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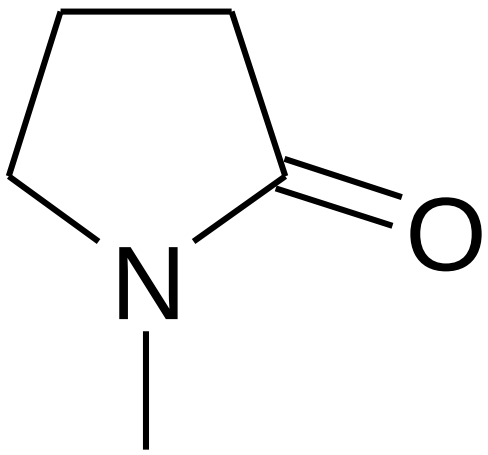
Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1-Methyl-) (NMP)

CASRN: 872-50-4



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ABBREVIATIONS

°C	Degrees Celsius
2-HMSI	2-hydroxy-N-methylsuccinimide
5-HNMP	5-hydroxy-N-methyl-2-pyrrolidone
ACA	American Coatings Association
ACR	Acute-to-chronic Ratio
ADR	Acute Dose Rate
AF	Assessment Factor
AIHA	American Industrial Hygiene Association
APF	Assigned Protection Factor
atm	Atmosphere(s)
ATSDR	Agency for Toxic Substances and Disease Registry
AUC	Area Under the Curve
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
BIOWIN	EPI Suite™ model that estimates Biodegradation rates
BLS	Bureau of Labor Statistics
BMD	Benchmark Dose
BMDL	Benchmark Dose Lower Confidence Limit
BMR	Benchmark Response
CAA	Clean Air Act
CARB	California Air Resources Board
CASRN	Chemical Abstracts Service Registry Number
CBI	Confidential Business Information
CCL	Contaminant Candidate List
CDR	Chemical Data Reporting
CEHD	Chemical Exposure Health Data
CEM	Consumer Exposure Model
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
CHIRP	Chemical Risk Information Platform
ChV	Chronic Value
cm^2	Square Centimeter(s)
cm^3	Cubic Centimeter(s)
C_{max}	Peak Serum Concentration
COC	Concentration of Concern
COU	Condition of Use
CPDat	Chemical and Products Database
CWA	Clean Water Act
DTSC	Department of Toxic Substances Control
EC	European Commission
EC_{50}	Effective Concentration with 50% immobilized test organisms
ECHA	European Chemicals Agency
ECOTOX	ECOTOXicology Knowledgebase System
E-FAST	Exposure and Fate Assessment Screening Tool
EPA	Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act

ER	Extra Risk
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
GD(s)	Gestational Day
HESIS	Hazard Evaluation System and Information Service
HPV	High Production Volume
Hr	Hour
IMAP	Inventory Multi-Tiered Assessment and Prioritisation
IPCS	International Programme on Chemical Safety
IRIS	Integrated Risk Information System
kg	Kilogram(s)
L	Liter(s)
LOAEL	Lowest Observed Adverse Effect Level
LOD	Limit of Detection
LOEC	Lowest Observed Effect Concentration
lb	Pound(s)
LC_{50}	Lethal Concentration to 50% of test organisms
Log K_{oc}	Logarithmic Soil Organic Carbon:Water Partition Coefficient
Log K_{ow}	Logarithmic Octanol:Water Partition Coefficient
m^3	Cubic Meter(s)
MADL	Maximum Allowable Dose Level
mg	Milligram(s)
MOE	Margin of Exposure
NIH	National Institutes of Health
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NPDES	National Pollutant Discharge Elimination System
PVL	Liquid Permeability Constant
µg	Microgram(s)
mmHg	Millimeter(s) of Mercury
mPa·s	Millipascal(s)-Second
MITI	Ministry of International Trade and Industry
SDS	Safety Data Sheet
MSDS	Material Safety Data Sheet
MSI	N-methylsuccinimide
MSW	Municipal Solid Waste
N/A	Not Applicable
NAICS	North American Industry Classification System
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NIOSH	National Institute for Occupational Safety and Health
NMP	n-Methylpyrrolidone
OCSPP	Office of Chemical Safety and Pollution Prevention
OECD	Organisation for Economic Co-operation and Development
OEHHA	Office of Environmental Health Hazard Assessment
OEL	Occupational Exposure Limits
OES	Occupational Exposure Scenario
ONU	Occupational Non-User

OPPT	Office of Pollution Prevention and Toxics
OSHA	Occupational Safety and Health Administration
OW	Office of Water
PBPK	Physiologically based Pharmacokinetic
PDE	Permissible Daily Exposure
PDM	Probabilistic Dilution Model
PECO	Populations, Exposures, Comparisons, Outcomes
PEL	Permissible Exposure Limit
PESS	Potentially Exposed or Susceptible Subpopulations
PF	Protection Factor
PND	Postnatal Day
POD	Point of Departure
POTW	Publicly Owned Treatment Works
ppb	Part(s) per Billion
PPE	Personal Protective Equipment
ppm	Part(s) per Million
QAPP	Quality Assurance Project Plan
RCRA	Resource Conservation and Recovery Act
RD	Relative Deviation
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RfC	Reference Concentration
RQ	Risk Quotient
SCBA	Self-Contained Breathing Apparatus
SDS	Safety Data Sheets
SDWA	Safe Drinking Water Act
SIA	Semiconductor Industry Association
SIC	Standard Industrial Classification
SIDS	Screening Information Data Set
SVHC	Substance of Very High Concern
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	Time-Weighted Average
UF	Uncertainty Factor
UF_A	Interspecies Uncertainty Factor
UF_H	Intraspecies Uncertainty Factor
U.S.	United States
U.S.C.	United States Code
VOC	Volatile Organic Compound
WF	Weight Fraction
WOE	Weight of the Scientific Evidence
Yr	Years

EXECUTIVE SUMMARY

This risk evaluation for n-methylpyrrolidone (NMP) was performed in accordance with the Frank R. Lautenberg Chemical Safety for the 21st Century Act and is being issued following public comment and peer review. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, in June 2016. Under the amended statute, EPA is required, under TSCA Section 6(b), to conduct risk evaluations to determine whether a chemical substance presents unreasonable risk of injury to health or the environment, under the conditions of use, without consideration of costs or other non-risk factors, including an unreasonable risk to potentially exposed or susceptible subpopulations, identified as relevant to the risk evaluation. Also, as required by TSCA Section (6)(b), EPA established, by rule, a process to conduct these risk evaluations, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726) (Risk Evaluation Rule). This risk evaluation is in conformance with TSCA Section 6(b), and the Risk Evaluation Rule, and is to be used to inform risk management decisions. In accordance with TSCA Section 6(b), if EPA finds unreasonable risk from a chemical substance under its conditions of use in any final risk evaluation, the Agency will propose actions to address those risks within the timeframe required by TSCA. However, any proposed or final determination that a chemical substance presents unreasonable risk under TSCA Section 6(b) is not the same as a finding that a chemical substance is "imminently hazardous" under TSCA Section 7. The conclusions, findings, and determinations in this final risk evaluation are for the purpose of identifying whether the chemical substance presents unreasonable risk or no unreasonable risk under the conditions of use, in accordance with TSCA Section 6, and are not intended to represent any findings under TSCA Section 7.

TSCA Sections 26(h) and (i) require EPA, when conducting risk evaluations, to use scientific information, technical procedures, measures, methods, protocols, methodologies and models consistent with the best available science and to base its decisions on the weight of the scientific evidence.[1] To meet these TSCA Section 26 science standards, EPA used the TSCA systematic review process described in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018a). The data collection, evaluation, and integration stages of the systematic review process are used to develop the exposure, fate, and hazard assessments for risk evaluations. To satisfy requirements in TSCA Section 26(j)(4) and 40 CFR 702.51(e), EPA has provided a list of studies considered in carrying out the risk evaluation, and the results of those studies are included in the Systematic Review Data Quality Evaluation Documents (see Appendix B, items 1*a-j*).

n-Methylpyrrolidone (CASRN 872-50-4), also called n-methyl-2-pyrrolidone, or 1-methyl-2-pyrrolidone, is a water-miscible, organic solvent that is often used as a substitute for halogenated solvents. NMP exhibits a unique set of physical and chemical properties that have proven useful in a range of industrial, commercial and consumer applications. NMP has low volatility and high affinity for aromatic hydrocarbons, which makes it effective for solvent extraction in petrochemical processing and pharmaceutical manufacturing. NMP is also valued for its high polarity and low surface tension which are considered desirable for solvent cleaning and surface treatment of metals, textiles, resins, and plastics. NMP is subject to federal and state regulations and reporting requirements. NMP has been a

[1] Weight of the scientific evidence is defined in EPA regulations as a "systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance." 40 CFR 702.33.

reportable Toxics Release Inventory (TRI) chemical substance under Section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) since January 1, 1995.

NMP is widely used in the chemical manufacturing, petrochemical processing and electronics industries. There is also growing demand for NMP use in semiconductor fabrication and lithium ion battery manufacturing (FMI, 2015). In the commercial sector, NMP is primarily used for producing and removing paints, coatings and adhesives. Other applications include, but are not limited to, use in solvents, reagents, sealers, inks and grouts. EPA evaluated the following categories of conditions of use for NMP: manufacturing; processing; distribution in commerce, industrial, commercial and consumer uses and disposal.[2] The total aggregate production volume for NMP decreased slightly from 164 to 160 million pounds between 2012 and 2015.

Approach

EPA used reasonably available information (defined in 40 CFR 702.33 as "*information that EPA possesses, or can reasonably generate, obtain, and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation*") in a "fit-for-purpose" approach, to develop a risk evaluation that relies on the best available science and is based on the weight of the scientific evidence. EPA used previous analyses as a starting point for identifying key and supporting studies to inform the exposure, fate, and hazard assessments. EPA also evaluated other studies that were published since these reviews. EPA reviewed the information and evaluated the quality of the methods and reporting of results of the individual studies using the evaluation strategies described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

In the problem formulation document, EPA identified the NMP conditions of use and presented three conceptual models and an analysis plan for the risk evaluation. These have been carried into this final risk evaluation where EPA has quantitatively and qualitatively evaluated the risk to the environment and human health using both monitoring data (when reasonably available) and modeling approaches for the conditions of use within the scope of the risk evaluation. In the problem formulation document, EPA performed a screening level analysis to evaluate risks to the general population and to terrestrial and sediment-dwelling aquatic species from exposure to water, sediment, soil, and air based on physical and chemical properties, environmental fate properties, and environmental release estimates. Screening-level analyses can be conducted with limited data based on high-end exposure assumptions and were used by EPA during problem formulation to identify which exposure pathways warrant more analysis. EPA has since updated the screening level analysis for general population exposure to surface water based on more recent TRI data. As part of this risk evaluation, EPA also quantitatively evaluated:

- Risks to aquatic species from environmental releases to surface water associated with the manufacturing, processing, distribution, use and disposal of NMP.
- Risks to workers for acute and chronic inhalation, dermal, and vapor-through-skin exposures and risks to occupational non-users (*i.e.*, workers who do not directly handle NMP but perform work in an area where it is used) from acute and chronic inhalation and vapor-through-skin exposures.
- Risks to consumers from acute inhalation, dermal, and vapor-through-skin exposure and risks to consumer bystanders (*i.e.*, non-users who are incidentally exposed to NMP as a result of the use of consumer products containing NMP) from acute inhalation and vapor-through-skin exposure.

[2] Although EPA has identified both industrial and commercial uses here for purposes of distinguishing scenarios in this analysis, the Agency interprets the authority over "any manner or method of commercial use" under TSCA Section 6(a)(5) to reach both.

Exposures
EPA quantitatively evaluated acute and chronic exposures of aquatic species for ambient surface water exposures associated with NMP environmental releases from the manufacturing, processing, distribution, use and disposal (Section 2.3.2). EPA used environmental release data from EPA's TRI to derive estimates of NMP surface water concentrations (acute and chronic) near facilities reporting the highest NMP water releases.

NMP may occur in various environmental media including sediment, soil, water and air. As part of the NMP Problem Formulation (U.S. EPA, 2018c), EPA evaluated potential exposures and risks to the general population and to environmental receptors through ambient water, sediment, land-applied biosolids, and ambient air. Based on environmental fate properties of NMP and first-tier screening level analyses, EPA did not identify risks to environmental receptors or to the general population from these pathways. Because the approach used to evaluate risks to environmental receptors and the general population from ambient air, water, sediment and land-applied biosolids in the Problem Formulation was sufficient to make a risk determination, those analyses were brought forward to this document as justification for EPA's final risk determination. Before reaching a final risk determination for surface water exposures, however, EPA updated the screening level analysis approach used in the Problem Formulation to include more recent TRI release data.

EPA evaluated acute and chronic human exposures by the dermal and inhalation routes, including direct contact with NMP-containing liquids and indirect exposure from vapor-through-skin uptake. NMP has unique physicochemical properties (Section 1.1) that result in very efficient dermal absorption (Section 3.2.2). For each worker occupational use scenario (Section 2.4.1), EPA considered moderate and high-end exposure parameters and the impact of different combinations of personal protective equipment (PPE) on exposure. Empirical data were preferred for exposure estimation when reasonably available. In the absence of measured data, EPA used models to estimate exposure to the human receptors of interest. The models' underlying input parameters and assumptions were based on reasonably available information regarding NMP physical and chemical properties, NMP weight fraction in the product, and the activity patterns associated with use. Exposure to individuals located near those using NMP-containing products (*i.e.*, occupational non-users) were also estimated based on inhalation and vapor-through-skin uptake.

EPA estimated acute exposures to consumers and to adult and child bystanders. Because reasonably available information does not indicate that chronic exposures would occur during the use of the consumer products identified as containing NMP, EPA did not evaluate chronic consumer exposures. EPA varied the following input parameters: the activity pattern of the consumer in using the product (including the location or room of use), the duration of use and the mass of the product used to quantify the amount of NMP exposure to consumers (Section 2.4.2). EPA selected not only median but also high-end input parameters in order to develop high-intensity use scenarios to capture the exposures to those consumers who may use the products in greater quantities and for a longer duration.

Hazards
EPA identified acute and chronic Concentrations of Concern (COCs) for aquatic organisms based on the reasonably available acute and chronic hazard data for NMP (Section 3.1). These acute and chronic COCs are compared to the estimated surface water concentrations of NMP from the exposure assessment.

EPA identified human health hazards based on reasonably available human and animal evidence. Reported outcomes in laboratory animal studies range from irritation to decreased body weight and

adverse systemic effects (*e.g.*, liver, kidney, spleen, thymus, testes, brain). EPA reviewed the reasonably available information on human health hazard potential and selected sensitive and robust reproductive and developmental toxicity endpoints in rodents (*i.e.*, post-implantation loss and decreased fertility) as the critical effects for dose-response analysis and risk estimation. EPA identified post-implantation loss as the critical endpoint for acute exposures and reduced fertility as the critical endpoint for chronic exposures (Section 3.2). As a result of additional analysis performed in response to peer-review comments, the point of departure (POD) used as the quantitative basis for evaluating risk from acute exposures for all conditions of use (COUs) has changed from 216 mg/L C_{max} to 437 mg/L C_{max} since the draft risk evaluation and since EPA's *TSCA Work Plan Chemical Risk Assessment n-Methylpyrrolidone: Paint Stripping Use* (U.S. EPA, 2015c). This change in acute POD resulted in some changes to acute risk estimates and risk determinations.

Other outcomes, including adverse systemic effects, may occur at higher exposure concentrations. Because the risk determinations in the current document are based on adverse reproductive and developmental effects observed in a potentially exposed or susceptible subpopulation (*e.g.*, pregnant women and women of childbearing age who may become pregnant) and at lower levels of exposure than other effects, they are expected to be protective of all other outcomes and potentially exposed or susceptible subpopulations.

Human Populations Considered in This Risk Evaluation

EPA assumed those who use NMP-containing products would be adults of either sex (≥16 years old), including pregnant women, and evaluated risks to individuals who do not use NMP but may be indirectly exposed due to their proximity to the user who is directly handling NMP or the product containing NMP.

The risk evaluation is based on potential effects on fertility as well as developmental toxicity. The lifestages of greatest concern for developmental effects are pregnant women and women of childbearing age who may become pregnant. Lifestages of concern for effects on reproductive health and fertility include men and women of reproductive age as well as children and adolescents. The risk estimates developed as part of this risk evaluation are intended to be protective of these groups and other potentially exposed or susceptible subpopulations, including people with pre-existing conditions and people with genetic variations that make them more susceptible. Exposures that do not present risks based on sensitive reproductive and developmental endpoints are not expected to present risks for other potential health effects of NMP because other health effects occur at higher levels of exposure.

Risk Characterization

This risk evaluation characterizes the environmental (Section 4.1) and human health (Section 4.2) risks from NMP under the conditions of use, including manufacture (including import), processing, distribution, use, and disposal.

Environmental Risks: For environmental risk, EPA utilized a risk quotient (RQ) to compare the estimated acute and chronic NMP exposure concentrations in surface water to respective acute and chronic COCs to characterize the risk to aquatic organisms. An RQ that does not exceed 1 indicates that the exposure concentrations of NMP are less than the concentrations expected to produce an adverse effect. Surface water concentrations were estimated for direct and indirect discharges of NMP and RQs and days of exceedance were used to characterize risk to aquatic organisms from acute and chronic exposures to NMP. Based on these values (acute RQs all < 1, and chronic RQs < 1 or RQ > 1 but < 20 days of exceedance) risk to aquatic organisms from acute or chronic exposure pathways was not

indicated. NMP is not likely to accumulate in sediment based on its physical and chemical properties and is not expected to adsorb to sediment due to its water solubility and low partitioning to organic matter. Because NMP toxicity to sediment-dwelling organisms is expected to be comparable to that of aquatic organisms, minimal risks are anticipated for sediment-dwelling organisms. NMP exhibits low volatility and readily biodegrades under aerobic conditions; therefore, the concentrations in ambient air are unlikely to reach levels that would present risks for terrestrial organisms. Details of these estimates are in Section 4.1.

Human Health Risks: For human health risks to workers and consumers, EPA identified non-cancer human health risks. Based on the exposure scenarios evaluated, risks may be anticipated for individuals who are not directly exposed to liquid NMP (*e.g.*, occupational non-user, consumer bystander) as a result of indirect exposure via inhalation and vapor through skin exposures. Generally, risks identified for workers are linked to chronic exposures, whereas risks for consumers are linked to acute exposures. Although glove use may be effective in reducing NMP exposure, some glove types do not provide adequate protection. Further discussion and examples of appropriate glove use are included in Appendix F.

Strengths, Limitations and Uncertainties in the Risk Characterization

EPA's assessments, risk estimations, and risk determinations accounted for uncertainties throughout the risk evaluation (Section 4.3). EPA used reasonably available information, in a fit-for-purpose approach, to develop a risk evaluation that relies on the best available science and is based on the weight of the scientific evidence. For instance, systematic review was conducted to identify reasonably available information related to NMP hazards and exposures. If no applicable monitoring data were identified, exposure scenarios were assessed using a modeling approach that requires the input of various chemical parameters and exposure factors. When possible, default model input parameters were modified based on chemical-specific inputs available in literature databases. Each of the Agency's risk determinations are supported by substantial evidence; consideration of uncertainties as set forth in detail in later sections of this final risk evaluation supports EPA's determinations.

The exposure estimates EPA used to evaluate human health risks were based on a large amount of monitoring data and were supported by modeling data for many conditions of use. The availability of validated rat and human physiologically based pharmacokinetic (PBPK) models that include a dermal compartment allowed EPA to evaluate all exposures and hazards in terms of internal dose metrics and to evaluate risks from aggregate exposures from simultaneous dermal, inhalation, and vapor-through-skin exposures. Robust evidence of a continuum of adverse reproductive and developmental effects support the hazard endpoints EPA used as the basis for evaluating risks from acute and chronic exposures. In addition, PBPK modeling reduces uncertainties around the relevance of animal data for human health. Uncertainties around the representativeness of exposure monitoring data, activity pattern information, PPE use and efficacy, and incomplete information on some hazard endpoints and factors that may contribute to increased exposure and susceptibility to NMP contribute to the overall uncertainties of the risk estimates. Overall, EPA has medium to high confidence in the risk estimates presented in this risk characterization (described in Section 4.2).

Potentially Exposed or Susceptible Subpopulations (PESS)

TSCA Section 6(b)(4) requires that EPA conduct a risk evaluation of PESS to "*determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of cost or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administration, under the conditions of use*." TSCA § 3(12) states that "*the term* '*potentially exposed or susceptible*

subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the risk evaluation, EPA analyzed the reasonably available information to ascertain whether some human receptor groups may have greater exposure or greater susceptibility than the general population to the hazard posed by a chemical. EPA assessed NMP exposures to potentially exposed or susceptible subpopulations of interest, including workers and ONUs, consumers and bystanders, males and females of reproductive age, pregnant females and the developing embryo/fetus, infants, children and adolescents, people with pre-existing conditions, and people with lower metabolic capacity due to life stage, genetic variation, or impaired liver function. See additional discussions in Sections 2.5.1, 3.2.5.3, and 4.4. EPA's decisions for unreasonable risk are based on high-end exposure estimates for workers and high intensity use scenarios for consumers and bystanders because these exposure estimates represent the high-end of exposures expected for PESS.

Aggregate and Sentinel Exposures

EPA evaluated aggregate risks from dermal and inhalation routes of exposure for each COU. Validated rat and human PBPK models including a dermal compartment allowed EPA to integrate aggregate exposures across routes by translating exposure concentrations into internal doses (human blood concentrations). While this assessment evaluated specific COUs based on exposure estimates that incorporate multiple routes of exposure, it did not consider the potential for aggregate exposures from multiple conditions of use. EPA considered sentinel exposure in the form of high-end estimates for consumer and occupational exposure scenarios which incorporate dermal and inhalation exposure, as these routes are expected to present the highest exposure potential. EPA's decision for unreasonable risk are based on high-end exposure estimates to capture individuals with sentinel exposure.

Risk Determination

Unreasonable Risk Determination: In each risk evaluation under TSCA Section 6(b), EPA determines whether a chemical substance presents an unreasonable risk of injury to health or the environment, under the conditions of use. The determination does not consider costs or other non-risk factors. In making this determination, EPA considers relevant risk-related factors, including, but not limited to: the effects of the chemical substance on health and human exposure to such substance under the conditions of use (including cancer and non-cancer risks); the effects of the chemical substance on the environment and environmental exposure under the conditions of use; the population exposed (including any potentially exposed or susceptible subpopulations, as determined by EPA); the severity of hazard (including the nature of the hazard, the irreversibility of the hazard); and uncertainties. EPA also takes into consideration the Agency's confidence in the data used in the risk estimate. This includes an evaluation of the strengths, limitations, and uncertainties associated with the information used to inform the risk estimate and the risk characterization. The rationale for the unreasonable risk determination is discussed in Section 5.2. The Agency's risk determinations are supported by substantial evidence, as set forth in detail in later sections of this final risk evaluation.

In the final risk evaluation, EPA updated the POD for acute exposures from the draft risk evaluation based on updated analyses performed in response to peer review comments. This updated POD for acute exposures resulted in some changes to acute risk estimates, which impacted unreasonable risk determinations.

While use of NMP as an inert ingredient in wood preservatives was included in the problem formulation and draft risk evaluation as a condition of use within the scope of the evaluation, upon further analysis ,

EPA has determined that this use falls outside the definition of chemical substance as regulated by TSCA. Under TSCA Section 3(2)(B)(ii), the definition of "chemical substance" does not include any pesticide (as defined in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)) when manufactured, processed, or distributed in commerce for use as a pesticide. Because NMP is used in wood preservative as an approved inert under FIFRA, NMP falls outside TSCA's definition of a chemical substance when used for this purpose. As a result, the use of NMP in wood preservatives is not included in the scope of this risk evaluation.

Two uses of NMP in pharmaceutical manufacturing were included in the problem formulation and draft risk evaluation, namely as one of the uses of NMP as a functional fluid in a closed system and as one of the uses of NMP as an intermediate and reactant. Upon further analysis of the details of this process, EPA has determined that these uses fall outside TSCA's definition of "chemical substance." Under TSCA Section 3(2)(B)(iv), the definition of "chemical substance" does not include any food, food additive, drug, cosmetic, or device (as such terms are defined in Section 201 of the Federal Food, Drug and Cosmetic Act) when manufactured, processed or distributed in commerce for use as a food, food additive, drug, cosmetic, or device. While EPA has identified industrial and commercial use of NMP as a functional fluid (closed system) and processing of NMP as a reactant or intermediate as conditions of use of NMP when under the TSCA definition of chemical substance, EPA has removed mention of pharmaceutical applications in these conditions of use. EPA has concluded that both uses of NMP fall within the aforementioned definitional exclusion and NMP, for these uses, is not a "chemical substance" under TSCA.

Unreasonable Risk of Injury to the Environment: EPA conducted a screening-level approach to integrate relevant pathways of environmental exposure with available environmental hazard data to evaluate unreasonable risk to relevant environmental receptors. Based on the qualitative assessment described in the problem formulation for NMP, exposures to terrestrial species are assumed to be negligible and exposures to sediment-dwelling organisms are assumed to be less than exposures to aquatic species in the water column. As a result, EPA focused the quantitative assessment of ecological receptors in the risk evaluation on aquatic species in the water column. For all conditions of use, EPA did not identify any exceedances of benchmarks to aquatic organisms from exposures to NMP in surface waters. EPA characterized the environmental hazards based on one high quality study.

Unreasonable Risk of Injury to Health: EPA's determination of unreasonable risk for specific conditions of use of NMP listed below are based on health risks to workers, occupational non-users, consumers, or bystanders from consumer use. For acute exposures, EPA evaluated unreasonable risk of developmental toxicity based on animal studies (*i.e.*, post-implantation loss (resorptions and fetal mortality)). For chronic exposures, EPA based the unreasonable risk determination on reproductive toxicity (decreased male fertility). Risk determinations based on this sensitive endpoint are expected to be protective of other less sensitive non-cancer effects (*e.g.*, liver toxicity, kidney toxicity, immunotoxicity, neurotoxicity, irritation and sensitization).

Unreasonable Risk of Injury to Health of the General Population: NMP exposures to the general population may occur from the conditions of use due to releases to air, water or land. During the course of the risk evaluation process for NMP, OPPT worked closely with the offices within EPA that administer and implement regulatory programs under the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), the Resource Conservation and Recovery Act (RCRA), and the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). As explained in more detail in Section 1.4.2, EPA believes it is both reasonable and prudent to tailor TSCA risk evaluations when other EPA offices have expertise and experience to address

specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with the statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadlines for completing risk evaluations. EPA has therefore tailored the scope of the risk evaluation for NMP using authorities in TSCA Sections 6(b) and 9(b)(1). EPA did not evaluate exposures to the general population from drinking water or disposal pathways because they are addressed by other EPA-administered statutes and regulatory programs

EPA evaluated general population exposure through ambient water, ambient air, and land-applied biosolids using a screening level analysis during Problem Formulation. EPA has updated the screening level analysis of surface water exposures based on more recent TRI data. For the general population, based on a screening level analysis, EPA determined there is no unreasonable risk to the general population for these pathways – ambient water (including surface water), ambient air, and land applied biosolids.

Unreasonable Risk of Injury to Health of Workers: EPA evaluated non-cancer effects from acute and chronic inhalation and dermal exposures (including uptake of vapor through skin) to determine if there was unreasonable risk of injury to workers' health. The drivers for EPA's determination of unreasonable risk for non-cancer effects for workers are reproductive effects from chronic inhalation and dermal exposures; generally, risks identified for workers are linked to chronic exposures.

EPA generally assumes compliance with Occupational Safety and Health Administration (OSHA) requirements for protection of workers including the implementation of the hierarchy of controls. In support of this assumption, EPA used reasonably available information, including public comments indicating that some employers, particularly in the industrial setting, are providing appropriate engineering, administrative controls, or PPE to their employees consistent with OSHA requirements. OSHA has not issued a specific permissible exposure limit (PEL) for NMP. While EPA does not have similar information to support this assumption for each condition of use, EPA does not believe that the Agency must presume, in the absence of such information, a lack of compliance with existing regulatory programs and practices. Rather, EPA assumes there is compliance with worker protection standards unless case-specific facts indicate otherwise, and therefore existing OSHA regulations for worker protection and hazard communication will result in use of appropriate PPE in a manner that achieves the stated assigned protection factor (APF) or PF. EPA's decisions for unreasonable risk to workers are based on high-end exposure estimates, in order to account for the uncertainties related to whether or not workers are using PPE. EPA believes this is a reasonable and appropriate approach that reflects workplace practices, accounts for reasonably available information related to worker protection practices, and addresses uncertainties regarding available and use of PPE. For each condition of use of NMP with an identified risk for workers, EPA assumes the use of appropriate respirators with APF 10 and gloves with a PF of 1 to 20.

The unreasonable risk determinations reflect the severity of the effects associated with the occupational exposures to NMP and incorporate consideration of the PPE that EPA assumes. A full description of EPA's unreasonable risk determination for each condition of use is in Section 5.2.

Unreasonable Risk of Injury to Health of Occupational Non-Users (ONUs): ONUs are workers who do not directly handle NMP-containing liquids but perform work in an area where NMP is present in the

air. EPA evaluated non-cancer effects to ONUs from acute and chronic inhalation and vapor-through-skin occupational exposures to determine if there was unreasonable risk of injury to ONUs' health. The unreasonable risk determinations reflect the severity of the effects associated with the occupational exposures to NMP and the assumed absence of PPE for ONUs, since ONUs do not directly handle the chemical and are instead doing other tasks in the vicinity. Effects from ONU exposures due to dermal contact with liquids were not evaluated because EPA assumes ONUs do not have dermal contact with liquids containing NMP. For exposures by inhalation and vapor-through-skin, EPA, where possible, estimated ONUs' exposures and described the risks separately from workers directly exposed. When the difference between ONUs' exposures and workers' exposures to airborne NMP cannot be quantified, EPA assumed that ONUs' exposures to airborne NMP are lower than workers' exposures to airborne NMP. A full description of EPA's unreasonable risk determination for each condition of use is in Section 5.2.

Unreasonable Risk of Injury to Health of Consumers: EPA evaluated non-cancer effects to consumers from acute inhalation, dermal, and vapor-through-skin exposures to determine if there was unreasonable risk of injury to consumers' health. EPA conducted a screening level analysis of oral exposures due to mouthing of children's products and high-end exposure was below levels that could result in unreasonable risk. EPA did not further analyze the oral pathway for exposure. Further information can be found in Section 2.4.2.2. A full description of EPA's unreasonable risk determination for each condition of use is in Section 5.2.

Unreasonable Risk of Injury to Health of Bystanders (from Consumer Uses): EPA evaluated non-cancer effects to bystanders from acute inhalation and vapor-through-skin exposures to determine if there was unreasonable risk of injury to bystanders' health. EPA did not evaluate dermal exposures to bystanders because bystanders do not have direct dermal exposure to NMP. A full description of EPA's unreasonable risk determination for each condition of use is in Section 5.2.

Summary of Unreasonable Risk Determinations:
In conducting risk evaluations, "EPA will determine whether the chemical substance presents an unreasonable risk of injury to health or the environment under each condition of use within the scope of the risk evaluation…" 40 CFR 702.47. Pursuant to TSCA Section 6(i)(1), a determination of "no unreasonable risk" shall be issued by order and considered to be final agency action. Under EPA's implementing regulations, "[a] determination by EPA that the chemical substance, under one or more of the conditions of use within the scope of the risk evaluation, does not present an unreasonable risk of injury to health or the environment will be issued by order and considered to be a final Agency action, effective on the date of issuance of the order." 40 CFR 702.49(d).

EPA has determined that the following conditions of use of NMP do not present an unreasonable risk of injury to health or the environment. These determinations are considered final agency action and are being issued by order pursuant to TSCA Section 6(i)(1). The details of these determinations are in Section 5.2, and the TSCA Section 6(i)(1) order is contained in Section 5.4.1 of this final risk evaluation.

Conditions of Use that Do Not Present an Unreasonable Risk
• Distribution in commerce • Industrial and commercial use in ink, toner and colorant products in printer ink and inks in writing equipment • Industrial and commercial use in other uses in soldering materials

- Industrial and commercial use in other uses in fertilizer and other agricultural chemical manufacturing, processing aids and solvents
- Consumer use in paint and coating removers
- Consumer use in adhesive removers
- Consumer use in paints and coatings in lacquers, stains, varnishes, primers and floor finishes
- Consumer use in paint additives and coating additives not described by other codes in paints and arts and crafts paints
- Consumer use in other uses in automotive care products
- Consumer use in other uses in cleaning and furniture care products, including wood cleaners and gasket removers
- Consumer use in other uses in lubricant and lubricant additives, including hydrophilic coatings

EPA has determined that the following conditions of use of NMP present an unreasonable risk of injury to health or the environment. EPA will initiate TSCA Section 6(a) risk management actions on these conditions of use as required under TSCA Section 6(c)(1). Pursuant to TSCA Section 6(i)(2), the unreasonable risk determinations for these conditions of use are not considered final agency action. The details of these determinations are in Section 5.2.

Manufacturing that Presents an Unreasonable Risk

- Domestic manufacture
- Import

Processing that Presents an Unreasonable Risk

- As a reactant or intermediate in plastic material and resin manufacturing and other non-incorporative processing
- Incorporation into a formulation, mixture or reaction product in multiple industrial sectors
- Incorporation into articles in lubricants and lubricant additives in machinery manufacturing
- Incorporation into articles in paint additives and coating additives not described by other codes in transportation equipment manufacturing
- Incorporation into articles as a solvent (which becomes part of a product formulation or mixture) including in textiles, apparel and leather manufacturing
- Incorporation into articles in other sectors, including in plastic product manufacturing
- Repackaging in wholesale and retail trade
- Recycling

Industrial and Commercial Uses that Present an Unreasonable Risk

- Industrial and commercial use in paints, coatings, and adhesive removers
- Industrial and commercial use in paints and coatings in lacquers, stains, varnishes, primers and floor finishes, and powder coatings in surface preparation
- Industrial and commercial use in paint additives and coating additives not described by other codes in computer and electronic product manufacturing in electronic parts manufacturing
- Industrial and commercial use in paint additives and coating additives not described by other codes in computer and electronic product manufacturing for use in semiconductor manufacturing

- Industrial and commercial use in in paint additives and coating additives not described by other codes in multiple manufacturing sectors
- Industrial and commercial use as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing
- Industrial and commercial use as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing for use in semiconductor manufacturing
- Industrial and commercial use in processing aids, specific to petroleum production in petrochemical manufacturing, in other uses in oil and gas drilling, extraction and support activities, and in functional fluids (closed systems)
- Industrial and commercial use in adhesives and sealants including binding agents, single component glues and adhesives, including lubricant adhesives, and two-component glues and adhesives including some resins
- Industrial and commercial use in other uses in anti-freeze and de-icing products, automotive care products, and lubricants and greases
- Industrial and commercial use in other uses in metal products not covered elsewhere, and lubricant and lubricant additives including hydrophilic coatings
- Industrial and commercial use in other uses in laboratory chemicals
- Industrial and commercial uses in other uses in lithium ion battery manufacturing
- Industrial and commercial use in other uses in cleaning and furniture care products, including wood cleaners and gasket removers

Consumer Uses that Present an Unreasonable Risk

- Consumer use in adhesives and sealants in glues and adhesives, including lubricant adhesives and sealants

Disposal that Presents an Unreasonable Risk

- Disposal

1 INTRODUCTION

This document presents the risk evaluation for NMP under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended TSCA, the Nation's primary chemicals management law, in June 2016.

The Agency published the Scope of the Risk Evaluation for NMP (U.S. EPA, 2017c) in June 2017, and the problem formulation in June, 2018 (U.S. EPA, 2018c), which represented the analytical phase of risk evaluation whereby "the purpose for the assessment is articulated, the problem is defined, and a plan for analyzing and characterizing risk is determined," as described in Section 2.2 of the *Framework for Human Health Risk Assessment to Inform Decision Making*. EPA received comments on the published problem formulation for NMP and has considered the comments specific to NMP, as well as more general comments regarding EPA's chemical risk evaluation approach for developing the risk evaluations for the first 10 TSCA Workplan chemicals.

During problem formulation, EPA identified the NMP conditions of use and presented the associated conceptual models and an analysis plan. In this risk evaluation, EPA evaluated risks to workers and occupational non-users from acute and chronic exposures as well as risks to consumers and bystanders from acute exposures. EPA evaluated human health risks by comparing the exposure estimates for acute or chronic scenarios to the related human health hazards.

While NMP is present in various environmental media such as ground water, surface water, and air, EPA determined during problem formulation that no further analysis of the environmental release pathways associated with ecological exposures via ambient water, sediments, land-applied biosolids, and ambient air was needed based on a qualitative assessment of the physical and chemical properties and fate of NMP in the environment and a quantitative comparison of the hazards and exposures identified for aquatic organisms. Risk determinations were not made as part of problem formulation; therefore, the results from these analyses are used to inform the risk determination section of this final risk evaluation. In this risk evaluation, EPA has updated the screening level analysis of surface water exposures based on more recent TRI release data.

EPA used reasonably available information consistent with the best available science for physical and chemical and fate properties, potential exposures, and relevant hazards according to the systematic review process. For the human exposure pathways, EPA evaluated inhalation exposures to vapors and mists for workers, occupational non-users, consumer and bystanders. EPA evaluated dermal exposures via skin contact with liquids for workers and consumer and evaluated vapor through skin uptake for workers, occupational non-users, consumers and bystanders. EPA characterized risks to ecological receptors from exposures via surface water, sediment, land-applied biosolids, and ambient air in the risk characterization section of this final risk evaluation based on the analyses presented in the problem formulation.

As per EPA's final rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726) (hereinafter "Risk Evaluation Rule"), this risk evaluation was subject to both public comment and peer review, which are distinct but related processes. EPA provided 60 days for public comment on all aspects of the draft risk evaluation, including the submission of any additional information that might be relevant to the science underlying the risk evaluation. This satisfies TSCA [15 U.S.C 2605(b)(4)(H)], which requires EPA to provide public notice and an opportunity for comment on a draft risk evaluation prior to publishing a final risk evaluation.

Peer review was conducted in accordance with EPA's regulatory procedures for chemical risk evaluations, including using the *EPA Peer Review Handbook* and other methods consistent with Section 26 of TSCA (see 40 CFR Section 702.45). As explained in the Risk Evaluation Rule, the purpose of peer review is for the independent review of the science underlying the risk evaluation. Peer review therefore addressed aspects of the underlying science as outlined in the charge to the peer review panel such as hazard assessment, assessment of dose-response, exposure assessment, and risk characterization. Peer review supports scientific rigor and enhances transparency in the risk evaluation process.

As explained in the Risk Evaluation Rule, it is important for peer reviewers to consider how the underlying risk evaluation analyses fit together to produce an integrated risk characterization, which forms the basis of an unreasonable risk determination. EPA believes peer reviewers are most effective in this role if they receive the benefit of public comments on draft risk evaluations prior to peer review. For this reason, and consistent with standard Agency practice, the public comment period began prior to peer review on the draft risk evaluation. EPA responded to public and peer review comments and explained changes made to the draft risk evaluation in response to those comments in this final risk evaluation and the associated response to comments document.

EPA also solicited input on the first 10 chemicals, including NMP, as it developed use dossiers, scope documents, and problem formulations. At each step, EPA received information and comments specific to individual chemicals and of a more general nature relating to various aspects of the risk evaluation process, technical issues, and the regulatory and statutory requirements. EPA has considered comments and information received at each step in the process and factored in the information and comments as the Agency deemed appropriate and relevant including comments on the published problem formulation of NMP.

In this final risk evaluation, the Introduction (Section 1) presents the basic physical and chemical properties of NMP, and background information on its regulatory history, conditions of use and conceptual models, with emphasis on any changes since the publication of the problem formulation. This section also includes a discussion of the systematic review process utilized in this risk evaluation. Exposures (Section 2) provides a discussion and analysis of the exposures, both human and environmental, that can be expected based on the conditions of use identified for NMP. Hazards (Section 3), discusses the environmental and human health hazards of NMP. The Risk Characterization (Section 4), integrates the reasonably available information on human health and environmental hazards and exposures, as required by TSCA (15 U.S.C 2605(b)(4)(F)). This section also includes a discussion of the uncertainties that underly the assessment and how they impact the risk evaluation. As required under TSCA 15 U.S.C. 2605(b)(4), a determination of whether the risk posed by this chemical substance, under the conditions of use, is unreasonable is presented in the Risk Determination (Section 5).

1.1 Physical and Chemical Properties

Physical and chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the conditions of use, exposure pathways, routes and hazards that EPA considers. During problem formulation, EPA considered the measured or estimated physical and chemical properties set forth in Table 1-1. Based on EPA’s review of reasonably available literature, the vapor pressure previously reported for NMP was updated (0.345 mmHg) to conform with EPA’s data quality criteria. This value is considered more reliable than the original value (0.19 mmHg) which was taken from a secondary source.

NMP is a high boiling, polar aprotic solvent with low viscosity and low volatility. It is miscible with water and most organic solvents and exhibits low flammability and no explosivity. It is not readily oxidizable; variations in temperature and humidity can produce a range of saturation concentrations in ambient air (U.S. EPA, 2020a, 2017c).

Table 1-1. Physical and Chemical Properties of NMP

Property	Value [a]	Reference
Molecular formula	C_5H_9ON	
Molecular weight	99.1 g/mol	O'Neil et al. (2006)
Physical form	Colorless liquid	O'Neil et al. (2006)
Melting point	-25°C	Ashford (1994)
Boiling point	202°C	O'Neil et al. (2006)
Density	1.03 at 25°C	O'Neil et al. (2006)
Vapor pressure	0.345 mmHg at 25°C	Daubert and Danner (1989)
Vapor density	3.4 (air = 1)	NFPA (1997)
Water solubility	1,000 g/L at 25°C (miscible)	O'Neil et al. (2006)
Octanol:water partition coefficient (log K_{ow})	-0.38 at 25°C	Sasaki et al. (1988)
Henry's Law constant	3.2×10^{-9} atm·m^3/mol	Kim et al. (2000)
Flash point	95°C (open cup)	Riddick et al. (1986)
Auto flammability	Not available	
Viscosity	1.65 mPa·s at 25°C	O'Neil et al. (2006)
Refractive index	Not applicable	
Dielectric constant	Not applicable	

[a] Measured unless otherwise noted.

1.2 Uses and Production Volume

1.2.1 Data and Information Sources

The summary of use and production volume information presented below is based on research conducted for the *Problem Formulation Document for n-Methylpyrrolidone (NMP)* (U.S. EPA, 2018c) and any additional information obtained since the publication of that document. The previous research was based on reasonably available information, including the *Use and Market Profile for NMP*, (EPA-HQ-OPPT-2016-0743); public meetings and meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying and verifying the conditions of use included in this risk evaluation.

NMP is a solvent that is widely used in the manufacture and production of electronics, petroleum products, pharmaceuticals, polymers and other specialty chemicals. It has numerous industrial, commercial, and consumer applications. Some of the major areas of use identified for NMP are listed below (Harreus et al., 2011; Ash and Ash, 2009):

1. Petrochemical processing: acetylene recovery from cracked gas, extraction of aromatics and butadiene, gas purification (removal of CO_2 and H_2S), lube oil extraction
2. Engineering plastics: reaction medium for production of high-temperature polymers such as polyether sulfones, polyamideimides and polyaramids
3. Coatings: solvent for acrylic and epoxy resins, polyurethane paints, waterborne paints or finishes, printing inks, synthesis/diluent of wire enamels, coalescing agent
4. Specialty chemicals: solvent and/or co-solvent for liquid formulations
5. Electronics: cleaning agent for silicon wafers, photoresist stripper, auxiliary in printed circuit board technology
6. Industrial and domestic cleaning: component in paint strippers and degreasers

In addition to the uses in industrial, commercial, and consumer settings, NMP is used in ways considered as mission critical to federal agencies.

The Chemical Data Reporting (CDR) Rule under TSCA (40 CFR Part 711) requires that U.S. manufacturers and importers provide EPA with information on chemicals they manufacture (including imports). For the 2016 CDR cycle, data collected for each chemical include the company name, volume of each chemical manufactured/imported, the number of workers employed at each site, and information on whether the chemical is used in the commercial, industrial, and/or consumer sector. Only those companies that manufactured or imported at least 25,000 pounds of NMP per site were required to report under the CDR rule during the 2015 calendar year (U.S. EPA, 2016a). The 2016 CDR reporting data for NMP are provided in Table 1-2.

Table 1-2. Production Volume of NMP in CDR Reporting Period (2012 to 2015)

Reporting Year [a]	2012	2013	2014	2015
Total Aggregate Production Volume (lbs)	164,311,844	168,187,596	171,095,221	160,818,058

[a] The CDR data for the 2016 reporting period is available via ChemView (https://chemview.epa.gov/chemview). The CDR data presented in the risk evaluation document is more specific than currently in ChemView.

NMP is widely used in the chemical manufacturing, petrochemical processing and electronics industries (FMI 2015). In the commercial sector, it is primarily used for producing and removing paints, coatings and adhesives. Other commercial applications include, but are not limited to, use in solvents, reagents, sealers, inks and grouts. There is also growing demand for NMP use in semiconductor fabrication and lithium ion battery manufacturing. Data reported for the 2016 CDR period (U.S. EPA, 2016a) indicate over 160 million pounds of NMP were manufactured (including imports) in the United States in 2015 (U.S. EPA, 2016a).

NMP is used in paint removers, and as a solvent/reagent for the electronics and pharmaceutical industries. It is also used as a solvent for hydrocarbon recovery in the petrochemical processing industry, and for the desulfurization of natural gas (Global Newswire, 2016; FMI, 2015). While paint removers represent a large product category for NMP, growth in this sector is uncertain as a result of the potential risks identified in the previous risk assessment published by EPA (U.S. EPA, 2015c).

NMP is a key cleaning component for the manufacture of semiconductors used in electronics, and for the manufacture of printed circuit boards. As the consumer demand for electronics rises, especially in the Asia Pacific region, the global demand for NMP is expected to grow. Similar increases in NMP use

may occur in other regions, albeit to a lesser degree (Grand View Research, 2016). The U.S. market revenue for NMP is also expected to increase over the next ten years despite variations in the oil and gas industry. NMP is primarily used in downstream processes, which makes it more resilient to market volatility in this sector (Grand View Research, 2016).

1.2.2 Toxics Release Inventory Data

Under the EPCRA Section 313, NMP is a TRI-reportable substance effective January 1, 1995. During problem formulation, EPA further analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from specific types of land disposal (*e.g.*, RCRA) Subtitle C hazardous landfill and Class I underground injection wells) and incineration. EPA also examined how NMP is treated at industrial facilities.

Table 1-3 provides production-related waste management data for NMP reported by subject facilities to the TRI program from reporting years 2015 to 2018.[3] In reporting year 2018, 395 facilities reported a total of approximately 247 million pounds of NMP production-related waste managed. Of this total amount, roughly 220 million pounds were recycled, 7 million pounds were recovered for energy, 10 million pounds were treated, and 9 million pounds were disposed of or otherwise released to the environment.

Table 1-3. Summary of NMP TRI Production-Related Waste Managed from 2015-2018 (lbs)

Year	Number of Facilities	Recycling	Energy Recovery	Treatment	Releases [a,b,c]	Total Production Related Waste
2015	398	197,244,994	7,130,768	15,736,406	8,825,595	228,937,764
2016	403	193,273,728	7,835,194	14,644,977	10,135,833	225,889,732
2017	390	245,399,644	7,397,620	10,620,139	10,545,761	273,963,164
2018	395	219,677,076	7,691,498	10,332,809	9,390,133	247,091,516

Data source: 2015-2018 TRI Data (Updated October 2020) (U.S. EPA, 2017e).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] Does not include releases due to one-time events not associated with production such as remedial actions or earthquakes.
[c] Counts all releases including release quantities transferred and release quantities disposed of by a receiving facility reporting to TRI.

Table 1-4 provides a summary of NMP releases to the environment reported to TRI for the same reporting years as Table 1-3. Approximately 6,292 pounds of NMP water releases, 1,548,343 pounds of NMP air releases, and roughly 6,550,696 pounds of NMP land releases were reported to TRI in 2018. In addition to the quantities reported in Table 1-4 as "disposed of in Class I underground injection wells and RCRA Subtitle C landfills" in 2018, other reported land disposal techniques included; disposal to landfills other than RCRA Subtitle C (2,262,919 pounds), land treatment/application farming (1,627 pounds), and other land disposal such as waste piles, spills and leaks (7,002 pounds).[4]

While production-related waste managed shown in Table 1-3 excludes any quantities reported as catastrophic or one-time releases (TRI Section 8 data), release quantities shown in Table 1-4 include

[3] Data presented in Table 1-3 and Table 1-4 were queried using TRI Explorer and uses the 2019 National Analysis data set (released to the public in October 2020). This dataset includes revisions for the years 1988 to 2018 processed by EPA.
[4] Other releases of NMP as shown in Table 1-4 include other TRI data elements such as quantities transferred to a waste broker off-site for disposal (403,456 pounds), storage of NMP off-site (19,536 pounds), other off-site management of NMP (26,424 pounds), and unknown off-site waste management practices (44,499 pounds) in 2018.

both production-related and non-routine quantities (TRI Section 5 and Section 6 data) for 2015-2018. As a result, release quantities may differ slightly and may further reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2017e).

Table 1-4. Summary of NMP TRI Releases to the Environment from 2015-2018 (lbs)

Year	Number of Facilities	Air Releases		Water Releases	Land Disposal			Other Releases [a]	Total On- and Off-Site Disposal or Other Releases [b, c]
		Stack Air Releases	Fugitive Air Releases		Class I Under-ground Injection	RCRA Subtitle C Landfills	All Other Land Disposal [a]		
2015	398	887,309	546,060	14,885	3,625,939	93,217	2,737,671	387,083	8,292,165 [d]
		1,433,370 [d]			6,456,827 [d]				
2016	403	1,179,654	581,790	15,869	4,865,286	118,134	2,401,377	445,132	9,607,242 [d]
		1,761,443 [d]			7,384,797 [d]				
2017	390	1,134,869	433,270	19,053	5,243,982	356,574	1,948,441	614,589	9,750,779 [d]
		1,568,139 [d]			7,548,997 [d]				
2018	395	1,097,116	451,227	6,292	4,122,586	156,562	2,271,548	619,613	8,724,945 [d]
		1,548,343 [d]			6,550,696 [d]				

Data source: 2015-2018 TRI Data (Updated October 2020) (U.S. EPA, 2017e).

[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.

[b] These release quantities do include releases due to one-time events not associated with production such as remedial actions or earthquakes.

[c] Counts release quantities once at final disposition, accounting for transfers to other TRI reporting facilities that ultimately dispose of the chemical waste.

[d] Value shown may be different than the summation of individual data elements due to decimal rounding.

1.3 Regulatory and Assessment History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to NMP. EPA compiled the summary information provided in Table 1-5 from reasonably available data from federal, state, international and other government sources, as cited in Appendix A.

Federal Laws and Regulations

NMP is subject to federal statutes or regulations, other than TSCA, that are implemented by other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

State Laws and Regulations

NMP is subject to state statutes or regulations. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

Laws and Regulations in Other Countries and International Treaties or Agreements

NMP is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.3.

EPA identified previous assessments conducted by other organizations (see Table 1-5). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations.

Table 1-5. Assessment History of NMP

Authoring Organization	Assessment
EPA Assessments	
U.S. EPA, Office of Pollution Prevention and Toxics (OPPT)	TSCA Work Plan Chemical Risk Assessment n-Methylpyrrolidone: Paint Stripping Use CASRN 872-50-4 (U.S. EPA, 2015c)
U.S. EPA, OPPT	Re-assessment of Pesticide Inert Ingredient Exemption under the Food Quality Protection Act (U.S. EPA, 2006b)
Other U.S.-Based Organizations	
California Office of Environmental Health Hazard Assessment (OEHHA)	Proposition 65 Maximum Allowable Dose Level for Reproductive Toxicity (OEHHA, 2003)
International	
National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Australian Government	Human Health Tier III assessment (NICNAS, 2013)
Government of Canada, Environment Canada, Health Canada	Draft Screening Assessment of Risks to Human and Ecological Receptors (Environment Canada, 2017)
European Commission (EC), Scientific Committee on Occupational Exposure Limits (OELs)	Evaluation of OELs for NMP (EC, 2016)
Organisation for Economic Co-operation and Development (OECD), Cooperative Chemicals Assessment Program	NMP: Screening Information Data Set (SIDS) Initial Assessment Profile (OECD, 2007)
World Health Organization (WHO) International Programme on Chemical Safety (IPCS)	Concise International Chemical Assessment Document 35 N-METHYLPYRROLIDONE (WHO, 2001)
Danish Ministry of the Environment Environmental Protection Agency	Survey of NMP - Miljøstyrelsen (Danish Ministry of the Environment, 2015)

1.4 Scope of the Evaluation

1.4.1 Conditions of Use Included in the Risk Evaluation

TSCA (U.S.C. Section 3(4)) defines the conditions of use as ‘‘the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.” The conditions of use are described below in Table 1-6. EPA has not exercised its authority in TSCA Section 6(b)(4)(D) to exclude any NMP conditions of use from the scope of the NMP risk evaluation.

Use categories include the following: “industrial use” means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed; “commercial use” means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial

enterprise providing saleable goods or services; "consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2016a).

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, Figure 1-1 depicts the life cycle diagram and includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR reporting (U.S. EPA, 2016a); however, the life cycle diagram for NMP does not include specific production volumes because the information was confidential business information (CBI).

EPA did not identify any "legacy uses" (*i.e.,* circumstances associated with activities that do not reflect ongoing or prospective manufacturing, processing, or distribution) or "associated disposal" (*i.e*., future disposal from legacy uses) of NMP, as those terms are described in EPA's Risk Evaluation Rule, 82 FR 33726, 33729 (July 20, 2017). Therefore, no such uses or disposals were added to the scope of the risk evaluation for NMP following the issuance of the opinion in *Safer Chemicals, Healthy Families v. EPA*, 943 F.3d 397 (9th Cir. 2019). EPA did not evaluate "legacy disposal" (*i.e*., disposals that have already occurred) in the risk evaluation, because legacy disposal is not a "condition of use" under *Safer Chemicals*, 943 F.3d 397.

To help characterize the life cycle of NMP, EPA developed a national mass balance to evaluate how much of the volume of NMP can be accounted for from cradle-to-grave. The inputs into the mass balance included data from the 2016 CDR, 2015 TRI, literature, and public comments. The result of the mass balance is provided in Figure 1-2. The total mass accounted for at the end-of-life stage, which includes wastes from manufacturing, processing, use, waste treatment and disposal facilities, is approximately 83% of the 2015 production volume. The unaccounted-for volume is most likely due to limitations in reporting requirements for TRI causing wastes and emissions from certain sites to go unreported. There is also uncertainty in the total accounted for volume due to combining data from different years. There is additional uncertainty arising from the potential to double count TRI volumes reported as transferred off-site for energy recovery, treatment, and recycling that are then received by another TRI site that reports this volume in its on-site waste management activities. Finally, the true export volume is higher than presented in the mass balance as nine sites reporting to 2016 CDR claimed their export volume as CBI. Additional details on the development of the mass balance can be found in Appendix C.

Additional worker monitoring data were provided to EPA during the public comment period for the NMP problem formulation. This information was incorporated into the occupational exposure estimates for semiconductor and electronics manufacturing.

Table 1-6. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category [a]	Subcategory [b]	References
Manufacturing	Domestic Manufacture	Domestic Manufacture	U.S. EPA (2016a)
	Import	Import	U.S. EPA (2016a)

Life Cycle Stage	Category [a]	Subcategory [b]	References
Processing	Processing as a reactant or intermediate	Intermediate in Plastic Material and Resin Manufacturing	U.S. EPA (2016a), Public comments EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0015, EPA-HQ-OPPT-2016-0743-0017
		Other Non-Incorporative Processing	U.S. EPA (2016a)
	Incorporated into formulation, mixture or reaction product	Adhesives and sealant chemicals in Adhesive Manufacturing	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0011
		Anti-adhesive agents in Printing and Related Support Activities	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060
		Paint additives and coating additives not described by other codes in Paint and Coating Manufacturing; and Print Ink Manufacturing	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0013
		Processing aids not otherwise listed in Plastic Material and Resin Manufacturing	U.S. EPA (2016a), Public comments EPA-HQ-OPPT-2016-0743-0015, EPA-HQ-OPPT-2016-0743-0017, EPA-HQ-OPPT-2016-0743-0035, EPA-HQ-OPPT-2016-0743-0038
		Solvents (for cleaning or degreasing) in Non-Metallic Mineral Product Manufacturing; Machinery Manufacturing; Plastic Material and Resin Manufacturing; Primary Metal Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Services; Wholesale and Retail Trade	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0027, EPA-HQ-OPPT-2016-0743-0028

Life Cycle Stage	Category [a]	Subcategory [b]	References
		Surface active agents in Soap, Cleaning Compound and Toilet Preparation Manufacturing	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060
		Plating agents and surface treating agents in Fabricated Metal Product Manufacturing	U.S. EPA (2016a)
		Solvents (which become part of product formulation or mixture) in Electrical Equipment, Appliance and Component Manufacturing; Other Manufacturing; Paint and Coating Manufacturing; Print Ink Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Wholesale and Retail Trade	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0019, EPA-HQ-OPPT-2016-0743-0024, EPA-HQ-OPPT-2016-0743-0031, EPA-HQ-OPPT-2016-0743-0034
		Other uses in Oil and Gas Drilling, Extraction and Support Activities; Plastic Material and Resin Manufacturing; Services	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comment EPA-HQ-OPPT-2016-0743-0016
	Incorporation into articles	Lubricants and lubricant additives in Machinery Manufacturing	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060
		Paint additives and coating additives not described by other codes in Transportation Equipment Manufacturing	U.S. EPA (2016a)
		Solvents (which become part of product formulation or mixture), including in Textiles, Apparel and Leather Manufacturing	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comment EPA-HQ-OPPT-2016-0743-0027

Life Cycle Stage	Category [a]	Subcategory [b]	References
		Other, including in Plastic Product Manufacturing	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, EPA-HQ-OPPT-2016-0743-0067
	Repackaging	Wholesale and Retail Trade	U.S. EPA (2016a)
	Recycling	Recycling	U.S. EPA (2017e), U.S. EPA (2016a), Public comments EPA-HQ-OPPT-2016-0743-0017, EPA-HQ-OPPT-2016-0743-0031
Distribution in commerce	Distribution	Distribution in Commerce	U.S. EPA (2017e), U.S. EPA (2016a); Use document EPA-HQ-OPPT-2016-0743-0003
Industrial/ commercial use	Paints and coatings	Paint and coating removers	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0008, EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0023, EPA-HQ-OPPT-2016-0743-0025, EPA-HQ-OPPT-2016-0743-0035
		Adhesive removers	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0018
		Lacquers, stains, varnishes, primers and floor finishes	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0032, EPA-HQ-OPPT-2016-0743-0035
		Powder coatings (surface preparation)	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0016
	Paint additives and coating additives not described by other codes	Use in Computer and Electronic Product Manufacturing in Electronic Parts Manufacturing	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0006, EPA-HQ-OPPT-2016-0743-0013,

Life Cycle Stage	Category [a]	Subcategory [b]	References
			EPA-HQ-OPPT-2016-0743-0031, EPA-HQ-OPPT-2016-0743-0032, EPA-HQ-OPPT-2016-0743-0064
		Use in Computer and Electronic Product Manufacturing for Use in Semiconductor Manufacturing	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0019, EPA-HQ-OPPT-2016-0743-0024, EPA-HQ-OPPT-2016-0743-0027, EPA-HQ-OPPT-2016-0743-0063
		Use in Construction, Fabricated Metal Product Manufacturing, Machinery Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Primary Metal Manufacturing, Transportation Equipment Manufacturing, Wholesale and Retail Trade	U.S. EPA (2016a), Public comments, EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0011, , EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0023, , EPA-HQ-OPPT-2016-0743-0035, EPA-HQ-OPPT-2016-0743-0036,
	Solvents (for cleaning or degreasing)	Use in Electrical Equipment, Appliance and Component Manufacturing	U.S. EPA (2016a), Public comments EPA-HQ-OPPT-2016-0743-0006, EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0023, EPA-HQ-OPPT-2016-0743-0024, EPA-HQ-OPPT-2016-0743-0027
		Use in Electrical Equipment, Appliance and Component Manufacturing for Use in Semiconductor Manufacturing	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0019, EPA-HQ-OPPT-2016-0743-0024, EPA-HQ-OPPT-2016-0743-0027, EPA-HQ-OPPT-2016-0743-0063
	Ink, toner and colorant products	Printer ink	U.S. EPA (2016a), Use document, EPA-HQ-OPPT-2016-0743-0003, Public comments EPA-HQ-OPPT-2016-0743-0006, EPA-HQ-OPPT-2016-0743-0016, EPA-HQ-OPPT-2016-0743-0018

Life Cycle Stage	Category [a]	Subcategory [b]	References
		Inks in writing equipment	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comment EPA-HQ-OPPT-2016-0743-0018
	Processing aids, specific to petroleum production	Petrochemical Manufacturing	U.S. EPA (2016a), Public comment, EPA-HQ-OPPT-2016-0743-0031
	Other uses	Other uses in Oil and Gas Drilling, Extraction and Support Activities	U.S. EPA (2016a),
		Functional Fluids (closed systems)	U.S. EPA (2016a), Public comment EPA-HQ-OPPT-2016-0743-0031
	Adhesives and sealants	Adhesives and sealant chemicals including binding agents	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0006, EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0016, EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0023
		Single component glues and adhesives, including lubricant adhesives	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0035, EPA-HQ-OPPT-2016-0743-0036
		Two-component glues and adhesives, including some resins	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0016, EPA-HQ-OPPT-2016-0743-0018
	Other uses	Soldering materials	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0023

Life Cycle Stage	Category [a]	Subcategory [b]	References
		Anti-freeze and de-icing products	U.S. EPA (2016a)
		Automotive care products	U.S. EPA (2016a), Public comment, EPA-HQ-OPPT-2016-0743-0035
		Lubricants and greases	U.S. EPA (2016a)
		Metal products not covered elsewhere	U.S. EPA (2016a), Public comment, EPA-HQ-OPPT-2016-0743-0027, EPA-HQ-OPPT-2016-0743-0028 Public comment, EPA-HQ-OPPT-2016-0743-0027, EPA-HQ-OPPT-2016-0743-0028
		Lubricant and lubricant additives, including hydrophilic coatings	Market profile EPA-HQ-OPPT-2016-0743-0060
		Laboratory chemicals	U.S. EPA (2016a), Public comments EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009
		Lithium ion battery manufacturing	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comment EPA-HQ-OPPT-2016-0743-0005
		Cleaning and furniture care products, including wood cleaners, gasket removers	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comment EPA-HQ-OPPT-2016-0743-0025, EPA-HQ-OPPT-2016-0743-0035
		Fertilizer and other agricultural chemical manufacturing - processing aids and solvents	U.S. EPA (2016a), Public comment EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0036
Consumer uses	Paints and coatings	Paint and coating removers	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, Public comments EPA-HQ-OPPT-2016-0743-0008,
		Adhesive removers	Market profile EPA-HQ-OPPT-2016-0743-0060
		Lacquers, stains, varnishes, primers and floor finishes	Market profile EPA-HQ-OPPT-2016-0743-0060

Life Cycle Stage	Category [a]	Subcategory [b]	References
	Paint additives and coating additives not described by other codes	Paints and arts and crafts paints	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, EPA-HQ-OPPT-2016-0743-0018,
	Adhesives and sealants	Glues and adhesives, including lubricant adhesives	U.S. EPA (2016a), Market profile EPA-HQ-OPPT-2016-0743-0060, EPA-HQ-OPPT-2016-0743-0018,
	Other uses	Automotive care products	U.S. EPA (2016a)
		Cleaning and furniture care products, including wood cleaners, gasket removers	Market profile EPA-HQ-OPPT-2016-0743-0060, Public comment EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0025
		Lubricant and lubricant additives including hydrophilic coatings	Market profile EPA-HQ-OPPT-2016-0743-0060
Disposal	Disposal	Industrial pre-treatment	U.S. EPA (2017e)
		Industrial wastewater treatment	U.S. EPA (2017e) U.S. EPA (2017e)
		Publicly owned treatment works (POTW)	
		Underground injection	U.S. EPA (2017e), Public comment EPA-HQ-OPPT-2016-0743-0031
		Landfill (municipal, hazardous or other land disposal)	U.S. EPA (2017e), Public comment EPA-HQ-OPPT-2016-0743-0031
		Emissions to air	
		Incinerators (municipal and hazardous waste)	

[a] These categories of conditions of use appear in the life cycle diagram, reflect CDR codes and broadly represent NMP conditions of use in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of NMP.

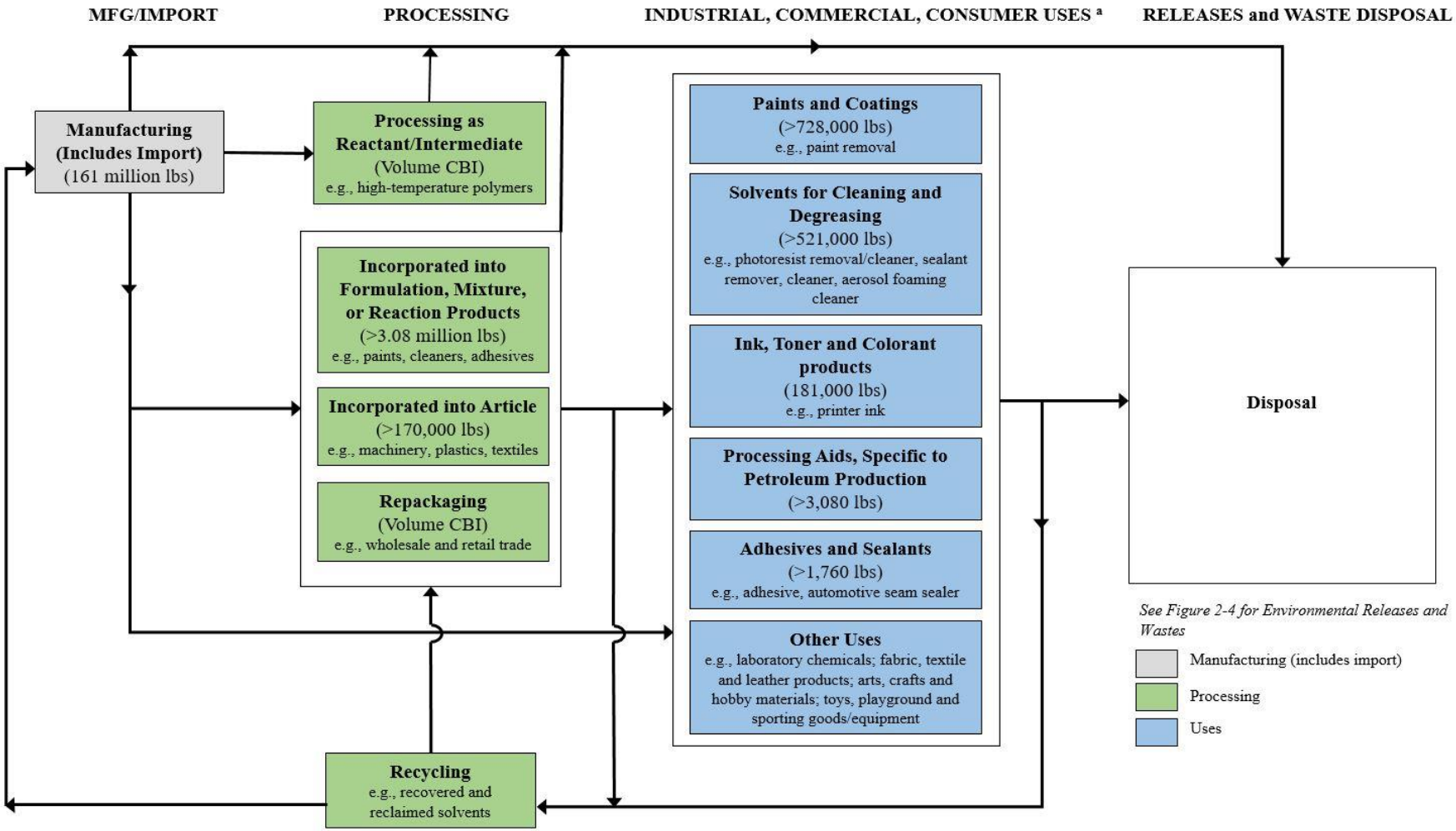


Figure 1-1. NMP Life Cycle Diagram

The life cycle diagram depicts the conditions of use that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period (U.S. EPA, 2016a). Activities related to distribution (*e.g.*, loading, unloading) will be considered throughout the NMP life cycle, rather than using a single distribution scenario.

[a] See Table 1-6 for additional uses not mentioned specifically in this diagram.

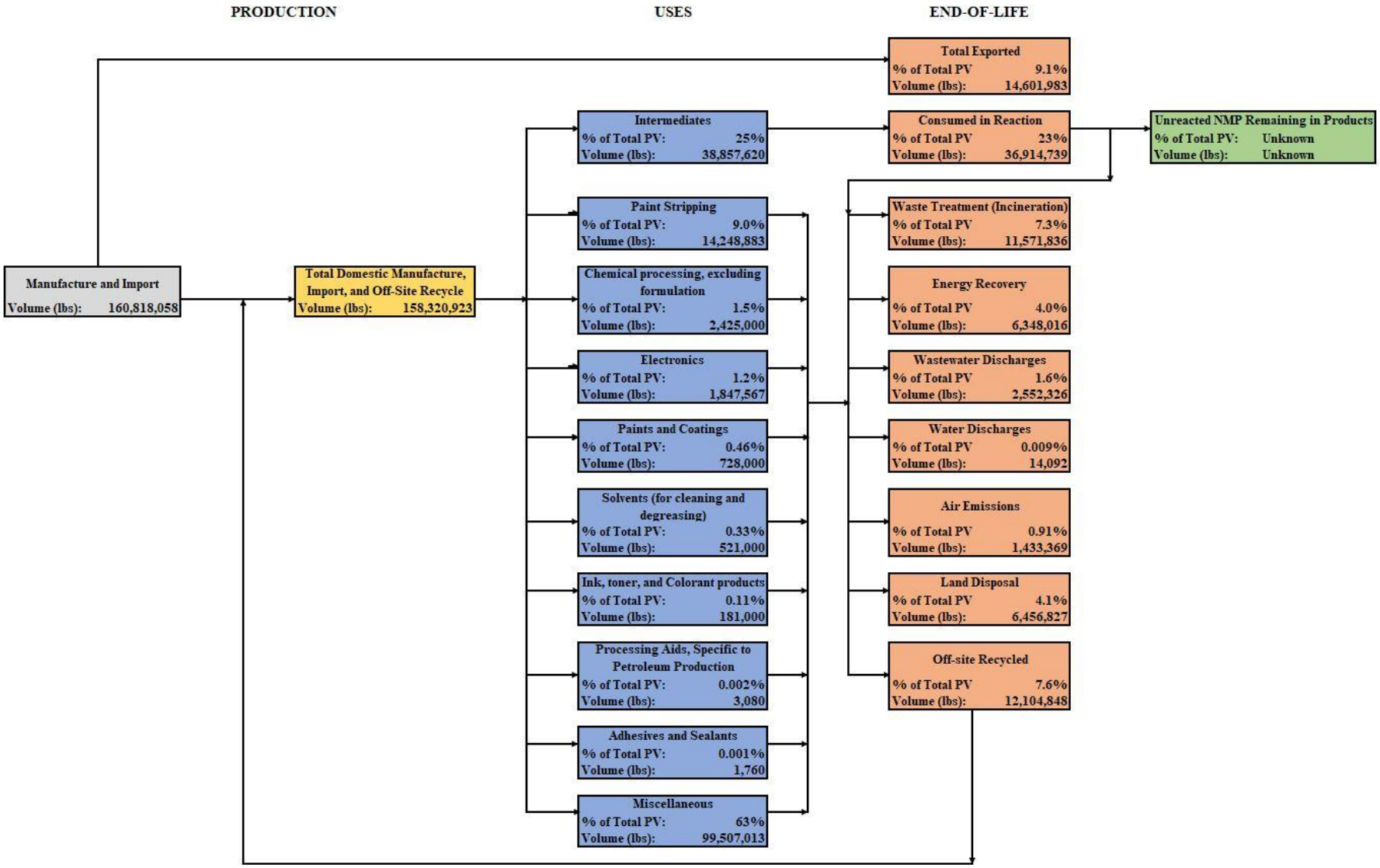


Figure 1-2. NMP Mass Balance

1.4.2 Exposure Pathways and Risks Addressed by Other EPA Statutes

In its TSCA Section 6(b) risk evaluations, EPA is coordinating action on certain exposure pathways and risks falling under the jurisdiction of other EPA-administered statutes or regulatory programs. More specifically, EPA is exercising its TSCA authorities to tailor the scope of its risk evaluations, rather than focusing on environmental exposure pathways addressed under other EPA-administered statutes or regulatory programs or risks that could be eliminated or reduced to a sufficient extent by actions taken under other EPA-administered laws. EPA considers this approach to be a reasonable exercise of the Agency's TSCA authorities, which include:

- TSCA Section 6(b)(4)(D): "The Administrator shall, not later than 6 months after the initiation of a risk evaluation, publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider…"
- TSCA Section 9(b)(1): "The Administrator shall coordinate actions taken under this chapter with actions taken under other Federal laws administered in whole or in part by the Administrator. If the Administrator determines that a risk to health or the environment associated with a chemical substance or mixture could be eliminated or reduced to a sufficient extent by actions taken under the authorities contained in such other Federal laws, the Administrator shall use such authorities to protect against such risk unless the Administrator determines, in the Administrator's discretion, that it is in the public interest to protect against such risk by actions taken under this chapter."
- TSCA Section 9(e): "…[I]f the Administrator obtains information related to exposures or releases of a chemical substance or mixture that may be prevented or reduced under another Federal law, including a law not administered by the Administrator, the Administrator shall make such information available to the relevant Federal agency or office of the Environmental Protection Agency."
- TSCA Section 2(c): "It is the intent of Congress that the Administrator shall carry out this chapter in a reasonable and prudent manner, and that the Administrator shall consider the environmental, economic, and social impact of any action the Administrator takes or proposes as provided under this chapter."

<u>TSCA authorities supporting tailored risk evaluations and intra-agency referrals</u>

TSCA Section 6(b)(4)(D)

TSCA Section 6(b)(4)(D) requires EPA, in developing the scope of a risk evaluation, to identify the hazards, exposures, conditions of use, and potentially exposed or susceptible subpopulations the Agency "expects to consider" in a risk evaluation. This language suggests that EPA is not required to consider all conditions of use, hazards, or exposure pathways in risk evaluations.

In the problem formulation documents for many of the first 10 chemicals undergoing risk evaluation, EPA applied this authority and rationale to certain exposure pathways, explaining that "EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes." This approach is informed by the legislative history of the amended TSCA, which supports the Agency's exercise of discretion to focus the risk evaluation on conditions of use that raise the greatest potential for risk, especially given that some conditions of use pose greater potential for exposure than others and the risks from many conditions of use are deemed negligible or already

well controlled. See June 7, 2016 Cong. Rec., S3519-S3520. Consistent with the approach articulated in the problem formulation documents, and as described in more detail below, EPA is exercising its authority under TSCA to tailor the scope of exposures evaluated in TSCA risk evaluations, rather than focusing on environmental exposure pathways addressed under other EPA-administered, media-specific statutes and regulatory programs.

TSCA Section 9(b)(1)

In addition to TSCA Section 6(b)(4)(D), the Agency also has discretionary authority under the first sentence of TSCA Section 9(b)(1) to "coordinate actions taken under [TSCA] with actions taken under other Federal laws administered in whole or in part by the Administrator." This broad, freestanding authority provides for intra-agency coordination and cooperation on a range of "actions." In EPA's view, the phrase "actions taken under [TSCA]" in the first sentence of Section 9(b)(1) is reasonably read to encompass more than just risk management actions, and to include actions taken during risk evaluation as well. More specifically, the authority to coordinate intra-agency actions exists regardless of whether the Administrator has first made a definitive finding of risk, formally determined that such risk could be eliminated or reduced to a sufficient extent by actions taken under authorities in other EPA-administered Federal laws, and/or made any associated finding as to whether it is in the public interest to protect against such risk by actions taken under TSCA. TSCA Section 9(b)(1) therefore provides EPA authority to coordinate actions with other EPA offices without ever making a risk finding, or following an identification of risk. This includes coordination on tailoring the scope of TSCA risk evaluations to focus on areas of greatest concern rather than exposure pathways addressed by other EPA-administered statutes and regulatory programs, which does not involve a risk determination or public interest finding under TSCA Section 9(b)(2).

In a narrower application of the broad authority provided by the first sentence of TSCA Section 9(b)(1), the remaining provisions of Section 9(b)(1) provide EPA authority to identify risks and refer certain of those risks for action by other EPA offices. Under the second sentence of Section 9(b)(1), "[i]f the Administrator determines that a risk to health or the environment associated with a chemical substance or mixture could be eliminated or reduced to a sufficient extent by actions taken under the authorities contained in such other Federal laws, the Administrator shall use such authorities to protect against such risk unless the Administrator determines, in the Administrator's discretion, that it is in the public interest to protect against such risk by actions taken under [TSCA]." Coordination of intra-agency action on risks under TSCA Section 9(b)(1) therefore entails both an identification of risk, and a referral of any risk that could be eliminated or reduced to a sufficient extent under other EPA-administered laws to EPA office(s) responsible for implementing those laws (absent a finding that it is in the public interest to protect against the risk by actions taken under TSCA).

Risk may be identified by OPPT or another EPA office, and the form of the identification may vary. For instance, OPPT may find that one or more conditions of use for a chemical substance present(s) a risk to human or ecological receptors through specific exposure routes and/or pathways. This could involve a quantitative or qualitative assessment of risk based on reasonably available information (which might include, *e.g.*, findings or statements by other EPA offices or other federal agencies). Alternatively, risk could be identified by another EPA office. For example, another EPA office administering non-TSCA authorities may have sufficient monitoring or modeling data to indicate that a particular condition of use presents risk to certain human or ecological receptors, based on expected hazards and exposures. This risk finding could be informed by information made available to the relevant office under TSCA Section 9(e), which supports cooperative actions through coordinated information-sharing.

Following an identification of risk, EPA would determine if that risk could be eliminated or reduced to a sufficient extent by actions taken under authorities in other EPA-administered laws. If so, TSCA requires EPA to "use such authorities to protect against such risk," unless EPA determines that it is in the public interest to protect against that risk by actions taken under TSCA. In some instances, EPA may find that a risk could be sufficiently reduced or eliminated by future action taken under non-TSCA authority. This might include, *e.g.*, action taken under the authority of the SDWA to address risk to the general population from a chemical substance in drinking water, particularly if the Office of Water has taken preliminary steps such as listing the subject chemical substance on the Contaminant Candidate List. This sort of risk finding and referral could occur during the risk evaluation process, thereby enabling EPA to use more a relevant and appropriate authority administered by another EPA office to protect against hazards or exposures to affected receptors.

Legislative history on TSCA Section 9(b)(1) supports both broad coordination on current intra-agency actions, and narrower coordination when risk is identified and referred to another EPA office for action. A Conference Report from the time of TSCA's passage explained that Section 9 is intended "to assure that overlapping or duplicative regulation is avoided while attempting to provide for the greatest possible measure of protection to health and the environment." S. Rep. No. 94-1302 at 84. See also H. Rep. No. 114-176 at 28 (stating that the 2016 TSCA amendments "reinforce TSCA's original purpose of filling gaps in Federal law," and citing new language in Section 9(b)(2) intended "to focus the Administrator's exercise of discretion regarding which statute to apply and to encourage decisions that avoid confusion, complication, and duplication"). Exercising TSCA Section 9(b)(1) authority to coordinate on tailoring TSCA risk evaluations is consistent with this expression of Congressional intent.

Legislative history also supports a reading of Section 9(b)(1) under which EPA coordinates intra-agency action, including information-sharing under TSCA Section 9(e), and the appropriately positioned EPA office is responsible for the identification of risk and actions to protect against such risks. See, *e.g.*, Senate Report 114-67, 2016 Cong. Rec. S3522 (under TSCA Section 9, "if the Administrator finds that disposal of a chemical substance may pose risks that could be prevented or reduced under the Solid Waste Disposal Act, the Administrator should ensure that the relevant office of EPA receives that information"); H. Rep. No. 114-176 at 28, 2016 Cong. Rec. S3522 (under Section 9, "if the Administrator determines that a risk to health or the environment associated with disposal of a chemical substance could be eliminated or reduced to a sufficient extent under the Solid Waste Disposal Act, the Administrator should use those authorities to protect against the risk"). Legislative history on Section 9(b)(1) therefore supports coordination with and referral of action to other EPA offices, especially when statutes and associated regulatory programs administered by those offices could address exposure pathways or risks associated with conditions of use, hazards, and/or exposure pathways that may otherwise be within the scope of TSCA risk evaluations.

TSCA Section 2(c) & 18(d)(1)

Finally, TSCA Sections 2(c) and 18(d) supports coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs. Section 2(c) directs EPA to carry out TSCA in a "reasonable and prudent manner" and to consider "the environmental, economic, and social impact" of its actions under TSCA. Legislative history from around the time of TSCA's passage indicates that Congress intended EPA to consider the context and take into account the impacts of each action under TSCA. S. Rep. No. 94-698 at 14 ("the intent of Congress as stated in this subsection should guide each action the Administrator takes under other sections of the bill").

Section 18(d)(1) specifies that state actions adopted or authorized under any Federal law are not preempted by an order of no unreasonable risk issued pursuant to TSCA Section 6(i)(1) or a rule to address unreasonable risk issued under TSCA Section 6(a). Thus, even if a risk evaluation were to address exposures or risks that are otherwise addressed by other federal laws and, for example, implemented by states, the state laws implementing those federal requirements would not be preempted. In such a case, both the other federal and state laws, as well as any TSCA Section 6(i)(1) order or TSCA Section 6(a) rule, would apply to the same issue area. See also TSCA Section 18(d)(1)(A)(iii). In legislative history on amended TSCA pertaining to Section 18(d), Congress opined that "[t]his approach is appropriate for the considerable body of law regulating chemical releases to the environment, such as air and water quality, where the states have traditionally had a significant regulatory role and often have a uniquely local concern." Sen. Rep. 114-67 at 26.

EPA's careful consideration of whether other EPA-administered authorities are available, and more appropriate, for addressing certain exposures and risks is consistent with Congress' intent to maintain existing federal requirements and the state actions adopted to locally and more specifically implement those federal requirements, and to carry out TSCA in a reasonable and prudent manner. EPA believes it is both reasonable and prudent to tailor TSCA risk evaluations in a manner reflective of expertise and experience exercised by other EPA and State offices to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. This approach furthers Congressional direction and EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing risk evaluations.

EPA-administered statutes and regulatory programs that address specific exposure pathways and/or risks

During the course of the risk evaluation process for NMP, OPPT worked closely with the offices within EPA that administer and implement regulatory programs under the SDWA, and the RCRA. Through intra-agency coordination, EPA determined that specific exposure pathways are well-regulated by the EPA statutes and regulations described in the following paragraphs.

Drinking Water Pathway

SDWA requires EPA to publish a Contaminant Candidate List (CCL) every 5 years. The CCL is a list of unregulated contaminants that are known or anticipated to occur in public water systems and that may require regulation. As provided by the SDWA, the Agency places those contaminants on the list that present the greatest health concern. The SDWA also requires EPA to make Regulatory Determinations (RegDet) to regulate (or not) at least five CCL contaminants every 5 years. To make a determination to regulate a contaminant, EPA must conclude the contaminant may have adverse health effects, occurs or is substantially likely to occur in public water systems at a level of concern, and that regulation, in the sole judgement of the Administrator, presents a meaningful opportunity for health risk reduction for persons served by public water systems, in accordance with SDWA Section 1412(b)(1)(A). If after considering public comment on a preliminary determination, the Agency makes a determination to regulate a contaminant, EPA will initiate the process to propose and promulgate a national primary drinking water regulation. The statutory time frame provides for Agency proposal of a regulation within 24 months and action on a final regulation within 18 months of proposal. When proposing and promulgating drinking water regulations, the Agency must conduct a number of analyses.

Currently, there is no National Primary Drinking Water regulation for NMP under SDWA. NMP is one of 109 contaminants listed on EPA's fourth Contaminant Candidate List (CCL 4), see 81 FR 81099. NMP is on the CCL because EPA's Office of Water (OW) concluded that based on occurrence and health information the chemical is anticipated to occur in public water systems and may require regulation.

OCSPP has coordinated with OW regarding NMP. In March 2020, OW published a notice with Preliminary Regulatory Determinations for Contaminants on the Fourth Drinking Water Contaminant Candidate List (85 FR 14098 (Mar. 10, 2020)). In accordance with OW's process, the Agency did not consider NMP for regulatory determinations as the Agency found that the available health effects and occurrence data were not sufficient for the Agency to conduct evaluations necessary to begin a regulatory determination. EPA does not have sufficient data to make a regulatory determination for NMP under SDWA and will continue to evaluate new information on NMP and other contaminants as it develops future CCLs under SDWA. Because the drinking water exposure pathway for NMP is being addressed under the regular analytical processes used to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under SDWA, EPA has not included this pathway in the risk evaluation for NMP under TSCA.

As described above, EPA has regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under SDWA. OW evaluates the regulatory determination criteria under SDWA Section 1412(b)(1)(A) to determine whether or not to initiate the development of a National Primary Drinking Water Regulation. EPA promulgates National Primary Drinking Water Regulations (NPDWRs) under SDWA when the Agency concludes a contaminant may have adverse health effects, occurs or is substantially likely to occur in public water systems at a level of concern and that regulation, in the sole judgement of the Administrator, presents a meaningful opportunity for health risk reduction. For each contaminant with NPDWRs, EPA sets an enforceable Maximum Contaminant Level (MCL) as close as feasible to a health based, non-enforceable Maximum Contaminant Level Goals (MCLG) or establishes a treatment technique. Feasibility refers to both the ability to treat water to meet the MCL and the ability to monitor water quality at the MCL. Public water systems generally monitor for the regulated chemical based on a standardized monitoring schedule to ensure compliance with the maximum contaminant level (MCL). Under SDWA, EPA must also review existing drinking water regulations every 6 years, and if appropriate, revise them. SDWA, originally passed by Congress in 1974, is the main federal statute to protect public drinking water by regulating the nation's public drinking water supply and authorizing EPA to set national health-based standards and take other actions to protect against contaminants that may be found in drinking water.

EPA's Office of Water will continue to evaluate NMP under SDWA authorities and will consider the information produced in the risk evaluation process as part of future SDWA actions.

Disposal Pathway

NMP is not classified as a RCRA hazardous waste. NMP containing solid wastes are not expected to be sent to Subtitle C incinerators because NMP is not a hazardous waste and due to higher cost of such incineration as compared with municipal solid waste (MSW) or other incinerators. Emissions from hazardous waste incinerators were not evaluated. However, it is possible that NMP containing solid wastes could be sent to subtitle C incinerators due to other chemicals in an NMP-containing solid waste mixture that are hazardous waste.

EPA did not evaluate on-site NMP land releases that go to underground injection or associated exposures to the general population or terrestrial species in the risk evaluation. Most of the on-site land disposal reported for NMP in the 2015 TRI was to Class I underground injection wells (approximately 3.6 million pounds), with no reported environmental releases via underground injection to Class II-VI wells (U.S. EPA, 2017b). Environmental disposal of NMP via injection into Class I wells is covered under the jurisdiction of SDWA and disposal of NMP via underground injection is not likely to result in environmental and general population exposures. See 40 CFR part 144.

EPA did not evaluate on-site releases to land from RCRA Subtitle C hazardous waste landfills or exposures of the general population or terrestrial species from such releases in this evaluation. Based on the 2015 TRI data, approximately 93,217 pounds of NMP were transferred to RCRA Subtitle C landfills; smaller amounts (approximately 25,648 pounds) were characterized as "other" land disposal and off-site land treatment (approximately 330 pounds) (U.S. EPA, 2017b). Design standards for Subtitle C landfills require double liner, double leachate collection and removal systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and ground water monitoring system. Bulk liquids may not be disposed in Subtitle C landfills. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. See 40 CFR part 264; Appendix A.

EPA did not include releases to land from RCRA Subtitle D MSW landfills or exposures to the general population or terrestrial species from such releases in the risk evaluation. As NMP is not classified as a RCRA hazardous waste, NMP containing solid waste may be sent to RCRA Subtitle D MSW landfills. While permitted and managed by individual states, MSW landfills established after 1989 are required by federal regulations to implement some of the same requirements as Subtitle C landfills. Newer MSW landfills must have a liner system with leachate collection and conduct ground water monitoring and corrective action when releases are detected. MSW landfills are also subject to closure and post-closure care requirements, as well as providing financial assurance for funding of any needed corrective actions. MSW landfills have been designed to allow for the small amounts of hazardous waste generated by households and very small quantity waste generators (< 220 pounds per month). Bulk liquids, such as free solvent, may not be disposed of in MSW landfills. See 40 CFR part 258.

1.4.3 Conceptual Model

EPA considered the hazards that may result from exposure pathways outlined in the preliminary conceptual models of the NMP Scope document (U.S. EPA, 2017c). These conceptual models considered potential exposures resulting from consumer activities and uses (Figure 1-4), industrial and commercial activities (Figure 1-3), environmental releases and waste disposal (Figure 1-5). During problem formulation EPA modified the initial conceptual models provided in the NMP Scope document based on reasonably available information identified for NMP (U.S. EPA, 2018c). For reasons described below, the conceptual model for consumer activities and uses was modified to indicate that the oral route of exposure will not be further analyzed.

During risk evaluation, EPA considered oral exposures that may result from consumer use of NMP-containing products (*e.g.*, infant mouthing behaviors). EPA reviewed experimental product-testing

information on NMP content in consumer articles and determined which products are likely to be mouthed (*e.g.*, blankets, toys). EPA then identified information sources that measured NMP content in various consumer products and considered additional contextual information regarding product use, including the extent of NMP migration from these products (DTI, 2004). Using the Consumer Exposure Model, EPA estimated the exposure to NMP due to mouthing of fabric articles such as blankets, dolls, or stuffed animals to young children. EPA evaluated NMP exposure for 3 lifestages, infant (<1 year), infant (1-2 years), and small child (3-5 years). Infants younger than one year would have the greatest possible exposure via mouthing, however the estimated levels of NMP exposure of 15 μg are significantly less than the migration amount reported in the Danish study (200 μg) and well below the oral dose of 48 mg/kg/day that could result in risk. EPA did not further analyze NMP exposure via the oral pathway in this risk evaluation.

The conceptual model presented in the NMP Problem Formulation also listed dust as a potential NMP exposure pathway for consumers. There is limited information reasonably available on NMP levels in dust, but EPA expects the impacts of this uncertainty to be negligible, as this exposure source is encompassed within the conservative estimates derived for dermal and inhalation exposures (Environment Canada, 2017).

Lastly, EPA analyzed NMP exposures to bystanders (*i.e.*, those located in the same home as the consumer during product use) who do not have direct contact with NMP-containing consumer products. Though EPA's 2015 Paint Remover risk assessment showed no risks to bystanders from indirect exposure to NMP air concentrations associated with consumer use, the supplemental paint remover analysis in the risk assessment consisted of several scenarios resulting in high NMP air concentrations that could expose other individuals in the home (see Appendix G) (U.S. EPA, 2015c). Given the evaluation of a greater number of conditions of use in addition to paint removers, EPA estimated NMP exposures to bystanders for consumer uses other than paint removers that resulted in high exposures.

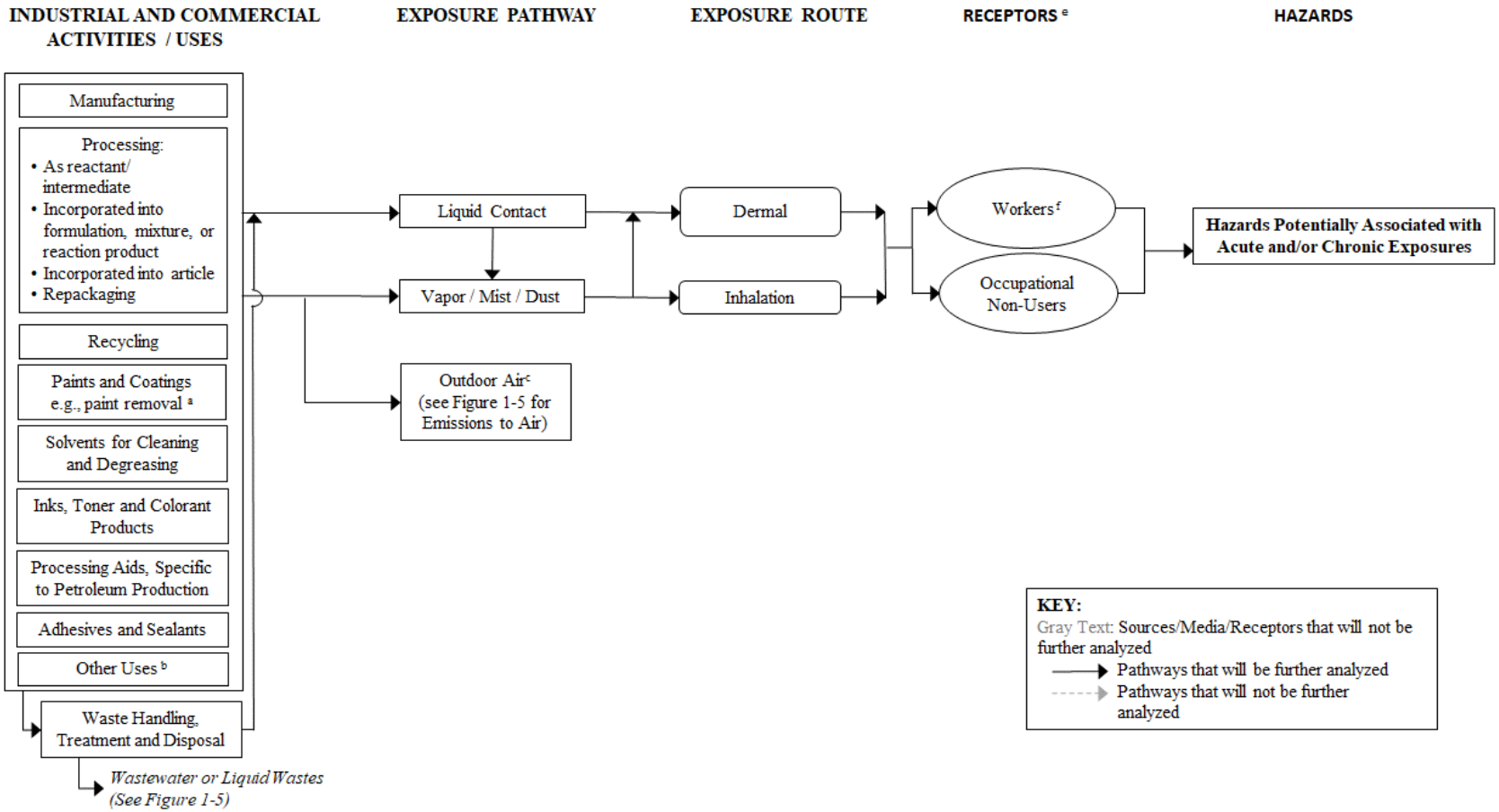


Figure 1-3. NMP Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The conceptual model presents exposure pathways, routes and hazards to human receptors from industrial and commercial uses of NMP.

[a] U.S. EPA (2015c) assessed NMP use in paint removal; these uses will be considered during risk evaluation to ensure previous assessments are aligned with the Procedures for Chemical Risk Evaluation under the Amended TSCA (40 CFR Part 702).

[b] Some products are used in both commercial and consumer applications. Additional uses of NMP are included in Table 1-6.

[c] Emissions to outdoor air include stack emissions and fugitive emissions such as fugitive equipment leaks from valves, pump seals, flanges, compressors, sampling connections and open-ended lines; evaporative losses from surface impoundment and spills; and releases from building ventilation systems.

[d] Oral exposure via incidental ingestion of inhaled vapor/mist will be considered as an inhalation exposure.

[e] Receptors include potentially exposed or susceptible subpopulations.

[f] When data and information are reasonably available to support the analysis, EPA expects to consider the effect that engineering controls and/or PPE have on occupational exposure levels.

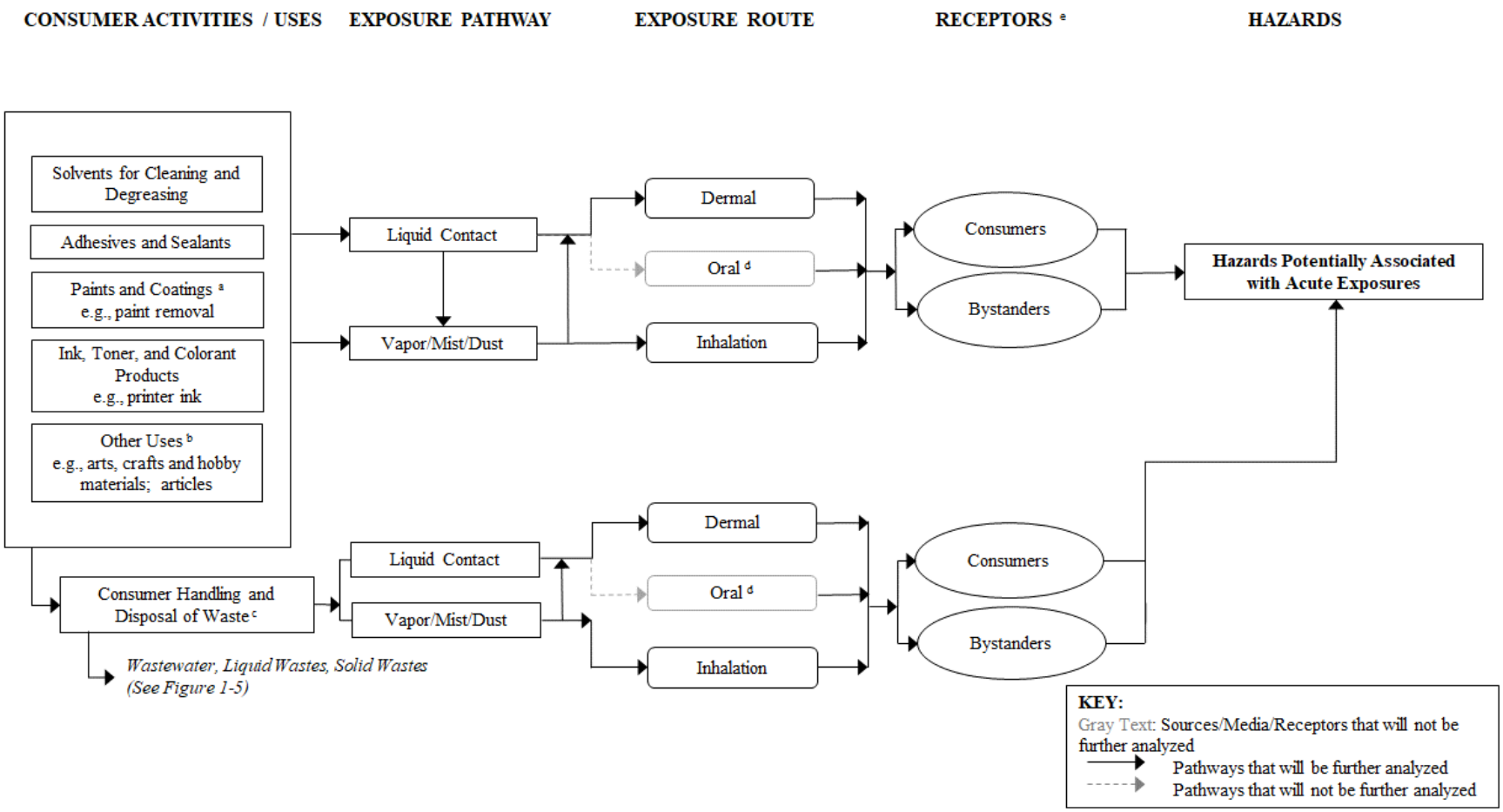


Figure 1-4. NMP Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

The conceptual model presents the exposure pathways, routes and hazards to human receptors from consumer activities and uses of NMP.

[a] U.S. EPA (2015c) assessed NMP use in paint and coating removal; these uses will be considered during risk evaluation to ensure previous assessments are aligned with the Procedures for Chemical Risk Evaluation under the Amended TSCA (40 CFR Part 702).

[b] Some products are used in both commercial and consumer applications; additional uses of NMP are included in Table 1-6.

[c] Consumers may also be exposed while handling municipal wastes; however, the pathway is uncertain.

[d] Oral exposure via incidental ingestion of inhaled vapor/mist/dust will be considered as an inhalation exposure.

[e] Receptors include potentially exposed or susceptible subpopulations.

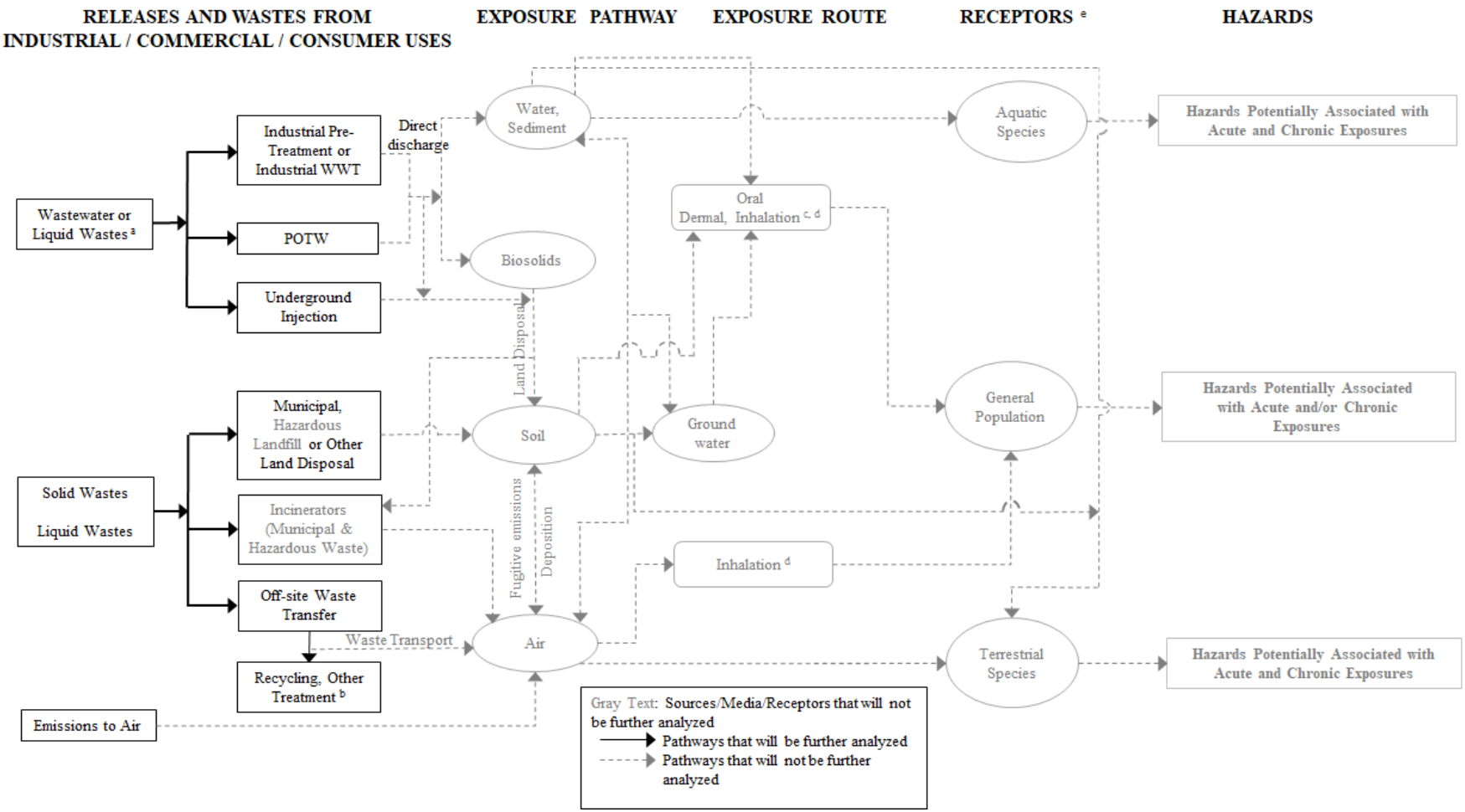


Figure 1-5. NMP Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The conceptual model presents the exposure pathways, routes and hazards to human and environmental receptors from NMP environmental releases.

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge). For consumer uses, such wastes may be released directly to POTW (*i.e.*, down the drain). Drinking water will undergo further treatment in drinking water treatment plant. Ground water may also be a source of drinking water.

[b] Additional releases may occur from recycling and other waste treatment.

[c] Volatilization from or contact with NMP-containing drinking/tap water during showering, bathing and washing represents another potential exposure pathway.

[d] Presence of mist is unlikely; inhalation and oral exposure are expected to be negligible.

[e] Receptors include potentially exposed or susceptible subpopulations.

1.5 Systematic Review

TSCA requires EPA to use scientific information, technical procedures, measures, methods, protocols, methodologies and models consistent with the best available science and base decisions under Section 6 on the weight of the scientific evidence. Within the TSCA risk evaluation context, the weight of the scientific evidence is defined as "*a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance*" (40 C.F.R. 702.33).

To meet the TSCA Section 26(h) science standards, EPA used the TSCA systematic review process described in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018a). The process complements the risk evaluation process in that the data collection, data evaluation, and data integration stages of the systematic review process are used to develop the exposure and hazard assessments based on reasonably available information. EPA defines "reasonably available information" to mean information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation (40 C.F.R. 702.33).

EPA is implementing systematic review methods and approaches within the regulatory context of the amended TSCA. Although EPA adopted as many best practices as practicable from the systematic review community, EPA modified the process to ensure that the identification, screening, evaluation and integration of data and information can support timely regulatory decision making under the timelines of the statute.

1.5.1 Data and Information Collection

EPA planned and conducted a comprehensive literature search based on key words related to the discipline-specific evidence supporting the risk evaluation (*e.g.*, environmental fate and transport; engineering releases and occupational exposure; exposure to general population, consumers and environmental exposure; and environmental and human health hazards). EPA then developed and applied inclusion and exclusion criteria during the title and abstract screening to identify information potentially relevant for the risk evaluation process. The literature and screening strategy as specifically applied to NMP is described in the *Strategy for Conducting Literature Searches for NMP: Supplemental File to the TSCA Scope document* (U.S. EPA, 2017d); results of the title and abstract screening process are published in the *n-Methylpyrrolidone (CASRN 872-50-4) Bibliography: Supplemental File to the TSCA Scope Document* (U.S. EPA, 2017b).

For studies determined to be on-topic after title and abstract screening, EPA conducted a full text screening to further exclude references that were not relevant to the risk evaluation. Screening decisions were made based on eligibility criteria documented in the form of the populations, exposures, comparators, and outcomes (PECO) framework or a modified framework.[5] Data sources that met the criteria were carried forward to the data evaluation stage. The inclusion and exclusion criteria for full text screening for NMP are available in Appendix G of the *Problem Formulation of the Risk Evaluation for n-Methylpyrrolidone* (U.S. EPA, 2018c).

[5] A PESO statement was used during the full text screening of environmental fate and transport data sources. PESO stands for Pathways and Processes, Exposure, Setting or Scenario, and Outcomes. A RESO statement was used during the full text screening of the engineering and occupational exposure literature. RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes.

In addition to the comprehensive literature search and screening process described above, EPA leveraged information presented in previous assessments[6] when identifying relevant key and supporting data[7] and information for developing the NMP risk evaluation. This is discussed in the *Strategy for Conducting Literature Searches for NMP: Supplemental Document to the TSCA Scope document* (U.S. EPA, 2017d). In general, many of the key and supporting data sources were identified in the *NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017b). However, there were instances where EPA missed relevant sources that were not captured in the initial categorization of the on-topic references. EPA found additional data and information using backward reference searching, a technique that will be included in future search strategies. This issue was discussed in Section 4 of the *Application of Systematic Review for TSCA Risk Evaluations* (U.S. EPA, 2018a). Other relevant key and supporting studies were identified through targeted supplemental searches conducted to inform the analytical approaches and methods used in the NMP risk evaluation (*e.g.*, to identify specific information needed for exposure modeling) or to identify new information published after the date of the initial search.

EPA used previous chemical assessments to quickly identify relevant key and supporting studies in order to expedite the data quality evaluation of these data sources, but many were already captured in the comprehensive literature search strategy described above. EPA also considered newer information not covered by previous chemical assessments, as described in the *Strategy for Conducting Literature Searches for NMP: Supplemental Document to the TSCA Scope document* (U.S. EPA, 2017d). EPA then evaluated the confidence of this information rather than evaluating the confidence of all underlying evidence ever published on NMP fate and transport, environmental releases, and environmental and human exposure and hazard potential. Such a comprehensive evaluation would be extremely labor intensive and could not be achieved under the TSCA statutory deadlines for most chemical substances, especially those that are data rich. EPA also considered how this approach to data evaluation would change the conclusions presented in previous assessments.

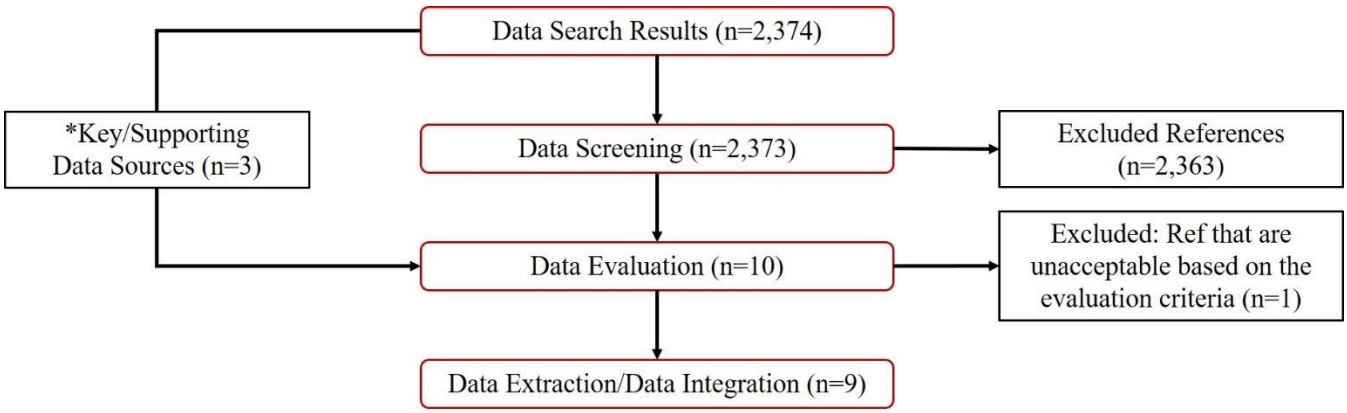
Using this pragmatic approach, EPA maximized the scientific and analytical efforts of other regulatory and non-regulatory agencies by accepting for the most part, the relevant scientific knowledge gathered and analyzed by others, except for influential information sources that may impact the weight of the scientific evidence underlying EPA's risk findings. This influential information (*i.e.*, key/supporting studies) came from a smaller pool of information sources subjected to the rigor of the TSCA systematic review process to ensure that the best available science is incorporated into the weight of the scientific evidence used to support the NMP risk evaluation.

The literature flow diagrams shown in Figure 1-6, Figure 1-7, Figure 1-8, Figure 1-9, and Figure 1-10 highlight the results obtained for each scientific discipline based on this approach. Each diagram provides the total number of references considered at the start of each systematic review stage (*i.e.*, data search, data screening, data evaluation, data extraction/data integration) and those excluded based on the criteria guiding EPA's screening and data quality evaluation decisions.

[6] Examples of existing assessments are EPA's chemical assessments (*e.g.*, previous work plan risk assessments, problem formulation documents), Agency for Toxic Substances and Disease Registry's (ATSDR) Toxicological Profiles and EPA's Integrated Risk Information System (IRIS) assessments. This is described in more detail in the *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (https://www.epa.gov/sites/production/files/2017-06/documents/14-dioxane_lit_search_strategy_053017.pdf).

[7] Key and supporting data and information are those that support key analyses, arguments, and/or conclusions in the risk evaluation.

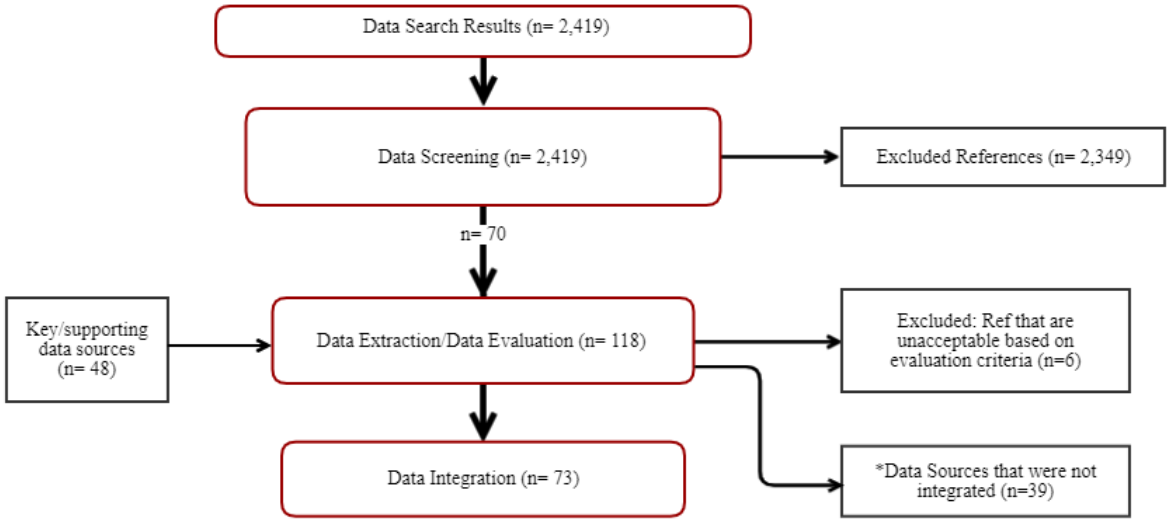
EPA made the decision to bypass the data screening step for data sources that were highly relevant to the risk evaluation as described above. These data sources are depicted as "key/supporting data sources" in the literature flow diagrams. Note that the number of "key/supporting data sources" were excluded from the total count during the data screening stage and added, for the most part, to the data evaluation stage depending on the discipline-specific evidence. The exception was the engineering releases and occupational exposure data sources that were subject to a combined data extraction and evaluation step (Figure 1-7).



*These are key and supporting studies from existing assessments (e.g., EPA IRIS assessments, ATSDR assessments, ECHA dossiers) that were highly relevant for the TSCA risk evaluation. These studies bypassed the data screening step and moved directly to the data evaluation step.

Figure 1-6. Literature Flow Diagram for Fate and Transport

The number of publications considered in each step of the systematic review of the NMP fate and transport literature is summarized in Figure 1-6. Literature on the environmental fate and transport of NMP were gathered and screened as described in Appendix C of the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). Additional information regarding the literature search and screening strategy for NMP is provided in EPA's *Strategy for Conducting Literature Searches for n-Methylpyrrolidone (NMP): Supplemental File to the TSCA Scope Document* (U.S. EPA, 2017d). The results of this screening are published in the *NMP (CASRN 872-50-4) Bibliography: Supplemental File to the TSCA Scope Document* (U.S. EPA, 2017b).



*The quality of data in these sources (n=39) were acceptable for risk assessment purposes, but they were ultimately excluded from further consideration based on EPA's integration approach for environmental release and occupational exposure data/information. EPA's approach uses a hierarchy of preferences that guide decisions about what types of data/information are included for further analysis, synthesis and integration into the environmental release and occupational exposure assessments. EPA prefers using data with the highest rated quality among those in the higher level of the hierarchy of preferences (i.e., data > modeling > occupational exposure limits or release limits). If warranted, EPA may use data/information of lower rated quality as supportive evidence in the environmental release and occupational exposure assessments.

Figure 1-7. Literature Flow Diagram for Releases and Occupational Exposures

As shown in Figure 1-7, the literature search strategy for NMP environmental releases and occupational exposures yielded 2,419 data sources. Of these, 70 data sources were determined to be relevant to the NMP risk evaluation during the data screening process. These relevant data sources progressed to the data extraction/evaluation phase. After data extraction/evaluation, EPA identified several data gaps and performed a supplemental, targeted search to fill these gaps (*e.g.*, to locate information needed for exposure modeling). This supplemental search and the identification of relevant data and information contained in public comments that were submitted following the publication of the risk evaluation yielded 48 relevant data sources that bypassed the initial data screening step. These new data sources were added to the 70 data sources originally determined to be relevant during the data screening process; all were evaluated and extracted in accordance with the process described in Appendix D of the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018a). Of the 118 sources evaluated, six were rated as containing only unacceptable data based on serious flaws detected during data evaluation. Of the 112 sources considered for data integration, lower quality data from 39 sources were not integrated based on EPA's integration approach (*i.e.*, higher quality data from other sources were used; in these cases, the hierarchy of preferences was not a factor in the decision). Data from the remaining 73 sources were integrated into the NMP risk evaluation. The data integration approach for releases and occupational exposure data is discussed in Appendix C of the document titled *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020t).

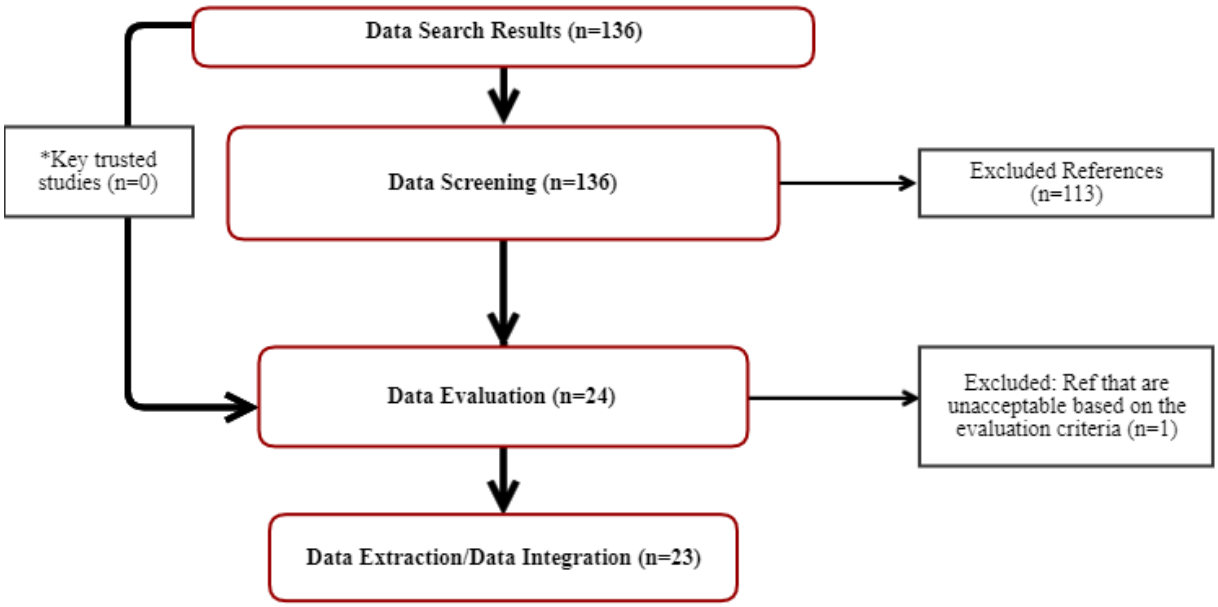


Figure 1-8. Literature Flow Diagram for General Population, Consumer and Environmental Exposures

The number of data and information sources considered in each step of the systematic review of NMP literature on general population, consumer and environmental exposure is summarized in Figure 1-8. The literature search results for general population, consumer and environmental exposures yielded 132 data sources. Of these data sources, 22 were determined to be relevant to the NMP risk evaluation through the data screening process. These relevant data sources were evaluated in accordance with Appendix E of the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018a).

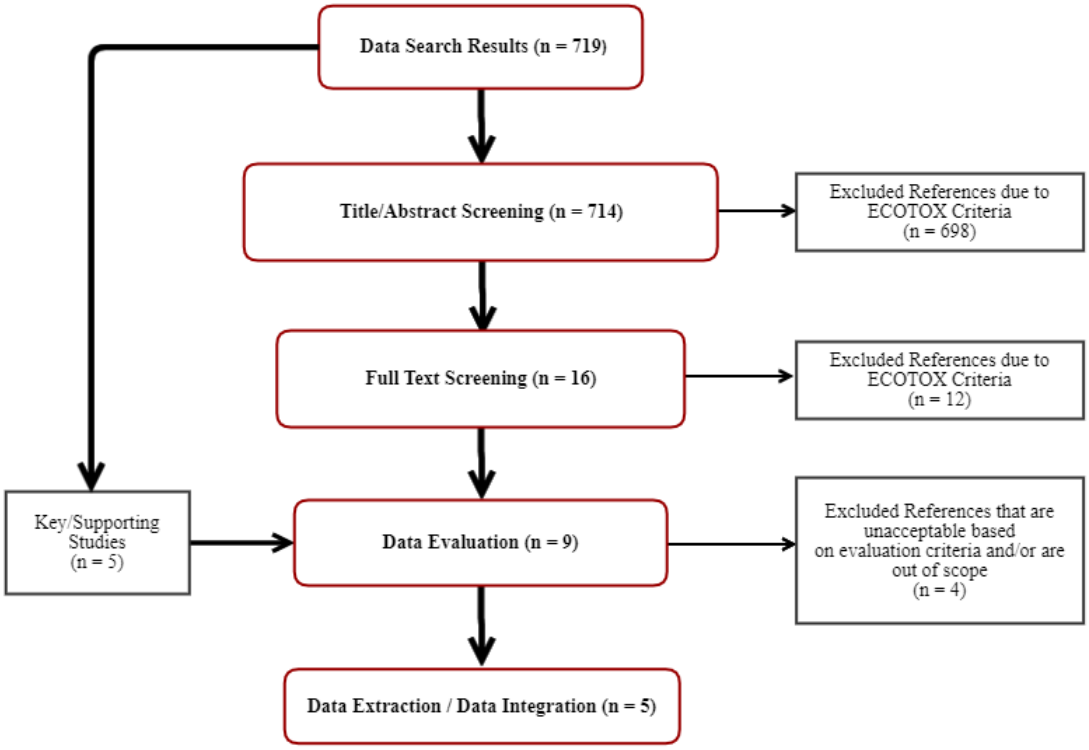


Figure 1-9. Literature Flow Diagram for Environmental Hazards

The environmental hazard data sources for NMP were identified through literature searches and screening strategies using the ECOTOXicology knowledgebase system (ECOTOX) Standing Operating Procedures. For studies determined to be on-topic after title and abstract screening, EPA conducted a full text screening to further exclude citations that were not considered relevant to the NMP risk evaluation. Screening decisions were made based on eligibility criteria as documented in the ECOTOX User Guide (U.S. EPA, 2018b). Additional details can be found in the *Strategy for Conducting Literature Searches for NMP: Supplemental Document to the TSCA Scope Document* (U.S. EPA, 2017d).

The literature search strategy for environmental hazard data identified 719 citations for NMP Figure 1-9). At the title and abstract screening phase, 698 of these citations were excluded as "off-topic" based on EPA's ECOTOX knowledgebase criteria. The remaining 16 citations underwent a more thorough (full-text) screening process using the same ECOTOX criteria to determine which should proceed to data evaluation. Several citations were determined to be "out of scope" during the initial screening steps and were therefore excluded from data evaluation. Five "Key/Supporting Citations" for Environmental Hazard were identified by EPA as a result of a review of the OECD HPV SIDS Document for NMP (OECD, 2009). EPA obtained the full study reports from BASF and GAF (only summaries are provided in the OECD document). Of these five citations, three were translated from German. These five citations were found independently from the ECOTOX process.

EPA developed data quality evaluation criteria based on a combination of EPA's ECOTOXicology knowledgebase (ECOTOX) criteria and the Criteria for Reporting and Evaluating ecotoxicity Data (CRED), as discussed in the *Applications of Systematic Review for TSCA Risk Evaluations* (U.S. EPA, 2018a). Nine citations went through the data evaluation process using the data quality evaluation criteria

for NMP. EPA analyzed each individual toxicity study in each of these citations using the data quality evaluation to determine the overall study quality. Four citations were excluded during data evaluation. In total, five citations were evaluated for data extraction/integration in the NMP risk evaluation.

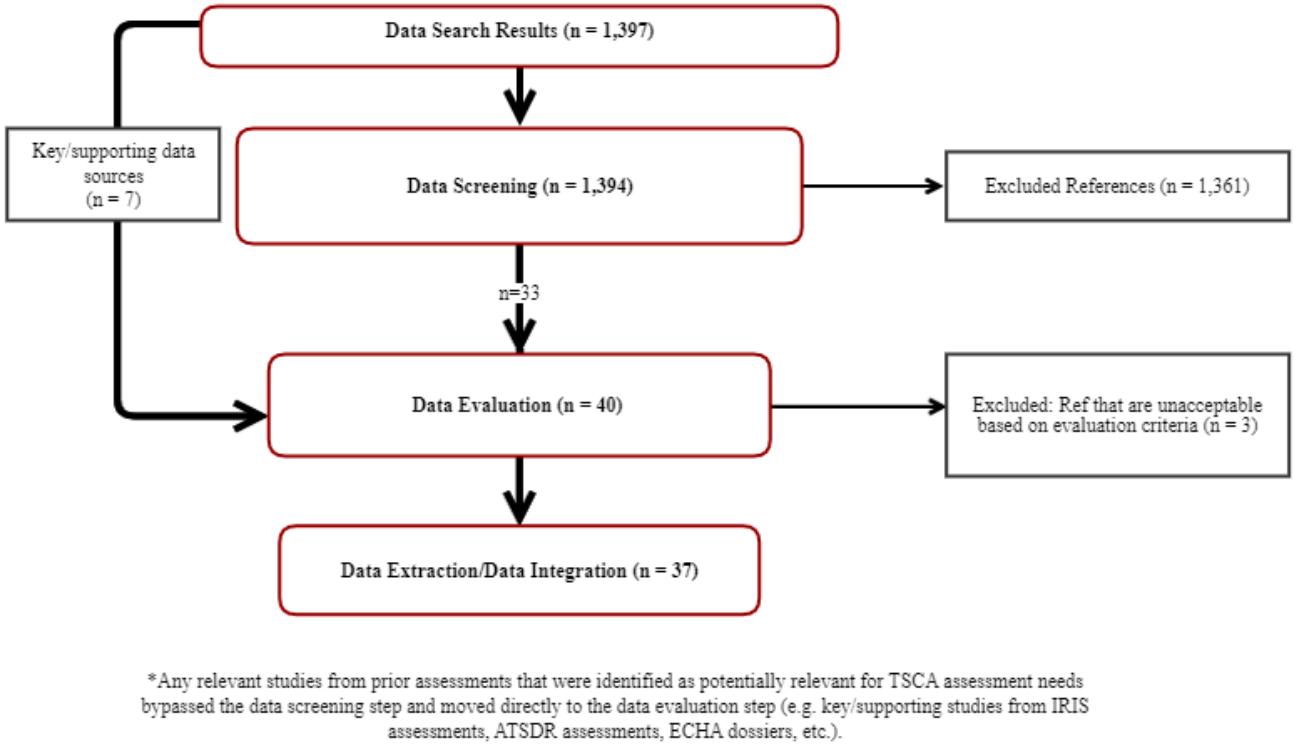


Figure 1-10. Literature Flow Diagram for Human Health Key/Supporting Data Sources

The literature search strategy used to gather human health hazard information for NMP yielded 1,397 studies. This included three key and supporting studies (identified from previous regulatory assessments) that skipped the initial screening process and proceeded directly to the data evaluation phase. Of the 1,394 studies identified for NMP, 1,361 were excluded as off topic during the title and abstract screening phase. The remaining human health hazard studies advanced to full text screening; 33 were determined to be relevant to the NMP risk evaluation. These relevant data sources were evaluated and extracted in accordance with the process described in Appendix G of the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018a). Additional details can be found in EPA's *Strategy for Conducting Literature Searches for n-Methylpyrrolidone (NMP): Supplemental File to the TSCA Scope* document (U.S. EPA, 2017d). The results of this screening process are published in the *NMP (CASRN 872-50-4) Bibliography: Supplemental File to the TSCA Scope Document* (U.S. EPA, 2017b).

1.5.2 Data Evaluation

During the data evaluation stage, EPA assessed the quality of the data sources using the evaluation strategies and criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). EPA evaluated the quality of all data sources that passed full-text screening. Each data source received an overall confidence rating of high, medium, low or unacceptable.

The results of the data quality evaluations are summarized in Sections 2.1 (Fate and Transport), 2.2 (Releases to the Environment), 2.3 (Environmental Exposures), 2.4 (Human Exposures), 3.1 (Environmental Hazards), and 3.2 (Human Health Hazards). Supplemental files 1a-1j (see list of

supplemental files in Appendix B) also provide details of the data evaluations including individual metric scores and the overall study score for each data source.

1.5.3 Data Integration

Data integration includes analysis, synthesis and integration of information for the risk evaluation. During data integration, EPA considers quality, consistency, relevance, coherence and biological plausibility to make final conclusions regarding the weight of the scientific evidence. As stated in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a), data integration involves transparently discussing the significant issues, strengths, and limitations as well as the uncertainties of the reasonably available information and the major points of interpretation (U.S. EPA, 2018d).

EPA used previous assessments to identify key and supporting information and then analyzed and synthesized reasonably available lines of evidence regarding NMP's chemical properties, environmental fate and transport properties and its potential for exposure and hazard. EPA's analysis also considered recent data sources that were not considered in the previous assessments (Section 1.5.1) as well as reasonably available information on potentially exposed or susceptible subpopulations.

The exposures and hazards sections describe EPA's analysis of the relevant lines of evidence that were found acceptable for the risk evaluation based on the data quality reviews provided in the supplemental files.

2 EXPOSURES

This section describes EPA's approach to assessing environmental and human exposures. First, the fate and transport of NMP in the environment is characterized. Then, NMP environmental releases are assessed. Last, this information is integrated into an assessment of occupational and consumer exposures (including potentially exposed or susceptible subpopulations). For all exposure-related disciplines, EPA screened, evaluated, extracted and integrated reasonably available empirical data. In addition, EPA used models to estimate exposures. Both empirical data and modeled estimates were considered when selecting values for use in the exposure assessment.

The exposure pathways evaluated in the current assessment include dermal, vapor-through-skin, and inhalation. NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (Bader et al., 2008; Keener et al., 2007). NMP diluted in water has reduced dermal absorption (Keener et al., 2007; Payan et al., 2003) while NMP diluted in other solvents, such as d-limonene, can increase the absorption of NMP (Huntingdon Life, 1998) and prolonged exposures to neat (*i.e.*, pure) NMP increases the permeability of the skin (RIVM, 2013). NMP is also absorbed via inhalation (Akesson and Paulsson, 1997) but the low vapor pressure and mild volatility can limit the amount of NMP available for inhalation. For nearby non-users, exposures were limited to inhalation and vapor-through-skin exposure routes. In all cases, internal doses integrating the different exposure routes were derived using a PBPK model. PBPK model inputs and outputs underwent a quality control check in accordance with methods outlined in an umbrella Quality Assurance Project Plan (QAPP) for PBPK models (EPA, 2018e).

The previously published PBPK model for NMP (Poet et al., 2010) was adapted for use by EPA as described in Appendix J. The model predicted absorption of liquid or vapor from the NMP concentration, duration of contact and physiological descriptions such as body weight. The physiological parameters of body weight and skin surface area used were specific to pregnant women and females of childbearing age for acute exposures and to adolescent and adult men for chronic exposures. Absorption of NMP via inhalation depended on the NMP concentrations in air. Dermal absorption of NMP depended on the NMP weight fraction in liquid, NMP vapor concentration and skin surface area exposed to liquid and vapor. The thickness of the liquid film did not factor directly into the estimate of liquid NMP absorption. As a conservative estimate for user scenarios it was assumed that fresh material would be constantly deposited over the time of use such that the concentration on the skin would remain essentially constant at the formulation concentration. For example, a thin layer of compound is assumed to cover the surface area of the hands due the activities of the condition use, which may include use of sponges or rags with either both hands or one hand covered for high end and central tendency, respectively. The exposure parameters used to estimate internal NMP doses for the occupational and consumer exposure scenarios are described below.

Exposure equations and selected values used in the exposure assessment are presented in the following sections. More specific information is provided in Supplementary Files.

Following inclusion of NMP on EPA's TSCA Chemical Work Plan list in 2012, EPA published an assessment of the human health risks associated with NMP use in paint and coating removal (U.S. EPA, 2015c) prior to passage of the Lautenberg Act amendments to TSCA. Since that time, EPA has published the Scope (U.S. EPA, 2017c) and Problem Formulation (U.S. EPA, 2018c) for the current risk evaluation.

2.1 Fate and Transport

The environmental fate studies considered for this assessment are summarized in Table 2-1. Much of this information was previously provided in the NMP Problem Formulation (U.S. EPA, 2018c).

2.1.1 Fate and Transport Approach and Methodology

Environmental fate data were evaluated using the environmental fate data quality criteria outlined in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). The study evaluation results are documented in the data evaluation tables presented in EPA-HQ-OPPT-2019-0236. Environmental fate data from studies which met data quality requirements (as indicated by high, medium, or low data quality scores) were extracted and integrated into the current risk evaluation to characterize the environmental fate of NMP.

EPA gathered and evaluated environmental fate information according to the process described in the Application of Systematic Review in TSCA Risk Evaluations (U.S. EPA, 2018a). Reasonably available environmental fate data were selected for use in the current evaluation. EPA also used environmental fate and transport characteristics of NMP described in previous regulatory and non-regulatory assessments to inform the environmental fate and transport information discussed in this section and in Appendix D. EPA has high confidence in the information used in the previous assessments to describe the environmental fate and transport of NMP and thus used it to make scoping decisions.

Although EPA conducted a comprehensive literature search and screening process as described in Section 1.5, information reported in previous chemical assessments was also used to identify key and supporting studies that could inform the current analysis (*i.e.*, information supporting key assumptions, arguments, and/or conclusions). Where applicable, EPA also considered newer information that was not considered in the previous chemical assessments. EPA did not critically evaluate all underlying evidence ever published on the environmental fate and transport of NMP, but instead focused its data evaluation efforts on key and supporting studies identified previously, and any relevant information identified subsequently. Using this pragmatic approach, EPA maximized its own resources and the scientific and analytical efforts of other regulatory and non-regulatory agencies by accepting, for the most part, the scientific knowledge gathered and analyzed by others. As a result, a smaller pool of information was subjected to the TSCA systematic review process to ensure that the NMP risk evaluation uses the best available science to support the weight of the scientific evidence.

Other data sources may be cited as part of the reasonably available evidence presented on the fate and transport properties of NMP. For instance, EPA assessed the quality of a study on the ready biodegradability of NMP (U.S. EPA, 2020h) based on the data quality criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a) and the study was determined to be of medium confidence. Other fate estimates were based on modeling results from EPI Suite™ (U.S. EPA, 2012c), a predictive tool for physical and chemical and environmental fate properties. The data evaluation tables describing the review of key and supporting fate data sources can be found in the supplemental document, *Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies* (U.S. EPA, 2020h).

The NMP physical and chemical properties and environmental fate characteristics used in the current assessment are presented in Table 1-1 and Table 2-1, respectively. EPA used EPI Suite™ estimations and reasonably available fate data to characterize the environmental fate and transport of NMP. During problem formulation, EPA also analyzed the air, water, sediment, land and biosolids pathways. These results are described in the NMP Problem Formulation document (U.S. EPA, 2018c).

Environmental fate data from studies were evaluated using the environmental fate data quality criteria outlined in *The Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). The study evaluation results are documented in Appendix D. Environmental fate data from acceptable studies were extracted and integrated during risk evaluation. Based on the results obtained from the data quality evaluation process EPA has high confidence in the studies used to characterize the environmental fate of NMP. The data extracted from environmental fate studies are shown in Appendix D and the full environmental fate data quality ratings are presented in the supplemental file (U.S. EPA, 2020h).

NMP does not persist in the environment. Upon release into the atmosphere, it is degraded via reaction with photochemically produced hydroxyl radicals in ambient air. The half-life for this reaction is approximately 5.8 hours, assuming a hydroxyl radical concentration of 1.5×10^6 hydroxyl radicals/cm^3 air and a 12-hour day (U.S. EPA, 2015c). NMP is hygroscopic and can dissolve in water droplets. Atmospheric releases may be removed by condensation or further reaction with hydroxyl radicals.

Although neat NMP is slightly volatile, volatilization from water and moist soils is not likely based on its Henry's Law constant (3.2×10^{-9} atm·m^3/mol). NMP is not subject to hydrolysis under environmental conditions (U.S. EPA, 2015c). It is not expected to adsorb to suspended solids or sediment upon release to water due to its estimated soil organic carbon/water partition coefficient (log K_{oc} = 0.9). NMP exhibits high mobility in soil, so environmental releases are expected to migrate from soil to ground water (U.S. EPA, 2012c).

EPI Suite™ (U.S. EPA, 2012c) modules were used to predict removal of NMP from wastewater treatment plants, lakes and rivers. The EPI Suite™ module that estimates chemical removal in sewage treatment plants ("STP" module) was run to evaluate the potential for NMP to biodegrade, volatilize to air or adsorb to sludge during wastewater treatment. The STP module, using BIOWIN predictions for biodegradation rates, estimates that most of NMP releases to wastewater (> 90%) will be removed by biodegradation. BIOWIN model predictions further indicate negligible removal of NMP (< 1%) via sorption to sludge or volatilization to air. The EPI Suite™ input values are listed in Appendix D, Figure_Apx D-1 and the EPI Suite™ outputs are listed in the NMP Fate Supplementary Document (U.S. EPA, 2020h).

The EPI Suite™ module that estimates volatilization from lakes and rivers was run using default settings to evaluate the potential for NMP to volatilize from surface water. The model results indicate that volatilization from surface water is unlikely to be a significant removal pathway for NMP. Aerobic biodegradation is expected to be the primary removal pathway for NMP in many surface water environments based on measured data (see Table 2-1).

Experimental data and EPI Suite™ model predictions indicate that NMP will degrade in aerobic environments. However, the BIOWIN module within EPI Suite™ that estimates anaerobic biodegradation potential (BIOWIN 7) (U.S. EPA, 2020h, 2012c) predicts that NMP will not rapidly biodegrade under anaerobic conditions. These model predictions are consistent with previous assessments of NMP degradation potential (Křížek et al., 2015; OECD, 2007; Toxicology and Regulatory Affairs, 2003; WHO, 2001; U.S. EPA, 1998; Chow and Ng, 1983; Gerike and Fischer, 1979).

Table 2-1. Environmental Fate Characteristics of NMP

Property or Endpoint	Value [a]	Reference	Study Quality
Direct photo-degradation	Not available		
Indirect photo-degradation	5.8 hours (estimated half-life for reaction with hydroxyl radicals) [b]	U.S. EPA (2012c)	High
Hydrolysis half-life	Does not undergo hydrolysis	U.S. EPA (2015c)	N/A
Biodegradation	45% COD in 2 weeks; 95% in 2 weeks based on GC peak disappearance (aerobic in static die-away system test, sewage sludge inoculum, OECD 301A)	Chow and Ng (1983)	High (1.3)
	99% DOC in 1 day (coupled-units test; adaptation of the OECD confirmatory test)	Gerike and Fischer (1979)	High (1.6)
	99% DOC in 1 day (OECD 301E screening test)	Gerike and Fischer (1979)	High (1.6)
	98% DOC in 4 days (Zahn-Wellens/EMPA Test OECD 302B)	Gerike and Fischer (1979)	High (1.6)
	97% DOC in 28 days (EPA OPPTS 835.3110 (Ready Biodegradability); OECD 301B (Sturm))	Gerike and Fischer (1979)	High (1.6)
	95% DOC in 4 days (EPA OPPTS 835.3100 (Aerobic Aquatic Biodegradation; Ministry of International Trade and Industry (MITI); OECD 301C)	Gerike and Fischer (1979)	High (1.6)
	88% $BODT_{30}$ in 30 days (EPA OPPTS 835.3100 (Aerobic Aquatic Biodegradation; Closed Bottle); OECD 301D)	Gerike and Fischer (1979)	High (1.6)
	100% BOD in 4 days (aerobic in activated sludge, method adapted from Chow and Ng (1983).	Křížek et al. (2015)	High (1.4)
	73% in 28 days (aerobic in water, Ready Biodegradability, Modified MITI, OECD 301C)	Toxicology and Regulatory Affairs (2003)	Medium (1.8)
Bioconcentration factor (BCF)	3.16 (estimated) [b]	U.S. EPA (2012c)	High
Bioaccumulation factor (BAF)	0.9 (estimated) [b]	U.S. EPA (2012c)	High
Soil organic carbon/water partition coefficient (log K_{oc})	0.9 (estimated) [b]	U.S. EPA (2012c)	High

[a] Measured unless otherwise noted.
[b] Information was estimated using EPI Suite™ (U.S. EPA, 2012c)
N/A = not applicable

NMP has low potential for bioaccumulation and bioconcentration in the environment. Measured bioconcentration studies for NMP were not presented in EPA's previous evaluation of risks associated with NMP use in paint and coating removal (U.S. EPA, 2015c). However, based on the estimated BAF and BCF values (0.9 and 3.16, respectively), NMP is not expected to bioaccumulate or bioconcentrate in aquatic organisms (U.S. EPA, 2012c; OECD, 2007; U.S. EPA, 1999).

Several compounds can be formed by the action of natural processes on NMP. These include 4-(methylamino)butanoate, a putative biodegradation product (Chow and Ng, 1983), and 5-hydroxy-N-methyl-2-pyrrolidone (5-HNMP), N-methylsuccinimide (MSI), and 2-hydroxy-N-methylsuccinimide (2-HMSI), the major metabolites of NMP in humans (discussed further in Section 3). 4-(Methylamino)butanoate is predicted by EPI Suite™ to be readily biodegradable (U.S. EPA, 2012c), meaning that it is likely a transitory intermediate on the way to complete mineralization of NMP. Similarly, MSI is a potential product of the atmospheric oxidation of NMP (Aschmann and Atkinson, 1999), but is itself likely transitory in the atmosphere, being subject to oxidation by hydroxyl radicals with an estimated half-life on the order of hours (U.S. EPA, 2012c). 5-HNMP, MSI, and 2-HMSI are even more polar than NMP, and are thus expected to have similar environmental fate properties, including miscibility in water, low Henry's law constants, and minimal sorption to soil, sediment, and other organic surfaces. There are no reasonably available environmental monitoring data on these metabolites, meaning that a quantitative risk evaluation is not feasible. However, given that they are expected to have similar fate properties as NMP, are either as toxic or less so (Section 3.2.4), and are expected to occur in lower concentrations, they are qualitatively unlikely to pose risk to the aquatic environment.

2.2 Releases to the Environment

Releases to the environment from conditions of use (*e.g.*, industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure that may be derived from reported data obtained through direct measurement, calculations based on empirical data and/or model assumptions.

Under the EPCRA Section 313, NMP has been a TRI-reportable substance effective January 1, 1995. The TRI database includes information on disposal and other releases of NMP to air, water, and land, in addition to how it is managed through recycling, treatment, and burning for energy recovery. EPA analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from specific types of land disposal (*i.e.*, RCRA Subtitle C hazardous landfills and Class I underground injection wells) and incineration. EPA also examined how NMP is treated at industrial facilities. Based on 2015 TRI reporting, an estimated 14,093 lbs of NMP was released to surface water from industrial sources. See Table_Apx E-1 in Appendix E for a TRI summary table and further details on recent releases of NMP to various media.

2.3 Environmental Exposures

NMP may occur in various environmental media including sediment, soil, water and air. As part of the NMP Problem Formulation (U.S. EPA, 2018c), EPA completed a preliminary analysis of environmental exposures for aquatic and terrestrial species to NMP in these environmental media. No additional information has been received or otherwise identified by EPA that would alter the conclusions presented in the NMP Problem Formulation (U.S. EPA, 2018c). EPA concluded that no further analysis of environmental release pathways for environmental receptors is necessary based on a qualitative assessment of the physical and chemical and fate properties of NMP and the levels of NMP exposure that may be expected for organisms that inhabit these environmental compartments.

The evaluation of environmental exposures from the NMP Problem Formulation (U.S. EPA, 2018c) is summarized in the following subsections on potential presence in biological tissues (biota), and possible exposures for aquatic and terrestrial receptors. The information is provided for clarity in this RE and the conclusions remain unchanged from the NMP Problem Formulation (U.S. EPA, 2018c).

2.3.1 Presence in the Environment and Biota

NMP exhibits low potential for bioaccumulation and bioconcentration in the environment. Based on the estimated BAF and BCF values (0.9 and 3.16, respectively) (see Table 2-1), NMP is not expected to bioaccumulate or bioconcentrate in aquatic organisms (U.S. EPA, 2012c; OECD, 2007; U.S. EPA, 1999).

2.3.2 Aquatic Environmental Exposures

EPA used data from EPA's TRI and EPA's Exposure and Fate Assessment Screening Tool, Version 2014 (E-FAST 2014;) to estimate the concentrations of NMP released to surface water near discharging facilities. The environmental exposure assessment for NMP was conducted using data for each of nine direct dischargers and the top ten indirect dischargers of NMP reporting to the TRI in 2015 and most recently updated to include 2018 data.

Using the 2018 TRI data and EPA's first-tier, Probabilistic Dilution Model (PDM) within E-FAST, surface water concentrations of NMP were modeled based on the assumption of 12 or 300 days of release. The 12-day release scenario represents an acute exposure scenario (wherein periodic maintenance and cleaning activities could result in monthly releases). The 300-day release scenario represents a chronic exposure scenario (wherein standard operations may result in continuous discharges of NMP) (see Appendix E). The PDM portion of E-FAST 2014 was run for free-flowing water bodies. The PDM predicts the number of days per year that a chemical's COC in an ambient water body will be exceeded. COCs are threshold concentrations below which adverse effects on aquatic life are expected to be minimal. The model is based on a simple mass balance approach presented by Di Toro (1984) that uses probability distributions as inputs to reflect that streams follow a highly variable seasonal flow pattern and there are numerous variables in a manufacturing process that can affect the chemical concentration and flow rate of the effluent. PDM does not estimate exceedances for chemicals discharged to still waters, such as lakes, bays, or estuaries. For these water bodies, the days of exceedance is assumed to be zero unless the predicted surface water concentration exceeds the COC.

These predicted acute and surface water concentrations are compared to the COCs identified for aquatic organisms in Section 3.1 for Environmental Hazards (Effects) to estimate Environmental Risk in Section 4.1. This exposure analysis is included in Appendix E of this risk evaluation.

2.4 Human Exposures

EPA evaluated acute and chronic exposures to workers and occupational non-users and acute exposures to consumers by non-immersive dermal contact with liquid films, vapor-through-skin, and inhalation routes in association with NMP use in industrial, commercial, and consumer applications. EPA assessed these exposures by inputting exposure parameters into a physiologically based pharmacokinetic (PBPK) model, which is described in Appendix J.

The conditions of use to be assessed were described in Table 1-6. Due to expected similarities in or the lack of data to distinguish between exposure scenarios for different conditions of use, occupational exposures or consumer exposures for several of the subcategories of use in Table 1-6 were grouped and assessed together during risk evaluation. For example, formulation of paints, coatings, adhesives and

sealants may generally have similar worker activities, and EPA does not have data to distinguish whether workers are differently exposed for these different formulations. Therefore, EPA has grouped these formulating conditions of use into one occupational exposure scenario group (Incorporation into Formulation, Mixture, or Reaction Product). Occupational groupings and consumer groupings are assessed separately. A crosswalk of the conditions of use listed in Table 1-6 with the occupational and consumer exposure scenarios assessed in this report is provided in Table 2-2. EPA crosswalked/ mapped the exposure scenarios to conditions of use using professional judgment based on reasonably available data and information.

Table 2-2. Crosswalk of Conditions of Use to Occupational and Consumer Scenarios Assessed in the Risk Evaluation

Life Cycle Stage	Category [a]	Subcategory [b]	Exposure Scenario
Manufacturing	Domestic Manufacture	Domestic Manufacture	Occupational Section 2.4.1.2.1 - Manufacturing
	Import	Import	Occupational Section 2.4.1.2.2 - Repackaging
Processing	Processing as a reactant or intermediate	Intermediate in Plastic Material and Resin Manufacturing	Occupational Section 2.4.1.2.3 - Chemical Processing, Excluding Formulation
		Other Non-Incorporative Processing	
	Incorporated into formulation, mixture or reaction product	Adhesives and sealant chemicals in Adhesive Manufacturing	Occupational Section 2.4.1.2.4 - Incorporation into Formulation, Mixture, or Reaction Product
		Anti-adhesive agents in Printing and Related Support Activities	Occupational Section 2.4.1.2.4 - Incorporation into Formulation, Mixture, or Reaction Product
		Paint additives and coating additives not described by other codes in Paint and Coating Manufacturing; and Print Ink Manufacturing	Occupational Section 2.4.1.2.4 - Incorporation into Formulation, Mixture, or Reaction Product
		Processing aids not otherwise listed in Plastic Material and Resin Manufacturing	Occupational Section 2.4.1.2.4 - Incorporation into

Life Cycle Stage	Category [a]	Subcategory [b]	Exposure Scenario
			Formulation, Mixture, or Reaction Product
		Solvents (for cleaning or degreasing) in Non-Metallic Mineral Product Manufacturing; Machinery Manufacturing; Plastic Material and Resin Manufacturing; Primary Metal Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Services; Wholesale and Retail Trade	Occupational Section 2.4.1.2.4 - Incorporation into Formulation, Mixture, or Reaction Product
		Surface active agents in Soap, Cleaning Compound and Toilet Preparation Manufacturing	Occupational Section 2.4.1.2.4 - Incorporation into Formulation, Mixture, or Reaction Product
		Plating agents and surface treating agents in Fabricated Metal Product Manufacturing	Occupational Section 2.4.1.2.4 - Incorporation into Formulation, Mixture, or Reaction Product
		Solvents (which become part of product formulation or mixture) in Electrical Equipment, Appliance and Component Manufacturing; Other Manufacturing; Paint and Coating Manufacturing; Print Ink Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Wholesale and Retail Trade	Occupational Section 2.4.1.2.4 - Incorporation into Formulation, Mixture, or Reaction Product

Life Cycle Stage	Category [a]	Subcategory [b]	Exposure Scenario
		Other uses in Oil and Gas Drilling, Extraction and Support Activities; Plastic Material and Resin Manufacturing; Services	Occupational Section 2.4.1.2.4 - Incorporation into Formulation, Mixture, or Reaction Product
	Incorporation into articles	Lubricants and lubricant additives in Machinery Manufacturing	Occupational Section 2.4.1.2.5 - Metal Finishing
		Paint additives and coating additives not described by other codes in Transportation Equipment Manufacturing	Occupational Section 2.4.1.2.6 - Application of Paints, Coatings, Adhesives, and Sealants
		Solvents (which become part of product formulation or mixture), including in Textiles, Apparel and Leather Manufacturing	Occupational Section 2.4.1.2.4 - Incorporation into Formulation, Mixture, or Reaction Product
		Other, including in Plastic Product Manufacturing	Occupational Section 2.4.1.2.3 - Chemical Processing, Excluding Formulation
	Repackaging	Wholesale and Retail Trade	Occupational Section 2.4.1.2.2 - Repackaging
	Recycling	Recycling	Occupational Section 2.4.1.2.7 - Recycling and Disposal
Distribution in commerce	Distribution	Distribution in Commerce	Occupational Section 2.4.1.2.2 - Repackaging
Industrial/ commercial use	Paints and coatings	Paint and coating removers	Occupational Section 2.4.1.2.8 - Removal of Paints, Coatings, Adhesives, and Sealants

Life Cycle Stage	Category [a]	Subcategory [b]	Exposure Scenario
		Adhesive removers	Occupational Section 2.4.1.2.8 - Removal of Paints, Coatings, Adhesives, and Sealants
		Lacquers, stains, varnishes, primers and floor finishes	Occupational Section 2.4.1.2.6 - Application of Paints, Coatings, Adhesives, and Sealants
		Powder coatings (surface preparation)	Occupational Section 2.4.1.2.6 - Application of Paints, Coatings, Adhesives, and Sealants
	Paint additives and coating additives not described by other codes	Use in Computer and Electronic Product Manufacturing in Electronic Parts Manufacturing	Occupational Section 2.4.1.2.9 – Other Electronics Manufacturing
		Use in Computer and Electronic Product Manufacturing for Use in Semiconductor Manufacturing	Occupational Section 2.4.1.2.10 – Semiconductor Manufacturing
		Use in Construction, Fabricated Metal Product Manufacturing, Machinery Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Primary Metal Manufacturing, Transportation Equipment Manufacturing, Wholesale and Retail Trade	Occupational Section 2.4.1.2.6 - Application of Paints, Coatings, Adhesives, and Sealants
Industrial/commercial use	Solvents (for cleaning or degreasing)	Use in Electrical Equipment, Appliance and Component Manufacturing	Occupational Section 2.4.1.2.9 – Other Electronics Manufacturing
		Use in Electrical Equipment, Appliance and Component Manufacturing for Use in Semiconductor Manufacturing	Occupational Section 2.4.1.2.10 – Semiconductor Manufacturing

Life Cycle Stage	Category [a]	Subcategory [b]	Exposure Scenario
	Ink, toner and colorant products	Printer ink	Occupational Section 2.4.1.2.11 - Printing and Writing
		Inks in writing equipment	Occupational Section 2.4.1.2.11 - Printing and Writing
	Processing aids, specific to petroleum production	Petrochemical Manufacturing	Occupational Section 2.4.1.2.3 - Chemical Processing, Excluding Formulation
	Other uses	Other uses in Oil and Gas Drilling, Extraction and Support Activities	Occupational Section 2.4.1.2.3 - Chemical Processing, Excluding Formulation
		Functional Fluids (closed systems)	Occupational Section 2.4.1.2.3 - Chemical Processing, Excluding Formulation
	Adhesives and sealants	Adhesives and sealant chemicals including binding agents	Occupational Section 2.4.1.2.6 - Application of Paints, Coatings, Adhesives, and Sealants
Industrial/ commercial use		Single component glues and adhesives, including lubricant adhesives	Occupational Section 2.4.1.2.6 - Application of Paints, Coatings, Adhesives, and Sealants
		Two-component glues and adhesives, including some resins	Occupational Section 2.4.1.2.6 - Application of Paints, Coatings, Adhesives, and Sealants

Life Cycle Stage	Category [a]	Subcategory [b]	Exposure Scenario
	Other uses	Soldering materials	Occupational Section 2.4.1.2.12 - Soldering
		Anti-freeze and de-icing products	Occupational Section 2.4.1.2.13 - Commercial Automotive Serving
		Automotive care products	Occupational Section 2.4.1.2.13 - Commercial Automotive Serving
		Lubricants and greases	Occupational Section 2.4.1.2.13 - Commercial Automotive Serving
		Metal products not covered elsewhere	Occupational Section 2.4.1.2.5 - Metal Finishing
		Lubricant and lubricant additives, including hydrophilic coatings	Occupational Section 2.4.1.2.5 - Metal Finishing
		Laboratory chemicals	Occupational Section 2.4.1.2.14 - Laboratory Use
		Lithium ion battery manufacturing	Occupational Section 2.4.1.2.15 - Lithium Ion Cell Manufacturing [c]
		Cleaning and furniture care products, including wood cleaners, gasket removers	Occupational Section 2.4.1.2.15 - Cleaning
		Fertilizer and other agricultural chemical manufacturing - processing aids and solvents	Occupational Section 2.4.1.2.17 - Fertilizer Application
Consumer uses	Paints and coatings	Paint and coating removers	Consumer Section 2.4.2 - Paint Removers
		Adhesive removers	Consumer Section 2.4.2 - Adhesive Removers

Life Cycle Stage	Category [a]	Subcategory [b]	Exposure Scenario
		Lacquers, stains, varnishes, primers and floor finishes	Consumer Section 2.4.2 - Stains, Varnishes, Finishes
	Paint additives and coating additives not described by other codes	Paints and arts and crafts paints	Consumer Section 2.4.2 – Paint; Arts and Crafts Paints
	Adhesives and sealants	Glues and adhesives, including lubricant adhesives	Consumer Section 2.4.2 – Adhesives and Sealants
	Other uses	Automotive care products	Consumer Section 2.4.2 - Auto Interior Liquid Cleaner; Auto Interior Spray Cleaner
		Cleaning and furniture care products, including wood cleaners, gasket removers	Consumer Section 2.4.2 - Cleaners/ Degreasers; Engine Cleaner/ Degreaser
		Lubricant and lubricant additives including hydrophilic coatings	Consumer Section 2.4.2 - Spray Lubricant
Disposal	Disposal	Industrial pre-treatment	Occupational Section 2.4.1.2.7 - Recycling and Disposal
		Industrial wastewater treatment	Occupational Section 2.4.1.2.7 - Recycling and Disposal
		Publicly owned treatment works (POTW)	
		Underground injection	Occupational Section 2.4.1.2.7 - Recycling and Disposal
		Landfill (municipal, hazardous or other land disposal)	Occupational Section 2.4.1.2.7 -
		Emissions to air	

Life Cycle Stage	Category [a]	Subcategory [b]	Exposure Scenario
		Incinerators (municipal and hazardous waste)	Recycling and Disposal

[a] These categories of conditions of use appear in the life cycle diagram, reflect CDR codes and broadly represent NMP conditions of use in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of NMP.
[c] The process for manufacture of lithium ion cells for these batteries uses NMP, and this manufacturing process is covered in the OES for Lithium Ion Cell Manufacturing.

2.4.1 Occupational Exposures

For the purpose of this assessment, EPA considered occupational exposure of the total workforce of exposed users and non-users, which include but are not limited to male and female workers of reproductive age who are 16 or more years of age. Female workers of reproductive age are 16 to less than 50 years old. Adolescents (16 to <21 years old) are a small part of this total workforce. The occupational exposure assessment is applicable to and covers the entire workforce who are exposed to NMP.

EPA evaluated acute and chronic exposures to workers and ONUs associated with dermal contact with liquids (workers only), vapor-through-skin, and inhalation routes in association with NMP use in industrial and commercial applications, which are shown in Table 2-2. Oral exposure via incidental ingestion of inhaled vapor/mist/dust will be considered as an inhalation exposure as noted in Figure 1-3 because EPA does not have data or methods to fractionate the total NMP inhaled into the inhalable amount of NMP that deposits in the upper respiratory system and the respirable amount of NMP that enters the lung.

EPA assessed these exposures by inputting exposure parameters into a PBPK model, which is described in Appendix J. Parameter development for each occupational exposure scenario assessed is described in Section 2.4.1.1. More detailed information about the parameter development may be found in the supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f).

A primary difference between workers and ONUs is that workers may have direct dermal contact with liquid chemicals that they handle, whereas ONUs located in the general vicinity of workers do not have direct dermal contact with liquids handled by the workers. Examples of ONUs include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in direct dermal contact with liquids. EPA expects that ONUs are exposed to lower air concentrations than workers since they may be further from the emission source than workers.

Based on the lack of acute ONU risk for the scenario with the highest air concentration, acute ONU exposures were not further characterized. EPA analyzed the highest exposure scenario for ONUs, paint removers – miscellaneous stripping, calculating an 8-hr time-weighted average (TWA) air concentration of 64 mg/m^3, and resulting in a peak blood concentration of 1.53 mg/L. Based on an acute POD, the acute margin of exposure (MOE) for the ONUs with the highest acute exposure is 285, well above the benchmark MOE of 30. Therefore, EPA did not further analyze acute ONU exposure for additional COUs.

2.4.1.1 Occupational Exposures Approach and Methodology

This section summarizes the occupational dermal and inhalation exposure parameters and concentrations for NMP in the various industries and scenarios shown in Table 2-2. These parameters were used as PBPK model inputs for the risk evaluation. The supplemental document, *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides background details on industries that may use NMP, worker activities, processes, numbers of sites and numbers of potentially exposed workers. This supplemental document also provides detailed discussion on the values used for the dermal exposure parameters and air concentrations and associated worker inhalation parameters presented in this section.

Key Parameters for PBPK Modeling

To derive internal exposure estimates for acute and chronic occupational exposures, the PBPK model required a set of input parameters related to exposures by the dermal and inhalation routes:

- NMP weight fraction in the liquid product;
- Total skin surface area in contact with the liquid product;
- Glove protection factor (if applicable);
- Duration of dermal contact with the liquid product;
- Air concentration for inhalation and vapor-through-skin exposure; and
- Body weight of the exposed worker.

The primary route of exposure for individuals may vary depending upon a variety of factors including NMP weight fraction in the liquid product contacted, skin surface areas in contact with the liquid product and with vapor, durations of dermal contact with liquid product and with vapor, air concentration for inhalation and vapor-through-skin exposure, body weight of the exposed person, and glove protection factor and respirator assigned protection factor (if applicable). Table 4-54 illustrates the variations in relative contributions of dermal contact with liquid for different OESs and Table 4-55 illustrates the relative contributions of inhalation exposure and dermal exposure to risk for different OESs.

EPA assumed that the skin was exposed dermally to NMP at the specified liquid weight fraction and skin surface area and that there was simultaneous exposure by inhalation and vapor-through-skin absorption for unobstructed skin areas. As described below, air concentrations were adjusted to duration of contact of liquid on the skin, which is assumed to usually be removed by cleaning at the end of the work period. Acute scenarios assumed 1 day of exposure and chronic scenarios assumed 5 days of exposure per week.

EPA used literature sources for estimating many of these occupational exposure parameters. EPA used modeling or generic assumptions when data were not reasonably available.

For most PBPK input parameters, EPA did not find enough data to determine statistical distributions of the actual exposure parameters and concentrations. Within the distributions, central tendencies describe 50th percentile or the substitute that most closely represents the 50th percentile. The high-end of a distribution describes the range of the distribution above 90th percentile (U.S. EPA, 1992). Ideally, EPA would use the 50th and 95th percentiles for each parameter. Where these statistics were unknown, the mean or mid-range (mean is preferable to mid-range) served as substitutes for 50th percentile and the high-end of ranges served as a substitute for 95th percentile. However, these substitutes were uncertain and not ideal substitutes for the percentiles. EPA could not determine whether these substitutes were suitable to represent statistical distributions of exposure scenarios.

EPA selected grouped sets of individual input parameter values intended to represent central tendency and high-end occupational exposure scenarios. To generate each central tendency scenario result, EPA used a group of all central tendency input parameter values relevant to the scenario. To generate each high-end scenario result, EPA used a group of mostly high-end input parameter values relevant to the scenario except body weight, which is a median value. Using mostly high-end input values is a plausible approach to estimate a high-end PBPK result for the periods of acute and chronic exposures of 1 and 5 days, respectively.
To demonstrate some potential variations beyond central tendency and high-end scenarios, EPA modified relevant scenarios to change parameters, mainly contact durations based on known tasks or monitoring times for the uses, to generate what-if task duration-based scenarios. Also, EPA added scenarios with groups of parameters provided by industry commenters to generate industry-proposed what-if scenarios.

Weight Fraction
To support this risk evaluation, EPA determined the weight fraction of NMP in various products through information provided in the reasonably available literature, previous risk assessments and the 2017 NMP Market Profile (ABT, 2017). This Market Profile was prepared in part by searching Safety Data Sheets (SDSs) of products that contain NMP and compiling the associated name, use, vendor and NMP concentration associated with each of these products. Where a data point was provided as range of NMP concentrations for a certain product (*e.g.*, paints and coatings), EPA utilized the mid-range (middle) and high-end (maximum) weight fractions to estimate potential exposures. Where multiple data points for a given type of product (*e.g.*, paints and coatings) were available, EPA estimated exposures using the central tendency (50^{th} percentile) and high-end (95^{th} percentile) NMP concentrations.

Skin Surface Area
EPA has no reasonably available information on actual surface area of contact with liquids. For both consumer and occupational user dermal exposure for liquid contact, EPA assumed skin surface area values both for the hands of females and for the hands of males, obtained from the 2011 edition of EPA's Exposure Factors Handbook (Table 7-13) (U.S. EPA, 2011). These values are assumed to represent adequate surrogates for most uses' central tendency and high-end surface areas of contact with liquid that may sometimes include exposures to much of the hands and also beyond the hands, such as wrists, forearms, neck, or other parts of the body. These values overestimate exposures for younger members of the workforce whose hand surface areas would be smaller. One exception is for the OES that includes Writing, 1 cm^2 was assumed based on a literature estimate for writing inks (Australian Government Department of Health, 2016). For the remainder of the occupational dermal exposure assessment, EPA used the following values:

- high-end value, which represents two full hands in contact with a liquid: 890 cm^2 (female), 1070 cm^2 (males);
- central tendency value, which is half of two full hands (equivalent to one full hand) in contact with a liquid and represents only the palm-side of both hands exposed to a liquid: 445 cm^2 (females), 535 cm^2 (males).

ONUs are not expected to have direct contact with NMP-based liquid products unless an incident (*e.g.*, spill) were to occur. However, PBPK modeling of ONU (no liquid contact) used a skin surface area value of 0.1 cm^2 (about 0.1% of values used for occupational users) for liquid exposure to prevent a division by zero error in model equations.

For dermal exposure to vapor for both occupational users and ONUs, the PBPK modeled up to 25% of the total skin surface area, corresponding to the face, neck, arms and hands, as exposed to and capable of absorbing vapors, minus any area covered by PPE. This area, which is programmed into the PBPK model, is not a variable input value.

Glove Usage

Glove protection factors (PFs) are also inputs into the PBPK model. Where workers wear gloves, workers are exposed to NMP-based product that penetrates the gloves, including potential seepage through the cuff from improper donning of the gloves, permeation of NMP through the glove material, and the gloves may occlude the evaporation of NMP from the skin. Where workers do not wear gloves, workers are exposed through direct contact with NMP.

Overall, EPA understands that workers may potentially wear gloves but does not know the likelihood that workers wear gloves of the proper type and have training on the proper usage of gloves. Some sources indicate that workers wear chemical-resistant gloves (NIOSH, 2014; Meier et al., 2013), while others indicate that workers likely wear gloves that are more permeable than chemical-resistant gloves (RIVM, 2013). For most occupational exposure scenarios, no information on employee training was found; if information was found for a scenario, this information is presented in the appropriate subsection of Section 2.4.1.2. Data on the prevalence of glove use is not reasonably available for most uses of NMP. For semiconductor manufacturing and lithium ion cell manufacturing, public comments provided information indicating that all employees wear gloves when performing tasks involving NMP, indicating that the glove material is chosen to be resistant to NMP and that employees receive training on proper glove usage, donning, and doffing before working with NMP (EaglePicher Technologies, 2020a; Intel Corporation, 2019; Semiconductor Industry Association, 2019a). One anecdotal survey of glove usage among workers performing graffiti removal indicates that 87% of workers wear gloves, although the glove materials varied and were sometimes not protective; only a small fraction of these workers used gloves made of optimal material for protection against NMP and some used cloth or leather gloves (Anundi et al., 2000).

Prior to the initiation of this risk evaluation EPA had gathered information in support of understanding glove use for handling pure NMP and for paint and coatings removal using NMP formulations. This information may be generally useful for a broader range of uses of NMP and is presented for illustrative purposes in Appendix F.1.1. SDSs found by EPA recommend glove use (see Appendix F.1.2). Initial literature review suggests that there is unlikely to be enough data to justify a specific probability distribution for effective glove use for a chemical or industry. Instead, the impact of effective glove use is explored by considering different protection factors, which are further discussed below and compiled in Table 2-3.

Gloves only offer barrier protection until the chemical breaks through the glove material. Using a conceptual model, Cherrie (2004) proposed a glove workplace protection factor (PF) – the ratio of estimated uptake through the hands without gloves to the estimated uptake though the hands while wearing gloves: this protection factor is driven by glove usage practices and by flux, which varies with time. The ECETOC TRA v3 model represents the protection factor of gloves as a fixed, assigned protection factor equal to 5, 10, or 20 (Marquart et al., 2017). Given the limited state of knowledge about the protection afforded by gloves in the workplace, it is reasonable to utilize the PF values of the ECETOC TRA v3 model (Marquart et al., 2017), rather than attempt to derive new values. EPA also considered potential dermal exposure in cases where exposure is occluded. If occlusion were to occur, contact duration would be extended and glove protection factors could be reduced, although such

extensions and reductions could not be quantified for this evaluation due to lack of reasonably available data. Additional explanation of occlusion is included in the supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f).

EPA conducted modeling of exposures for the full range of dermal contacts including no glove use, non-protective glove use, and protective glove use (using PFs of 1, 5, 10, and 20) to determine impacts on exposures as what-if scenarios. For the purpose of PBPK modeling, PFs were assumed to reduce workers' surface areas of contact with liquids (*i.e.*, surface areas of contact were divided by PF values). As indicated in Table 2-3, use of PFs above 1 is recommended only for glove materials that have been tested for and shown to be effective for preventing permeation of the NMP-containing liquids associated with the condition of use.

Table 2-3. Glove Protection Factors for Different Dermal Protection Strategies from ECETOC TRA v3

Dermal Protection Characteristics	Setting	Protection Factor, PF
a. No gloves used, or any glove / gauntlet without permeation data and without employee training	Industrial and Commercial Uses	1
b. Gloves with reasonably available permeation data indicating that the material of construction offers good protection for the substance		5
c. Chemically resistant gloves (*i.e.*, as *b* above) with "basic" employee training		10
d. Chemically resistant gloves in combination with specific activity training (*e.g.*, procedure for glove removal and disposal) for tasks where dermal exposure can be expected to occur	Industrial Uses Only	20

Duration of Dermal Contact with Liquid

EPA found no reasonably available data on actual duration of dermal contact with liquids. In lieu of dermal duration data or task-based durations from inhalation monitoring data, EPA based it assumptions of contact duration on the length of a shift. EPA assumed a minimum contact duration of 1 hour/day, which is a reasonable assumption considering the initial contact time with the formulation containing NMP plus the time after direct contact when the thin film evaporates from and absorbs into the skin. For a standard 8-hour shift, EPA assumed a high-end contact duration value of 8 hours/day (*i.e.*, a full shift). As a central tendency estimate, EPA assumed a mid-range contact duration value of 4 hours/day (the calculated mid-point of 4.5 was rounded to 4 hours/day, or a half of a shift). The low-end and high-end values are consistent with EPA's documented standard model assumptions for occupational dermal exposure modeling (U.S. EPA, 1991a). If an OES was found to have 12-hour shifts, the central tendency and high-end contact durations were assumed to be 6 hours (half-shift) and 12 hours (full shift), respectively. Shift-based contact duration assumptions of full shifts for high-ends account for the possibility of repeated contact with NMP such that NMP does not fully volatilize from the skin before the next contact event, resulting in prolonged exposure. Where available, EPA utilized exposure durations from the reasonably available task-based inhalation monitoring data for generating what-if type exposure scenarios assuming that the workers were contacting NMP-containing liquids over only the monitoring duration (*i.e.*, the entire task duration). Task-based duration estimates do not account for

either liquid remaining on the skin after the task is completed or for workers performing a task multiple times during their shift.

Air Concentration for Inhalation and Vapor-through-Skin Exposure

EPA reviewed workplace inhalation monitoring data collected by government agencies such as Occupational Safety and Health Administration (OSHA) and National Institute for Occupational Safety and Health (NIOSH), and monitoring data found in published literature (*i.e.*, personal exposure monitoring data and area monitoring data). Data were evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a), and the evaluation details are shown in two supplemental files: *Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Data Quality Evaluation for Occupational Exposure and Release Data* (U.S. EPA, 2020j) and *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1-Methyl-) Systematic Review Supplemental File: Data Quality Evaluation of Environmental Releases and Occupational Exposure Common Sources* (U.S. EPA, 2020k). Where reasonably available, EPA used air concentration data and estimates found in government or published literature sources to serve as inputs to the PBPK modeling for occupational exposures to NMP. There is not a known correlation between weight fraction of NMP in the material being handled / used and the concentration of NMP in air. Where air concentration data were not reasonably available, modeling estimates were used. Details on which models EPA used are included in Section 2.4.1.2 for the applicable OESs and discussion of the uncertainties associated with these models is included in Section 2.4.1.4. EPA has modeled inhalation air concentrations for workers in 11 of 17 OESs. EPA has exhausted all modeling opportunities with the parameter data that are reasonably available and therefore was unable to model air concentrations of the remaining 6 OESs. For these 6 OESs, air monitoring data for workers was reasonably available and used when modeling was not possible.

EPA evaluated personal monitoring data or modeled near-field exposure concentrations potential inhalation and vapor-through-skin exposures for workers. Since ONUs do not directly handle NMP, EPA reviewed personal monitoring data, modeled far-field exposure concentrations, and area monitoring data in evaluating potential inhalation and vapor-through-skin exposures for ONUs. Because modeled results are typically intended to capture exposures in the near-field, modeling that does not contain a specific far-field component are not considered to be suitable for ONUs. EPA has modeled far-field inhalation air concentrations for ONUs in 1 of 17 OESs. EPA has exhausted all far-field modeling opportunities with the parameter data that are reasonably available and therefore was unable to model air concentrations for ONUs in the remaining 16 OESs. For these 16 OESs, air monitoring data or modeling estimates for workers were reasonably available and used when modeling for ONUs was not possible. Area monitoring data may potentially represent ONU exposures depending on the monitor placement and the intended sample population. Inhalation data sources did not usually indicate whether NMP exposure concentrations were for occupational users or ONUs.

For PBPK modeling, the duration of inhalation exposure must equal the duration of dermal exposure. Therefore, for activities where air monitoring or modeling durations (usually full-shift) do not equal the duration of dermal contact with liquid assumptions (usually less than a full shift), EPA adjusted NMP air concentrations by multiplying by a ratio of duration of the air concentration averaging time to duration of dermal contact with liquid, which is discussed above. These adjusted air concentrations, which are used for worker and ONU exposure estimates, assure that the PBPK model accounts for the full amount of inhalation and vapor-through-skin exposure and is referred to as “duration-based NMP air concentration.”

Few literature sources indicate the use of respirators for reducing worker exposures to NMP by inhalation. Therefore, EPA central tendency and high-end scenarios do not incorporate protection factors for respirator use. Regarding respirator use, only one of the NMP studies containing worker inhalation data specified the type of respirator used by the workers in the study. This respirator, a half mask air-purifying respirator with organic vapor cartridges (NIOSH, 1993), is classified as having an assigned protection factor (APF) of 10. Therefore, EPA conducted additional modeling representing scenarios below central tendency (*i.e.*, these scenarios represent the low percentiles of worker exposure) for the use of respirators providing an APF of 10. This modeling reduces inhalation concentrations by a factor of 10 when this type of respirator is used in accordance with OSHA's Respiratory Protection standard (29 CFR 1910.134). While respirators with other APFs may be used, EPA only included this APF in additional modeling. The results of this additional modeling are shown in Section 4.2.2 and in the *Supplemental Excel File on Occupational Risk Calculations*.

Body Weight

Both the consumer and occupational dermal exposure assessments used the 50th percentile body weights for pregnant women in their first trimester, which is 74 kg, and for males, which is 88 kg, for both central tendency and high-end exposure scenarios. EPA obtained these values from the 2011 edition of EPA's Exposure Factors Handbook (Table 8-29) (U.S. EPA, 2011).

2.4.1.2 Occupational Exposure Scenarios

The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides details of the PBPK input data and assumptions, air concentration modeling, and associated exposure-related information for each of the Occupational Exposure Scenarios (OES) listed in Table 2-2 and in the OES subsections below.

The following subsections contain a summary of dermal and inhalation parameter estimates for each OES. Information on the number of potentially exposed workers and ONUs can be found in Table 2-4. Details on the parameter estimates as well as process descriptions, numbers of sites and potentially exposed workers, and worker activities for each OES are available in the supplemental document (U.S. EPA, 2020f). Key strengths and limitations of each PBPK input parameter set are listed and used to determine qualitative overall confidence ratings, and these lists and ratings are provided at the end of each OES subsection. The data integration strategy and factors impacting the overall confidence ratings are available in Appendix C of the supplemental document (U.S. EPA, 2020f).

A summary set of all central tendency and high-end scenarios parameter inputs to the PBPK model is shown in Table 2-72. A summary set of all central tendency and high-end scenarios results from the PBPK model is shown in Table 2-73. Key uncertainties toward exposure estimates are summarized in Section 2.4.1.4.

EPA estimated numbers of workers in the assessed industries. Where reasonably available, EPA used CDR data to provide a basis to estimate the numbers of sites, workers, and ONUs. EPA supplemented the reasonably available CDR data with U.S. economic data using the following method:

1. Identify the North American Industry Classification System (NAICS) codes for the industry sectors associated with these uses.
2. Estimate total employment by industry/occupation combination using the Bureau of Labor Statistics' (BLS) Occupational Employment Statistics (OES) data (U.S. BLS, 2016).

3. Refine the OES estimates where they are not sufficiently granular by using the U.S. Census' Statistics of US Businesses (SUSB) data on total employment by 6-digit NAICS.
4. Use market penetration data to estimate the percentage of employees likely to be using NMP instead of other chemicals.
5. Combine the data generated in Steps 1 through 4 to produce an estimate of the number of employees using NMP in each industry/occupation combination, and sum these to arrive at a total estimate of the number of employees with exposure.

Market penetration data for NMP are not reasonably available at this time; therefore, site, worker, and ONU estimates do not take this into account and likely overestimate the number of sites, workers, and ONUs potentially exposed to NMP. Where end-use sector is not clear, relevant U.S. EPA Generic Scenarios and OECD Emission Scenario Documents are used to estimate the number of sites and workers, such as for metal finishing.

Table 2-4. Estimated Numbers of Workers in the Assessed Industry Uses of NMP

Occupational Exposure Scenario	Number of Workers [a,b]
Manufacturing	2,800 [c]
Repackaging	1,100 [c]
Chemical Processing, Excluding Formulation	5,000 [c]
Incorporation into Formulation, Mixture, or Reaction Product	1,800 [c]
Metal Finishing	530,000
Application of Paints, Coatings, Adhesives and Sealants	2,000,000
Recycling and Disposal	200 [c]
Removal of Paints, Coatings, Adhesives and Sealants	410,000
Other Electronics Manufacturing	610,000
Semiconductor Manufacturing	43,000
Printing and Writing	53,000
Soldering	4,000,000
Commercial Automotive Servicing	910,000
Laboratory Use	420,000
Lithium Ion Cell Manufacturing	9,800
Cleaning	190,000
Fertilizer Application	1,300,000

[a] The number of worker estimates are based on industry-specific data that are independent of NMP usage and the portion of workers that are exposed to NMP within these industries is unknown.
[b] These numbers are rounded to two significant figures.
[c] The number of sites associated with these occupational exposure scenarios were determined from CDR or TRI data. However, the number of workers that are exposed to NMP at these sites is unknown.

Estimated numbers of occupational workers in the assessed industries are shown in Table 2-4. The number of workers exposed to NMP for these industries is not known. Additionally, the proportion of workers that are exposed in an industrial versus commercial setting is unknown. Details of these estimates may be found in the supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f).

2.4.1.2.1 Manufacturing

For this industrial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures from the loading of various containers (*i.e.*, drums, tank trucks, rail cars) with pure NMP. While EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work, EPA expects that loading activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin

EPA found no monitoring data specific to the manufacture of NMP. EPA found European modeling estimates for the manufacturing of NMP in the RIVM *Annex XV Proposal for a Restriction – NMP* report (RIVM, 2013). EPA modeled potential NMP air concentrations during the loading of bulk storage containers (*i.e.*, tank trucks and rail cars) and drums using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* and the *Drum Loading and Unloading Release and Inhalation Exposure Model* and compared them to the European modeled exposures. EPA's *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* involves deterministic modeling and the *Drum Loading and Unloading Release, and Inhalation Exposure Model* involves probabilistic modeling. EPA's modeled exposure concentrations are similar in value and the same order of magnitude as the European modeling estimates. EPA's modeled concentrations represent a larger range of potential NMP air concentrations than those presented by RIVM. EPA assessed the range of NMP air concentrations modeled by EPA for this scenario.

The inhalation exposure concentrations modeled by EPA for loading of NMP are summarized into the input parameters used for the PBPK modeling in Table 2-5. Note that the exposure duration for the central tendency and high-end exposure scenarios for loading into drums are the same because the unloading rate does not vary in that model. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides additional details.

Table 2-5. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Manufacturing

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Loading NMP into bulk containers	Central Tendency (50^{th} percentile)	0.047	0.760 (duration = 0.5 hr)	*Tank Truck and Railcar Loading and Unloading Release and Inhalation*	N/A [a]

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
	High-end (95th percentile)	0.190	1.52 (duration = 1 hr)	*Exposure Model* (U.S. EPA, 2015a)	
Loading NMP into drums	Central Tendency (50th percentile)	0.427	1.65 (duration = 2.06 hr)	*Drum Loading and Unloading Release and Inhalation Exposure Model* (U.S. EPA, 2015a)	
	High-end (95th percentile)	1.51	5.85 (duration = 2.06 hr)		

[a] EPA models are standard sources used by EPA for occupational exposure assessments. EPA did not systematically review models that were developed by EPA.
N/A = not applicable

ONUs for this scenario include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the manufacturing of NMP. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from NMP manufacturing. Since ONUs do not directly handle NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

Table 2-6 summarizes the parameters used to assess dermal exposure during the manufacturing of NMP. For this life cycle stage, EPA assessed dermal exposures during the loading of pure NMP into bulk containers and into drums. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from 2016 CDR and literature sources to determine the NMP weight fraction. These underlying data have data quality ratings of high.

Table 2-6. Summary of Parameters for Worker Dermal Exposure to Liquids During Manufacturing

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Loading NMP into bulk containers	Central Tendency	1	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-end	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	1	445 (f) 535 (m)	0.5	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	1	
Loading NMP into drums	Central Tendency	1	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-end	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	1	445 (f) 535 (m)	2.06	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	2.06	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-7.

The numeric parameters corresponding to the characterizations presented in Table 2-7 are summarized in Table 2-8. These are the inputs used in the PBPK model.

Table 2-7. Characterization of PBPK Model Input Parameters for Manufacturing of NMP

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Loading of bulk containers	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	N/A - 100% is assumed
High-end	Loading of drums	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	N/A - 100% is assumed
What-if (task duration-based)	Loading of bulk containers	Central Tendency (50^{th} percentile)	Duration calculated by model	1-Hand	N/A - 100% is assumed

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
What-if (task duration-based)	Loading of drums	High-end (95^{th} percentile)	Duration calculated by model	2-hand	N/A - 100% is assumed
N/A = not applicable because a weight fraction distribution is not known for this OES, and therefore pure NMP is assumed for these scenarios and work activities.					

Table 2-8. PBPK Model Input Parameters for Manufacturing of NMP

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Loading of bulk containers	0.10	4	445 (f) 535 (m)	1	74 (f) 88 (m)
High-end	Loading of drums	1.51	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Loading of bulk containers	0.76	0.5	445 (f) 535 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Loading of drums	5.85	2.06	890 (f) 1,070 (m)	1	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. Modeling, in the middle of the approach hierarchy, was used to estimate occupational air concentrations for both the loading of NMP into bulk containers and into drums. For

modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, for modeling of air concentrations during the loading of drums, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic for the loading activities, as the durations are based on the length of time to load NMP into specific container sizes (*i.e.*, tank trucks, rail cars, and drums).

Primary Limitations

Due to lack of data, EPA has no method to determine the representativeness of the estimates of duration of inhalation and dermal exposure for the loading activities toward the true distribution for all worker activities. NMP concentration is reported to CDR as a range and EPA assessed only the upper end of the range since a central value cannot be ascertained for this scenario. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. EPA is uncertain of the accuracy of the emission factors used to estimate fugitive NMP emissions and thereby to model NMP air concentrations. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.2 Repackaging

For this industrial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures from the unloading of various containers (*i.e.*, drums, tank trucks, rail cars) containing pure NMP. While EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work, EPA expects that unloading activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin

Since no monitoring data or modeling estimates were found for Repackaging, EPA determined the same monitoring data and modeled exposure estimates for manufacturing could be applied to this occupational exposure scenario, due to the similarity in work activities (*e.g.*, loading vessels) and corresponding NMP concentrations between the two occupational exposure scenarios. The air concentration estimates from Section 2.4.1.2.1 for manufacturing are used for this occupational exposure scenario.

ONUs for repackaging include supervisors, managers, and tradesmen that may be in the repackaging area but do not perform tasks that result in the same level of exposures as repackaging workers. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from repackaging of NMP. Since ONUs do not directly handle NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

EPA compiled the same dermal exposure parameters for this occupational exposure scenario as for manufacturing. The dermal exposure parameters from Section 2.4.1.2.1 for manufacturing are used for this occupational exposure scenario.

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-9.

The numeric parameters corresponding to the characterizations presented in Table 2-9 are summarized in Table 2-10. These are the inputs used in the PBPK model.

Table 2-9. Characterization of PBPK Model Input Parameters for Repackaging

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Unloading NMP from bulk containers	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	N/A - 100% is assumed
High-end	Unloading NMP from drums	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	N/A - 100% is assumed
What-if (task duration-based)	Unloading NMP from bulk containers	Central Tendency (50^{th} percentile)	Duration calculated by model	1-hand	N/A - 100% is assumed
What-if (task duration-based)	Unloading NMP from drums	High-end (95^{th} percentile)	Duration calculated by model	2-hand	N/A - 100% is assumed

N/A = not applicable because a weight fraction distribution is not known for this OES, and therefore pure NMP is assumed for these scenarios and work activities.

Table 2-10. PBPK Model Input Parameters for Repackaging

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Unloading NMP from bulk containers	0.10	4	445 (f) 535 (m)	1	74 (f) 88 (m)
High-end	Unloading NMP from drums	1.51	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Unloading NMP from bulk containers	0.76	0.5	445 (f) 535 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Unloading NMP from drums	5.85	2.06	890 (f) 1,070 (m)	1	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations for both the unloading of NMP from bulk containers and from drums. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, for modeling of air concentrations during the loading of drums, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic, as the durations are based on the length of time to load NMP into specific container sizes (*i.e.*, tank trucks, rail cars, and drums).

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the unloading activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. NMP concentration is reported to CDR as a range and EPA assessed only the upper end of the range since a central value cannot be ascertained for this scenario. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. EPA is uncertain of the accuracy of the emission factors used to estimate fugitive NMP emissions and thereby to model NMP air concentrations. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.3 Chemical Processing, Excluding Formulation

This scenario includes the use of NMP for processing activities other than formulation (*i.e.*, non-incorporative processing). Specifically, this may include the use of NMP as an intermediate, as a media for synthesis, extractions, and purifications, or as some other type of processing aid. EPA identified the following industries that use NMP in this manner (RIVM, 2013; U.S. EPA, 2016a):

- Agricultural chemical manufacturing
- Functional fluids (closed systems)
- Petrochemical manufacturing
- Polymer product manufacturing

For this industrial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures from the unloading of various containers (*i.e.*, drums, tank trucks, rail cars) with pure NMP. While EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work, EPA expects that unloading activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin

EPA found limited monitoring data for the use of NMP in non-incorporative processing activities (*e.g.*, use of NMP as an intermediate, as a media for synthesis, extractions, and purifications, or as some other type of processing aid), and the monitoring data found lacks data on worker activities, the function of NMP within the industry of use, and the sampling duration. Due to limited relevance and quality of monitoring data and modeling estimates for chemical processing with NMP found in the published literature, EPA modeled air concentrations using the *Drum Loading and Unloading Release and Inhalation Exposure Model*, which involves probabilistic modeling.

The inhalation exposure concentrations modeled by EPA for loading of NMP are summarized into the input parameters used for the PBPK modeling in Table 2-11. The modeled exposure concentrations are the same as those for Manufacturing and Repackaging; however, the exposure durations are different because they are based on the NMP volume unloaded for the exposure scenario. Note that the exposure

duration for the central tendency and high-end exposure scenarios are the same because the unloading rate does not vary in this model. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides additional details.

Table 2-11. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Chemical Processing

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Unloading liquid NMP from drums	Central Tendency (50^{th} percentile)	0.075	1.65 (duration = 0.36 hr)	*Drum Loading and Unloading Release and Inhalation Exposure Model* (U.S. EPA, 2015a)	N/A [a]
	High-end (95^{th} percentile)	0.265	5.85 (duration = 0.36 hr)		

[a] EPA models are standard sources used by EPA for occupational exposure assessments. EPA did not systematically review models that were developed by EPA.
N/A = not applicable

ONUs include supervisors, managers, and tradesmen that may be in the processing area but do not perform tasks that result in the same level of exposures as workers. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from chemical processing of NMP. Since ONUs do not directly handle NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

Table 2-12 summarizes the parameters used to assess dermal exposure during NMP use in non-incorporative processing activities. EPA assessed dermal exposures during the unloading of pure NMP from drums. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from 2016 CDR, public comments, and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The underlying data rated by EPA have data quality ratings of high.

Table 2-12. Summary of Parameters for Worker Dermal Exposure to Liquids During Chemical Processing, Excluding Formulation

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Unloading liquid NMP from drums	Central Tendency	1	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	1	445 (f) 535 (m)	0.36	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	0.36	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-13.

The numeric parameters corresponding to the characterizations presented in Table 2-13 are summarized in Table 2-14. These are the inputs used in the PBPK model.

Table 2-13. Characterization of PBPK Model Input Parameters for Chemical Processing, Excluding Formulation

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Unloading drums	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	N/A - 100% is assumed
High-end	Unloading drums	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	N/A - 100% is assumed
What-if (task duration-based)	Unloading drums	Central Tendency (50^{th} percentile)	Duration calculated by model	1-hand	N/A - 100% is assumed
What-if (task duration-based)	Unloading drums	High-end (95^{th} percentile)	Duration calculated by model	2-hand	N/A - 100% is assumed

N/A = not applicable because a weight fraction distribution is not known for this OES, and therefore pure NMP is assumed for these scenarios and work activities.

Table 2-14. PBPK Model Input Parameters for Chemical Processing, Excluding Formulation

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Unloading drums	0.15	4	445 (f) 535 (m)	1	74 (f) 88 (m)
High-end	Unloading drums	0.26	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Unloading drums	1.65	0.36	445 (f) 535 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Unloading drums	5.85	0.36	890 (f) 1,070 (m)	1	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations for both the unloading of NMP from bulk containers and from drums. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic, as the duration is based on the length of time to load NMP into drums.

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the unloading activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. NMP concentration is reported to CDR as a range and EPA assessed only the upper end of the range since a central value cannot be ascertained for this scenario. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. EPA is uncertain of the

accuracy of the emission factors used to estimate fugitive NMP emissions and thereby to model NMP air concentrations. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence
Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.4 Incorporation into Formulation, Mixture, or Reaction Product

This scenario includes the use of NMP for incorporation into a formulation, mixture or reaction product, which refers to the process of mixing or blending of several raw materials to obtain a single product or preparation. The uses of NMP that may require incorporation into a formulation include adhesives, sealants, paints, coatings, inks, metal finishing chemicals, cleaning and degreasing products, agricultural products, and petrochemical products including lube oils.

For this industrial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures from the unloading of various containers (*i.e.*, drums, tank trucks, rail cars) with pure NMP and from maintenance, bottling, shipping, and loading of NMP in formulations.

Inhalation and Vapor-through-Skin
EPA compiled inhalation monitoring data and modeled exposure concentration data for the incorporation of NMP into a formulation, mixture or reaction product. Because EPA favors the use of monitoring data over modeled data, monitoring data with the highest data quality was used to assess exposure for this use. EPA used the monitoring data for the central tendency and high-end full-shift worker exposure concentrations presented in Table 2-15. The American Coatings Association (ACA) additionally provided one full-shift personal breathing zone monitoring point taken for a worker during paint formulation (ACA, 2020). Because this data point is within the range of other data and modeling estimates, EPA did not include this data point in the quantitative analysis for this condition of use.

In addition to this monitoring data, EPA also modeled short-term worker inhalation exposure from unloading NMP. The *Drum Loading and Unloading Release and Inhalation Exposure Model* involves probabilistic modeling. The concentrations obtained from modeling are summarized into the input parameters used for the PBPK modeling in Table 2-17 and Table 2-18. In addition to the formulation of liquid products, EPA identified formulation activities that may result in potential worker exposures to solids containing NMP. EPA estimated inhalation exposure concentration of NMP in particulates; however, EPA does not use these exposure concentrations as input to the PBPK model because the PBPK model does not account for solids, and the range of input parameters for the other exposure scenarios capture these concentrations. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides additional details.

Table 2-15. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Incorporation into Formulation, Mixture or Reaction Product

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Liquid – unloading drums	Central Tendency (50th percentile)	0.075	1.65 (duration = 0.36 hr)	*Drum Loading and Unloading Release and Inhalation Exposure Model* (U.S. EPA, 2015a)	N/A [a]
	High-end (95th percentile)	0.26	5.85 (duration = 0.36 hr)		
Liquid – Misc. (Maintenance, analytical, loading)	Central Tendency (50th percentile)	0.344	No data	Fujifilm Holdings America Corporation (2020); Bader et al. (2006)	High
	High-end (95th percentile)	6.28	No data		
Solid – loading into drums	Central Tendency (50th percentile)	0.75	No data	EPA's OSHA PNOR PEL model (U.S. EPA, 2015a) and NMP concentration data	N/A
	High-end (95th percentile)	0.96	No data		

[a] EPA models are standard sources used by EPA for occupational exposure assessments. EPA did not systematically review models that were developed by EPA.
N/A = not applicable

ONUs for formulation sites include supervisors, managers, and tradesmen that may be in the processing area, but do not perform tasks that result in the same level of exposures as production workers. EPA has not identified personal data on or parameters for modeling potential ONU inhalation exposures. Limited area monitoring data were identified (see the supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f). However, the representativeness of these data for ONU exposures is not clear because of uncertainty concerning the intended sample population and the selection of the specific monitoring location. EPA assumed that the area monitoring data were not appropriate surrogates for ONU exposure due to lack of necessary metadata, such as monitoring location and distance from worker activities, to justify its use. Since ONUs do not directly handle formulations containing NMP EPA expects ONU inhalation exposures to be lower than worker inhalation exposures. Information on processes and worker activities is insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified using modeling.

Dermal

Table 2-16 summarizes the parameters used to assess dermal exposure during the incorporation of NMP into formulations, mixtures, and reaction products. For this life cycle stage, EPA assessed dermal exposures during the unloading of pure NMP from drums. As indicated above, the PBPK model does not account for solids so EPA did not include loading of solids in the dermal parameter summary. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from 2016 CDR, public comments, literature, and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The underlying data rated by EPA have data quality ratings ranging from medium to high.

Table 2-16. Summary of Parameters for Worker Dermal Exposure to Liquids During Incorporation into Formulation, Mixture, or Reaction Product

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Liquid - Unloading drums	Central Tendency	1	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	1	445 (f) 535 (m)	0.36	
	What-if (task duration-based)	1	445 (f) 535 (m)	0.36	
Liquid – Misc. (Maintenance, analytical, loading)	Central Tendency	0.31	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.99	890 (f) 1,070 (m)	8	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-17. EPA only presents these scenarios for handling of liquid NMP, to present conservative assessments of potential exposures.

The numeric parameters corresponding to the characterizations presented in Table 2-17 are summarized in Table 2-18. These are the inputs used in the PBPK model.

Table 2-17. Characterization of PBPK Model Input Parameters for Incorporation into Formulation, Mixture or Reaction Product

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Liquid - Drum unloading	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	N/A - 100% is assumed

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
High-end	Liquid - Drum unloading	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	N/A - 100% is assumed
What-if (task duration-based)	Liquid - Drum unloading	Central Tendency (50^{th} percentile)	Duration calculated by model	1-hand	N/A - 100% is assumed
What-if (task duration-based)	Liquid - Drum unloading	High-end (95^{th} percentile)	Duration calculated by model	2-hand	N/A - 100% is assumed
Central Tendency	Liquid – Misc. (Maintenance, analytical, loading)	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	Central Tendency (50^{th} percentile)
High-end	Liquid – Misc. (Maintenance, analytical, loading)	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	High-end (95^{th} percentile)
N/A = not applicable because a weight fraction distribution is not known for this OES, and therefore pure NMP is assumed for these scenarios and work activities.					

Table 2-18. PBPK Model Input Parameters for Incorporation into Formulation, Mixture or Reaction Product

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Hand Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Liquid – Drum unloading	0.15	4	445 (f) 535 (m)	1	74 (f) 88 (m)
High-end	Liquid – Drum unloading	0.26	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Liquid – Drum unloading	1.65	0.36	445 (f) 535 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Liquid – Drum unloading	5.85	0.36	890 (f) 1,070 (m)	1	74 (f) 88 (m)
Central Tendency	Liquid – Misc. (Maintenance, analytical, loading)	0.69	4	445 (f) 535 (m)	0.31	74 (f) 88 (m)

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Hand Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
High-end	Liquid – Misc. (Maintenance, analytical, loading)	6.28	8	890 (f) 1,070 (m)	0.99	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations for the unloading of NMP from drums. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic, as the duration is based on the length of time to load NMP into drums. EPA assessed worker inhalation exposure during maintenance, bottling, shipping, and loading of NMP using directly applicable monitoring data, which is the highest of the approach hierarchy, taken at an adhesive formulation facility. The data quality rating for the monitoring data used by EPA is high. EPA expects the duration of inhalation and dermal exposure to be realistic for the unloading of drums, as the duration is based on the length of time to load NMP into drums.

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. NMP concentration is reported to CDR as a range and EPA assessed only the upper end of the range since a central value cannot be ascertained for this scenario (NMP concentration is lower in the formulated products). Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. EPA estimated worker inhalation exposure concentration during the loading of NMP in solid formulations using EPA's OSHA PEL for PNOR model U.S. EPA (2015a), which is the lowest approach on the hierarchy. EPA did not use these inhalation exposure concentrations for the PBPK modeling because the PBPK model does not account for solids and because both the inhalation and dermal exposure potential are captured within other occupational exposure scenarios.

EPA is uncertain of the accuracy of the emission factors used to estimate fugitive NMP emissions and thereby to model NMP air concentrations. For the maintenance, bottling, shipping, and loading of liquid NMP, the monitoring data consists of only 7 data points from 1 source. The representativeness of the modeling and the monitoring data toward the true distribution of inhalation concentrations for these occupational exposure scenarios is uncertain.

Overall Confidence
Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.5 Metal Finishing

This scenario includes the use of metal finishing products containing NMP. For this industrial and commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to metal finishing products containing NMP from the following application methods:

- Spray application;
- Dip application; and
- Brush application.

While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that application activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin
EPA compiled inhalation monitoring data for NMP-based metal finishing applications from published literature sources, including 8-hour TWA, short-term and partial shift sampling results. Where reasonably available, EPA used monitoring data for metal finishing or surrogate monitoring data (surrogate work activities using NMP) for the use of NMP during the Application of Paints, Coatings, Adhesives, and Sealants (Section 2.4.1.2.6) and Cleaning (Section 2.4.1.2.16) that had the highest quality rating to assess exposure. Where monitoring data were not reasonably available for an application type, EPA used modeling estimates from literature with the highest data quality to assess exposure.

EPA found limited data on the application of metal finishing chemicals and thus assessed spray application using data from the Application of Paints, Coatings, Adhesives, and Sealants occupational exposure scenario (Section 2.4.1.2.6) as a surrogate for the worker activities in this occupational exposure scenario. EPA also used data for dip cleaning from the Cleaning occupational exposure scenario (Section 2.4.1.2.16) as a surrogate for the worker activities in this occupational exposure scenario. EPA used these data as surrogate because of the lack of more applicable data and due to the similarity in work activities (*e.g.*, spray and dip activities are similar between these OESs) between the occupational exposure scenarios. Finally, EPA used a modeled exposure estimate for the brush application of a substance containing NMP.

The monitoring data and the modeled exposure estimates for metal finishing are summarized according to the input parameters used for the PBPK modeling in Table 2-19. The supplemental document *Risk*

Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment (U.S. EPA, 2020f) provides additional details.

Table 2-19. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Metal Finishing

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Spray Application	Low-end (of range)	0.04	0.04 (duration = 4 hr)	NIOSH (1998)	High
	Mean	0.53	0.53 (duration = 4 hr)		
	High-end (of range)	4.51	4.51 (duration = 4 hr)		
Dip Application	Central Tendency (50^{th} percentile)	0.99	No data	Surrogate data (surrogate work activities using NMP) from: RIVM (2013); Nishimura et al. (2009); Bader et al. (2006); Xiaofei et al. (2000); Ifa (2010)	Medium to high
	High-end (95^{th} percentile)	2.75	No data		
Brush Application	Single estimate	4.13	No data	RIVM (2013)	High

ONUs for this scenario include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal data on or parameters for modeling potential ONU inhalation exposures. Limited area monitoring data were identified (see the supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f)). However, the representativeness of these data for ONU exposures is not clear because of uncertainty concerning the intended sample population and the selection of the specific monitoring location. EPA assumed that the area monitoring data were not appropriate surrogates for ONU exposure due to lack of necessary metadata, such as monitoring location and distance from worker activities, to justify its use. Since ONUs do not directly handle formulations containing NMP, EPA expects ONU inhalation exposures to be lower than worker inhalation exposures. Information on processes and worker activities is insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified using modeling.

Dermal

Table 2-20 summarizes the parameters used to assess dermal exposure during application of metal finishing formulations containing NMP. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from the 2012 and 2016 CDR to determine the NMP weight fraction, which indicate that the weight concentration of NMP in formulation is greater than 60 percent but less than 90 percent. Due to lack of additional information, EPA assesses a low-end weight fraction of 0.6 and a high-end weight fraction of 0.9. The CDR data have a data quality rating of high.

Table 2-20. Summary of Parameters for Worker Dermal Exposure to Liquids During Metal Finishing

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
All forms of application listed above	Central Tendency	0.6	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-end	0.9	890 (f) 1,070 (m)	8	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-21. The numeric parameters corresponding to the characterizations presented in Table 2-21 are summarized in Table 2-22. These are the inputs used in the PBPK model.

Table 2-21. Characterization of PBPK Model Input Parameters for Metal Finishing

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Spray application	Mean	Assumed 4 hours	1-hand	Central Tendency
High-end	Spray application	High-end (of range)	Assumed 8 hours	2-hand	High-end
Central Tendency	Dip application	Central Tendency (50^{th} percentile)	Assumed 4 hours	1-hand	Central Tendency
High-end	Dip application	High-end (95^{th} percentile)	Assumed 8 hours	2-hand	High-end
Central Tendency	Brush application	Single estimate	Assumed 4 hours	1-hand	Central Tendency
High-end	Brush application	Single estimate	Assumed 8 hours	2-hand	High-end

Table 2-22. PBPK Model Input Parameters for Metal Finishing

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Spray application	0.530	4	445 (f) 535 (m)	0.6	74 (f) 88 (m)
High-end	Spray application	4.51	8	890 (f) 1,070 (m)	0.9	74 (f) 88 (m)
Central Tendency	Dip application	1.98	4	445 (f) 535 (m)	0.6	74 (f) 88 (m)
High-end	Dip application	2.75	8	890 (f) 1,070 (m)	0.9	74 (f) 88 (m)
Central Tendency	Brush application	8.26	4	445 (f) 535 (m)	0.6	74 (f) 88 (m)
High-end	Brush application	4.13	8	890 (f) 1,070 (m)	0.9	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. To estimate inhalation exposure during spray application, EPA used surrogate monitoring data (surrogate work activities using NMP), which is in the middle of the approach hierarchy, including 26 data points. These data have a data quality rating of high. To estimate inhalation exposure during dip application, EPA used surrogate monitoring data for the use of NMP design dip cleaning, which is in the middle of the approach hierarchy, including data from 5 sources. These data have data quality ratings of medium to high. To estimate inhalation exposure during brush application, EPA used modeled data from the RIVM report (RIVM, 2013), which has a data quality rating of high. The use of modeling is in the middle of the approach hierarchy. EPA used durations associated with inhalation monitoring data to estimate duration of inhalation and dermal exposure during spray application.

Primary Limitations

EPA did not find exposure data for this occupational exposure scenario and used surrogate or modeled data to assess occupational inhalation exposures. For occupational exposure scenarios other than spray application, EPA did not find reasonably available data on actual duration of liquid contact and assumed a high-end of 8 hours because the surrogate data or modeled values are 8-hour TWA values. EPA assumed a mid-range of 4 hours for central tendency duration of liquid contact. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Due to lack of data, EPA could not calculate central tendency and high-end NMP concentration in metal finishing products and used the low-end and high-end of the NMP concentration range reported in 2016 CDR. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are “what-if” assumptions and are uncertain. The available monitoring data for spray application is from 1996. The extent to which these data are representative of current worker inhalation exposure potential is uncertain. The worker activities associated with the surrogate data used to assess worker inhalation exposure during dip application are not detailed for all sample points. The modeled inhalation exposure concentration during roller/brush application was obtained from RIVM (2013) and not generated by EPA. For all occupational exposure scenarios, representativeness of the monitoring data, surrogate monitoring data, or modeled data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher

certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.6 Application of Paints, Coatings, Adhesives and Sealants

This scenario includes the application of paints, coatings, adhesives, and sealants containing NMP. For this industrial and commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to paints, coatings, adhesives, and sealants containing NMP from the following application methods:

- Spray application;
- Roll / curtain application;
- Dip application; and
- Roller / brush and syringe / bead application.

While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that application activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin

EPA compiled inhalation monitoring data and modeled exposure data for NMP-based paint, coating, adhesive, and sealant application from published literature sources, including 8-hour TWA, short-term, and partial shift sampling results. Where reasonably available, EPA compiled surrogate monitoring data (surrogate work activities using NMP) for the use of NMP during cleaning, which is described in Section 2.4.1.2.16. Where monitoring data were not reasonably available for an application type, EPA used surrogate monitoring data (surrogate work activities using NMP) with the highest data quality or modeled estimates to assess exposure, as further described below.

EPA found limited to no inhalation monitoring data on roll / curtain application, dip application, or roller /brush and syringe / bead application with NMP-containing formulations, so either surrogate data for the use of NMP during the Cleaning occupational exposure scenario or modeling data were used to determine the modeling parameters for these application methods. The *EPA/OPPT UV Roll Coating Model* was used for roll / curtain coating application and involved deterministic modeling.

The monitoring data and the modeled exposures for this life cycle stage are summarized in Table 2-23. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides additional details.

Table 2-23. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Application

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Spray Application	Low-end (of range)	0.04	0.04 (duration = 4 hr)	NIOSH (1998)	High
	Mean	0.53	0.53 (duration = 4 hr)		
	High-end (of range)	4.51	4.51 (duration = 4 hr)		
Roll / Curtain Application	Central Tendency (50^{th} percentile)	0.03	No data	*EPA/OPPT UV Roll Coating Model* (U.S. EPA, 2015a)	N/A [a]
	High-end (95^{th} percentile)	0.19	No data		
Dip Application	Central Tendency (50^{th} percentile)	0.99	No data	Surrogate data (surrogate work activities using NMP) from: RIVM (2013); IFA (2010); Nishimura et al. (2009); Bader et al. (2006); Xiaofei et al. (2000)	Medium to high
	High-end (95^{th} percentile)	2.75	No data		
Roller / Brush and Syringe / Bead Application	Single estimate	4.13	No data	RIVM (2013)	High

[a] EPA models are standard sources used by EPA for occupational exposure assessments. EPA did not systematically review models that were developed by EPA.
N/A = not applicable

ONUs for this scenario include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal data on or parameters for modeling potential ONU inhalation exposures. Limited area monitoring data were identified (see the supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f). However, the representativeness of these data for ONU exposures is not clear because of uncertainty concerning the intended sample population and the selection of the specific monitoring location. EPA assumed that the

area monitoring data were not appropriate surrogates for ONU exposure due to lack of necessary metadata, such as monitoring location and distance from worker activities, to justify its use. Since ONUs do not directly handle formulations containing NMP, EPA expects ONU inhalation exposures to be lower than worker inhalation exposures. Information on processes and worker activities is insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified using modeling.

Dermal

Table 2-24 summarizes the parameters used to assess dermal exposure during application of paints, coatings, adhesives, and sealants containing NMP. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from public comments, literature, and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The underlying data rated by EPA have data quality ratings ranging from medium to high.

Table 2-24. Summary of Parameters for Worker Dermal Exposure to Liquids During Application of Paints, Coatings, Adhesives and Sealants

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
All forms of application listed above	Central Tendency	0.02	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.534	890 (f) 1,070 (m)	8	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-25. The numeric parameters corresponding to the characterizations presented in Table 2-25 are summarized in Table 2-26. These are the inputs used in the PBPK model.

Table 2-25. Characterization of PBPK Model Input Parameters for Application of Paints, Coatings, Adhesives, and Sealants

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Spray application	Mean	Half shift (4 hours)	1-hand	Central Tendency
High-end	Spray application	High-end (of range)	Full shift (8 hours)	2-hand	High-end
Central Tendency	Roll / curtain application	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	Central Tendency

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
High-end	Roll / curtain application	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	High-end
Central Tendency	Dip application	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	Central Tendency
High-end	Dip application	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	High-end
Central Tendency	Brush application	Single estimate	Half shift (4 hours)	1-hand	Central Tendency
High-end	Brush application	Single Estimate	Full shift (8 hours)	2-hand	High-end

Table 2-26. PBPK Model Input Parameters for Application of Paints, Coatings, Adhesives and Sealants

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Spray application	0.530	4	445 (f) 535 (m)	0.02	74 (f) 88 (m)
High-end	Spray application	4.51	8	890 (f) 1,070 (m)	0.534	74 (f) 88 (m)
Central Tendency	Roll / curtain application	0.06	4	445 (f) 535 (m)	0.02	74 (f) 88 (m)
High-end	Roll / curtain application	0.19	8	890 (f) 1,070 (m)	0.534	74 (f) 88 (m)
Central Tendency	Dip application	1.98	4	445 (f) 535 (m)	0.02	74 (f) 88 (m)
High-end	Dip application	2.75	8	890 (f) 1,070 (m)	0.534	74 (f) 88 (m)
Central Tendency	Brush application	8.26	4	445 (f) 535 (m)	0.02	74 (f) 88 (m)
High-end	Brush application	4.13	8	890 (f) 1,070 (m)	0.534	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.						

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from 79 values from a variety of data sources with data quality ratings ranging from medium to high. The spread of the 79 values of weight fraction was more pronounced than other OESs, leading to a larger than average difference of central tendency and high-end exposures; however, this data set is stronger than average and reduces uncertainties. To estimate inhalation exposure during spray application, EPA used directly applicable personal monitoring data, the highest of the approach hierarchy, including 26 data points. These data have a data quality rating of high. To estimate inhalation exposure during roll/curtain application, EPA used modeling, which is in the middle of the approach hierarchy. To estimate inhalation exposure during dip application, EPA used surrogate monitoring data for the use of NMP during dip cleaning, which is in the middle of the approach hierarchy, including data from 5 sources. These data have data quality ratings of medium to high. To estimate inhalation exposure during roller / brush and syringe/bead application, EPA used modeled data from the RIVM report RIVM (2013), which has a data quality rating of high. The use of modeling is in the middle of the approach hierarchy. EPA used durations associated with short-term inhalation monitoring data to estimate duration of inhalation and dermal exposure during spray application.

Primary Limitations

For occupational exposure scenarios other than spray application, EPA did not find reasonably available data on actual duration of liquid contact and assumed a high-end of 8 hours because the surrogate data or modeled values are 8-hour TWA values. EPA assumed a mid-range of 4 hours for central tendency duration of liquid contact. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are “what-if” assumptions and are uncertain.

The reasonably available monitoring data for spray application is from 1996 and the surrogate monitoring data used in the model for roll / curtain application is from 1994 or earlier. The extent to which these data are representative of current worker inhalation exposure potential is uncertain. The

worker activities associated with the surrogate data (surrogate work activities using NMP) used to assess worker inhalation exposure during dip application are not detailed for all sample points. The modeled inhalation exposure concentration during roller / brush application was obtained from RIVM (2013) and not generated by EPA. For all occupational exposure scenarios, representativeness of the monitoring data, surrogate monitoring data, or modeled data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence
Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.7 Recycling and Disposal

For this industrial and commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures from the unloading of various containers (*i.e.*, drums, tank trucks, rail cars) containing waste NMP. While EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work, EPA expects that unloading activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin
EPA did not find monitoring data on the handling of NMP wastes at disposal and recycling sites. EPA therefore compiled the same monitoring and modeled exposure concentration data for this life cycle stage as that for manufacturing. As described for Manufacturing in Section 2.4.1.2.1, due to limited relevance and quality of monitoring data and modeling estimates found in the published literature, EPA modeled air concentrations for this use, using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model,* which involves deterministic modeling, and the *Drum Loading and Unloading Release and Inhalation Exposure Model,* which involves probabilistic modeling.

The inhalation exposure concentrations modeled by EPA for unloading of NMP are summarized into the input parameters used for the PBPK modeling in Table 2-27. The modeled exposure concentrations are the same as those for Manufacturing and Repackaging; however, the exposure durations are different because they are based on the NMP volume unloaded for the exposure scenario. Note that the exposure duration for the central tendency and high-end exposure scenarios are the same for unloading drums because the unloading rate does not vary in that model. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides additional details.

Table 2-27. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Recycling and Disposal

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Unloading bulk containers	Central Tendency (50th percentile)	0.048	0.760 (duration = 0.5 hr)	*Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* (U.S. EPA, 2015a)	N/A[a]
	High-end (95th percentile)	0.190	1.52 (duration = 1 hr)		
Unloading drums	Central Tendency (50th percentile)	0.124	1.65 (duration = 0.603 hr)	*Drum Loading and Unloading Release and Inhalation Exposure Model* (U.S. EPA, 2015a)	N/A [a]
	High-end (95th percentile)	0.441	5.85 (duration = 0.603 hr)		

[a] EPA models are standard sources used by EPA for occupational exposure assessments. EPA did not systematically review models that were developed by EPA.
N/A = not applicable

ONUs for disposal and recycling sites include supervisors, managers, and tradespeople that may be in the processing and disposal area but do not perform tasks that result in the same level of exposures as workers that directly handle NMP wastes. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from recycling and disposal NMP. Since ONUs do not directly handle formulations containing NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

Table 2-28 summarizes the parameters used to assess dermal exposure during worker handling of wastes containing NMP. Most parameters were determined based on assumptions described in Section 2.4.1.1. The data submitted by SIA for the use of NMP in the production of semiconductors (discussed in Section 2.4.1.2.10) include one inhalation monitoring data point for the loading of trucks with waste NMP. This data point indicates that NMP is 92% in the handled waste material (Semiconductor Industry Association, 2019c). EPA uses this concentration for the central tendency NMP weight fraction. Due to lack of additional information on the concentration of NMP in waste solvents, for the high-end value, EPA assumes that waste NMP may contain very little impurities and be up to 100 weight percent NMP

(*e.g.*, residues of pure NMP in shipping containers that have been unloaded and sent without cleaning for reclamation or disposal).

Table 2-28. Summary of Parameters for Worker Dermal Exposure During Recycling and Disposal

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Unloading bulk containers	Central Tendency	0.92	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.92	445 (f) 535 (m)	0.5	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	1	
Unloading drums	Central Tendency	0.92	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.92	445 (f) 535 (m)	0.603	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	0.603	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-29. The numeric parameters corresponding to the characterizations presented in Table 2-29 are summarized in Table 2-30. These are the inputs used in the PBPK model.

Table 2-29. Characterization of PBPK Model Input Parameters for Recycle and Disposal

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Unloading bulk containers	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	Central Tendency
High-end	Unloading drums	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	High-end
What-if (task	Unloading bulk containers	Central Tendency (50^{th} percentile)	Duration calculated by model	1-hand	Central Tendency

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
duration-based)					
What-if (task duration-based)	Unloading drums	High-end (95^{th} percentile)	Duration calculated by model	2-hand	High-end

Table 2-30. PBPK Model Input Parameters for Recycle and Disposal

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Unloading bulk containers	0.10	4	445 (f) 535 (m)	0.92	74 (f) 88 (m)
High-end	Unloading drums	0.44	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Unloading bulk containers	0.76	0.5	445 (f) 535 (m)	0.92	74 (f) 88 (m)
What-if (task duration-based)	Unloading drums	5.85	0.603	890 (f) 1,070 (m)	1	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations for both the unloading of NMP from bulk containers and from drums. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, for modeling of air concentrations during the unloading of drums, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic for the unloading activities, as the durations are based on the length of time to unload NMP from specific container sizes (*i.e.*, tank trucks, rail cars, and drums).

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the unloading activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. EPA did not find NMP concentration data and assumed waste NMP may contain very little impurities and be up to 100% NMP. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. For the modeling of NMP air concentrations, EPA is uncertain of the accuracy of the emission factors used to estimate fugitive NMP emissions and thereby estimate worker inhalation exposure concentration. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.8 Removal of Paints, Coatings, Adhesives and Sealants

This scenario includes the use of paint, coating, adhesive, and sealant removal products containing NMP. For this industrial and commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to paint, coating, adhesive, and sealant removal products containing NMP from the following activities:

- Miscellaneous paint and coating removal; and
- Graffiti removal.

While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that removal activities present the largest range of potential exposures.

Worker activities for the removal of paints, coatings, adhesives, and sealants involve the application of products containing high concentrations of NMP onto open surfaces from which evaporation will occur. This results in higher NMP air concentrations and potential worker exposures relative to other occupational exposure scenarios in this risk evaluation.

Inhalation and Vapor-through-Skin

EPA compiled inhalation monitoring data for NMP-based paint, coating, adhesive, and sealant removal from published literature sources, including 8-hour TWA, short-term, and partial shift sampling results. This data is summarized into low-end (lowest concentration), high-end (highest concentration), and mean or mid-range values in Table 2-31. EPA used the reasonably available monitoring data with the highest data quality to assess exposure for this use. The data presented in Table 2-31 are the input parameters used for the PBPK modeling for workers. The supplemental document Risk Evaluation *for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides additional details.

Table 2-31. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Removal of Paints, Coatings, Adhesives and Sealants

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Miscellaneous paint, coating, adhesive, and sealant removal	Low end (of range)	1.0	6.1 (duration = 1 hr)	NMP Producers Group (2012); WHO (2001); NIOSH (1993) as cited in U.S. EPA (2015c) Akesson et al. (2000) as cited in WHO (2001) [a]	High
	Mid-range	32.5	13.2 (duration = 1 hr)		
	High end (of range) [a]	64	280 (duration = 1 hr)		
Graffiti removal	Low end (of range)	0.03	No data	Anundi et al. (2000) as cited in U.S. EPA (2015c)	High
	Mean	1.01	No data		
	High end (of range)	4.52	No data		

[a] These values are cited in WHO, 2001, and are from the unpublished source "Akesson B, Jönsson B. 2000. Occupational study in paint stripping industries. Draft Report Lund University Hospital, Department of Occupational & Environmental Health."

ONUs for this scenario include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from paint, coating, adhesive, and sealant removal. Since ONUs do not directly handle formulations containing NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be

present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

Table 2-32 summarizes the parameters used to assess dermal exposure during paint, coating, adhesive, and sealant removal. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from public comments, literature sources, and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The underlying data have data quality ratings ranging from medium to high. One anecdotal survey of glove usage among workers performing graffiti removal indicates that most workers wear gloves, although the glove materials varied and were sometimes not protective (Anundi et al., 2000).

Table 2-32. Summary of Parameters for PBPK Modeling of Worker Dermal Exposure to Liquids During Removal of Paints, Coatings, Adhesives and Sealants

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Miscellaneous paint, coating, adhesive, and sealant removal	Central Tendency	0.305	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.695	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.305	445 (f) 535 (m)	1	
	What-if (task duration-based)	0.695	890 (f) 1,070 (m)	1	
Graffiti removal	Central Tendency	0.5	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.6125	890 (f) 1,070 (m)	8	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-33. The numeric parameters corresponding to the characterizations presented in Table 2-33 are summarized in Table 2-34. These are the inputs used in the PBPK model.

Table 2-33. Characterization of PBPK Model Input Parameters for Removal of Paints, Coatings, Adhesives and Sealants

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Miscellaneous paint, coating, adhesive, and sealant removal	Mid-range	Half shift (4 hours)	1-hand	Central Tendency
High-end	Miscellaneous paint, coating, adhesive, and sealant removal	High-end (of range)	Full shift (8 hours)	2-hand	High-end
What-if (task duration-based)	Miscellaneous paint, coating, adhesive, and sealant removal	Mid-range	Based on 1-hour TWA data	1-hand	Central Tendency
What-if (task duration-based)	Miscellaneous paint, coating, adhesive, and sealant removal	High-end (of range)	Based on 1-hour TWA data	2-hand	High-end
Central Tendency	Graffiti removal	Mean	Half shift (4 hours)	1-hand	Central Tendency
High-end	Graffiti removal	High-end (of range)	Full shift (8 hours)	2-hand	High-end

Table 2-34. PBPK Model Input Parameters for Removal of Paints, Coatings, Adhesives and Sealants

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Miscellaneous paint, coating, adhesive, and sealant removal	65	4	445 (f) 535 (m)	0.305	74 (f) 88 (m)
High-end	Miscellaneous paint, coating, adhesive, and sealant removal	64	8	890 (f) 1,070 (m)	0.695	74 (f) 88 (m)
What-if (task duration-based)	Miscellaneous paint, coating, adhesive, and sealant removal	13.2	1	445 (f) 535 (m)	0.305	74 (f) 88 (m)

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
What-if (task duration-based)	Miscellaneous paint, coating, adhesive, and sealant removal	280	1	890 (f) 1,070 (m)	0.695	74 (f) 88 (m)
Central Tendency	Graffiti removal	2.02	4	445 (f) 535 (m)	0.5	74 (f) 88 (m)
High-end	Graffiti removal	4.52	8	890 (f) 1,070 (m)	0.6125	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50^{th} and 95^{th} percentiles, respectively, from a variety of data sources with data quality ratings ranging from medium to high. To estimate inhalation exposure during miscellaneous paint and coating removal, EPA used directly applicable personal monitoring data, the highest of the approach hierarchy, including data from three studies. These data have a data quality rating of high. To estimate inhalation exposure during graffiti removal, EPA used directly applicable personal monitoring data, the highest of the approach hierarchy, including 25 data points. These data have a data quality rating of high. EPA used durations associated with inhalation monitoring data to estimate duration of inhalation and dermal exposure during miscellaneous paint, coating, adhesive, and sealant removal.

Primary Limitations

For graffiti removal, EPA did not find data other than 8-hour TWA values. EPA assumed a high-end duration of liquid contact equal to 8 hours and a central tendency duration of liquid contact of 4 hours, which is the mid-range of a full shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The short-term inhalation exposure concentrations for miscellaneous removal are based on data from 1993 and the extent to which these data are representative of current worker inhalation exposure potential is uncertain. For graffiti removal, EPA used the minimum, mean, and maximum air concentrations reported by one literature source for 25 datapoints. Because the source did not report these 25 data points individually, EPA could not calculate 50th and 95th percentile values. The representativeness of the monitoring data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.9 Other Electronics Manufacturing

This scenario includes the use of NMP in other electronics industry (exclusion lithium ion cell manufacturing and semiconductor manufacturing). For this industrial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to NMP from Capacitor, resistor, coil, transformer, and other inductor manufacturing (OSHA, 2017).

While operations for the various types of electronics manufacturing that are included in this occupational exposure scenario may vary, EPA expects these activities present the largest range of potential exposures for other electronics manufacturing activities.

Inhalation and Vapor-through-Skin

EPA used NMP monitoring data from OSHA's Chemical Exposure Health Data (CEHD), which includes four NMP data points related to capacitor, resistor, coil, transformer, and other inductor (OSHA, 2017). These data points are personal breathing zone, full-shift measurements. These were summarized into the PBPK modeling full-shift input parameters in Table 2-35. Confidential air concentration data were submitted for several additional work activities for this industry and are not included in this evaluation.

Table 2-35. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Other Electronics Manufacturing

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hour TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Capacitor, Resistor, Coil, Transformer, and Other Inductor Mfg.	Central Tendency (50^{th} percentile)	2.96	No data	OSHA (2017)	High
	High-end (95^{th} percentile)	44.2	No data		

ONUs for this scenario include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures. Since ONUs do not directly handle formulations containing NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on processes and worker activities is insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified using modeling.

Dermal

Table 2-36 summarizes the parameters used to assess dermal exposure during use of NMP in in the electronics industries. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from public comments, literature, and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The weight fraction data has a data quality rating of high. Public comments indicate workers wear gloves in the electronics manufacturing industries (National Electrical Manufacturers, 2020; Roberts, 2017).

Table 2-36. Summary of Parameters for Worker Dermal Exposure During Other Electronics Manufacturing

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Capacitor, Resistor, Coil, Transformer, and Other Inductor Mfg.	Central Tendency	0.60	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	8	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-37.

The numeric parameters corresponding to the characterizations presented in Table 2-37 are summarized in Table 2-38. These are the PBPK model inputs determined by EPA.

Table 2-37. Characterization of PBPK Model Input Parameters for Other Electronics Manufacturing

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	All activities	Central Tendency (50^{th} percentile)	Mid-point of shift duration (4 hours)	1-hand	Central Tendency
High-end	All activities	High-end (95^{th} percentile)	High-end of shift duration (8 hours)	2-hand	High-end

Table 2-38. PBPK Model Input Parameters for Other Electronics Manufacturing

Work Activity	Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Capacitor, Resistor, Coil, Transformer, and Other Inductor Mfg.	Central Tendency	5.92	4	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	High-end	44.2	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths
EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from OSHA data (OSHA, 2017), which has a data quality rating of high. EPA used directly applicable inhalation monitoring data, which is the highest of the approach hierarchy, to estimate worker inhalation exposure during one electronics manufacturing operation. These data have a data quality rating of high.

Primary Limitations
The OSHA data (OSHA, 2017) monitoring data were provided as 8-hour TWA values. EPA assumed 8 hours as the high-end duration of liquid contact and mid-range of 4 hours as the central tendency duration of liquid contact. The representativeness of the estimates of duration of inhalation and dermal exposure for the assessed activity toward the true distribution of duration for all worker activities in this occupational exposure scenario beyond capacitor, resistor, coil, transformer, and other inductor manufacturing is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The OSHA data (OSHA, 2017) monitoring data only include capacitor, resistor, coil, transformer, and other inductor manufacturing. The representativeness of the monitoring data for capacitor, resistor, coil, transformer, and other inductor manufacturing toward the true distribution of inhalation concentrations for all worker activities in this occupational exposure scenario is uncertain.

Overall Confidence
Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.10 Semiconductor Manufacturing

This scenario includes the use of NMP in the electronics industry. For this industrial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to NMP from the following work activities (Semiconductor Industry Association, 2019b):

- Container handling, small containers
- Container handling, drums
- Fab worker
- Maintenance
- Virgin NMP truck unloading
- Waste truck loading

While operations for semiconductor manufacturing may vary, EPA expects these activities present the largest range of potential exposures. This OES applies to two conditions of use, one for coatings and another for solvents. The work activities above all apply to the solvent use, and all except the virgin NMP truck unloading apply to the coatings use because virgin NMP delivered to these sites is used as a solvent and not as a coating.

Inhalation and Vapor-through-Skin

For semiconductor manufacturing, EPA uses data received from the Semiconductor Industry Association (SIA), which include full-shift personal breathing zone sampling results at semiconductor fabrication facilities during container handling of both small containers and drums, workers inside the fabrication rooms, maintenance workers, workers that unload trucks containing virgin NMP (100%), and workers that load trucks with liquid waste NMP (92%) (Semiconductor Industry Association, 2019c). The SIA monitoring data were summarized into the PBPK modeling full-shift input parameters in Table 2-39. The majority (96% of all samples) of samples in SIA (2019c) were non-detect for NMP. Because the geometric standard deviation of the data set is greater than three, EPA used the limit of detection (LOD) divided by two to calculate central tendency and high-end values where samples were non-detect for NMP (U.S. EPA, 1994b). Due to the high amount of non-detect results, this method may result in bias. This is further described in the supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f). The SIA data included samples of both 8-hour TWA and 12-hour TWA values, with much of the data being 12-hour TWA. EPA used the 12-hour TWA values to assess occupational exposures in this occupational exposure scenario, as there is more data available for this exposure duration, indicating that typical shifts in this industry are 12 hours. Note, however, that the single data points available for the last two tasks in Table 2-39 are 8-hour TWA values.

Table 2-39. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Semiconductor Manufacturing

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8- or 12-hour TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Semiconductor manufacturing - Container handling, small containers	Central Tendency (50^{th} percentile)	0.507	No data	Semiconductor Industry Association (2019b)	High
	High-end (95^{th} percentile)	0.608	No data		
Semiconductor manufacturing - Container handling, drums	Central Tendency (50^{th} percentile)	0.013	No data		
	High-end (95^{th} percentile)	1.54	No data		
Semiconductor manufacturing - Fab worker	Central Tendency (50^{th} percentile)	0.138	No data		
	High-end (95^{th} percentile)	0.405	No data		
Semiconductor manufacturing - Maintenance	Central Tendency (50^{th} percentile)	0.020	No data		
	High-end (95^{th} percentile)	0.690	No data		

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8- or 12-hour TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Semiconductor manufacturing - Virgin NMP truck unloading	Single value	4.78 [a]	No data		
Semiconductor manufacturing - Waste truck loading	Single value	0.709 [a]	No data		
[a] These are 8-hour TWA values.					

ONUs for this scenario include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal data on or parameters for modeling potential ONU inhalation exposures. Limited area monitoring data were identified (see the supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f). However, the representativeness of these data for ONU exposures is not clear because of uncertainty concerning the intended sample population and the selection of the specific monitoring location. EPA assumed that the area monitoring data were not appropriate surrogates for ONU exposure due to lack of necessary metadata, such as monitoring location and distance from worker activities, to justify its use. Since ONUs do not directly handle formulations containing NMP, EPA expects ONU inhalation exposures to be lower than worker inhalation exposures. Information on processes and worker activities is insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified using modeling.

Dermal

Table 2-40 summarizes the parameters used to assess dermal exposure during use of NMP in semiconductor manufacturing. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from SIA (2019c), public comments, literature, and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The weight fraction data has a data quality rating of high. Workers typically wear chemical resistant aprons with sleeves and chemical resistant gloves (Intel Corporation, 2020, 2019; Semiconductor Industry Association, 2019a). Workers receiving training on PPE usage, including when PPE is required, what PPE is required, and the proper donning and doffing of PPE (Intel Corporation, 2020, 2019; Semiconductor Industry Association, 2019a).

Table 2-40. Summary of Parameters for Worker Dermal Exposure During Semiconductor Manufacturing

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Semiconductor manufacturing - Container handling, small containers	Central Tendency	0.6	445 (f) 535 (m)	6	74 (f) 88 (m)
	High-End	0.75	890 (f) 1,070 (m)	12	
	What-if (task duration-based)	0.6	445 (f) 535 (m)	5 min	
	What-if (task duration-based)	0.75	890 (f) 1,070 (m)	60 min	
Semiconductor manufacturing - Container handling, drums	Central Tendency	0.5	445 (f) 535 (m)	6	74 (f) 88 (m)
	High-End	0.75	890 (f) 1,070 (m)	12	
	What-if (task duration-based)	0.5	445 (f) 535 (m)	2 min	
	What-if (task duration-based)	0.75	890 (f) 1,070 (m)	20 min	
Semiconductor manufacturing - Fab worker	Central Tendency	0.05	445 (f) 535 (m)	6	74 (f) 88 (m)
	High-End	0.025	890 (f) 1,070 (m)	12	
	What-if (task duration-based)	0.05	445 (f) 535 (m)	10.5	
	What-if (task duration-based)	0.025	890 (f) 1,070 (m)	10.5	
Semiconductor manufacturing - Maintenance	Central Tendency	0.50	445 (f) 535 (m)	6	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	12	
	What-if (task duration-based)	0.50	445 (f) 535 (m)	7 min	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	11	

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Semiconductor manufacturing - Virgin NMP truck unloading	Central Tendency	1	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	1	445 (f) 535 (m)	2	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	2	
Semiconductor manufacturing - Waste truck loading	Central Tendency	0.92	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.92	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.92	445 (f) 535 (m)	2	
	What-if (task duration-based)	0.92	890 (f) 1,070 (m)	2	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-41.

The numeric parameters corresponding to the characterizations presented in Table 2-41 are summarized in Table 2-42. These are the PBPK model inputs determined by EPA. In addition to the PBPK inputs determined by EPA in Table 2-63, EPA also modeled PBPK input parameters that were proposed by the SIA in a public comment (Semiconductor Industry Association, 2020). The SIA proposed PBPK inputs are presented in Table 2-43.

Table 2-41. Characterization of PBPK Model Input Parameters for Semiconductor Manufacturing

Scenario	Work Activity	Air Concentration Data Characterization [a]	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	All activities	Central Tendency (50^{th} percentile)	Mid-point of shift duration (6 or 4 hours)	1-hand	Central Tendency
High-end	All activities	High-end (95^{th} percentile)	High-end of shift duration (8 or 12 hours)	2-hand	High-end

Scenario	Work Activity	Air Concentration Data Characterization [a]	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
What-if (task duration-based)	All activities	Central Tendency (50th percentile)	Task-based duration	1-hand	Central Tendency
What-if (task duration-based)	All activities	High-end (95th percentile)	Task-based duration	2-hand	High-end

[a] Only a single estimate was reasonably available for virgin NMP truck unloading and waste truck loading. This single air concentration value was used with both central tendency and high-end duration and dermal parameters.

Table 2-42. PBPK Model Input Parameters for Semiconductor Manufacturing

Work Activity	Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Semiconductor manufacturing - Container handling, small containers	Central Tendency	0.507	6	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	High-end	0.608	12	890 (f) 1,070 (m)	0.75	74 (f) 88 (m)
	What-if (task duration-based)	0.507	5 min	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	What-if (task duration-based)	0.608	1	890 (f) 1,070 (m)	0.75	74 (f) 88 (m)
Semiconductor manufacturing - Container handling, drums	Central Tendency	0.013	6	445 (f) 535 (m)	0.5	74 (f) 88 (m)
	High-end	1.54	12	890 (f) 1,070 (m)	0.75	74 (f) 88 (m)
	What-if (task duration-based)	0.013	2 min	445 (f) 535 (m)	0.5	74 (f) 88 (m)
	What-if (task duration-based)	1.54	20 min	890 (f) 1,070 (m)	0.75	74 (f) 88 (m)
Semiconductor manufacturing - Fab Worker	Central Tendency	0.138	6	445 (f) 535 (m)	0.025	74 (f) 88 (m)
	High-end	0.405	12	890 (f)	0.05	74 (f)

Work Activity	Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
				1,070 (m)		88 (m)
	What-if (task duration-based)	0.138	10.5	445 (f) 535 (m)	0.025	74 (f) 88 (m)
	What-if (task duration-based)	0.405	10.5	890 (f) 1,070 (m)	0.05	74 (f) 88 (m)
Semiconductor manufacturing - Maintenance	Central Tendency	0.020	6	445 (f) 535 (m)	0.50	74 (f) 88 (m)
	High-end	0.690	12	890 (f) 1,070 (m)	1	74 (f) 88 (m)
	What-if (task duration-based)	0.020	7 min	445 (f) 535 (m)	0.50	74 (f) 88 (m)
	What-if (task duration-based)	0.690	11	890 (f) 1,070 (m)	1	74 (f) 88 (m)
Semiconductor manufacturing - Virgin NMP truck unloading	Inhalation - Single value; Dermal – Central Tendency	9.56	4	445 (f) 535 (m)	1	74 (f) 88 (m)
	Inhalation - Single value; Dermal – High-end	4.78	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)
	What-if (task duration-based)	19.12	2	445 (f) 535 (m)	1	74 (f) 88 (m)
	What-if (task duration-based)	19.12	2	890 (f) 1,070 (m)	1	74 (f) 88 (m)

Work Activity	Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Semiconductor manufacturing - Waste truck loading	Inhalation - Single value; Dermal – Central Tendency	0.709	4	445 (f) 535 (m)	0.92	74 (f) 88 (m)
	Inhalation - Single value; Dermal – High-end	0.709	8	890 (f) 1,070 (m)	0.92	74 (f) 88 (m)
	What-if (task duration-based)	0.709	2	445 (f) 535 (m)	0.92	74 (f) 88 (m)
	What-if (task duration-based)	0.709	2	890 (f) 1,070 (m)	0.92	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Table 2-43. Industry Proposed PBPK Model Input Parameters for Semiconductor Manufacturing (Semiconductor Industry Association, 2020)

Activity	Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Semiconductor manufacturing - Container handling, small containers	Central Tendency	0.511	0.33	20.03 (f) 24.08 (m)	0.6	74 (f) 88 (m)
	High-end	0.613	1	66.75 (f) 80.25 (m)	0.75	74 (f) 88 (m)
Semiconductor manufacturing - Container handling, drums	Central Tendency	0.013	0.33	20.03 (f) 24.08 (m)	0.5	74 (f) 88 (m)
	High-end	1.557	1	66.75 (f) 80.25 (m)	0.75	74 (f) 88 (m)

Activity	Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Semiconductor manufacturing - Fab Worker with Container Changeout	Central Tendency	0.139	0.33	20.03 (f) 24.08 (m)	0.025	74 (f) 88 (m)
	High-end	0.409	1	66.75 (f) 80.25 (m)	0.05	74 (f) 88 (m)
Semiconductor manufacturing – Typical Fab Worker (*e.g.*, ONU)	Central Tendency	0.139	0 [d]	0 [d]	0 [d]	74 (f) 88 (m)
	High-end	0.409	0 [d]	0 [d]	0 [d]	74 (f) 88 (m)
Semiconductor manufacturing - Maintenance	Central Tendency	0.020	0.33	222.5 (f) 267.5 (m)	0.50	74 (f) 88 (m)
	High-end	0.696	1	311.5 (f) 374.5 (m)	1	74 (f) 88 (m)
Semiconductor manufacturing - Virgin NMP truck unloading	Inhalation - Single value; Dermal – Central Tendency	4.822	0.33	66.75 (f) 80.25 (m)	1	74 (f) 88 (m)
	Inhalation - Single value; Dermal – High-end	4.822	1	222.5 (f) 267.5 (m)	1	74 (f) 88 (m)
Semiconductor manufacturing - Waste truck loading	Inhalation - Single value; Dermal – Central Tendency	0.715	0.33	66.75 (f) 80.25 (m)	0.92	74 (f) 88 (m)
	Inhalation - Single value; Dermal – High-end	0.715	1	222.5 (f) 267.5 (m)	0.92	74 (f) 88 (m)

[a] SIA proposed exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

[b] SIA proposed PF = 20 for all occupational exposure scenarios.

[c] EPA assessed a skin surface area exposed of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs (except for the Typical Fab Worker scenario, for which EPA assessed PF = 20 per SIA).

[d] For the Typical Fab Worker scenario, SIA proposed no dermal contact with NMP, corresponding to a duration of liquid contact of 0 hours, 0 cm^2 of skin exposed, and an NMP weight fraction of 0. Because exposure duration is needed for the inhalation exposure estimate, EPA assessed a duration equal to a full shift (12 hours). In addition, to avoid a model error, EPA assessed 0.1 cm^2 for skin surface area exposed.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths
EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from the data provided by SIA (2019c), which has a data quality rating of high. EPA used directly applicable inhalation monitoring data, which is the highest of the approach hierarchy, to estimate worker inhalation exposure during a variety of semiconductor manufacturing tasks. These data have a data quality rating of high.

Primary Limitations
The SIA (2019c) monitoring data were provided as 8-hour or 12-hour TWA values. EPA assumed 8 or 12 hours as the high-end duration of liquid contact and mid-range of 4 or 6 hours as the central tendency duration of liquid contact. The representativeness of the estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The majority of the data points in SIA (2019c) were non-detect for NMP and, for these samples, EPA used the LOD/2 to calculate central tendency and high-end inhalation exposure concentration values (U.S. EPA, 1994). The extent to which the use of LOD/2 accurately represents the actual inhalation concentrations is uncertain. The representativeness of the SIA monitoring data for semiconductor manufacturing toward the true distribution of inhalation concentrations for all worker activities in this occupational exposure scenario is uncertain. The uncertainty in the representativeness of the data may result in either overestimation or underestimation of exposures, depending on the true distribution of inhalation concentrations.

Overall Confidence
Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.11 Printing and Writing

This scenario includes printing and writing with inks containing NMP. For this industrial and commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to inks containing NMP during printing activities. Additionally, EPA assessed dermal exposures to inks containing NMP during writing activities.

While EPA does expect that workers may perform additional activities during this scenario, such as unloading or maintenance activities, EPA expects that printing and writing activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin
EPA used NMP monitoring data for commercial printing (except screen printing) that were identified in OSHA's Chemical Exposure Health Data (CEHD) (OSHA, 2017). These data include six personal breathing zone, partial shift measurements. EPA calculated central tendency (50th percentile) and high-

end exposures (95th percentile) with these data. For the calculations, where non-detect values were included in the dataset, EPA used the LOD divided by two (U.S. EPA, 1994b).

EPA did not find inhalation monitoring data for the use of writing utensils containing NMP. EPA did not assess potential inhalation exposures during the use of NMP-based writing inks based on information indicating these exposures may be negligible from a NICNAS assessment (Australian Government Department of Health, 2016) and the likely outdoor use of the one writing product that was identified (weather-resistant marker).

The monitoring data presented in Table 2-44 represent input parameters used for the PBPK modeling. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides additional details.

Table 2-44. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Printing and Writing

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Printing	Central Tendency (50th percentile)	0.037	0.037 (duration = 50 mins)	OSHA (2017)	High
	High-end (95th percentile)	0.109	0.827 (duration = 50 mins)		
Writing	Not assessed				

ONUs for this scenario include supervisors, managers, and other employees that may be in the printing areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from printing and writing. Since ONUs do not directly handle formulations containing NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

Table 2-45 summarizes the parameters used to assess dermal exposure during printing and writing activities. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from public comments and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The underlying data have a data quality rating of high. Because writing inks are contained within markers and pens, EPA expects the surface area of skin potentially exposed to NMP to be smaller than the surface area of one or two hands. EPA used data from Australian Government Department of Health (2016), which has a data quality rating of medium, for the skin surface area exposed during writing.

Table 2-45. Summary of Parameters for Worker Dermal Exposure to Liquids During Printing and Writing

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Printing	Central Tendency	0.05	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.07	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.05	445 (f) 535 (m)	0.83	
	What-if (task duration-based)	0.07	890 (f) 1,070 (m)	0.83	
Writing	Central Tendency	0.1	1 [b]	0.5	74 (f) 88 (m)
	High-End	0.2	1 [b]	0.5	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] This surface area was assumed for both males and females based on (Australian Government Department of Health, 2016).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-46.

The numeric parameters corresponding to the characterizations presented in Table 2-46 are summarized in Table 2-47. These are the inputs used in the PBPK model.

Table 2-46. Characterization of PBPK Model Input Parameters for Printing and Writing

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed (cm^2)	NMP Weight Fraction Characterization
Central Tendency	Printing	Central tendency (50^{th} percentile)	Half-shift (4 hours)	1-hand	Central Tendency
High-end	Printing	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	High-end
What-if (task duration-based)	Printing	Central tendency (50^{th} percentile)	Duration based on monitoring data (50 mins)	1-hand	Central Tendency
What-if (task duration-based)	Printing	High-end (95^{th} percentile)	Duration based on monitoring data (50 mins)	2-hand	High-end
Central Tendency	Writing	Inhalation exposure not assessed	Based on one contact event	1 cm^2	Central tendency

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed (cm^2)	NMP Weight Fraction Characterization
High-end	Writing	Inhalation exposure not assessed	Based on one contact event	1 cm^2	High-end

Table 2-47. PBPK Model Input Parameters for Printing and Writing

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Printing	0.016	4	445 (f) 535 (m)	0.05	74 (f) 88 (m)
High-end	Printing	0.172	8	890 (f) 1,070 (m)	0.07	74 (f) 88 (m)
What-if (task duration-based)	Printing	0.037	0.83	445 (f) 535 (m)	0.05	74 (f) 88 (m)
What-if (task duration-based)	Printing	0.827	0.83	890 (f) 1,070 (m)	0.07	74 (f) 88 (m)
Central Tendency	Writing	0	0.5	1	0.1	74 (f) 88 (m)
High-end	Writing	0	0.5	1	0.2	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for use of NMP in printing. Only dermal exposure is expected for use of NMP in writing activities. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

For printing activities, EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from a variety of data sources with data quality ratings of high. For writing activities, EPA assessed dermal exposure to 10 to 20% NMP based on one writing product identified in the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017). For worker dermal exposure during writing, EPA determined the skin surface area dermally

exposed to writing ink using a literature source with a data quality rating of high. To estimate worker inhalation exposure during printing, EPA used surrogate monitoring data, which is in the middle of the approach hierarchy. These data include 48 samples and have a data quality rating of high. EPA used durations associated with inhalation monitoring data to estimate duration of inhalation and dermal exposure during printing activities.

Primary Limitations

For writing, EPA did not find reasonably available data on actual duration of liquid contact and assumed a high-end of 8 hours based on the length of a full shift and a central tendency of 4 hours based on the mid-range of a shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed printing and writing activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. For printing, skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. The surrogate monitoring data used to estimate occupational inhalation exposure during printing is from 1983. The extent to which these data are representative of current worker inhalation exposure potential is uncertain. The representativeness of the surrogate monitoring data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.12 Soldering

This scenario includes soldering with solder materials containing NMP. For this industrial and commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to NMP during soldering.

While EPA does expect that workers may perform additional activities during this scenario, such as equipment maintenance activities, EPA expects that soldering presents the largest range of potential exposures.

Inhalation and Vapor-through-Skin

Due to the low NMP content in the one identified soldering production containing NMP (one to 2.5 weight percent NMP), the potential for worker and ONU inhalation exposures is likely small. While the increased temperature during soldering may increase the potential for NMP vapor production, some of the NMP may be combusted in the soldering process, reducing the potential for inhalation exposures.

Due to the lack of data for this occupational exposure scenario, EPA uses a modeled exposure for brush application of products containing NMP as surrogate for soldering. The modeled exposure is from the RIVM *Annex XV Proposal for a Restriction - NMP* report and is presented in Table 2-48 below.

Table 2-48. Summary of Parameters for Soldering

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hour TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Brush Application	Single estimate	4.13	No data	RIVM (2013)	High

ONUs for this scenario include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from soldering. Since ONUs do not directly handle formulations containing NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

Table 2-49 summarizes the parameters used to assess dermal exposure during the use of soldering products containing NMP. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction.

Table 2-49. Summary of Parameters for Worker Dermal Exposure During Soldering

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Soldering	Central Tendency	0.01	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-end	0.025	890 (f) 1,070 (m)	8	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-50.

The numeric parameters corresponding to the characterizations presented in Table 2-50 are summarized in Table 2-51. These are the inputs used in the PBPK model.

Table 2-50. Characterization of PBPK Model Input Parameters for Soldering

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Soldering	Single estimate	Half shift (4 hours)	1-hand	Central Tendency
High-end	Soldering	Single estimate	Full shift (8 hours)	2-hand	High-end

Table 2-51. PBPK Model Input Parameters for Soldering

Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	8.26	4	445 (f) 535 (m)	0.01	74 (f) 88 (m)
High-end	4.13	8	890 (f) 1,070 (m)	0.025	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed worker dermal exposure to 1 – 2.5% NMP based on one soldering product identified in the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017).

Primary Limitations

EPA did not find inhalation monitoring data specific to this use and used modeled data for the bush application of a substance containing NMP as surrogate. The representativeness of this modeled data towards this use is uncertain. EPA did not find reasonably available data on actual duration of liquid contact and assumed a high-end of 8 hours based on the length of a full shift and a central tendency of 4 hours based on the mid-range of a shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is low to medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.13 Commercial Automotive Servicing

This scenario includes automotive servicing with products containing NMP. For this commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to products containing NMP during aerosol degreasing of automotive brakes.

While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that aerosol degreasing activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin

EPA did not find monitoring data for the use of NMP products during automotive servicing. Because EPA did not find relevant monitoring data for this use in the published literature, modeling estimates were used to assess exposure for this use, as described below.

In lieu of monitoring data, EPA modeled potential occupational inhalation exposures for workers using EPA's model for Occupational Exposures during Aerosol Degreasing of Automotive Brakes. The *Occupational Exposures during Aerosol Degreasing of Automotive Brakes Model* involves probabilistic modeling. This model uses a near-field/far-field approach, where an aerosol application located inside the near-field generates a mist of droplets, and indoor air movements lead to the convection of the droplets between the near-field and far-field. Workers are assumed to be exposed to NMP droplet concentrations in the near-field, while ONUs are exposed at concentrations in the far-field. ONUs for this scenario include supervisors, managers, and other mechanics that may be in the automotive servicing areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. Consistent with the approach for other OESs, EPA uses the central tendency worker air concentration to evaluate ONU exposure and further refines this estimate using far-field modeling or applicable area monitoring data if the ONU MOE was below the benchmark MOE. Refinement was not necessary for this OES since the ONU MOE was above the benchmark MOE. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) includes background information on this model, including model results and EPA's rationale for using it.

Table 2-52. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Commercial Automotive Servicing

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Aerosol Degreasing	Central Tendency (50th percentile)	6.39	19.96 (duration = 1 hr)	*Occupational Exposures during Aerosol Degreasing of Automotive Brakes Model*	N/A[a]
	High-end (95th percentile)	43.4	128.8 (duration = 1 hr)		

[a] EPA models are standard sources used by EPA for occupational exposure assessments. EPA did not systematically review models that were developed by EPA.
N/A = not applicable

Dermal

Table 2-53 summarizes the parameters used to assess dermal exposure during cleaning activities. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from public comments and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The underlying data have a data quality rating of high.

Table 2-53. Summary of Parameters for Worker Dermal Exposure to Liquids During Commercial Automotive Servicing

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Commercial Automotive Servicing	Central Tendency	0.025	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-end	0.33	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.025	445 (f) 535 (m)	1	
	What-if (task duration-based)	0.33	890 (f) 1,070 (m)	1	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-54. The numeric parameters corresponding to the characterizations presented in Table 2-54 are summarized in Table 2-55. These are the inputs used in the PBPK model.

Table 2-54. Characterization of PBPK Model Input Parameters for Commercial Automotive Servicing

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Aerosol degreasing	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	Central Tendency
High-end	Aerosol degreasing	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	High-end
What-if (task duration-based)	Aerosol degreasing	Central Tendency (50^{th} percentile)	Based on time for one job	1-hand	Central Tendency
What-if (task duration-based)	Aerosol degreasing	High-end (95^{th} percentile)	Based on time for one job	2-hand	High-end

Table 2-55. PBPK Model Input Parameters for Commercial Automotive Servicing

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Aerosol degreasing	12.78	4	445 (f) 535 (m)	0.025	74 (f) 88 (m)
High-end	Aerosol degreasing	43.4	8	890 (f) 1,070 (m)	0.33	74 (f) 88 (m)
What-if (task duration-based)	Aerosol degreasing	19.96	1	445 (f) 535 (m)	0.025	74 (f) 88 (m)
What-if (task duration-based)	Aerosol degreasing	128.8	1	890 (f) 1,070 (m)	0.33	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from a variety of data sources with data quality ratings of high. Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic, as the duration is based on the length of time to conduct aerosol degreasing of automotive brakes.

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the aerosol brake degreasing activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. For the modeling of NMP air concentrations, EPA used aerosol product use rate and application frequency from one literature source (CARB, 2000) on brake servicing. The extent to which this is representative of other aerosol degreasing applications involving NMP is uncertain. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.14 Laboratory Use

This scenario includes the use of NMP in a laboratory setting. For this industrial and commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to 100% NMP during laboratory activities.

While EPA does expect that workers may perform additional activities during this scenario, such as unloading, EPA expects that laboratory use activities present the largest range of potential exposures.

Inhalation and Vapor-Through-Skin

EPA only found one data source that had inhalation monitoring data, representing the preparation of NMP for use in samples, sample preparation involving the dissolving of solids in NMP, and sample analysis. These data were used as input into the PBPK model for a what-if task duration of 2-hours. EPA did not find additional monitoring data, thus used a modeled exposure for the use of NMP in a laboratory setting for the full-shift concentrations. As the quality of both the monitoring and modeled data is acceptable, EPA used all reasonably available data to assess this occupational exposure scenario.

The monitoring data and modeled exposure summarized in Table 2-56 are the input parameters used for the PBPK modeling. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-*

Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment (U.S. EPA, 2020f) provides additional details.

Table 2-56. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Laboratory Use

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Laboratory Use	Central Tendency (unknown statistical characterization)	2.07	0.200 (duration = 2 hr)	Solomon et al. (1996)	Medium
	High-end (unknown statistical characterization)	4.13	No data	RIVM (2013)	High

ONUs for this scenario include supervisors, managers, and other employees that may be in the laboratory but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from laboratory use of NMP. Since ONUs do not directly handle NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

Table 2-57 summarizes the parameters used to assess dermal exposure during use of NMP in laboratories. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. Because NMP is used as a carrier chemical, EPA expects that NMP may be used in pure form (*i.e.*, 100 percent NMP).

Table 2-57. Summary of Parameters for Worker Dermal Exposure During Laboratory Use

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Laboratory Use	Central Tendency	1	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-end	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	1	445 (f) 535 (m)	2	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	2	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-58.

The numeric parameters corresponding to the characterizations presented in Table 2-58 are summarized in Table 2-59. These are the inputs used in the PBPK model.

Table 2-58. Characterization of PBPK Model Input Parameters by Laboratory Use

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Laboratory activities	Central Tendency (unknown statistical characterization)	Half shift (4 hours)	1-hand	N/A - 100% is assumed
High-end	Laboratory activities	High-end (unknown statistical characterization)	Full shift (8 hours)	2-hand	N/A - 100% is assumed
What-if (task duration-based)	Laboratory activities	Single estimate	Based on 2-hour TWA data	1-hand	N/A - 100% is assumed
What-if (task duration-based)	Laboratory activities	Single estimate	Based on 2-hour TWA data	2-hand	N/A - 100% is assumed

N/A = not applicable because a weight fraction distribution is not known for this OES, and therefore pure NMP is assumed for these scenarios and work activities.

Table 2-59. PBPK Model Input Parameters for Laboratory Use

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Laboratory activities	0.10	4	445 (f) 535 (m)	1	74 (f) 88 (m)
High-end	Laboratory activities	4.13	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Laboratory activities	0.20	2	445 (f) 535 (m)	1	74 (f) 88 (m)
What-if (task duration-based)	Laboratory activities	0.20	2	890 (f) 1,070 (m)	1	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed occupational inhalation exposure using directly applicable personal monitoring data, which is the highest of the approach hierarchy, from one source with a data quality rating of medium. EPA also used a modeled inhalation exposure concentration value, which is in the middle of the approach hierarchy, from RIVM (2013). This data has a data quality rating of high. EPA determined central tendency exposure duration from the inhalation monitoring data. EPA expects the central tendency duration of inhalation and dermal exposure to be realistic, as the duration is task-based.

Primary Limitations

EPA assumed a high-end duration of liquid contact of 8 hours based on the length of a full shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. EPA did not find NMP concentration data and assumed workers may be exposed to up to 100% NMP since NMP is a carrier chemical, and carrier chemical concentrations may

be very high. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The monitoring data used for central tendency worker inhalation exposure is only one data point from a 1996 industrial hygiene report. The extent to which these data are representative of current worker inhalation exposure potential is uncertain. The modeled high-end inhalation exposure concentration was obtained from RIVM (2013) and not generated by EPA. The representativeness of the monitoring data and modeled exposure toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.15 Lithium Ion Cell Manufacturing

This scenario includes the use of NMP in lithium ion cell manufacturing. For this industrial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to NMP from the following occupation exposure scenarios (LICM, 2020a):

- Container handling, small containers;
- Container handling, drums;
- Cathode coating;
- Cathode mixing;
- Research and development;
- Miscellaneous

While operations for lithium ion cell manufacturing may vary, EPA expects these activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin

EPA used data provided by the Lithium Ion Cell Manufacturers' Coalition (LICM, 2020a). These data include 8-hour TWA personal breathing zone monitoring data for NMP during cathode coating, cathode mixing, research and development, and miscellaneous activities (*e.g.*, mix room, maintenance, and cleaning). Information from the Lithium Ion Cell Manufacturers' Coalition and EaglePicher also indicate that NMP may be unloaded from small containers and drums and that waste NMP may be loaded into drums (EaglePicher Technologies, 2020b; LICM, 2020b); therefore, EPA assessed occupational exposure scenarios for both small containers handling and drum handling. No monitoring data for small container handling or drum handling were reasonably available for the lithium ion cell manufacturing industry. EPA used monitoring data for these occupational exposure scenarios for semiconductor manufacturing, as described in Section 2.4.1.2.10. These data were summarized into the PBPK modeling full-shift input parameters in Table 2-60. Where non-detect measurements exist in a

dataset, EPA used the LOD divided by two for central tendency and high-end calculations (U.S. EPA, 1994b).

Table 2-60. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Lithium Ion Cell Manufacturing

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8- or 12-hour TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Lithium ion cell manufacturing – Container handling, small containers	Central Tendency (50^{th} percentile)	0.507	No data	Semiconductor Industry Association (2019b)	High
	High-end (95^{th} percentile)	0.608	No data		
Lithium ion cell manufacturing – Container handling, drums	Central Tendency (50^{th} percentile)	0.013	No data		
	High-end (95^{th} percentile)	1.54	No data		
Lithium ion cell manufacturing - Cathode coating	Central Tendency (50^{th} percentile)	4.87 [a]	No data	LICM (2020a)	High
	High-end (maximum)	39.7 [a]	No data		
Lithium ion cell manufacturing - Cathode mixing	Central Tendency (50^{th} percentile)	2.19 [a]	No data		
	High-end (95^{th} percentile)	9.61 [a]	No data		
Lithium ion cell manufacturing – Research and development	Central Tendency (50^{th} percentile)	0.373 [a]	No data		
	High-end (maximum)	4.05 [a]	No data		
Lithium ion cell manufacturing – Miscellaneous additional activities	Central Tendency (50^{th} percentile)	6.08 [a]	No data		
	High-end (maximum)	7.30 [a]	No data		

[a] These are 8-hour TWA values.

ONUs for this scenario include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures. Since ONUs do not directly handle formulations containing NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures.

Information on processes and worker activities is insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified using modeling.

Dermal

Table 2-61 summarizes the parameters used to assess dermal exposure during use of NMP in lithium ion cell manufacturing. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from the Lithium Ion Cell Manufacturers' Coalition and EaglePicher (EaglePicher Technologies, 2020b; LICM, 2020c), public comments, literature, and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The weight fraction data has a data quality rating of high. Public comments indicate that workers always wear PPE, including gloves specifically designed to protect against NMP exposure Saft, (EaglePicher Technologies, 2020a; LICM, 2020a, c; 2017). Public comments also indicated that employees receive training on PPE usage, which is supplemented with signage in the workplace and dedicated areas to don and doff PPE (EaglePicher Technologies, 2020a; LICM, 2020c).

Table 2-61. Summary of Parameters for Worker Dermal Exposure During Lithium Ion Cell Manufacturing

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Lithium ion cell manufacturing – Container handling, small containers	Central Tendency	0.99	445 (f) 535 (m)	6	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	12	
	What-if (task duration-based)	0.99	445 (f) 535 (m)	0.5	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	1	
Lithium ion cell manufacturing – Container handling, drums	Central Tendency	0.6	445 (f) 535 (m)	6	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	12	
	What-if (task duration-based)	0.6	445 (f) 535 (m)	0.5	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	1	
Lithium ion cell manufacturing - Cathode coating	Central Tendency	0.6	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.6	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.6	445 (f) 535 (m)	2	

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
	What-if (task duration-based)	0.6	890 (f) 1,070 (m)	6	
Lithium ion cell manufacturing - Cathode slurry mixing	Central Tendency	0.6	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.6	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.6	445 (f) 535 (m)	0.5	
	What-if (task duration-based)	0.6	890 (f) 1,070 (m)	0.5	
Lithium ion cell manufacturing – Research and development	Central Tendency	0.6	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.6	445 (f) 535 (m)	2.5	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	2.5	
Lithium ion cell manufacturing – Miscellaneous additional activities	Central Tendency	0.6	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	1	890 (f) 1,070 (m)	8	
	What-if (task duration-based)	0.6	445 (f) 535 (m)	1	
	What-if (task duration-based)	1	890 (f) 1,070 (m)	4	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-62. The numeric parameters corresponding to the characterizations presented in Table 2-62 are summarized in Table 2-63. These are the PBPK model inputs determined by EPA.

Table 2-62. Characterization of PBPK Model Input Parameters for Lithium Ion Cell Manufacturing

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	All activities	Central Tendency (50^{th} percentile)	Mid-point of shift duration (6 or 4 hours)	1-hand	Central Tendency
High-end	All activities	High-end (95^{th} percentile)	High-end of shift duration (8 or 12 hours)	2-hand	High-end
What-if (task duration-based)	All activities	Central Tendency (50^{th} percentile)	Task-based duration	1-hand	Central Tendency
What-if (task duration-based)	All activities	High-end (95^{th} percentile)	Task-based duration	2-hand	High-end

Table 2-63. PBPK Model Input Parameters for Lithium Ion Cell Manufacturing

Work Activity	Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Lithium ion cell manufacturing – Container handling, small containers	Central Tendency	0.507	6	445 (f) 535 (m)	0.99	74 (f)
	High-end	0.608	12	890 (f) 1,070 (m)	1	88 (m)
	What-if (task duration-based)	0.507	0.5	445 (f) 535 (m)	0.99	74 (f)
	What-if (task duration-based)	0.608	1	890 (f) 1,070 (m)	1	88 (m)
Lithium ion cell manufacturing – Container handling, drums	Central Tendency	0.013	6	445 (f) 535 (m)	0.6	74 (f)
	High-end	1.54	12	890 (f) 1,070 (m)	1	88 (m)
	What-if (task duration-based)	0.013	0.5	445 (f) 535 (m)	0.6	74 (f)

Work Activity	Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
	What-if (task duration-based)	1.54	1	890 (f) 1,070 (m)	1	88 (m)
Lithium ion cell manufacturing - Cathode coating	Central Tendency	9.74	4	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	High-end	39.7	8	890 (f) 1,070 (m)	0.6	74 (f) 88 (m)
	What-if (task duration-based)	23.4	2	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	What-if (task duration-based)	191	6	890 (f) 1,070 (m)	0.6	74 (f) 88 (m)
Lithium ion cell manufacturing - Cathode slurry mixing	Central Tendency	4.38	4	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	High-end	9.61	8	890 (f) 1,070 (m)	0.6	74 (f) 88 (m)
	What-if (task duration-based)	10.5	0.5	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	What-if (task duration-based)	46.1	0.5	890 (f) 1,070 (m)	0.6	74 (f) 88 (m)
Lithium ion cell manufacturing – Research and development	Central Tendency	0.746	4	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	High-end	4.05	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)
	What-if (task duration-based)	1.79	2.5	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	What-if (task duration-based)	19.4	2.5	890 (f) 1,070 (m)	1	74 (f) 88 (m)

Work Activity	Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Lithium ion cell manufacturing – Miscellaneous additional activities	Central Tendency	12.2	4	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	High-end	7.30	8	890 (f) 1,070 (m)	1	74 (f) 88 (m)
	What-if (task duration-based)	29.2	1	445 (f) 535 (m)	0.6	74 (f) 88 (m)
	What-if (task duration-based)	35.0	4	890 (f) 1,070 (m)	1	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from the data provided by Lithium Ion Cell Manufacturers' Coalition (LICM, 2020a) which has a data quality rating of high. EPA used directly applicable inhalation monitoring data, which is the highest of the approach hierarchy, to estimate worker inhalation exposure during a variety of lithium ion cell manufacturing tasks. These data have a data quality rating of high.

Primary Limitations

The Lithium Ion Cell Manufacturers' Coalition (LICM, 2020a) monitoring data were provided as 8-hour or 12-hour TWA values. EPA assumed 8 or 12 hours as the high-end duration of liquid contact and mid-range of 4 or 6 hours as the central tendency duration of liquid contact. The representativeness of the estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario beyond semiconductor manufacturing is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The representativeness of the monitoring data for lithium ion cell manufacturing toward the true distribution of inhalation concentrations for all worker activities in this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.16 Cleaning

This scenario includes the use of cleaning products containing NMP. For this industrial and commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to cleaning products containing NMP from the following activities:

- Dip cleaning / degreasing; and
- Spray / wipe cleaning.

While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that cleaning activities present the largest range of potential exposures.

Inhalation and Vapor-through-Skin

EPA compiled inhalation monitoring data and modeled exposure concentration data for NMP-based cleaning activities from published literature and used these data for the central tendency and high-end (for full-shift) worker exposure concentrations presented in Table 2-64. EPA used the reasonably available monitoring data for NMP use in cleaning that had the highest quality rating to assess exposure via this use. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides additional details.

Table 2-64. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Cleaning

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Dip Cleaning / Degreasing	Central Tendency (50^{th} percentile)	0.57	No data	RIVM (2013); IFA (2010); Nishimura et al. (2009); Bader et al. (2006); Xiaofei et al. (2000)	Medium to high
	High-end (95^{th} percentile)	2.68	No data		
Spray / Wipe Cleaning	Central Tendency (50^{th} percentile)	0.49	No data	OSHA (2017); RIVM (2013); IFA (2010); Nishimura et al. (2009); Bader et al. (2006)	Medium to high
	High-end (95^{th} percentile)	2.70	No data		

ONUs for this scenario include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in the same level of exposures as those workers that engage in tasks related to the use of NMP. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from cleaning with formulations containing NMP. Since ONUs do not directly handle formulations containing NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

Table 2-65 summarizes the parameters used to assess dermal exposure during cleaning activities. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from public comments, literature sources, and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The underlying data have data quality ratings ranging from medium to high.

Table 2-65. Summary of Parameters for Worker Dermal Exposure to Liquids During Cleaning

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Dip Cleaning and Degreasing	Central Tendency	0.845	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.999	890 (f) 1,070 (m)	8	
Spray/Wipe Cleaning	Central Tendency	0.313	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.989	890 (f) 1,070 (m)	8	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-66. The numeric parameters corresponding to the characterizations presented in Table 2-66 are summarized in Table 2-67. These are the inputs used in the PBPK model.

Table 2-66. Characterization of PBPK Model Input Parameters for Cleaning

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Dip cleaning	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	Central Tendency
High-end	Dip cleaning	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	High-end
Central Tendency	Spray / wipe cleaning	Central Tendency (50^{th} percentile)	Half shift (4 hours)	1-hand	Central Tendency
High-end	Spray / wipe cleaning	High-end (95^{th} percentile)	Full shift (8 hours)	2-hand	High-end

Table 2-67. PBPK Model Input Parameters for Cleaning

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Dip cleaning	1.14	4	445 (f) 535 (m)	0.845	74 (f) 88 (m)
High-end	Dip cleaning	2.68	8	890 (f) 1,070 (m)	0.999	74 (f) 88 (m)

Scenario	Work Activity	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	Spray / wipe cleaning	0.98	4	445 (f) 535 (m)	0.313	74 (f) 88 (m)
High-end	Spray / wipe cleaning	2.70	8	890 (f) 1,070 (m)	0.989	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50^{th} and 95^{th} percentiles, respectively, from a variety of data sources with data quality ratings ranging from medium to high. To estimate inhalation exposure during dip cleaning, EPA used directly applicable monitoring data, which is in the highest of the approach hierarchy, including data from 5 sources. These data have data quality ratings ranging from medium to high. To estimate inhalation exposure during spray / wipe application, EPA used directly applicable monitoring data, which is in the highest of the approach hierarchy, including data from 4 sources. These data have data quality ratings ranging from medium to high.

Primary Limitations

EPA did not find reasonably available data on actual duration of liquid contact and assumed a high-end of 8 hours based on the length of a full shift and a central tendency of 4 hours based on the mid-range of a shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed cleaning activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The worker activities associated with the monitoring data used to assess inhalation exposure during dip cleaning and spray/wipe cleaning were not detailed for all samples. Where EPA could not determine the type of cleaning activities associated with a data point, EPA used the data in the estimates for both dip and spray/wipe cleaning. For both occupational exposure scenarios, the representativeness of the

monitoring data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence
Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.2.17 Fertilizer Application

This scenario includes the use of fertilizers containing NMP. For this commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to NMP during application of fertilizers.

While EPA does expect that workers may perform additional activities during this scenario, such as unloading or maintenance activities, EPA expects that fertilizer application presents the largest range of potential exposures.

Inhalation and Vapor-through-Skin
EPA did not find inhalation monitoring data for the application of fertilizers containing NMP. EPA found modeled inhalation exposures during spray and fog application of agrochemicals (RIVM, 2013). EPA uses the modeled exposures to assess potential inhalation exposures during this life cycle stage. These data have a data quality rating of high.

The input parameters used for the PBPK modeling based on the modeled exposures are summarized in Table 2-68. EPA did not model data on short-term inhalation exposures during the application of fertilizers containing. The supplemental document *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f) provides additional details.

Table 2-68. Summary of Parameters for PBPK Modeling of Worker Inhalation Exposure During Fertilizer Application

Work Activity	Parameter Characterization	Full-Shift NMP Air Concentration (mg/m^3, 8-hr TWA)	Duration-Based NMP Air Concentration (mg/m^3)	Source	Data Quality Rating
Manual spray or boom application of fertilizers	Low-end (of range)	2.97	No data	RIVM (2013)	High
	High-end (of range)	5.27	No data		

ONUs for this scenario include farm managers and other farmers that may be near the fields that are receiving fertilizer application, but do not perform tasks that result in the same level of exposures as

those workers that apply fertilizer containing NMP. EPA has not identified personal or area data on or parameters for modeling potential ONU inhalation exposures from application of fertilizers containing NMP. Since ONUs do not directly handle formulations containing NMP, ONU inhalation exposures are expected to be lower than worker inhalation exposures. Information on activities where ONUs may be present are insufficient to determine the proximity of ONUs to workers and sources of emissions, so relative exposure of ONUs to workers cannot be quantified.

Dermal

Table 2-69 summarizes the parameters used to assess dermal exposure during the use of agricultural products containing NMP. Most of these parameters were determined based on assumptions described in Section 2.4.1.1. EPA used data from literature, public comments, and the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017) to determine the NMP weight fraction. The underlying data have a data quality rating of high.

Table 2-69. Summary of Parameters for Worker Dermal Exposure During Fertilizer Application

Work Activity	Parameter Characterization	NMP Weight Fraction	Skin Surface Area Exposed [a]	Duration of Liquid Contact	Body Weight [a]
		Unitless	cm^2	hr/day	kg
Manual spray or boom application of fertilizers	Central Tendency	0.001	445 (f) 535 (m)	4	74 (f) 88 (m)
	High-End	0.07	890 (f) 1,070 (m)	8	

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

PBPK Inputs

EPA assessed PBPK parameters for central tendency and high-end exposure scenarios based on the characterizations listed in Table 2-70. The numeric parameters corresponding to the characterizations presented in Table 2-70 are summarized in Table 2-71. These are the inputs used in the PBPK model.

Table 2-70. Characterization of PBPK Model Input Parameters for Fertilizer Application

Scenario	Work Activity	Air Concentration Data Characterization	Duration of Liquid Contact	Skin Surface Area Exposed	NMP Weight Fraction Characterization
Central Tendency	Manual spray or boom application	Low-end (of range)	Half shift (4 hours)	1-hand	Central Tendency
High-end	Manual spray or boom application	High-end (of range)	Full shift (8 hours)	2-hand	High-end

Table 2-71. PBPK Model Input Parameters for Fertilizer Application

Scenario	Duration-Based NMP Air Concentration (mg/m^3)	Duration of Liquid Contact (hr)	Skin Surface Area Exposed (cm^2) [a,b,c]	NMP Weight Fraction	Body Weight (kg) [a]
Central Tendency	5.94	4	445 (f) 535 (m)	0.001	74 (f) 88 (m)
High-end	5.27	8	890 (f) 1,070 (m)	0.07	74 (f) 88 (m)

[a] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).
[b] EPA modeled all glove protection factors (*e.g.*, 1, 5, 10, and 20) for workers in Section 4.2.2.
[c] EPA assessed a skin surface area exposed to liquid NMP of 0.1 cm^2 for ONUs for each scenario. However, EPA did not assess glove usage (protection factor = 1) for ONUs.

Summary

In summary, dermal and inhalation exposures are expected for this use. EPA has not identified additional uncertainties for this use beyond those included in Section 2.4.1.4. EPA identified primary strengths and limitations and assigned an overall confidence to the occupational exposure scenario inputs to the PBPK model, as discussed below. EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence. Note that the effects of the limitations on this assessment are discussed in Section 2.4.1.4.

Primary Strengths

EPA assessed dermal exposure to 0.1 to 7% NMP, based on data from public comments and literature, which have data quality ratings of high. EPA assessed occupational inhalation exposure during fertilizer application using a modeled inhalation exposure concentration value, which is in the middle of the approach hierarchy, from RIVM (2013). This data has a data quality rating of high.

Primary Limitations

EPA did not find reasonably available data on actual duration of liquid contact and assumed a high-end of 8 hours based on the length of a full shift and a central tendency of 4 hours based on the mid-range of a shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. The modeled inhalation exposure concentration was obtained from RIVM (2013) and not generated by EPA. The representativeness of the modeled exposure toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be

quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

2.4.1.3 Summary of Occupational Exposure Assessment

Table 2-72 shows the occupational dermal and inhalation exposure parameters used in the PBPK modeling for this assessment. The skin surface area and body weight dermal parameters were specific to PESS of interest: adolescent and adult males, pregnant women, and females (adolescent and adult) of childbearing age who may become pregnant. For each Occupational Exposure Scenario, a central scenario and a higher-end scenario are provided. Table 2-73 shows the results of the PBPK modeling. Table 2-72 shows the inputs and Table 2-73 shows the PBPK exposure results using a PF of 1, the most protective assumption, and using PF 5, 10, and 20 to determine how protective glove use could impact exposures. PKPK exposure results include acute exposures, which are peak blood concentrations (C_{max} in mg/L), and chronic exposures, which are area under the curve (AUC in hr mg/L). The full range of this modeling is presented in the spreadsheet Supplemental File on Occupational Risk Calculations.

Table 2-72. Parameter Inputs to PBPK for Central and High-End Scenarios by Use [a]

Use Scenario	Scenario Characterization	Sub-scenario	Weight Fraction in Formulation	Surface Area exposed to liquid (cm^2) [b]	Liquid Contact duration (hr)	Duration-based Air Conc. (mg/m^3)
Section 2.4.1.2.1 Manufacturing	Central Tendency	Bulk container loading	1	445 (f) 535 (m)	4	0.10
	High-end	Drum loading	1	890 (f) 1,070 (m)	8	1.51
	What-if (task duration-based)	Bulk container loading	1	445 (f) 535 (m)	0.5	0.76
	What-if (task duration-based)	Drum loading	1	890 (f) 1,070 (m)	2.06	5.85
Section 2.4.1.2.2 Repackaging	Central Tendency	Bulk container loading	1	445 (f) 535 (m)	4	0.10
	High-end	Drum loading	1	890 (f) 1,070 (m)	8	1.51
	What-if (task duration-based)	Bulk container loading	1	445 (f) 535 (m)	0.5	0.76
	What-if (task duration-based)	Drum loading	1	890 (f) 1,070 (m)	2.06	5.85
Section 2.4.1.2.3 Chemical Processing, Excluding Formulation	Central Tendency	Drum unloading	1	445 (f) 535 (m)	4	0.15
	High-end	Drum unloading	1	890 (f) 1,070 (m)	8	0.26
	What-if (task duration-based)	Drum unloading	1	445 (f) 535 (m)	0.36	1.65
	What-if (task duration-based)	Drum unloading	1	890 (f) 1,070 (m)	0.36	5.85
Section 2.4.1.2.4 Incorporation into Formulation,	Central Tendency	Drum unloading	1	445 (f) 535 (m)	4	0.15
	High-end	Drum unloading	1	890 (f) 1,070 (m)	8	0.26

Use Scenario	Scenario Characterization	Sub-scenario	Weight Fraction in Formulation	Surface Area exposed to liquid (cm^2) [b]	Liquid Contact duration (hr)	Duration-based Air Conc. (mg/m^3)
Mixture, or Reaction Product	What-if (task duration-based)	Drum unloading	1	445 (f) 535 (m)	0.36	1.65
	What-if (task duration-based)	Drum unloading	1	890 (f) 1,070 (m)	0.36	5.85
	Central Tendency	Maintenance, analytical, loading	0.31	445 (f) 535 (m)	4	0.69
	High-end	Maintenance, analytical, loading	0.99	890 (f) 1,070 (m)	8	6.28
Section 2.4.1.2.5 Metal Finishing	Central Tendency	Spray application	0.6	445 (f) 535 (m)	4	0.53
	High-end	Spray application	0.9	890 (f) 1,070 (m)	8	4.51
	Central Tendency	Dip application	0.6	445 (f) 535 (m)	4	1.98
	High-end	Dip application	0.9	890 (f) 1,070 (m)	8	2.75
	Central Tendency	Brush application	0.6	445 (f) 535 (m)	4	8.26
	High-end	Brush application	0.9	890 (f) 1,070 (m)	8	4.13
Section 2.4.1.2.6 Application of Paints, Coatings, Adhesives and Sealants	Central Tendency	Spray application	0.02	445 (f) 535 (m)	4	0.53
	High-end	Spray application	0.534	890 (f) 1,070 (m)	8	4.51
	Central Tendency	Roll/curtain application	0.02	445 (f) 535 (m)	4	0.06
	High-end	Roll/curtain application	0.534	890 (f) 1,070 (m)	8	0.19
	Central Tendency	Dip application	0.02	445 (f) 535 (m)	4	1.98
	High-end	Dip application	0.534	890 (f) 1,070 (m)	8	2.75
	Central Tendency	Brush application	0.02	445 (f) 535 (m)	4	8.26
	High-end	Brush application	0.534	890 (f) 1,070 (m)	8	4.13
Section 2.4.1.2.7	Central Tendency	Bulk container unloading	0.92	445 (f) 535 (m)	4	0.10

Use Scenario	Scenario Characterization	Sub-scenario	Weight Fraction in Formulation	Surface Area exposed to liquid (cm^2) [b]	Liquid Contact duration (hr)	Duration-based Air Conc. (mg/m^3)
Recycling and Disposal	High-end	Drum unloading	1	890 (f) 1,070 (m)	8	0.44
	What-if (task duration-based)	Bulk container unloading	0.92	445 (f) 535 (m)	0.5	0.76
	What-if (task duration-based)	Drum unloading	1	890 (f) 1,070 (m)	0.603	5.85
Section 2.4.1.2.8 Removal of Paints, Coatings, Adhesives and Sealants	Central Tendency	Miscellaneous removal	0.305	445 (f) 535 (m)	4	65
	High-end	Miscellaneous removal	0.695	890 (f) 1,070 (m)	8	64
	What-if (task duration-based)	Miscellaneous removal	0.305	445 (f) 535 (m)	1	13.2
	What-if (task duration-based)	Miscellaneous removal	0.695	890 (f) 1,070 (m)	1	280
	Central Tendency	Graffiti removal	0.5	445 (f) 535 (m)	4	2.02
	High-end	Graffiti removal	0.613	890 (f) 1,070 (m)	8	4.52
Section 2.4.1.2.9 Other Electronics Manufacturing	Central Tendency	Capacitor, Resistor, Coil, Transformer, and Other Inductor Mfg	0.6	445 (f) 535 (m)	4	5.92
	High-end	Capacitor, Resistor, Coil, Transformer, and Other Inductor Mfg	1	890 (f) 1,070 (m)	8	44.2
Section 2.4.1.2.10 Semiconductor Manufacturing	Central Tendency	Semiconductor manufacturing - Container handling, small containers	0.6	445 (f) 535 (m)	6	0.507
	High-end	Semiconductor manufacturing - Container handling, small containers	0.75	890 (f) 1,070 (m)	12	0.608
	What-if (task duration-based)	Semiconductor manufacturing - Container handling, small containers	0.6	445 (f) 535 (m)	5 min	0.507
	What-if (task duration-based)	Semiconductor manufacturing - Container handling, small containers	0.75	890 (f) 1,070 (m)	1	0.608

Use Scenario	Scenario Characterization	Sub-scenario	Weight Fraction in Formulation	Surface Area exposed to liquid (cm^2) [b]	Liquid Contact duration (hr)	Duration-based Air Conc. (mg/m^3)
	Central Tendency	Semiconductor manufacturing - Container handling, drums	0.5	445 (f) 535 (m)	6	0.013
	High-end	Semiconductor manufacturing - Container handling, drums	0.75	890 (f) 1,070 (m)	12	1.54
	What-if (task duration-based)	Semiconductor manufacturing - Container handling, drums	0.5	445 (f) 535 (m)	2 min	0.013
	What-if (task duration-based)	Semiconductor manufacturing - Container handling, drums	0.75	890 (f) 1,070 (m)	20 min	1.54
	Central Tendency	Semiconductor manufacturing - Fab worker	0.025	445 (f) 535 (m)	6	0.138
	High-end	Semiconductor manufacturing - Fab worker	0.05	890 (f) 1,070 (m)	12	0.405
	What-if (task duration-based)	Semiconductor manufacturing - Fab worker	0.025	445 (f) 535 (m)	10.5	0.138
	What-if (task duration-based)	Semiconductor manufacturing - Fab worker	0.05	890 (f) 1,070 (m)	10.5	0.405
	Central Tendency	Semiconductor manufacturing - Maintenance	0.50	445 (f) 535 (m)	6	0.020
	High-end	Semiconductor manufacturing - Maintenance	1	890 (f) 1,070 (m)	12	0.690
	What-if (task duration-based)	Semiconductor manufacturing - Maintenance	0.50	445 (f) 535 (m)	7 min	0.020
	What-if (task duration-based)	Semiconductor manufacturing - Maintenance	1	890 (f) 1,070 (m)	11	0.690
	Central Tendency	Semiconductor manufacturing - Virgin NMP truck unloading	1	445 (f) 535 (m)	4	9.56
	High-end	Semiconductor manufacturing - Virgin NMP truck unloading	1	890 (f) 1,070 (m)	8	4.78

Use Scenario	Scenario Characterization	Sub-scenario	Weight Fraction in Formulation	Surface Area exposed to liquid (cm^2) [b]	Liquid Contact duration (hr)	Duration-based Air Conc. (mg/m^3)
	What-if (task duration-based)	Semiconductor manufacturing - Virgin NMP truck unloading	1	445 (f) 535 (m)	2	19.12
	What-if (task duration-based)	Semiconductor manufacturing - Virgin NMP truck unloading	1	890 (f) 1,070 (m)	2	19.12
	Central Tendency	Semiconductor manufacturing - Waste truck loading	0.92	445 (f) 535 (m)	4	0.709
	High-end	Semiconductor manufacturing - Waste truck loading	0.92	890 (f) 1,070 (m)	8	0.709
	What-if (task duration-based)	Semiconductor manufacturing - Waste truck loading	0.92	445 (f) 535 (m)	2	0.709
	What-if (task duration-based)	Semiconductor manufacturing - Waste truck loading	0.92	890 (f) 1,070 (m)	2	0.709
Section 2.4.1.2.11 Printing and Writing	Central Tendency	Printing	0.05	445 (f) 535 (m)	4	0.074
	High-end	Printing	0.07	890 (f) 1,070 (m)	8	0.109
	What-if (task duration-based)	Printing	0.05	445 (f) 535 (m)	0.83	0.037
	What-if (task duration-based)	Printing	0.07	890 (f) 1,070 (m)	0.83	0.827
	Central Tendency	Writing	0.1	1	0.5	0
	High-end	Writing	0.2	1	0.5	0
Section 2.4.1.2.12 Soldering	Central Tendency	Soldering	0.01	445 (f) 535 (m)	4	8.26
	High-end	Soldering	0.025	890 (f) 1,070 (m)	8	4.13
Section 2.4.1.2.13 Commercial Automotive Servicing	Central Tendency	Aerosol Degreasing	0.025	445 (f) 535 (m)	4	12.78
	High-end	Aerosol Degreasing	0.33	890 (f) 1,070 (m)	8	43.4
	What-if (task duration-based)	Aerosol Degreasing	0.025	445 (f) 535 (m)	1	19.96
	What-if (task duration-based)	Aerosol Degreasing	0.33	890 (f) 1,070 (m)	1	128.8
	Central Tendency	Laboratory use	1	445 (f)	4	0.10

Use Scenario	Scenario Characterization	Sub-scenario	Weight Fraction in Formulation	Surface Area exposed to liquid (cm^2) [b]	Liquid Contact duration (hr)	Duration-based Air Conc. (mg/m^3)
				535 (m)		
Section 2.4.1.2.14 Laboratory Use	High-end	Laboratory use	1	890 (f) 1,070 (m)	8	4.13
	What-if (task duration-based)	Laboratory use	1	445 (f) 535 (m)	2	0.20
	What-if (task duration-based)	Laboratory use	1	890 (f) 1,070 (m)	2	0.20
Section 2.4.1.2.15 Lithium Ion Cell Manufacturing	Central Tendency	Lithium ion cell manufacturing - Container handling, small containers	0.99	445 (f) 535 (m)	6	0.507
	High-end	Lithium ion cell manufacturing - Container handling, small containers	1	890 (f) 1,070 (m)	12	0.608
	What-if (task duration-based)	Lithium ion cell manufacturing - Container handling, small containers	0.99	445 (f) 535 (m)	0.5	0.507
	What-if (task duration-based)	Lithium ion cell manufacturing - Container handling, small containers	1	890 (f) 1,070 (m)	1	0.608
	Central Tendency	Lithium ion cell manufacturing - Container handling, drums	0.6	445 (f) 535 (m)	6	0.013
	High-end	Lithium ion cell manufacturing - Container handling, drums	1	890 (f) 1,070 (m)	12	1.54
	What-if (task duration-based)	Lithium ion cell manufacturing - Container handling, drums	0.6	445 (f) 535 (m)	0.5	0.013
	What-if (task duration-based)	Lithium ion cell manufacturing - Container handling, drums	1	890 (f) 1,070 (m)	1	1.54
	Central Tendency	Lithium ion cell manufacturing - Cathode coating	0.6	445 (f) 535 (m)	4	9.74

Use Scenario	Scenario Characterization	Sub-scenario	Weight Fraction in Formulation	Surface Area exposed to liquid (cm^2) [b]	Liquid Contact duration (hr)	Duration-based Air Conc. (mg/m^3)
	High-end	Lithium ion cell manufacturing - Cathode coating	0.6	890 (f) 1,070 (m)	8	39.7
	What-if (task duration-based)	Lithium ion cell manufacturing - Cathode coating	0.6	445 (f) 535 (m)	2	23.4
	What-if (task duration-based)	Lithium ion cell manufacturing - Cathode coating	0.6	890 (f) 1,070 (m)	6	191
	Central Tendency	Lithium ion cell manufacturing - Cathode mixing	0.6	445 (f) 535 (m)	4	4.38
	High-end	Lithium ion cell manufacturing - Cathode mixing	0.6	890 (f) 1,070 (m)	8	9.61
	What-if (task duration-based)	Lithium ion cell manufacturing - Cathode mixing	0.6	445 (f) 535 (m)	0.5	10.5
	What-if (task duration-based)	Lithium ion cell manufacturing - Cathode mixing	0.6	890 (f) 1,070 (m)	0.5	46.1
	Central Tendency	Lithium ion cell manufacturing – Research and development	0.6	445 (f) 535 (m)	4	0.746
	High-end	Lithium ion cell manufacturing – Research and development	1	890 (f) 1,070 (m)	8	4.05
	What-if (task duration-based)	Lithium ion cell manufacturing – Research and development	0.6	445 (f) 535 (m)	2.5	1.79
	What-if (task duration-based)	Lithium ion cell manufacturing – Research and development	1	890 (f) 1,070 (m)	2.5	19.4
	Central Tendency	Lithium ion cell manufacturing – Miscellaneous	0.6	445 (f) 535 (m)	4	12.2
	High-end	Lithium ion cell manufacturing – Miscellaneous	1	890 (f) 1,070 (m)	8	7.30
	What-if (task duration-based)	Lithium ion cell manufacturing – Miscellaneous	0.6	445 (f) 535 (m)	1	29.2

Use Scenario	Scenario Characterization	Sub-scenario	Weight Fraction in Formulation	Surface Area exposed to liquid (cm^2) [b]	Liquid Contact duration (hr)	Duration-based Air Conc. (mg/m^3)
	What-if (task duration-based)	Lithium ion cell manufacturing – Miscellaneous	1	890 (f) 1,070 (m)	4	35.0
Section 2.4.1.2.16 Cleaning	Central Tendency	Dip Cleaning	0.845	445 (f) 535 (m)	4	1.14
	High-end	Dip Cleaning	0.999	890 (f) 1,070 (m)	8	2.68
	Central Tendency	Spray / Wipe Cleaning	0.313	445 (f) 535 (m)	4	0.98
	High-end	Spray / Wipe Cleaning	0.989	890 (f) 1,070 (m)	8	2.70
Section 2.4.1.2.17 Fertilizer Application	Central Tendency	Manual spray or boom application	0.001	445 (f) 535 (m)	4	5.94
	High-end	Manual spray or boom application	0.07	890 (f) 1,070 (m)	8	5.27

[a] The prevalence of respirator use is not known but may be unlikely for most scenarios. Some "what-if" scenarios were generated assuming the use of APF 10 respirators. These scenarios are shown in Section 4.2.2.
[b] EPA assessed these exposure factors for both females and males. Values associated with females are denoted with (f) and values associated with males are denoted with (m).

Table 2-73. PBPK Exposure Results for Central and High-End Worker and ONU Scenarios by Use

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
Section 2.4.1.2.1 Manufacturing	Central Tendency	Bulk container loading	1	82	470	0.064
			5	14	65	N/A
			10	6.7	31	N/A
			20	3.3	15	N/A
	High-end	Drum loading	1	400	4500	0.41
			5	43	320	N/A
			10	19	140	N/A
			20	9.0	64	N/A
	What-if (task duration-based) - central tendency	Bulk container loading	1	18	40	0.016
			5	3.6	7.4	N/A
			10	1.8	3.7	N/A
			20	0.89	1.8	N/A
	What-if (task duration-based) - high-end	Drum loading	1	100	510	0.33
			5	19	68	N/A
			10	9.1	32	N/A
			20	4.5	16	N/A
	Central Tendency		1	82	470	0.064

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
Section 2.4.1.2.2 Repackaging		Bulk container loading	5	14	65	N/A
			10	6.7	31	N/A
			20	3.3	15	N/A
	High-end	Drum loading	1	400	4500	0.41
			5	43	320	N/A
			10	19	140	N/A
			20	9.0	64	N/A
	What-if (task duration-based) - central tendency	Bulk container loading	1	18	40	0.016
			5	3.6	7.4	N/A
			10	1.8	3.7	N/A
			20	0.89	1.8	N/A
	What-if (task duration-based) - high-end	Drum loading	1	100	510	0.33
			5	19	68	N/A
			10	9.1	32	N/A
			20	4.5	16	N/A
Section 2.4.1.2.3 Chemical Processing, Excluding Formulation	Central Tendency	Drum unloading	1	82	470	0.069
			5	14	65	N/A
			10	6.7	31	N/A
			20	3.3	15	N/A
	High-end	Drum unloading	1	400	4500	0.16
			5	43	320	N/A
			10	19	140	N/A
			20	8.9	63	N/A
	What-if (task duration-based) - central tendency	Drum unloading	1	15	28	0.020
			5	3.0	5.3	N/A
			10	1.5	2.7	N/A
			20	0.75	1.3	N/A
	What-if (task duration-based) - high-end	Drum unloading	1	31	60	0.058
			5	6.0	11	N/A
			10	3.0	5.4	N/A
			20	1.5	2.7	N/A
Section 2.4.1.2.4 Incorporation into Formulation, Mixture, or Reaction Product	Central Tendency	Drum unloading	1	82	470	0.069
			5	14	65	N/A
			10	6.7	31	N/A
			20	3.3	15	N/A
	High-end	Drum unloading	1	400	4500	0.16
			5	43	320	N/A
			10	19	140	N/A
			20	8.9	63	N/A

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
	What-if (task duration-based) - central tendency	Drum unloading	1	15	28	0.020
			5	3.0	5.3	N/A
			10	1.5	2.7	N/A
			20	0.75	1.3	N/A
	What-if (task duration-based) - high-end	Drum unloading	1	31	60	0.058
			5	6.0	11	N/A
			10	3.0	5.4	N/A
			20	1.5	2.7	N/A
	Central Tendency	Maintenance, analytical, loading	1	4.8	22	0.074
			5	0.95	4.3	N/A
			10	0.48	2.2	N/A
			20	0.25	1.1	N/A
	High-end	Maintenance, analytical, loading	1	390	4300	1.4
			5	42	320	N/A
			10	19	140	N/A
			20	8.9	63	N/A
Section 2.4.1.2.5 Metal Finishing	Central Tendency	Spray application	1	16	76	0.066
			5	3.1	14	N/A
			10	1.5	6.9	N/A
			20	0.76	3.4	N/A
	High-end	Spray application	1	260	2700	1.0
			5	31	230	N/A
			10	14	100	N/A
			20	6.8	48	N/A
	Central Tendency	Dip application	1	16	77	0.21
			5	3.1	14	N/A
			10	1.6	7.0	N/A
			20	0.80	3.6	N/A
	High-end	Dip application	1	260	2700	0.64
			5	31	230	N/A
			10	14	100	N/A
			20	6.8	48	N/A
	Central Tendency	Brush application	1	16	77	0.85
			5	3.2	15	N/A
			10	1.7	7.7	N/A
			20	0.94	4.2	N/A
	High-end	Brush application	1	260	2700	0.92
			5	31	230	N/A
			10	14	100	N/A

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
			20	6.8	48	N/A
Section 2.4.1.2.6 Application of Paints, Coatings, Adhesives and Sealants	Central Tendency	Spray application	1	0.31	1.4	0.054
			5	0.072	0.32	N/A
			10	0.042	0.19	N/A
			20	0.027	0.12	N/A
	High-end	Spray application	1	31	230	0.93
			5	5.4	38	N/A
			10	2.7	19	N/A
			20	1.4	9.9	N/A
	Central Tendency	Roll / curtain application	1	0.30	1.4	6.3E-03
			5	0.061	0.28	N/A
			10	0.031	0.14	N/A
			20	0.016	0.074	N/A
	High-end	Roll / curtain application	1	31	230	0.055
			5	5.3	37	N/A
			10	2.6	18	N/A
			20	1.3	9.0	N/A
	Central Tendency	Dip application	1	0.35	1.6	0.20
			5	0.10	0.47	N/A
			10	0.074	0.33	N/A
			20	0.059	0.26	N/A
	High-end	Dip application	1	31	230	0.57
			5	5.4	38	N/A
			10	2.7	19	N/A
			20	1.4	9.5	N/A
	Central Tendency	Brush application	1	0.49	2.2	0.84
			5	0.25	1.1	N/A
			10	0.22	0.95	N/A
			20	0.20	0.88	N/A
	High-end	Brush application	1	31	230	0.85
			5	5.4	38	N/A
			10	2.7	19	N/A
			20	1.4	9.8	N/A
Section 2.4.1.2.7 Recycling and Disposal	Central Tendency	Bulk container unloading	1	64	350	0.053
			5	11	51	N/A
			10	5.4	25	N/A
			20	2.6	12	N/A
	High-end	Drum unloading	1	400	4500	0.20
			5	43	340	N/A

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
			10	19	140	N/A
			20	8.9	63	N/A
	What-if (task duration-based) - central tendency	Bulk container unloading	1	15	32	0.015
			5	2.9	6.0	N/A
			10	1.4	3.0	N/A
			20	0.72	1.5	N/A
	What-if (task duration-based) - high-end	Drum unloading	1	42	110	0.097
			5	8.1	18	N/A
			10	4.0	9.0	N/A
			20	2.0	4.5	N/A
Section 2.4.1.2.8 Removal of Paints, Coatings, Adhesives and Sealants	Central Tendency	Miscellaneous removal	1	6.3	29	6.7
			5	2.4	11	N/A
			10	1.9	8.6	N/A
			20	1.7	7.5	N/A
	High-end	Miscellaneous removal	1	98	810	13
			5	16	110	N/A
			10	8.6	60	N/A
			20	5.1	36	N/A
	What-if (task duration-based) - central tendency	Miscellaneous removal	1	2.1	5.6	0.34
			5	0.51	1.4	N/A
			10	0.31	0.84	N/A
			20	0.22	0.58	N/A
	What-if (task duration-based) - high-end	Miscellaneous removal	1	24	70	7.2
			5	6.7	18	N/A
			10	4.6	13	N/A
			20	3.6	9.8	N/A
	Central Tendency	Graffiti removal	1	7.9	36	0.21
			5	1.6	7.1	N/A
			10	0.80	3.6	N/A
			20	0.42	1.9	N/A
	High-end	Graffiti removal	1	57	440	0.94
			5	9.0	64	N/A
			10	4.4	31	N/A
			20	2.2	16	N/A
Section 2.4.1.2.9 Other Electronics Manufacturing	Central Tendency	Capacitor, Resistor, Coil, Transformer, and Other Inductor Mfg.	1	16	77	0.61
			5	3.2	14	N/A
			10	1.6	7.4	N/A
			20	0.88	4.0	N/A
	High-end		1	410	4500	9.2

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
		Capacitor, Resistor, Coil, Transformer, and Other Inductor Mfg.	5	46	340	N/A
			10	21	150	N/A
			20	10	74	N/A
Section 2.4.1.2.10 Semiconductor Manufacturing	Central Tendency	Semiconductor - Container handling, small containers	1	19	120	0.096
			5	3.5	21	N/A
			10	1.7	10	N/A
			20	0.87	5.2	N/A
	High-end	Semiconductor - Container handling, small containers	1	190	2100	0.26
			5	21	200	N/A
			10	9.4	89	N/A
			20	4.5	42	N/A
	What-if (task duration-based) - central tendency	Semiconductor - Container handling, small containers	1	1.6	1.4	1.3E-03
			5	0.32	0.28	N/A
			10	0.16	0.14	N/A
			20	0.081	0.071	N/A
	What-if (task duration-based) - high-end	Semiconductor - Container handling, small containers	1	26	78	0.022
			5	5.1	14	N/A
			10	2.5	6.8	N/A
			20	1.3	3.4	N/A
	Industry-proposed - ONU - central tendency	Semiconductor - Container handling, small containers	1	ONU only	ONU only	5.3E-03
	Industry-proposed - ONU - high-end		1	ONU only	ONU only	0.022
	Industry-proposed - worker - central tendency		20	9.6E-03	0.017	N/A
	Industry-proposed - worker - high-end		20	0.10	0.27	N/A
	Central Tendency	Semiconductor - Container handling, drums	1	9.1	55	0.011
			5	1.7	10	N/A
			10	0.86	5.1	N/A
			20	0.43	2.6	N/A
	High-end	Semiconductor - Container handling, drums	1	190	2100	0.54
			5	21	200	N/A
			10	9.4	89	N/A
			20	4.5	43	N/A

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
	What-if (task duration-based) - central tendency	Semiconductor - Container handling, drums	1	0.42	0.28	6.3E-05
			5	0.084	0.056	N/A
			10	0.042	0.028	N/A
			20	0.021	0.014	N/A
	What-if (task duration-based) - high-end	Semiconductor - Container handling, drums	1	13	24	0.015
			5	2.6	4.5	N/A
			10	1.3	2.3	N/A
			20	0.66	1.1	N/A
	Industry-proposed - ONU - central tendency	Semiconductor - Container handling, drums	1	ONU only	ONU only	6.3E-04
	Industry-proposed - ONU - high-end		1	ONU only	ONU only	0.046
	Industry-proposed - worker - central tendency		20	3.8E-03	6.4E-03	N/A
	Industry-proposed - worker - high-end		20	0.11	0.29	N/A
	Central Tendency	Semiconductor - Fab worker	1	0.43	2.6	0.021
			5	0.089	0.53	0.020
			10	0.046	0.27	0.020
			20	0.025	0.15	0.020
	High-end	Semiconductor - Fab worker	1	2.2	21	0.12
			5	0.44	4.2	0.12
			10	0.23	2.2	0.12
			20	0.12	1.1	0.12
	What-if (task duration-based) - central tendency	Semiconductor - Fab worker	1	0.53	4.5	0.038
			5	0.11	0.93	0.036
			10	0.056	0.48	0.036
			20	0.030	0.26	0.035
	What-if (task duration-based) - high-end	Semiconductor - Fab worker	1	2.1	18	0.11
			5	0.43	3.7	0.10
			10	0.22	1.9	0.10
			20	0.12	0.99	0.10
	Industry-proposed - ONU - central tendency	Semiconductor - Fab worker	20	ONU only	ONU only	0.041
	Industry-proposed - ONU - high-end		20	ONU only	ONU only	0.12
	Industry-proposed -	Semiconductor - Fab worker	20	8.0E-04	1.4E-03	1.1E-03

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
	worker and ONU - central tendency	with container changeout				
	Industry-proposed - worker and ONU - high-end		20	6.1E-03	0.016	0.010
	Central Tendency	Semiconductor - Maintenance	1	9.1	55	0.013
			5	1.7	10	N/A
			10	0.86	5.1	N/A
			20	0.43	2.6	N/A
	High-end	Semiconductor - Maintenance	1	700	9200	0.37
			5	55	540	N/A
			10	23	220	N/A
			20	10	97	N/A
	What-if (task duration-based) - central tendency	Semiconductor - Maintenance	1	0.98	0.98	2.4E-04
			5	0.20	0.20	N/A
			10	0.098	0.098	N/A
			20	0.049	0.049	N/A
	What-if (task duration-based) - high-end	Semiconductor - Maintenance	1	630	7900	0.34
			5	52	480	N/A
			10	22	200	N/A
			20	10	89	N/A
	Industry-proposed - ONU - central tendency	Semiconductor - Maintenance	1	ONU only	ONU only	6.9E-04
	Industry-proposed - ONU - high-end		1	ONU only	ONU only	0.031
	Industry-proposed - worker - central tendency		20	0.041	0.070	N/A
	Industry-proposed - worker - high-end		20	0.96	2.6	N/A
	Central Tendency	Semiconductor - Virgin NMP truck unloading	1	83	470	1.0
			5	14	66	N/A
			10	6.9	32	N/A
			20	3.5	16	N/A
	High-end	Semiconductor - Virgin NMP truck unloading	1	400	4500	1.1
			5	44	330	N/A
			10	19	140	N/A
			20	9.1	64	N/A
	What-if (task duration-based) - central tendency	Semiconductor - Virgin NMP	1	48	200	1.0
			5	9.1	32	N/A
			10	4.6	16	N/A

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
		truck unloading	20	2.4	8.3	N/A
	What-if (task duration-based) - high-end	Semiconductor - Virgin NMP truck unloading	1	100	500	1.0
			5	18	67	N/A
			10	9.1	32	N/A
			20	4.6	16	N/A
	Industry-proposed - ONU - central tendency	Semiconductor - Virgin NMP truck unloading	1	ONU only	ONU only	0.045
	Industry-proposed - ONU - high-end		1	ONU only	ONU only	0.14
	Industry-proposed - worker - central tendency		20	0.13	0.22	N/A
	Industry-proposed - worker - high-end		20	0.73	1.9	N/A
	Central Tendency	Semiconductor - Waste truck loading	1	64	350	0.12
			5	11	51	N/A
			10	5.4	25	N/A
			20	2.7	12	N/A
	High-end	Semiconductor - Waste truck loading	1	280	3000	0.23
			5	34	250	N/A
			10	15	110	N/A
			20	7.1	50	N/A
	What-if (task duration-based) - central tendency	Semiconductor - Waste truck loading	1	38	150	0.058
			5	7.1	25	N/A
			10	3.5	12	N/A
			20	1.8	6.0	N/A
	What-if (task duration-based) - high-end	Semiconductor - Waste truck loading	1	81	370	0.058
			5	15	52	N/A
			10	7.1	25	N/A
			20	3.5	12	N/A
	Industry-proposed - ONU - central tendency	Semiconductor - Waste truck loading	1	ONU only	ONU only	0.010
	Industry-proposed - ONU - high-end		1	ONU only	ONU only	0.029
	Industry-proposed - worker - central tendency		20	0.089	0.15	N/A

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
	Industry-proposed - worker - high-end		20	0.56	1.5	N/A
Section 2.4.1.2.11 Printing and Writing	Central Tendency	Printing	1	0.76	3.4	0.023
			5	0.16	0.70	N/A
			10	0.080	0.36	N/A
			20	0.043	0.19	N/A
	High-end	Printing	1	2.8	20	0.024
			5	0.54	3.8	N/A
			10	0.27	1.9	N/A
			20	0.14	0.97	N/A
	What-if (task duration-based) - central tendency	Printing	1	0.29	0.73	0.023
			5	0.065	0.16	N/A
			10	0.037	0.092	N/A
			20	0.023	0.057	N/A
	What-if (task duration-based) - high-end	Printing	1	0.80	2.0	0.023
			5	0.17	0.42	N/A
			10	0.088	0.22	N/A
			20	0.048	0.12	N/A
	Central Tendency	Writing	1	9.3E-04	1.6E-03	1.6E-04
			5	1.9E-04	3.2E-04	N/A
	High-end	Writing	1	9.3E-04	1.6E-03	3.2E-04
			5	1.9E-04	3.2E-04	N/A
Section 2.4.1.2.12 Soldering	Central Tendency	Soldering	1	0.34	1.5	0.84
			5	0.22	0.95	N/A
			10	0.20	0.88	N/A
			20	0.19	0.84	N/A
	High-end	Soldering	1	1.1	7.7	0.84
			5	0.31	2.2	N/A
			10	0.22	1.5	N/A
			20	0.17	1.1	N/A
Section 2.4.1.2.13 Commercial Automotive Servicing	Central Tendency	Aerosol Degreasing	1	0.67	3.0	1.3
			5	0.36	1.6	N/A
			10	0.32	1.4	N/A
			20	0.31	1.3	N/A
	High-end	Aerosol Degreasing	1	16	110	8.9
			5	3.9	27	N/A
			10	2.6	18	N/A
			20	1.9	13	N/A
			1	0.35	0.92	0.51

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
	What-if (task duration-based) - central tendency	Aerosol Degreasing	5	0.21	0.57	N/A
			10	0.20	0.53	N/A
			20	0.19	0.51	N/A
	What-if (task duration-based) - high-end	Aerosol Degreasing	1	5.4	15	3.3
			5	2.0	5.5	N/A
			10	1.6	4.3	N/A
			20	1.4	3.7	N/A
Section 2.4.1.2.14 Laboratory Use	Central Tendency	Laboratory activities	1	82	470	0.064
			5	14	65	N/A
			10	6.7	31	N/A
			20	3.3	15	N/A
	High-end	Laboratory activities	1	400	4500	0.95
			5	44	330	N/A
			10	19	140	N/A
			20	9.1	64	N/A
	What-if (task duration-based) - central tendency	Laboratory activities	1	48	190	0.037
			5	8.8	31	N/A
			10	4.4	15	N/A
			20	2.2	7.4	N/A
	What-if (task duration-based) - high-end	Laboratory activities	1	100	490	0.037
			5	18	66	N/A
			10	8.8	31	N/A
			20	4.4	15	N/A
Section 2.4.1.2.15 Lithium Ion Cell Manufacturing	Central Tendency	Lithium ion - Container handling, small containers	1	110	790	0.16
			5	16	98	N/A
			10	7.6	46	N/A
			20	3.7	22	N/A
	High-end	Lithium ion - Container handling, small containers	1	700	9200	0.35
			5	55	540	N/A
			10	23	220	N/A
			20	10	97	N/A
	What-if (task duration-based) - central tendency	Lithium ion - Container handling, small containers	1	18	39	0.013
			5	3.5	7.2	N/A
			10	1.7	3.6	N/A
			20	0.87	1.8	N/A
	What-if (task duration-based) - high-end	Lithium ion - Container handling,	1	59	200	0.029
			5	11	31	N/A
			10	5.5	15	N/A
			20	2.7	7.4	N/A

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
		small containers				
	Central Tendency	Lithium ion - Container handling, drums	1	19	120	0.021
			5	3.5	21	N/A
			10	1.7	10	N/A
			20	0.85	5.1	N/A
	High-end	Lithium ion - Container handling, drums	1	700	9200	0.63
			5	55	540	N/A
			10	23	220	N/A
			20	10	97	N/A
	What-if (task duration-based) - central tendency	Lithium ion - Container handling, drums	1	4.1	8.6	1.7E-03
			5	0.82	1.7	N/A
			10	0.41	0.84	N/A
			20	0.21	0.42	N/A
	What-if (task duration-based) - high-end	Lithium ion - Container handling, drums	1	59	200	0.053
			5	11	31	N/A
			10	5.5	15	N/A
			20	2.8	7.4	N/A
	Central Tendency	Lithium ion - Cathode coating	1	16	78	1.0
			5	3.3	15	N/A
			10	1.7	7.8	N/A
			20	0.97	4.4	N/A
	High-end	Lithium ion - Cathode coating	1	54	410	8.2
			5	9.6	67	N/A
			10	5.2	37	N/A
			20	3.2	22	N/A
	What-if (task duration-based) - central tendency	Lithium ion - Cathode coating	1	11	37	0.99
			5	2.3	7.8	N/A
			10	1.3	4.4	N/A
			20	0.79	2.7	N/A
	What-if (task duration-based) - high-end	Lithium ion - Cathode coating	1	45	290	8.2
			5	8.7	52	N/A
			10	4.9	29	N/A
			20	3.1	18	N/A
	Central Tendency	Lithium ion - Cathode slurry mixing	1	16	77	0.46
			5	3.1	14	N/A
			10	1.6	7.3	N/A
			20	0.85	3.8	N/A
	High-end	Lithium ion - Cathode slurry mixing	1	53	400	2.0
			5	8.5	60	N/A
			10	4.3	30	N/A
			20	2.2	16	N/A
	What-if (task duration-based) - central tendency	Lithium ion - Cathode slurry mixing	1	4.4	9.0	0.45
			5	1.0	2.1	N/A
			10	0.61	1.3	N/A

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
			20	0.41	0.85	N/A
	What-if (task duration-based) - high-end	Lithium ion - Cathode slurry mixing	1	9.2	20	2.0
			5	2.5	5.3	N/A
			10	1.7	3.6	N/A
			20	1.3	2.7	N/A
	Central Tendency	Lithium ion - Research and development	1	16	77	0.088
			5	3.1	14	N/A
			10	1.5	6.9	N/A
			20	0.77	3.5	N/A
	High-end	Lithium ion - Research and development	1	400	4500	0.93
			5	44	330	N/A
			10	19	140	N/A
			20	9.0	64	N/A
	What-if (task duration-based) - central tendency	Lithium ion - Research and development	1	12	46	0.083
			5	2.3	8.7	N/A
			10	1.2	4.3	N/A
			20	0.59	2.2	N/A
	What-if (task duration-based) - high-end	Lithium ion - Research and development	1	120	670	0.86
			5	21	86	N/A
			10	11	40	N/A
			20	5.3	20	N/A
	Central Tendency	Lithium ion - Miscellaneous additional activities	1	17	78	1.2
			5	3.3	15	N/A
			10	1.8	8.1	N/A
			20	1.0	4.6	N/A
	High-end	Lithium ion - Miscellaneous additional activities	1	400	4500	1.6
			5	44	330	N/A
			10	19	140	N/A
			20	9.2	65	N/A
	What-if (task duration-based) - central tendency	Lithium ion - Miscellaneous additional activities	1	6.9	19	1.2
			5	1.7	4.6	N/A
			10	1.1	2.9	N/A
			20	0.76	2.0	N/A
	What-if (task duration-based) - high-end	Lithium ion - Miscellaneous additional activities	1	190	1300	1.5
			5	30	150	N/A
			10	14	67	N/A
			20	7.0	32	N/A
Section 2.4.1.2.16 Cleaning	Central Tendency	Dip Cleaning	1	50	260	0.15
			5	8.7	40	N/A
			10	4.3	20	N/A
			20	2.1	9.6	N/A
	High-end	Dip Cleaning	1	400	4400	0.65
			5	43	320	N/A
			10	19	140	N/A

Use Scenario	Scenario Characterization	Sub-scenario	Glove Protection Factor	Acute Exposure, Peak blood concentration (mg/L) (female)	Chronic Exposure, AUC (hr mg/L) (male)	Chronic Exposure, AUC (hr mg/L) (ONU)
			20	9.0	64	N/A
	Central Tendency	Spray / Wipe Cleaning	1	4.9	22	0.10
			5	0.97	4.4	N/A
			10	0.49	2.2	N/A
			20	0.26	1.2	N/A
	High-end	Spray / Wipe Cleaning	1	380	4200	0.65
			5	42	310	N/A
			10	19	130	N/A
			20	8.7	62	N/A
Section 2.4.1.2.17 Fertilizer Application	Central Tendency	Manual spray or boom application	1	0.15	0.66	0.60
			5	0.14	0.60	N/A
			10	0.13	0.59	N/A
			20	0.13	0.59	N/A
	High-end	Manual spray or boom application	1	2.9	21	1.1
			5	0.70	4.9	N/A
			10	0.42	2.9	N/A
			20	0.29	2.0	N/A
N/A = not applicable						

2.4.1.4 Summary of Uncertainties for Occupational Exposure Parameters

Key uncertainties in the occupational exposure parameters are summarized below. Most parameters are related specifically to the route of dermal contact with liquids by workers, while air concentrations are related to the routes of inhalation and vapor-through-skin exposure. The body weight parameter is related to all of these routes. The assumed values for human body weight have relatively lower uncertainties, and the median values used may underestimate exposures at the high-end of PBPK exposure results. The application of OESs and associated work activities increases uncertainties in PBPK parameter inputs for OESs that combine COUs, although the directional impacts due to this application of either overestimating or underestimating exposures estimated by PBPK modeling are not known.

Dermal Exposure Parameters

The dermal exposure parameters used in this assessment have uncertainties because many parameters lack data and were therefore based on assumptions. The assumed parameter values with the greatest uncertainties are glove use and effectiveness (using protection factors based on the ECETOC TRA model that are what-if type values as described in Section 2.4.1.1), durations of contact with liquid, and skin surface areas for contact with liquids, and these assumed values may or may not be representative of actual values. The assumed values for NMP concentrations in formulations have relatively lower uncertainties. The midpoints of some ranges serve as substitutes for 50^{th} percentiles of the actual distributions and high ends of ranges serve as substitutes for 95^{th} percentiles of the actual distributions. However, these substitutes are uncertain and are weak substitutes for the ideal percentile values.

Generally, EPA cannot determine whether most of these assumptions may overestimate or underestimate exposures. However, high-end duration of dermal contact estimates of 8 hours may be more likely to overestimate exposure potential to some extent, and some activity-based durations may be more likely to underestimate exposure potential to some extent. For many OESs, the high-end surface area assumption of contact over the full area of two hands likely overestimates exposures. Occupational non-users (ONUs) may have direct contact with NMP-based liquid products due to incidental exposure at shared work areas with workers who directly work with NMP, and the estimate of zero surface area contact may underestimate their exposure. The parameter values NMP concentrations are from reasonably available data and are likely to have a relatively low impact on the magnitude (less than an order of magnitude, or factor of 10) of overestimation or underestimation of exposure. The impact of vapors being trapped next to the skin during glove use is also uncertain.

Inhalation and Vapor-through-Skin Exposure Parameters

Where monitoring data are reasonably available, limitations of the data also introduce uncertainties into the exposures. The principal limitation of the air concentration data is the uncertainty in the representativeness of the data. EPA identified a limited number of exposure studies and data sets that provided data for facilities or job sites where NMP was used. Some of these studies primarily focused on single sites. This small sample pool introduces uncertainty as it is unclear how representative the data for a specific end use are for all sites and all workers across the US. Differences in work practices and engineering controls across sites can introduce variability and limit the representativeness of any one site relative to all sites. Age of the monitoring data can also introduce uncertainty due to differences in work practices and equipment used at the time the monitoring data were taken and those used currently, so the use of older data may over- or underestimate exposures. Additionally, some data sources may be inherently biased. For example, bias may be present if exposure monitoring was conducted to address concerns regarding adverse human health effects reported following exposures during use. The effects of these uncertainties on the occupational exposure assessment are unknown, as the uncertainties may result in either over or underestimation of exposures depending on the actual distribution of inhalation exposure concentrations and the variability of work practices among different sites. Dermal exposures to NMP vapor that may penetrate clothing fabrics and the potential for associated direct skin contact with clothing saturated with NMP vapor are not included in quantifying exposures, which could potentially result in underestimation of exposures.

The impact of these uncertainties precluded EPA from describing actual parameter distributions. In most scenarios where data were reasonably available, EPA did not find enough data to determine complete statistical distributions. Ideally, EPA would like to know 50^{th} and 95^{th} percentiles for each exposed population. In the absence of percentile data for monitoring, the means or midpoint of the range serve as substitutes for 50^{th} percentiles of the actual distributions and high ends of ranges serve as substitutes for 95^{th} percentiles of the actual distributions. However, these substitutes are uncertain and are weak substitutes for the ideal percentile values. The effects of these substitutes on the occupational exposure assessment are unknown, as the substitutes may result in either over or underestimation of exposures depending on the actual distribution.

Where data were not reasonably available, the modeling approaches used to estimate air concentrations also have uncertainties. Parameter values used in models did not all have distributions known to represent the modeled scenario. It is also uncertain whether the model equations generate results that represent actual workplace air concentrations. Some activity-based modeling does not account for exposures from other activities, which may result in underestimation of exposures. When EPA does not

have ONU-specific exposure data, EPA's assumption that 50th percentile air concentrations predicted for workers in these activities are a good approximation of exposure is uncertain. It is not known whether this assumption underestimates or overestimates exposure for ONUs. Additional model-specific uncertainties are included below. In general, unless specified otherwise, the effects of the below model-specific uncertainties on the exposure estimates are unknown, as the uncertainties may result in either over or underestimation on exposures depending on the actual distributions of each of the model input parameters.

Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model
For manufacturing; repackaging; and recycling and disposal, the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* was used to estimate the airborne concentration associated with generic chemical loading scenarios at industrial facilities. Specific uncertainties associated with this model are described below:

- After each loading event, the model assumes saturated air containing NMP that remains in the transfer hose and/or loading arm is released to air. The model calculates the quantity of saturated air using design dimensions of loading systems published in the OPW Engineered Systems catalog and engineering professional judgment. These dimensions may not be representative of the whole range of loading equipment used at industrial facilities handling NMP.
- The model estimates fugitive emissions from equipment leaks using total organic compound emission factors from EPA's *Protocol for Equipment Leak Emission Estimates* (U.S. EPA, 1995), and professional judgment on the likely equipment type used for transfer (*e.g.*, number of valves, seals, lines, and connections). The applicability of these emission factors to NMP, and the accuracy of EPA's assumption on equipment type are not known.

Drum Loading and Unloading Release and Inhalation Exposure Model
For chemical processing, excluding formulation and incorporation into formulation, mixture, or reaction product, the *Drum Loading and Unloading Release and Inhalation Exposure Model* was used to estimate the airborne concentration associated with generic chemical loading scenarios at industrial facilities. Specific uncertainties associated with this model are described below:

- The model estimates fugitive emissions using the *EPA/OAQPS AP-42 Loading Model.* The applicability of the emission factors used in this model to NMP is not known.
- EPA assigned statistical distributions based on reasonably available literature data or professional judgment to address the variability in Ventilation Rate (Q), Mixing Factor (k), Vapor Saturation Factor (f), and Exposed Working Years per Lifetime (WY). The selected distributions may vary from the actual distributions.

Model for Occupational Exposures during Aerosol Degreasing of Automotive Brakes
The aerosol degreasing assessment uses a near-field/far-field approach (uncertainties on this approach are presented below) to model worker exposure. Specific uncertainties associated with the aerosol degreasing scenario are presented below:

- The model references a CARB study (CARB, 2000) on brake servicing to estimate use rate and application frequency of the degreasing product. The brake servicing scenario may not be representative of the use rates for other aerosol degreasing applications involving NMP;
- Aerosol formulations were taken from reasonably available SDSs, and some were provided as ranges. For each Monte Carlo iteration the model selects an NMP concentration within the range

of concentrations using a uniform distribution. In reality, the NMP concentration in the formulation may be more consistent than the range provided.

Near-Field/Far-Field Model Framework
The near-field/far-field approach is used as a framework to model inhalation exposure for aerosol degreasing. The following describe uncertainties and simplifying assumptions generally associated with this modeling approach:

- There is some degree of uncertainty associated with each model input parameter. In general, the model inputs were determined based on review of reasonably available literature. Where the distribution of the input parameter is known, a distribution is assigned to capture uncertainty in the Monte Carlo analysis. Where the distribution is unknown, a uniform distribution is often used. The use of a uniform distribution will capture the low-end and high-end values but may not accurately reflect actual distribution of the input parameters.
- The model assumes the near-field and far-field are well mixed, such that each zone can be approximated by a single, average concentration.
- All emissions from the facility are assumed to enter the near-field. This assumption will overestimate exposures and risks in facilities where some emissions do not enter the airspaces relevant to worker exposure modeling.
- The exposure models estimate airborne concentrations. Exposures are calculated by assuming workers spend the entire activity duration in their respective exposure zones (*i.e.*, the worker in the near-field and the occupational non-user in the far-field). A worker may walk away from the near-field during part of the process. As such, assuming the worker is exposed at the near-field concentration for the entire activity duration may overestimate exposure.
- The exposure models represent model workplace settings for NMP used in aerosol degreasing of automotive brakes. The model has not been regressed or fitted with monitoring data.

2.4.2 Consumer Exposures

NMP is found in consumer products that are available for purchase at retail stores or via the internet (ABT, 2017). Use of these products can result in consumer exposures. As presented in the previous 2015 EPA NMP Paint Remover Risk Assessment, women of child-bearing age and pregnant women are the populations identified as at risk due to the hazards of NMP and exposures. That is, the hazard endpoint, identified in the Paint Remover Risk Assessment and confirmed in this Risk Evaluation affects the fetus, and could present a risk to women of child-bearing age or pregnant women (see Section 3.2 and U.S. EPA, 2015c).

2.4.2.1 Consumer Exposures Approach and Methodology

EPA selected currently available NMP-containing consumer products for exposure analysis that had uses covered under TSCA (see Table 2-74). EPA recognizes that there are numerous other products containing NMP which are not subject to TSCA, as noted in the NMP Problem Formulation. For example, NMP is found in cosmetics and pharmaceutical manufacture which are regulated by the Food and Drug Administration (FDA) and in pesticides (as an inert ingredient) regulated by EPA but under the Federal Insecticide Fungicide and Rodenticide Act. EPA also confirmed in the NMP Market Profile previous uses of NMP-containing products that are no longer in use such as a component of the inner layer of aluminum aerosol or spray cans used for hairspray or air fresheners and which are not based in EPA's professional judgement a reasonably foreseen use (EPA-HQ-OPPT-2016-0743-0060) (ABT, 2017).

EPA searched the National Institutes of Health (NIH) Household Products Database, various government and trade association sources for products containing NMP, company websites for product SDSs and the internet in general. Lists of consumer products were compiled and are found in EPA's 2017 Market Profile (ABT, 2017). These products ranging from 0.1 to >85 weight percent NMP were categorized according to their respective condition(s) of use and were included in this risk evaluation.

Table 2-74. Conditions of Use for Consumer Products Containing NMP

Consumer Conditions of Use	Form	No. of Products Identified [a]	Range of Product NMP Weight Fractions [b] (%)
Sealants	Liquid	3	0.3 – 1.0
Adhesives	Liquid	1	85.0
Adhesives Remover	Liquid	5	1.0 – 60.0
Auto Interior Cleaner	Liquid	1	1.0 – 5.0
Auto Interior Spray Cleaner	Aerosol	1	1.0
Cleaners/ Degreasers	Liquid	8	1.0 – 100.0
Engine Cleaner/ Degreaser	Liquid	1	15.0 – 40.0
Paint	Liquid	3	1.0 – 7.0
Paint and Coating Removers	Liquid	35	25.0 – 60.0 [c]
Spray Lubricant (Mold Release)	Aerosol	1	30.0 – 40.0
Stains, Varnishes, Finishes	Liquid	10	1.0 – 10.0
Arts and Crafts	Liquid	2	0.1 – 1.0

[a] The number of products identified is based on the product lists in EPA's 2017 Market and Use Report and Preliminary Information on Manufacturing, Processing, Distribution, Use and Disposal: n-methyl-2-pyrrolidone, as well as the 2016 Supplemental Consumer Exposure and Risk Estimation Technical Report for NMP in Paint and Coating Removal.
[b] Conditions of use with one value for weight fraction represent one product with a single value listed in the Manufacturer's Safety Data Sheet (MSDS). Several manufacturer's list a range of possible NMP weight fractions within a given product's MSDS.
[c] See the 2015 Paint Remover's Risk Assessment.

In the absence of reasonably available emissions and monitoring data for use of consumer products containing NMP, a modeling approach was utilized to assess consumer exposure. Appropriate use scenarios corresponding to the product use were selected for exposure modeling and parameterization of model inputs used consumer survey data where appropriate. The PBPK model was used to derive internal exposure estimates for consumer acute exposures. The PBPK model required a set of input parameters related to exposure by the dermal and inhalations routes:

- NMP weight fraction in the liquid product;
- Total skin surface area of hands in contact with the liquid product;
- Duration of dermal contact with the liquid product;
- Air concentration for inhalation and vapor-through-skin exposure; and
- Body weight of the exposed consumer/user.

Section 2.4.2.4 presents the input parameters in more detail. The specific PBPK model inputs and outputs are found in the NMP supplemental documents (U.S. EPA, 2020p).

EPA relied on information gathered through literature searches and data evaluation (see Section 1.5 above). In addition to product specific data from gray literature, surveys provided data needed to

parameterize model inputs. Many of the model defaults are based on data from EPA's 2011 Exposure Factors Handbook (see Consumer Exposure Model guide) but were supplemented with data found from scientific literature (U.S. EPA, 2017a). For the NMP consumer exposure assessment, existing assessments such as the 2015 U.S. EPA Paint Remover Risk Assessment and other assessments as listed in Table 2-74 also provided supplementary information and data.

Table 2-75 lists some of the key sources of information evaluated under the data evaluation process and used in the consumer exposure assessment. A description of the evaluation metrics and confidence scores for each of the sources is presented in the NMP supplemental document *Risk Evaluation for n-Methylpyrrolidone, Systematic Review Supplemental File: Data Quality Evaluation of Consumer and General Population Studies* (U.S. EPA, 2020g). The one indoor air monitoring study is discussed below in Section 2.4.2.5 under consumer use of paint removers.

Table 2-75. Consumer Exposures Assessment Literature Sources

Source Reference	Data Type	Confidence Rating
U.S. EPA (1994a)	Survey Data	Medium (1.8)
U.S. EPA (1987)	Survey Data	High (1.3)
ABT (1992)	Survey Data	Medium (1.8)
Danish Ministry of the Environment (2015)	Completed Assessments	High (1.5)
DTI (2004)	Completed Assessments	High (1.6)
ECHA (2014)	Completed Assessments	High (1.0)
Environment Canada (2017)	Completed Assessments	High (1.5)
NIOSH (1993)	Monitoring	Low (2.5)

2.4.2.2 Exposure Routes

Based on reasonably available information on the toxicity profile and physicochemical properties of NMP as well as the previous NMP Paint Remover Risk Assessment, the primary routes of exposure for human health concerns are dermal, including vapor through skin, and inhalation exposures.

Oral

EPA considered the oral pathway for consumers based on children's exposure potential via mouthing articles containing NMP (WSDE, 2014). EPA reviewed several NMP assessments (see Table 2-75 above), including a Danish assessment specific to consumer product mouthing and NMP migration. Based on an estimated NMP migration amount of 200µg, the Danish study concluded that NMP from articles such as toothbrushes do not pose a risk (DTI, 2004).

Using the Consumer Exposure Model, EPA estimated the exposure to NMP due to mouthing of fabric articles such as blankets, dolls, or stuffed animals to young children. EPA evaluated NMP exposure for 3 lifestages, infant (<1 year), infant (1-2 years), and small child (3-5 years) (see Table 2-76). Mouthing duration can vary significantly as cited in Babich et al. (2004) over a 24 hour period. EPA used the U.S. Consumer Protection and Safety Commission high-end mouthing duration data cited in CEM to estimate

a single event exposure per the data. Infants younger than one year would have the greatest possible exposure via mouthing, however levels of 15µg are significantly less than the migration amount reported in the Danish study and well below the oral dose of 48mg/kg/day that could result in risk. EPA did not further analyze NMP exposure via the oral pathway in this risk evaluation.

Table 2-76. NMP Oral Exposure to Children via Mouthing

Receptor	Fabric: blanket, doll, stuffed animal (weight fraction)	Mouthing Duration (min)	Body Weight (kg)	Acute Dose Rate (mg/kg/day)
Infant (<1 year)	1.0E-03	22.5	7.8	1.5E-02
Infant (1-2 years)	1.0E-03	22.5	12.6	9.2E-03
Small child (3-5 years)	1.0E-03	22.5	18.6	6.2E-03

Dermal

NMP has unique physicochemical properties such that it is very efficiently dermally absorbed. Dermal absorption was characterized for consumers as it was characterized in the previous NMP Paint Remover Risk Assessment most importantly in that consumers were assumed not to wear gloves when using NMP-containing products. For the consumer exposure evaluation, dermal absorption is an important route of NMP exposure for consumers.

NMP exposure to consumers via vapor through skin uptake was also considered for each of the scenarios. This pathway will most likely occur in the scenario where the product is spray applied.

Inhalation

For each of the product use scenarios except for paint removers, the air concentrations of NMP resulting from consumer use were modeled using EPA's Consumer Exposure Model (CEM). For paint removers, the Paint Remover Risk Assessment estimated air concentrations using the Multi-Chamber Concentration and Exposure Model (MCCEM). This model requires NMP emission data for the specific product and use conditions which was available through the specific paint remover study (Koontz et al., 1990). The PBPK model was used to estimate aggregate dermal, vapor through skin and inhalation exposures resulting from the uses of NMP (see Section 3.2.5.5 below and U.S. EPA (2015c) for details of the PBPK model).

Based on anticipated use patterns of each of the product categories by consumers in residential settings, acute exposures via the dermal and inhalation routes were the primary scenarios of interest. EPA assumed that consumer users would be females of childbearing age (16 – 49 years), because, in terms of hazard, they are the most sensitive subpopulation. Other individuals, adults and children alike may be exposed via inhalation as bystanders located in the same building as the user of the NMP-containing consumer product. According to the 2015 Paint Remover risk assessment as well as the supplemental analysis presented in Appendix G.2 bystanders or non-users are significantly less affected than the direct users of the product since they do not have direct dermal contact (U.S. EPA, 2015c). Bystander exposure via inhalation and vapor-through-skin was evaluated in this risk evaluation for three high-end scenarios. Since monitoring data is not reasonably available for most of the consumer product use scenarios, CEM was used to estimate air concentrations in the breathing zone of the user. These estimates were then used to predict acute inhalation exposure to NMP for the user using the PBPK modeling approaches.

2.4.2.3 Overview of Models used in Consumer Exposure Estimates

The Consumer Exposure Model (CEM) was selected for the consumer exposure modeling as the most appropriate model to use due to the lack of reasonably available emissions and monitoring data for NMP uses other than paint removers under consideration. Moreover, EPA did not have the input parameter data from specific NMP product chamber studies required to run more complex indoor air models for the consumer products under the scope of this assessment. Details of the CEM model and the advantages of using CEM in estimating consumer exposures to NMP are presented in Appendix G.

Modeling Dermal Exposure

Since consumers do not always wear gloves when using consumer products, EPA modeled dermal exposures for all NMP-containing products. Though CEM can estimate dermal exposures using a chemical permeability coefficient, EPA used the PBPK model to estimate the internal dose of NMP as it is absorbed through the skin both from direct contact of the liquid product and through absorption of vapor through skin. The PBPK model thus estimated the peak internal dose of NMP through combined routes of exposure: inhalation, dermal and vapor through skin and was also used to estimate exposures in the Paint Remover Risk Assessment.

2.4.2.4 Consumer Model Scenario and Input Parameters for Exposure to Specific NMP Uses

Table 2-77 describes the models and input parameters for women of child-bearing age that EPA evaluated in the NMP consumer exposure assessment. As indicated in Section 2.4.2.2, EPA assessed dermal and inhalation as the main exposure pathways.

Table 2-77. Product Use Input Parameters for CEM Modeling

Parameter	Units	Value / Description
CHEMICAL PROPERTIES		
Chemical of Interest	N/A	n-Methyl-2-pyrrolidone
CAS Number	N/A	872-50-4
Vapor Pressure	torr	0.345
Molecular Weight	g/mol	99.1
Chemical Saturation Concentration in Air	mg/m^3	1,840
Log Octanol-Water Partition Coefficient	N/A	0.38
Water Solubility	mg/mL	1,000
Henry's Law Coefficient	atm/M	3.2E-09
Gas Phase Mass Transfer Coefficient	m/hr	CEM estimate, if applicable
MODEL SELECTION / SCENARIO INPUTS		
Inhalation Model	N/A	PBPK
Dermal Model	N/A	PBPK
Emission Rate	N/A	Let CEM Estimate Emission Rate

Parameter	Units	Value / Description
Product User(s)	N/A	Women of Childbearing age: Adults (20-49 years) and Young Women/Female Adolescent (16 - <21 years)
Activity Pattern	N/A	"Stay at home": user spends most of their time at home (*i.e.*, includes room of use as well as indoor/outdoor user locations within a 24hr time period)
Product Use Start Time	N/A	9:00 AM
Background Concentration	mg/m^3	0
PRODUCT/ARTICLE PROPERTIES		
Frequency of Use (Acute)	events/day	Fixed at 1 event/day (CEM default)
Aerosol Fraction	-	CEM default (0.06)
Product Dilution Factor	unitless	Fixed at 1 (*i.e.*, no dilution)
ENVIRONMENT INPUTS		
Building Volume (Residence)	m^3	492
Air Exchange Rate, Zone 1 (Residence)	hr^{-1}	CEM default
Air Exchange Rate, Zone 2 (Residence)	hr^{-1}	CEM default
Air Exchange Rate, Near-Field Boundary	hr^{-1}	CEM default (402)
Interzone Ventilation Rate	m^3/hr	CEM default
RECEPTOR EXPOSURE FACTORS		
Body Weight	kg	74 (Adult Women) and 65.9 (Young Women/Female Adolescent 16 - <21 years)
Averaging Time	yrs/lifetime	Acute: 1 day
Inhalation Rate-During Use	m^3/hr	0.67 (Adult) and (Adolescent 16 - <21 years)
Inhalation Rate-After Use	m^3/hr	0.635 (Adult) and 0.57 (Adolescent 16 - <21 years)
Dermal Surface Area	cm^2	445 (Adult) and 415 (Adolescent 16 - <21 years)
N/A = not applicable		

Table 2-78. Consumer Conditions of Use and Modeling Input Parameters

Consumer Conditions of Use	Form	Selected U.S. EPA (1987) Survey Scenario [a]	Room of Use [b]	Duration of Use (min) [c,d]			Mass of Product Used (g, [oz]) [e]		
				10th	50th	95th	10th	50th	95th
Adhesives and Sealants	Liquid	Contact Cement, Super Glues, and Spray Adhesives	Bathroom/ Utility Room/ Outdoors	0.33	4.25	60	0.92 [0.03]	7.69 [0.25]	132.87 [4.32]
Adhesives Remover	Liquid	Adhesive Removers	Utility Room	3	60	480	17.85 [0.67]	213.17 [8]	1705.33 [64]
Auto Interior Cleaner	Liquid	Solvent-type Cleaning Fluids or Degreasers	Automobile	2	15	120	16.56 [0.56]	96.11 [3.25]	946.35 [32]
Auto Interior Spray Cleaner	Aerosol	Solvent-type Cleaning Fluids or Degreasers	Automobile	2	15	120	16.60 [0.56]	96.34 [3.25]	946.53 [32]
Cleaners/ Degreasers	Liquid	Solvent-type Cleaning Fluids or Degreasers	Utility Room	2	15	120	16.23 [0.56]	94.19 [3.25]	927.43 [32]
Engine Cleaner/ Degreaser	Liquid	Engine Cleaners/ Degreasers	Garage	5	15	120	73.15 [2.91]	291.60 [11.60]	1206.60 [48]
Paint	Liquid	Latex Paint	Garage	30	180	810	349.63 [10.67]	4194.24 [128]	23068.31 [704]
Paint and Coating Removers	Liquid	Paint Remover survey data from ABT (1992)	Bathroom/ Utility	--	90	396	--	540	1,944
Spray Lubricant (Mold release)	Aerosol	Other Lubricants (Non-Automotive)	Utility Room	0.08	2	30	3.40 [0.10]	18.71 [0.55]	170.05 [5.00]
Stains, Varnishes	Liquid	Stains, Varnishes, and Finishes	Living Room	10	60	360	61.07 [2.00]	366.42 [12.00]	3908.44 [128.00]
Arts and Crafts	Liquid	Latex Paint	Utility Room	30	180	810	5.44 [0.17]	65.27 [2.00]	358.98 [11.00]

Consumer Conditions of Use	Form	Selected U.S. EPA (1987) Survey Scenario [a]	Room of Use [b]	Duration of Use (min) [c,d]			Mass of Product Used (g, [oz]) [e]		
				10th	50th	95th	10th	50th	95th

[a] The U.S. EPA 1987 Survey was used to inform values used for duration of use and mass of product used. Where exact matches for conditions of use were not available, scenario selection was based on product categories that best met the description and usage patterns of the identified consumer conditions of use.
[b] The room of use was a selection within the Consumer Exposure Model to model the most likely location of the consumer product use and exposure.
[c] Duration of use is time of use per event and assumes only one use per day.
[d] Low-end durations of use reported by U.S.EPA 1987 that are less than 0.5 minutes are modeled as being equal to 0.5 minutes due to that being the minimum timestep available within the model.
[e] Mass of product used within U.S.EPA 1987 for given scenarios is reported in ounces but were converted to grams using reported densities in the product SDSs or MSDSs.

To estimate exposures to these products, numerous input parameters are required to generate a single exposure estimate. These parameters include the characteristics of the house, the behavior of the consumer and the emission rate of the chemical into the room of use. In the absence of measured values for many of the needed inputs, the CEM modeling for NMP used a combination of upper (95^{th}) percentile, mean, and median as well as low-end (10^{th} percentile) input parameters and assumptions in the calculation of potential exposure for consumer users. The 10^{th} percentile, 50^{th} percentile and 95^{th} percentile inputs parameters were selected for three parameters that varied among users and were included in the 1987 Westat survey, that is, duration of product use, mass of product used, and weight fraction. This approach represents high-intensity use (95^{th} percentile) in which the user uses a greater amount, higher NMP concentration product for a longer duration and a moderate intensity use (50^{th} percentile weight fraction/duration/mass used) and produces acute inhalation estimates that are hypothetical but representative of the range of consumer product use. The general input parameters and assumptions are summarized in Table 2-77. The input values specific to each use scenario are summarized and explained more fully in Table 2-78. Based on the previous NMP Paint Remover Risk Assessment, the combinations of input parameters associated with low intensity use did not result in risk. Thus, for this evaluation, only the medium intensity and high intensity use scenarios were further analyzed. The general input parameters and assumptions are summarized in Table 2-77. The input values specific to each use scenario are summarized and explained more fully in Table 2-78.

Consumer behavior pattern parameters in CEM include the mass of product used, the duration of use and the frequency of use. Although the default values in CEM for these consumer behavior parameters are set to high end values, they were *not* used in this risk assessment. The other parameters (*e.g.*, house volume) in CEM are set to mean or median values obtained from the literature. A combination of high end and mean or median values was utilized to produce high end acute inhalation exposure estimates, whereas a combination of mean and median values was used to produce central tendency acute inhalation exposure estimates.

To determine the appropriateness of the consumer behavior pattern parameters chosen in this risk evaluation, EPA examined the consumer categories available in the Westat U.S. EPA (1987) survey. The authors of the Westat U.S. EPA (1987) survey contacted thousands of Americans to gather information on consumer behavior patterns related to product categories that may contain halogenated solvents. The Westat U.S. EPA (1987) survey data aligned reasonably well with the description of the products that were used in this consumer exposure assessment. The data informed the values that EPA used for the mass of product used, and the time spent in the room of use when considering all surveyed individuals who identified as users of spray adhesives, spot removers, engine cleaners, brake cleaners or electronics cleaners.

The input parameter for house volume was taken from the Exposure Factors Handbook (2011). The room volume for aerosol spray adhesives and aerosol spot removers was calculated as a proxy utility room measuring 9 ft x 10 ft, with 8 ft ceilings (U.S. EPA, 2014). The designated room of use modeled for aerosol degreasers and cleaners (used as engine degreasers and brake cleaners) was the garage since users surveyed in the Westat U.S. EPA (1987) report reported use in the garage. The CEM model does not include a garage volume in its default room parameters, thus the median garage volume from a 2007 indoor air quality study (Batterman et al., 2007) of 15 homes in Michigan was used as a reasonable proxy value. The room of use for adhesives was reported in the product sheet as outdoors. Since CEM does not have an outdoors scenario, the garage was selected as the room of use but input parameters such as a high air exchange rate were modified to simulate the outdoors.

The user's body weight, inhalation rate, and inside of two hands surface area were set to adult (+21) and teen (16-20) women mean or the median values from the Exposure Factors Handbook (U.S. EPA, 2011) for the simulations used in this assessment.

The air exchange rate in the room of use does not take into consideration open windows or the use of an exhaust fan. While it is possible that some users may employ these exposure reduction techniques inside their homes, the goal of the consumer exposure assessment was to provide an acute exposure estimate for ventilation conditions representing average household air exchange rates. Moreover, residential users would not necessarily have the type of indoor exposure reduction tools/equipment (*e.g.*, gloves, exhaust ventilation) that workers are likely to have in occupational settings. Consumers may not necessarily be as aware of potential chemical hazards as workers and would not have a standard operating procedure in place to assure that they use exposure reduction techniques each time they use a product.

In this assessment it was assumed that there was no pre-existing concentration of NMP in the home before product use began. The outdoor air was also assumed to be free of NMP, meaning that the air exchange rate described the intake of air with no pre-existing NMP contamination.

The products were assumed to be brushed on as a liquid to varying surfaces, where a thin film of the product was assumed to build up, evaporate, and contribute to the air concentration of the chemical in the room. EPA relied on modeled emission rates because data from chamber studies were not reasonably available. To generate emission rates, CEM used empirical data from studies assessing the emission rates of pure solvents (Chinn, 1981). CEM used the Chinn study as surrogate data to calculate the rate of evaporation of NMP from the surface to the air in the home.

The use of an exponentially decaying emission rate for NMP from the application surface was based on vapor pressure and molecular weight the equations using the Chinn method. The adhesive application should be well modeled by the Chinn study since it contained over 85% NMP. On the other hand, the spray cleaner product may have more components, and the interaction of these chemicals could alter the evaporation rate of NMP. This introduces uncertainty into the assessment, however EPA did not identify a better data set reasonably available to model the emission rates. Within the current exposure assessment, the 24-hr exposure was not strongly dependent on the emission rate due to the amount of time the product user spends in the room of use (see Table 2-78 for details).

2.4.2.5 Consumer Exposure Scenarios

Adhesives and Sealants

Exposure to NMP found in NMP-containing adhesive and sealant products was based on four products with associated weight fraction data. Three of the products had a range of weight fractions from 0.1 to 1% and were similar use products, sealants. One product was an adhesive to glue boards used in deck construction. The duration of use and mass of product used were based on the 1987 Westat survey data, specifically the data found under the Contact Cement, Super Glues, and Spray Adhesives scenario and are listed in Table 2-79.

In order to differentiate the adhesives and sealants use scenarios of the outdoor product versus the scenario of the other adhesives and sealant products that were modeled for indoor use, the former was designated as a "High Weight Fraction Adhesives and Sealants" and the remaining as "Low Weight Fraction Adhesives and Sealants."

The Glues and Adhesives (small scale) default scenario within the Consumer Exposure Module (CEM) was chosen for conducting the modeling runs. This selection was the closest match to the liquid

adhesive scenario among the default CEM exposure scenarios. The common modeling inputs required to run CEM for all consumer single-use scenarios evaluated in this assessment are provided in Table 2-77. Table 2-77 also has a brief explanation of the source of each parameter and the justification for the parameter selection. Other scenario-specific input parameters are provided in Table 2-78.

CEM calculated air concentrations over the course of the simulation for the room of use and the rest of the house (Zone 1 and Zone 2). These concentrations were inputs to the PBPK model and used the body weights (74 kg, 65.9 kg), inside both hands surface areas (445 cm^2, 415 cm^2) and respiration rates (0.74 m^3/hr, 0.68 m^3/hr during use) for adult women (21-49 years) and adolescent females (16 to <21 years old), respectively and both age groups are considered of child-bearing age in calculating the internal dose of NMP (HHS, 2013). Though both young and adult women scenarios were modeled and are presented in Appendix J.2, the difference in exposures were very small. Exposures to adult women are presented below as they are expected to adequately represent the women of child-bearing age who may use these consumer products.

Table 2-79 presents the results of the indoor air concentrations (ppm) for both central tendency and high end estimated exposures for the consumer use scenarios based on the 50th percentile and 95th percentile input parameters. Calculations detailing the conversion from acute dose rates to air concentrations are provided in a supplemental Excel spreadsheet file (U.S. EPA, 2020d).

Table 2-79. Estimated NMP Air Concentrations (Time Averaged Over 1 Day) Based on Residential Use of Adhesives or Sealants

Scenario Description For Product User (Women of Childbearing Age)	Duration of Use (min)	Weight Fraction (%)	Mass of Product Used (g)	Air Concentration [a]		
				Max 8 hr TWA (mg/m^3)	Max 8 hr TWA (ppm)	Max 24 hr TWA (ppm)
High Weight Fraction Adhesives and Sealants						
Medium Intensity Use [b]	4.25	85	7.69	1.82E-01	4.48E-02	1.49E-02
High Intensity Use [c]	60	85	132.87	1.74	0.429	0.143
Low Weight Fraction Adhesives and Sealants						
Medium Intensity Use [b]	4.25	0.77	7.69	4.30E-02	1.06E-02	3.76E-03
High Intensity Use [c]	60	0.77	132.87	6.18E-01	1.52E-01	5.56E-02

[a] See Appendix G for details about the model inputs and the method used to estimate air concentrations of NMP.
[b] Medium intensity use estimate based on using 50th percentile values for use patterns from Westat Survey (1987).
[c] High intensity use estimate based on using 95th percentile values for use patterns from Westat Survey (1987).

The model output reports the peak concentration of NMP, however this air concentration was not used in the risk assessment. The peak concentration was the highest concentration among all 10-second time intervals that CEM simulated within a 24-hr period. The peak concentration may only exist in the room of use for a short duration and was not considered a good indicator of what the concentration of NMP would be for longer time periods. Thus, the peak concentration was not used in the risk assessment as it was not representative of a 24-hr exposure.

The maximum internal NMP dose (C_{max}) resulting from inhalation, dermal and vapor through skin exposures to women of childbearing age consumer use of adhesive or sealant products as estimated from the PBPK model is presented in Table 2-80.

Table 2-80. Estimated NMP Exposures (Time Averaged Over 1 Day) Based on Residential Use of Adhesives or Sealants

Scenario Description For Product User	Women of Childbearing Age C_{max} (mg/L)	Pregnant Women C_{max} (mg/L)
High Weight Fraction Adhesives and Sealants		
Medium Intensity Use	4.084	3.802
High Intensity Use	18.629	17.352
Low Weight Fraction Adhesives and Sealants		
Medium Intensity Use	0.011	0.011
High Intensity Use	0.070	0.068

Adhesives Removers

Exposure to NMP found in NMP-containing adhesive remover products was based on five products with associated weight fraction data. Weight fractions ranged from 1% to 60% and were similar use products. The duration of use and mass of product used were based on the 1987 Westat survey data, specifically the data found under the Adhesive Removers scenario and are listed in Table 2-81.

Table 2-81. Estimated NMP Air Concentrations (Time Averaged Over 1 Day) Based on Residential Use of Adhesives Removers

Scenario Description For Product User (Women of Childbearing Age)	Duration of Use (min)	Weight Fraction (%)	Mass of Product Used (g)	Air Concentration [a]		
				Max 8 hr TWA (mg/m^3)	Max 8 hr TWA (ppm)	Max 24 hr TWA (ppm)
Adhesive Remover						
Medium Intensity Use [b]	60	18.90	213.17	1.42	0.349	0.119
High Intensity Use [c]	480	25.00	1,705.33	21.70	5.34	1.89

[a] See Appendix G for details about the model inputs and the method used to estimate air concentrations of NMP.
[b] Medium intensity use estimate based on using 50th percentile values for use patterns from Westat Survey (1987).
[c] High intensity use estimate based on using 90th percentile values for use patterns from Westat Survey (1987).

The Adhesives/Caulk Removers default scenario within the Consumer Exposure Module (CEM) was chosen for conducting the modeling runs. This selection was the closest match to the liquid adhesive remover scenario among the default CEM exposure scenarios. The common modeling inputs required to run CEM for all consumer scenarios evaluated in this assessment are provided in Table 2-77. Other scenario-specific input parameters are provided in Table 2-78.

CEM calculated air concentrations over the course of the simulation for the room of use and the rest of the house (Zone 1 and Zone 2). These concentrations were inputs to the PBPK model and used the body weight and respiration rate for adult women (21-49 years) and adolescent females (16 to <21 years old), both considered of child-bearing age in calculating the internal dose of NMP.

Table 2-81 presents the results of the indoor air concentrations (ppm) both central tendency and high-end estimated exposures for the consumer use scenarios based on the 50th percentile and 95th percentile input parameters. Calculations detailing the conversion from acute dose rates to air concentrations are provided in a supplemental Excel spreadsheet file (U.S. EPA, 2020d).

Detailed CEM modeling results are provided in Table 2-78.

Total internal NMP dose (C_{max}) resulting from inhalation, dermal and vapor through skin exposures to women of childbearing age consumer use of adhesive remover products as estimated from the PBPK model is presented in Table 2-82.

Table 2-82. Estimated NMP Exposures (Time Averaged Over 1 Day) Based on Residential Use of Adhesive Removers

Scenario Description For Product User	Women of Childbearing Age C_{max} (mg/L)	Pregnant Women C_{max} (mg/L)
Adhesive Removers		
Medium Intensity Use	1.292	1.239
High Intensity Use	5.957	5.778

Auto Interior Liquid and Spray Cleaners

Exposure to NMP found in NMP-containing auto interior cleaner products was based on one product that was a liquid and one product that was a spray applied. The NMP weight fraction of the liquid cleaner was listed in the product SDS as a range between 1 and 5%. For the modeling scenarios, EPA assumed a typical or central tendency NMP amount of 3% and at a high-end of 5% NMP. The duration of use and mass of product used were based on the 1987 Westat survey data, specifically the data found under the Solvent-type Cleaning Fluids or Degreasers scenario and are listed in Table 2-83.

For the spray applied cleaner, the product data sheet listed the weight fraction as <1%. EPA conservatively used 1% for both scenarios with the other two parameters distinguishing the scenarios as either high-end or central tendency. The duration of use and mass of product used were based on the 1987 Westat survey data, specifically the data found under the Solvent-type Cleaning Fluids or Degreasers scenario and are listed in Table 2-83.

Table 2-83. Estimated NMP Air Concentrations (Time Averaged Over 1 Day) Based on Residential Use of Auto Interior Liquid or Spray Cleaners

Scenario Description For Product User (Women of Childbearing Age)	Duration of Use (min)	Weight Fraction (%)	Mass of Product Used (g)	Air Concentration [a]		
				Max 8 hr TWA (mg/m^3)	Max 8 hr TWA (ppm)	Max 24 hr TWA (ppm)
Auto Interior Liquid Cleaner						
Medium Intensity Use [b]	15	3	7.69	2.88	0.711	0.237
High Intensity Use [c]	120	5	132.87	54.4	13.4	4.48
Auto Interior Spray Cleaner						
Medium Intensity Use [b]	15	1	7.69	10.8	0.266	8.89E-02
High Intensity Use [c]	120	1	132.87	12.0	2.95	0.984

[a] See Appendix G for details about the model inputs and the method used to estimate air concentrations of NMP.
[b] Medium intensity use estimate based on using 50th percentile values for use patterns from Westat Survey (1987).
[c] High intensity use estimate based on using 95th percentile values for use patterns from Westat Survey (1987).

The All Purpose Liquid Cleaner and the All Purpose Spray Cleaner default scenarios within the Consumer Exposure Module (CEM) were chosen for conducting the modeling runs for the Auto Liquid Cleaner and Auto Spray Cleaner scenarios. This selection was the closest match to the liquid or spray cleaner scenario among the default CEM exposure scenarios. The common modeling inputs required to run CEM for all consumer scenarios evaluated in this assessment are provided in Table 2-77. Other scenario-specific input parameters are provided in Table 2-78.

CEM calculated air concentrations over the course of the simulation for the room of use and the rest of the house (Zone 1 and Zone 2). These concentrations were inputs to the PBPK model and used the body weight and respiration rate for adult women (21-49 years) and adolescent females (16 to <21 years old) both considered of child-bearing age in calculating the internal dose of NMP (cite EPA definition of childbearing age).

Table 2-83 presents the results of the indoor air concentrations (ppm) both central tendency and high-end estimated exposures for the consumer use scenarios based on the 50th percentile and 95th percentile input parameters. Calculations detailing the conversion from acute dose rates to air concentrations are provided in a supplemental Excel spreadsheet file (U.S. EPA, 2020d).

Total internal NMP dose (C_{max}) resulting from inhalation, dermal and vapor through skin exposures to women of childbearing age consumer use of various auto interior cleaner products as estimated from the PBPK model is presented in Table 2-84.

Table 2-84. Estimated NMP Exposures (Time Averaged Over 1 Day) Based on Residential Use of Auto Interior Liquid or Spray Cleaners

Scenario Description For Product User	Women of Childbearing Age C_{max} (mg/L)	Pregnant Women C_{max} (mg/L)
Auto Interior Liquid Cleaner		
Medium Intensity Use	0.256	0.249
High Intensity Use	4.355	4.245
Auto Interior Spray Cleaner		
Medium Intensity Use	0.093	0.091
High Intensity Use	0.183	0.177

Cleaners/Degreasers, Engine Cleaner/Degreaser and Spray Lubricant

Exposure to NMP found in consumer cleaner/degreaser and spray lubricant products containing NMP was based on product data found on a total of 10 products. Eight products ranging from oven cleaners to metal cleaners to resin cleaner had NMP weight fractions, as listed in the product SDSs, between 1% and 100%. The duration of use and mass of product used were based on the 1987 Westat survey data, specifically the data found under the Solvent-type Cleaning Fluids or Degreasers scenario and are listed in Table 2-85.

One product was specifically used as an engine cleaner (weight fraction between 15% and 40%) and one product was found as a spray lubricant (weight fraction between 30% to 40%). For the three modeling scenarios, EPA assumed the product could be available in a low-end formulation with 1% NMP, a typical or central tendency amount of 3% and at a high-end of 5% NMP. The duration of use and mass of product used were based on the 1987 Westat survey data, specifically the data found under the Engine Cleaners/Degreasers scenario and are listed in Table 2-85.

One product was identified as a mold release (*i.e.*, once a product is formed or shaped then hardened in a mold, it then can be easily removed). It was modeled differently since it is used as a spray product. The duration of use and mass of product used were based on the 1987 Westat survey data, specifically the data found under the Other Lubricants scenario and are listed in Table 2-85

Table 2-85. Estimated NMP Air Concentrations (Time Averaged Over 1 Day) Based on Residential Use of Cleaners/Degreasers, Engine Cleaner/Degreaser and Spray Lubricant

Scenario Description For Product User (Women of Childbearing Age)	Duration of Use (min)	Weight Fraction (%)	Mass of Product Used (g)	Air Concentration [a]		
				Max 8 hr TWA (mg/m^3)	Max 8 hr TWA (ppm)	Max 24 hr TWA (ppm)
Cleaners/Degreasers						
Medium Intensity Use [b]	15	25.46	94.19	18.5	4.56	1.61
High Intensity Use [c]	120	29.87	927.43	235	57.9	20.8
Engine Cleaner/Degreaser						

Scenario Description For Product User (Women of Childbearing Age)	Duration of Use (min)	Weight Fraction (%)	Mass of Product Used (g)	Air Concentration [a]		
				Max 8 hr TWA (mg/m^3)	Max 8 hr TWA (ppm)	Max 24 hr TWA (ppm)
Medium Intensity Use [b]	15	27.50	291.6	39.7	9.80	3.56
High Intensity Use [c]	120	40	1,206.60	281	69.3	25.5
Spray Lubricant						
Medium Intensity Use [b]	2	35	18.71	0.28	7.04E-02	2.48E-02
High Intensity Use [c]	30	40	170.05	2.65	0.65	0.23

[a] See Appendix G for details about the model inputs and the method used to estimate air concentrations of NMP.
[b] Medium intensity use estimate based on using 50th percentile values for use patterns from Westat Survey (1987).
[c] High intensity use estimate based on using 95th percentile values for use patterns from Westat Survey (1987).

The All Purpose Liquid Cleaner, All Purpose Spray Cleaner and Lubricant (spray) default scenarios within the Consumer Exposure Module (CEM) were chosen for conducting the modeling runs for the Cleaner/Degreaser, Engine Cleaner/Degreaser and Spray Lubricant scenarios, respectively. This selection was the closest match to the liquid or spray cleaner scenario among the default CEM exposure scenarios. The common modeling inputs required to run CEM for all consumer scenarios evaluated in this assessment are provided in Table 2-77. Other scenario-specific input parameters are provided in Table 2-78.

CEM calculated air concentrations over the course of the simulation for the room of use and the rest of the house (Zone 1 and Zone 2). These concentrations were inputs to the PBPK model and used the body weight and respiration rate for adult women (21-49 years) and adolescent females (16 to <21 years old) both considered of child-bearing age in calculating the internal dose of NMP.

Table 2-85 presents the results of the indoor air concentrations (ppm) both central tendency and high-end estimated exposures for the consumer use scenarios based on the 50th percentile and 95th percentile input parameters. Calculations detailing the conversion from acute dose rates to air concentrations are provided in a supplemental Excel spreadsheet file (U.S. EPA, 2020d).

The total internal NMP dose (C_{max}) resulting from inhalation, dermal and vapor through skin exposures to women of childbearing age consumer use of various types of cleaner/degreaser products as estimated from the PBPK model is presented in Table 2-86.

Table 2-86. Estimated NMP Exposures (Time Averaged Over 1 Day) Based on Residential Use of Cleaners/Degreasers, Engine Cleaner/Degreaser and Spray Lubricant

Scenario Description For Product User	Women of Childbearing Age C_{max} (mg/L)	Pregnant Women C_{max} (mg/L)
Cleaners/Degreasers		
Medium Intensity Use	1.033	1.016
High Intensity Use	13.40	13.00
Engine Cleaner/Degreaser		

Scenario Description For Product User	Women of Childbearing Age C_{max} (mg/L)	Pregnant Women C_{max} (mg/L)
Medium Intensity Use	1.682	1.640
High Intensity Use	16.46	15.97
Spray Lubricant		
Medium Intensity Use	0.332	0.322
High Intensity Use	2.853	2.801

Paints and Arts and Craft Paints

Exposure to NMP found in consumer paints and arts and crafts paints products containing NMP was based on product data found on a total of four products. Two paint products that contained NMP were paints such as concrete paint and truck bed coating and had NMP weight fractions ranging from 1% to 7%. For arts and crafts paints the NMP weight fractions were 0.1% to 1%. According to the manufacturer, these liquid enamel products classified as arts and crafts paints are for craft projects (sold in half-pint and quart sized containers) and recommended for application to wood, metal, plaster, masonry or unglazed ceramic. These products are neither intended for nor are assumed to be used by children.

The duration of use and mass of product used were based on the 1987 Westat survey data, specifically the data found under the Latex Paint scenario and are listed in Table 2-85. For the Arts and Craft scenario mass of product was adjusted lower (ratio of 64) by the craft volume sold (2 ounces) relative to the wall paint (gallon).

Table 2-87. Estimated NMP Air Concentrations (Time Averaged Over 1 Day) Based on Residential Use of Paints and Arts and Crafts Paints

Scenario Description For Product User (Women of Childbearing Age)	Duration of Use (min)	Weight Fraction (%)	Mass of Product Used (g)	Air Concentration [a]		
				Max 8 hr TWA (mg/m^3)	Max 8 hr TWA (ppm)	Max 24 hr TWA (ppm)
Paints						
Medium Intensity Use [b]	180	2.03	4,194.24	2.40	0.593	0.204
High Intensity Use [c]	810	3.63	23,068.31	18.3	4.51	2.52
Arts and Crafts Paints						
Medium Intensity Use [b]	180	0.55	65.30	1.41E-02	3.48E-03	1.19E-03
High Intensity Use [c]	810	1.00	359.00	1.01E-01	2.48E-02	1.39E-02

[a] See Appendix G for details about the model inputs and the method used to convert acute dose rates (ADRs) to air concentrations of NMP.
[b] Medium intensity use estimate based on using 50th percentile values for use patterns from Westat Survey (1987).
[c] High intensity use estimate based on using 95th percentile values for use patterns from Westat Survey (1987).

The Solvent-based Wall Paint and the Crafting Paint default scenarios within the Consumer Exposure Module (CEM) were chosen for conducting the modeling runs for the Paint and Arts and Crafts

scenarios, respectively. These selections were the closest match to each of the paint scenarios among the default CEM exposure scenarios. The common modeling inputs required to run CEM for all consumer scenarios evaluated in this assessment are provided in Table 2-77. Other scenario-specific input parameters are provided in Table 2-78.

CEM calculated air concentrations over the course of the simulation for the room of use and the rest of the house (Zone 1 and Zone 2). These concentrations were inputs to the PBPK model and used the body weight and respiration rate for adult women (21-49 years) and adolescent females (16 to <21 years old) both considered of child-bearing age in calculating the internal dose of NMP.

Table 2-87 presents the results of the indoor air concentrations (ppm) both central tendency and high-end estimated exposures for the consumer use scenarios based on the 50th percentile and 95th percentile input parameters. Calculations detailing the conversion from acute dose rates to air concentrations are provided in a supplemental Excel spreadsheet file (U.S. EPA, 2020d).

Total internal NMP dose (C_{max}) resulting from inhalation, dermal and vapor through skin exposures to women of childbearing age consumer use of paint products as estimated from the PBPK model is presented in Table 2-88.

Table 2-88. Estimated NMP Exposures (Time Averaged Over 1 Day) Based on Residential Use of Paints and Arts and Crafts Paints

Scenario Description For Product User	Women of Childbearing Age C_{max} (mg/L)	Pregnant Women C_{max} (mg/L)
Paints		
Medium Intensity Use	0.374	0.358
High Intensity Use	1.422	1.415
Arts and Crafts Paints		
Medium Intensity Use	0.071	0.068
High Intensity Use	0.222	0.219

Stains, Varnishes, Finishes (Coatings)

Exposure to NMP found in consumer stains, varnishes, finishes and other coatings products containing NMP was based on product data found on a total of nine products. The NMP weight fractions range was between 0.3% to 10% with the mean of 4.97% and the average high-end of 8.25% used to model consumer exposure estimates. The duration of use and mass of product used were based on the 1987 Westat survey data, specifically the data found under the Stains, Varnishes, and Finishes scenario and are listed in Table 2-89.

The Varnishes and Floor Finishes default scenarios within the Consumer Exposure Module (CEM) was chosen for conducting the modeling runs for the Stains, Varnishes, Finishes (Coatings) scenario. This selection was the closest match to the liquid coatings scenario among the default CEM exposure scenarios. The common modeling inputs required to run CEM for all consumer scenarios evaluated in this assessment are provided in Table 2-77. Other scenario-specific input parameters are provided in Table 2-78.

Table 2-89. Estimated NMP Air Concentrations (Time Averaged Over 1 Day) Based on Residential Use of Stains, Varnishes, Finishes (Coatings)

Scenario Description For Product User (Women of Childbearing Age)	Duration of Use (min)	Weight Fraction (%)	Mass of Product Used (g)	Air Concentration [a]		
				Max 8 hr TWA (mg/m^3)	Max 8 hr TWA (ppm)	Max 24 hr TWA (ppm)
Stains, Varnishes, Finishes (Coatings)						
Medium Intensity Use [b]	60	4.97	366.42	6.84E-01	1.68E-01	5.74E-02
High Intensity Use [c]	360	8.25	3,908.44	12.5	3.08	1.08

[a] See Appendix G for details about the model inputs and the method used to estimate air concentrations of NMP.
[b] Medium intensity use estimate based on using 50th percentile values for use patterns from Westat Survey (1987).
[c] High intensity use estimate based on using 95th percentile values for use patterns from Westat Survey (1987).

CEM calculated air concentrations over the course of the simulation for the room of use and the rest of the house (Zone 1 and Zone 2). These concentrations were inputs to the PBPK model and used the body weight and respiration rate for adult women (21-49 years) and adolescent females (16 to <21 years old) both considered of child-bearing age in calculating the internal dose of NMP.

Table 2-89 presents the results of the indoor air concentrations (ppm) both central tendency and high-end estimated exposures for the consumer use scenarios based on the 50th percentile and 95th percentile input parameters. Calculations detailing the conversion from acute dose rates to air concentrations are provided in a supplemental Excel spreadsheet file (U.S. EPA, 2020d).

Total internal NMP dose (C_{max}) resulting from inhalation, dermal and vapor through skin exposures to women of childbearing age consumer use of coatings products as estimated from the PBPK model is presented in Table 2-90.

Table 2-90. Estimated NMP Exposures (Time Averaged Over 1 Day) Based on Residential Use of Stains, Varnishes, Finishes (Coatings)

Scenario Description For Product User	Women of Childbearing Age C_{max} (mg/L)	Pregnant Women C_{max} (mg/L)
Stains, Varnishes, Finishes (Coatings)		
Medium Intensity Use	0.341	0.327
High Intensity Use	1.947	1.882

Paint and Coating Removers

Consumer exposure to NMP found in consumer paint and coating remover products containing NMP was assessed in the Final *Paint Remover Risk Assessments* (U.S. EPA, 2015c) as well as the *Supplemental Consumer Exposure and Risk Estimation Technical Report for NMP in Paint and Coating Removal* (see Appendix G.2). For the supplemental analysis, exposures were estimated for 18 scenarios. The E2 scenario was selected as a representative high intensity use scenario. The paint and coating remover product was modeled to remove paint from a bathtub and using 4 applications. The A2 scenario was selected as a representative medium intensity use scenario. The NMP paint and coating remover product was used to remove paint from a coffee table. For this final risk evaluation, the high-end weight

fraction of 60% was used for paint remover products for both scenarios. Appendix G.2 lists all of the evaluated scenarios for the paint and coating remover evaluation.

Table 2-91. Estimated NMP Air Concentrations (Time Averaged Over 1 Day) Based on Residential Use of Paint and Coating Removers

Scenario Description For Product User	Duration of Use (min)	Weight Fraction (%)	Mass of Product Used (g)	Air Concentration	
				Max 8 hr TWA (mg/m^3)	Max 8 hr TWA (ppm)
Paint and Coating Removers					
Medium Intensity Use	60	60	540	6.2	1.5
High Intensity Use	360	60	1944	232	57.3

As described in detail in the previous assessments, emissions data were reasonably available specifically for paint and coating remover product use. This data can then be used in a higher tier exposure model, the Multi-Chamber Concentration and Exposure Model (MCCEM) to estimate air concentration. In principle, as in the CEM, the MCCEM also estimates NMP air concentrations in various areas of the house depending on the user's activity pattern. MCCEM calculated air concentrations over the course of the simulation for the room of use and the rest of the house (Zone 1 and Zone 2). These concentrations were inputs to the PBPK model and used the body weight and respiration rate for adult women of child-bearing age in calculating the internal dose of NMP.

Table 2-92 presents the internal dose for women of childbearing age for the medium intensity use and high intensity use scenarios.

Table 2-92. Estimated NMP Exposures (Time Averaged Over 1 Day) Based on Residential Use of Paint and Coatings Removers

Scenario Description For Product User	Women of Childbearing Age C_{max} (mg/L)
Paint and Coating Removers	
Medium Intensity Use	2.014
High Intensity Use	15.12

EPA reviewed data from one study that specifically measured NMP air concentrations while an NMP-containing paint removal product was being used on floors in a house undergoing renovation (NIOSH, 1993). The study reported air concentrations ranging from 3.6 to 7.7 ppm in the room of use. In EPA's supplemental analysis of NMP use in paint and coating removal, the modeled paint removal use resulted in air concentrations of 11.1 ppm (8-hr time weighted average, see Appendix G.2, "Eight-hour TWA exposures for additional scenarios" table). Although this model estimated NMP air concentration is higher than the measured air concentration presented by NIOSH (1993), both represent the air concentration in the room that a non-user would be exposed to rather than the personal breathing zone concentration to which the user is directly exposed. EPA determined that the estimated NMP exposures incurred during floor paint removal do not present a risk to non-users (see Appendix G.2).

Exposure to Bystanders

In each of the consumer scenarios listed above, use of a product containing NMP is expected to result in air concentrations of NMP and user inhalation exposure to NMP in addition to dermal and vapor-through skin exposures. EPA also expects that the NMP air concentrations can be circulated through the house via the air ventilation system so that NMP exposures could occur to other occupants in the house during and after consumer use. The air concentration in Zone 2 (rest of the house) is presented in the supplemental document, *Risk Evaluation for n-Methylpyrrolidone, Supplemental Information on Consumer Exposure Assessment, Consumer Exposure Model Outputs* (U.S. EPA, 2020d).

EPA estimated the internal dose for indirect NMP exposures to adult bystanders as well as children aged 3-5 years due to their location in the rest of the house (Zone 2) and in the room of use together with the user or in other areas of the house during consumer use (see Table 2-93) (U.S. EPA, 2019p). The default bystander scenario in CEM is that the bystander is in another room within the home while the consumer product is being used. EPA, however, also considered the scenario of the bystander being exposed to the same NMP air concentration as the user. Though this may be highly unlikely, it does provide an upper bound exposure estimate. For example, this upper bound may reflect exposures of children in the same room as their parent using the NMP-containing consumer product.

Table 2-93. Estimated Bystander Exposure to NMP Consumer Use

Consumer Conditions of Use	Bystander Female Adult C_{max} (mg/L)		Bystander Child (3-5 yrs) C_{max} (mg/L)	
	In Room of Use [a]	In Rest of House	In Room of Use [a]	In Rest of House
Engine Cleaner/ Degreaser	8.2	5.5	10.6	6.5
Paint and Coating Removers	9.8	3.6	11.4	3.6
High Weight Fraction Adhesives and Sealants	0.16	0.0	0.2	0.0

[a] Bystander C_{max} estimates in room of use assume exposure to the same NMP air concentrations as the user.

2.4.2.6 Key Assumptions and Confidence

Given the absence of direct measurement and monitoring of consumer exposures during product use, modeling was used to evaluate consumer exposures resulting from the conditions of use summarized in Table 2-78. Modeling requires a number of input parameters, some of which rely on default modeling assumptions and some of which rely on user inputs or selections. As with any modeling approach, there are uncertainties associated with the assumptions and data used. An overall review of these factors can help develop a qualitative description of the confidence associated with the modeling approach and results.

Key Assumptions

Evaluation of acute consumer exposure is based on the assumption that the products used under the conditions of use summarized in Table 2-78, except paint removers, are only used once per day. This assumption considers a single use event which may occur over a 24-hour period and represents an expected consumer use pattern. This is a reasonable assumption for the average intensity user but may underestimate those high intensity users such as do-it-yourselfers (DIY) that could use a product multiple times in a day. The paint remover scenario as defined in the Paint Remover Risk Assessment, defines a user pattern in which the product is applied then scraped away with the paint and reapplied

again as is outlined in the product directions. This product-specific use is reflected in the use patterns for all of the products evaluated for consumer exposures.

Evaluation of consumer exposure for this evaluation is also based on the assumption that a consumer uses a single product or product type. For the products estimated under the conditions of use, this is a reasonable assumption.

This evaluation assumes consumer exposure is not chronic in nature. This assumption is based on the expected consumer use pattern and data found during systematic review that indicates frequency of use (days of use) of products containing the chemical of concern is not chronic in nature. This assumption is also based on the rapid elimination of NMP so that the use pattern and data would not be chronic in nature. This assumption may result in excluding certain consumer users who may be do-it-yourselfers.

This evaluation assumes a background concentration of zero for the chemical of concern during evaluation of consumer exposure. This assumption is primarily driven by the physical and chemical properties of the chemical of concern which is the high vapor pressure and expected quick dissipation of the chemical of concern.

Inputs
Inputs for the modeling were a combination of physical and chemical properties of the chemical of concern, default values within the models used, values from the Exposure Factors Handbook (U.S. EPA, 2011), and use pattern survey data found in the literature as part of the systematic review process (Westat Survey U.S. EPA, 1987). Physical and chemical properties of the chemical of concern are pre-defined and well established in the literature. These properties do not change under standard conditions and therefore have high confidence associated with them.

Default values within the models used are a combination of central tendency and high-end values derived from well-established calculations, modeling, literature, and from the Exposure Factors Handbook (U.S. EPA, 2011). The models used have a wide variety of parameters with default values, although certain default values can be changed (if information and data are reasonably available) prior to running the model. There is a high confidence associated with these values due to the number of parameters where defaults are available.

Values from the Exposure Factors Handbook (U.S. EPA, 2011) are a combination of central tendency and high-end values which are well established and commonly used for exposure evaluations and modeling. The values are derived from literature, modeling, calculations, and surveys. There is a high confidence associated with the Exposure Factors Handbook (U.S. EPA, 2011).

The Westat Survey (U.S. EPA, 1987) was previously described in this evaluation. It is an EPA-directed national survey which received over 4,920 completed questionnaires from across the United States. The survey aimed to answer multiple questions related to the use of solvent-containing consumer products within thirty-two different common household product categories. Multiple aspects of the survey and survey results were utilized in this evaluation. Most of the consumer uses summarized in Table 2-78 aligned well with one of the thirty-two product categories within the Westat Survey. There is a high confidence associated with cross-walking of consumer uses with the Westat product categories.

The representativeness of the consumer use patterns (duration of use, amount used, room of use, etc.) described in the Westat Survey (from 1987) is believed to remain strong when compared to present day consumer use patterns even though some aspects of the use may have changed (electronics cleaners

were applied to VCRs in 1987, but now are applied to computer motherboards or DVD players). However, ease of access to products on-line or in big box stores (like home improvement stores), readily accessible how-to videos, and a consumer movement toward more do-it-yourself projects with products containing the chemical of concern could impact the representativeness of the consumer use patterns described within the Westat Survey and may lead to an underestimation of overall consumer exposure. There is a high confidence associated with the representativeness of the consumer use patterns described within the Westat Survey and present-day consumer use patterns.

Other Uncertainties
There are several other factors to which some level of uncertainty may apply. These include, but are not limited to, product use/availability, model specific factors, building characteristics, and use of PPE or natural/engineered controls.

As described in Section 2.4.2.1, the market profile was developed in 2017 based on information reasonably available at that time. These do not take into consideration company-initiated formulation changes, product discontinuation, or other business or market-based factors that occurred after the documents were compiled. However, unless these factors were in process while the dossier and market profile were being developed, it is unlikely any significant changes occurred since such changes often require considerable time to research, develop, and implement. Even with discontinuation of products, while they may readily be removed from shelves, product already purchased or picked up to be sold online shortly before discontinuation will take some time to work out of the system. There is a medium confidence associated with the product use/availability of product containing the chemical of concern.

There are multiple model specific factors to which a level of uncertainty may apply including user groups (age groups), building characteristics, and inherent model parameters.

There are multiple building characteristics considered when modeling consumer exposure including, but not limited to, room size, ventilation rate, and building size. For this evaluation, we relied on default values within the models for these parameters. These default values were primarily obtained from the Exposure Factors Handbook (U.S. EPA, 2011). There is a medium to high confidence associated with these parameters.

Room size varied for this evaluation based on room of use obtained from the Westat Survey (1987) data. Room size relates to the volume of the room and is a sensitive parameter within the models. However, the room size of a standard bedroom, living room, kitchen, utility room, one or two car garage, etc. should be relatively consistent across building types (small or large residential homes, apartments, condominiums, or townhomes). Therefore, any uncertainty associated with room size is derived more from the room of use selected, rather than the wide variety of sizes of a particular room of use. Since the rooms of use selected for this evaluation are based on data collected by the Westat Survey, there is a high confidence associated with room sizes used for this evaluation.

Ventilation rate is another sensitive parameter within the models. Similar to the room of use, however, ventilation rates should be relatively consistent across building types where ventilation systems are properly maintained and balanced. Centralized ventilation systems are designed to deliver ventilation rates or air exchange rates which meet the American Society of Heating, Refrigeration, and Air Conditioning Engineers Standard Recommendations which are established for rooms, house types, commercial buildings, and others. Centralized ventilation systems may be larger for larger homes, but the ventilation rates delivered to the specific room of use should be relatively consistent across building types. Therefore, any uncertainty associated with ventilation rates is derived more from the proper

design, balancing, and maintenance of ventilation systems. Ventilation rates for a particular room of use could be impacted by use of fans or opening windows within the room of use, however, most respondents to the Westat Survey indicated they did not have an exhaust fan on when using the products. Most respondents kept the door to the room of use open but did not open doors or windows leading to the outside when using the products. There is a medium to high confidence associated with the ventilation rates used for this evaluation.

Building size is another sensitive parameter within the models, however, the sensitivity derives from more mixing and dissipation outside of the room of use. There will be more variability in building size across building types so there is a medium confidence associated with building size.

The use of PPE or natural/engineered controls by a consumer during product use is uncertain. It is not expected that consumers will utilize PPE like full face respirators, or engineering controls like hoods when using consumer products in a residence or building to reduce inhalation risks. While it may be slightly more likely that, for certain products, consumers may choose to wear gloves or eye protection, neither of these addresses inhalation exposure. Use of gloves by a consumer could decrease dermal exposure, assuming the gloves are high quality and chemical resistant. Latex gloves are readily available; however, such gloves tear easily, and may not be resistant to breakdown by certain products used. Although the use of gloves could reduce dermal exposure, if used improperly (for example fully immersing hands into a product) could allow for leakage into the glove.

Confidence

There is an overall medium confidence in all the results found for the consumer scenarios identified in Table 2-74 and evaluated in this evaluation. This confidence derives from a review of the factors discussed above as well as previous discussions about the strength of the models and data used, sensitivity of the models, and approaches taken for this evaluation.

The models used for this evaluation are peer reviewed models. The equations are derived, justified and substantiated by peer reviewed literature as described in the respective user guides and associated user guide appendices. The default values utilized in the model (and retained for this evaluation) are a combination of central tendency and high-end estimates from both peer reviewed literature and the Exposure Factors Handbook (U.S. EPA, 2011) providing a representative spectrum of modeling results. Even though some values have high end values (like building size or ventilation rates), it should be recognized that these parameters are correlated, and that "higher" building sizes or higher ventilation rates would be expected to result in more mixing and dissipation leading to a lower exposure.

The data used in lieu of default values within the model are a combination of central tendency, and high-end values from the Westat Survey, which was rated as a high-quality study as part of the systematic review process. The twelve use scenarios evaluated for this evaluation aligned well with specific scenarios within the Westat Survey, pre-defined model scenarios, and other approaches taken. The deterministic approach taken for consumer exposure in this evaluation involved varying three parameters that were either highly sensitive or representative of consumer use patterns or both. The three parameters varied also provided a broad spectrum of consumer use patterns covering low, moderate, and high intensity uses and therefore are not limited to a high-end, worst-case type situation or an upper bounding estimate. Other aspects of the deterministic approach taken (like a single product used once per day) may result in an underestimation of actual consumer exposure.

2.4.3 General Population Exposures

Since NMP is not designated a hazardous air pollutant, EPA considered human exposures that may result from inhalation of outdoor air containing NMP released from industrial and commercial facilities. A first-tier screening analysis was used to estimate the potential (near field) exposure to populations located downwind of facilities reporting the highest NMP air releases based on 2015 TRI data. Using EPA's SCREEN3 Model and the highest reported stack emissions, the estimated NMP concentration in ambient air was approximately 0.41 mg/m3.

In the previous NMP assessment, EPA used data on NMP-induced decreases in fetal body weight as the basis for risk estimation. Benchmark dose modeling of internal dose estimates based on physiologically-based pharmacokinetic modelling was used to determine a POD (48 mg/kg/day) for estimating risks associated with chronic exposure in humans (U.S. EPA (2015). This POD was converted to an inhalation dose (based on a total dose of 3,840 mg/day, and 80 kg bodyweight). EPA's EFAST model uses a default breathing rate of 0.61 m^3/hour over a 24-hour period (14.6 m^3/day). Hence the inhalation POD is: (3,840 mg/day)/(14.6 m^3/day) = 263 mg/m^3 (24-hour TWA).

NMP does not currently have established water quality criteria to protect human health under the CWA Section 304a. Therefore, in this evaluation, EPA considers potential general population exposures via the ambient water pathway through evaluating incidental oral and dermal exposures related to recreational activities such as swimming for adults and children 11-15 years. EPA considered the latter lifestage as representing worst-case exposure conditions when considering the age-specific ingestion rate, body weight and duration of exposure. Exposures to the general population via fish ingestion are not evaluated due to NMP's low bioaccumulation potential in fish.

2.4.3.1 General Population Exposure Approach and Methodology

Both estimated and measured levels of NMP in ambient water, or surface water, were used to estimate incidental oral and dermal exposures during recreational activities such as swimming. Based on the incidental nature of such exposures, the evaluation focuses on acute exposures.

2.4.3.2 Exposure Through Incidental Contact with Surface Water

Based on 2018 TRI reporting, EPA estimates annual releases, release days, and number of facilities to provide a range of daily water releases for each occupational exposure scenario (OES) (see Table 2-2). This evaluation of general population exposures via ambient water consisted of facilities reporting direct discharges into receiving waters and included the following OES: chemical processing, excluding formulation, electronics manufacturing, formulation, and metal finishing.

Using the described site-specific water release information (kg/site/day) and days of release based on OES categories and assumptions, environmental modeling was conducted using EPA's Exposure and Fate Assessment Screening Tool (E-FAST 2014) to predict surface water concentrations in near-facility ambient water bodies (U.S. EPA, 2014c). For more on the operation and inputs of the E-FAST model, refer to the Estimating Surface Water Concentrations Section of Appendix E and the E-FAST 2014 Documentation Manual (U.S. EPA, 2007).

In this evaluation, site-specific stream flows were applied within E-FAST, where available, and no wastewater treatment removal was applied. E-FAST does not incorporate degradation or volatilization once released and estimates concentrations at the point of release (not downstream).

Modeled Surface Water Concentrations

Table 2-94 displays the modeled surface water concentrations from direct dischargers obtained from E-FAST, as well as the site-specific water release inputs.

Table 2-94. Modeled Surface Water Concentrations

OES	Facility Name	Daily Release (kg/site-day)	Number of Days of Release	30Q5 Surface Water Concentration [a,b] (µg/L)
Chemical Processing, Excluding Formulation	Spruance Plant	7.1	300	3.4E+00
	BASF Corp., Alabama	8.0E-01	300	2.2E-01
	Fortron Industries LLC	3.8E-01	300	1.7E+00
	American Refining Group, Inc.	2.0E-02	300	1.1E-01
	BASF Corp, Michigan	1.7E-02	300	1.3E-04
Electronics Manufacturing	GlobalFoundries, Vermont	1.3	250	2.3E+00
	GlobalFoundries, New York	2.5E-02	250	1.4E+00
Formulation	Essex Group Inc. Chemical Processing Plant	6.7E-02	300	5.4E+00
Metal Finishing	Essex Group LLC	3.6E-03	250	7.7E-01

[a] Site specific modeling was conducted to estimate surface water concentrations.

[b] Predicted 30Q5 surface water concentrations are the concentrations predicted using a 30Q5 stream flow. The 30Q5 stream flow is the lowest 30-day mean stream flow for a recurrence interval of five years. For sites modeled using a generic SIC code, the values in this column correspond to concentrations predicted using the low-end *(i.e.*, 10th percentile) of the 30Q5 stream flow distribution for that SIC code. The 30Q5 concentrations are used in this evaluation over the mean or 7Q10 concentrations based on alignment with E-FAST guidance for assessing acute drinking water exposures (U.S. EPA, 2007).

2.4.3.2.1 Estimating Incidental Oral Exposures from Swimming

Predicted stream concentrations were used to estimate acute incidental oral exposure from swimming. Predicted surface water concentrations ranges from 1.3E-04 µg/L to 5.4 µg/L (see Table 2-94). Additional inputs/exposure factors used to estimate these acute oral exposures are included in Table 2-95. This evaluation focused on children 11-15 years, as they present the worst-case exposure conditions when considering the age-specific ingestion rate, body weight, and duration of exposure.

Table 2-95. Incidental Oral Exposure Factors

Description	Value	Notes
Age Class	Adult	Selected based on having highest dose based on permeability-based dermal exposure equation used in SWIMODEL, considering exposed surface area, duration, and body weight

Description	Value	Notes
Incidental Ingestion Rate	152 mL/hr	Upper-percentile hourly incidental ingestion rate from the Exposure Factors Handbook, Table 3-7 (U.S. EPA, 2019n)
Body Weight	74 kg	Mean body weight for adult female (EFH, Table 8-1)
Duration of Exposure	2 hrs	High-end default short-term duration default from EPA Swimmer Exposure Assessment Model (SWIMODEL); based on competitive swimmers in the child 11-15 age class (U.S. EPA, 2015b)
Daily Ingestion Rate	0.304 L/day	0.152 L/day * 2 hrs

The equation used to estimate the acute daily dose rate (ADR) for incidental oral ingestion is shown below (U.S. EPA, 2007):

$$ADR = \frac{SW\ x\ IR\ x\ CF}{BW}$$

Where,

SWC = Surface water concentration (µg/L)
IR = Drinking water intake rate (L/day)
CF = 0.001 mg/µg
BW = Body weight (kg)

2.4.3.2.2 Estimating Dermal Exposures from Swimming

Predicted stream concentrations were used to estimate incidental acute incidental oral exposure from swimming. Predicted surface water concentrations of NMP ranges from 1.3E-04 µg/L to 5.4 µg/L (see). Additional inputs/exposure factors used to estimate these acute oral exposures are included in Table 2-96. This evaluation focused on the adult age class, as they present the worst-case exposure conditions when considering the age-specific surface area to body weight ratio and duration of exposure.

Table 2-96. Dermal Exposure Factors

Description	Value	Notes
Age Class	Adult	Selected based on having highest dose based on permeability-based dermal exposure equation used in SWIMODEL, considering exposed surface area, duration, and body weight
Skin Surface Area	19,500 cm^2	Default dermal contact surface area for the adult age class in SWIMODEL (U.S. EPA, 2015b)
Body Weight	74 kg	Mean body weight for adult female (EFH, Table 8-1)
Exposure Duration	3 hrs	High-end short-term default duration from EPA Swimmer Exposure Assessment Model (SWIMODEL); based on competitive swimmers in the adult age class (U.S. EPA, 2015b)
Permeability Coefficient (Kp)	4.78E-04 cm/hr	NMP permeability coefficient (see Section 3.2.5.5)

The equation used to estimate the acute daily dose rate for dermal exposure from swimming shown below (U.S. EPA, 2015b):

$$ADR = \frac{CW\ x\ Kp\ x\ SA\ x\ ET\ x\ CF}{BW}$$

Where,

CW = Chemical concentration in water (mg/L)
Kp = Permeability coefficient (cm/hr)
SA = Skin surface area exposed (cm^2)
ET = Exposure time (hrs/day)
CF = Conversion factor (0.001 L/cm^3)
BW = Body Weight (kg)

2.4.3.3 General Population Exposure Results

Estimated acute incidental oral exposures range from 4.7E-10 to 2.0E-05 mg/kg/day, while estimated acute dermal exposures range from 4.8E-5 to 2.0 mg/kg/day. The highest doses are associated with releases from the formulation uses OES. This range of exposure estimates cover acute oral and dermal doses estimated using both modeled and measured surface water concentrations.

Table 2-97. Acute Oral Exposure Estimates Through Incidental Ingestion of Water and Dermal Exposure from Swimming

OES	Facility/Data Source [a]	30Q5 Surface Water Concentration [b] (µg/L)	Oral Acute Dose, Female (mg/kg/day) [c]	Dermal Acute Dose, Adult [d] (mg/kg/day)
Chemical Processing, Excluding Formulation	Spruance Plant	3.4E+00	1.3E-05	1.3E+00
	BASF Corp., Alabama	2.2E-01	8.2E-07	8.3E-02
	Fortron Industries LLC	1.7E+00	6.5E-06	6.6E-01
	American Refining Group, Inc.	1.1E-01	4.1E-07	4.2E-02
	BASF Corp., Michigan	1.3E-04	4.7E-10	4.8E-05
Electronics Manufacturing	GlobalFoundries, Vermont	2.3E+00	8.6E-06	8.7E-01
	GlobalFoundries, New York	1.4E+00	5.2E-06	5.2E-01
Formulation	Essex Group Inc. Chemical Processing Plant	5.4E+00	2.0E-05	2.0E+00

OES	Facility/Data Source [a]	30Q5 Surface Water Concentration [b] (µg/L)	Oral Acute Dose, Female (mg/kg/day) [c]	Dermal Acute Dose, Adult [d] (mg/kg/day)
Metal Finishing	Essex Group LLC	7.7E-01	2.9E-06	2.9E-01

[a] Site specific modeling was conducted to estimate surface water concentrations.
[b] Predicted 30Q5 surface water concentrations are the concentrations predicted using a 30Q5 stream flow. The 30Q5 stream flow is the lowest 30-day mean stream flow for a recurrence interval of five years. For sites modeled using a generic SIC code, the values in this column correspond to concentrations predicted using the low-end (*i.e.*, 10th percentile) of the 30Q5 stream flow distribution for that SIC code. The 30Q5 concentrations are used in this evaluation over the mean or 7Q10 concentrations based on alignment with E-FAST guidance for assessing acute drinking water exposures (U.S. EPA, 2007).
[c] Dose is based on high end incidental intake rate
[d] Dose is based on high-end competitive swimmer (3 hrs/day)

2.4.3.4 Uncertainties Related to Modeling Approach and Assumptions

Releases modeled using E-FAST 2014 were predicted based on engineering site-specific estimates based on TRI reporting databases. These data that form the basis for engineering estimates are self-reported by facilities subject to minimum reporting thresholds; therefore, they may not capture releases from certain facilities not meeting reporting thresholds (*i.e.*, environmental releases may be underestimated).

E-FAST 2014 estimates surface water concentrations at the point of release, without accounting for post-release environmental fate or degradation processes such as volatilization, biodegradation, photolysis, hydrolysis, or partitioning. Additionally, E-FAST does not estimate stream concentrations based on the potential for downstream transport and dilution. These considerations tend to lead to higher predicted surface water concentrations. Dilution is incorporated, but it is based on the stream flow applied. Therefore, there is uncertainty regarding the level of NMP that would be predicted downstream of a releasing facility or after accounting for potential volatilization from the water surface, which is dependent on the degree of mixing in a receiving water body.

The ambient water analysis assumes that members of the general population are incidentally exposed via swimming in ambient waters, but there is uncertainty surrounding the likelihood that such recreation and contact would occur at or near the point of release. If such activities occurred further from the point of release, this analysis may overestimate the water concentrations that swimmers would be exposed to. EPA's SWIMODEL was used as the source for exposure duration. This model is intended to assess exposure from swimming in pools, not ambient water bodies, so there is uncertainty about the application of swimming pool duration data in this analysis.

2.4.3.5 Confidence in General Population Exposure Estimates

Confidence ratings for general population ambient water exposure scenarios are informed by uncertainties surrounding inputs and approaches used in modeling surface water concentrations and estimating incidental oral and dermal doses. Estimated daily releases (kg/site-day) on a per occupational exposure scenario (OES) basis reflect moderate confidence.

Other considerations that impact confidence in the ambient water exposure scenarios include the model used (E-FAST 2014) and its associated default and user-selected values and related uncertainties. As described, there are uncertainties related to the ability of E-FAST 2014 to incorporate downstream fate and transport. Of note, as stated on EPA's E-FAST 2014 website, "modeled estimates of concentrations and doses are designed to reasonably overestimate exposures, for use in an exposure assessment in the absence of or with reliable monitoring data." Regarding the assumption that members of the general

population could reasonably be expected to swim at or near the point of release, there is relatively low confidence.

There are no readily available NMP surface water monitoring data available that reflect ambient water exposure levels in the United States (see Section 2.4.3.2) thus, EPA relied on facility submitted data as reported in TRI.

Based on the above considerations, the general population ambient water exposure assessment scenarios have an overall low to moderate confidence.

2.5 Other Exposure Considerations

2.5.1 Potentially Exposed or Susceptible Subpopulations

TSCA Section 6 requires that a risk evaluation "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of cost or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use." TSCA Section 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly."

In developing the risk evaluation, EPA analyzed reasonably available information to ascertain whether some human receptor groups may have greater exposure potential or susceptibility to NMP than the general population. Because risk determinations were based on potential reproductive and developmental effects of NMP exposure that may occur at sensitive lifestages, they account for risks to susceptible subpopulations, including males and females of reproductive age, pregnant females and the developing embryo/fetus, infants, children and adolescents. It was assumed that exposures which do not result in unreasonable risks for this population would also be protective of other populations because other health effects are expected to occur at high levels of NMP exposure.

EPA estimated exposures to children who may be located near the consumer user at the time of use and determined that these exposures were below the levels of concern identified for adverse developmental effects and would therefore be below the levels of concern for other hazard effects that may be associated with higher NMP exposure levels.

2.5.2 Aggregate and Sentinel Exposures

As a part of risk evaluation, Section 2605(b)(4)(F)(ii) of TSCA requires EPA to describe whether aggregate or sentinel exposures were considered under the identified conditions of use and the basis for their consideration. EPA has defined aggregate exposure as "the combined exposure to an individual from a single chemical substance across multiple routes and multiple pathways." (40 C.F.R. 702.33). EPA defines sentinel exposure as "exposure to a single chemical substance that represents the plausible upper bound relative to all other exposures within a broad category of similar or related exposures." (40 C.F.R. 702.33). EPA considered sentinel exposure in the form of high-end estimates for consumer and occupational exposure scenarios which incorporate dermal and inhalation exposure, as these routes are expected to present the highest exposure potential based on details provided for the manufacturing, processing and use scenarios discussed in the previous section. The exposure calculation used to

estimate dermal exposure to liquid is conservative for high-end occupational and consumer scenarios where it assumes full contact of both hands and no protective glove use.

3 HAZARDS

3.1 Environmental Hazards

3.1.1 Approach and Methodology

EPA identified environmental hazard data for NMP through an extensive literature search as described in detail in Section 1.5 and depicted in Figure 1-9. This process was completed in 2019 as part of this risk evaluation with a portion of the search completed in 2017 as part of the NMP problem formulation.

EPA in the NMP Problem Formulation (U.S. EPA, 2018c) did not conduct any further analyses on pathways of exposure for terrestrial receptors in line with Section 2.5.3.1 of the Problem Formulation. The Problem Formulation did not identify Environmental Hazards for either aquatic or terrestrial receptors. The analysis was based on a qualitative assessment of the physical and chemical properties and fate of NMP in the environment and a quantitative comparison of the hazards and exposures identified for aquatic organisms.

Subsequent to that analysis, an additional five "Key/Supporting" citations were identified by EPA after review of the OECD HPV SIDS Document for NMP (OECD, 2009). EPA obtained the full study reports from the NMP Producer's Group (BASF and GAF). As these studies raised concerns for Environmental Hazards associated with NMP and aquatic receptors, a quantitative evaluation of hazards to aquatic receptors is included as part of this risk evaluation. EPA conducted no further analyses of exposure and hazards for terrestrial receptors and instead relied on the analyses conducted as part of the NMP Problem Formulation.

3.1.2 Hazard Identification

EPA quantitatively evaluated impacts to aquatic organisms, including fish, aquatic invertebrates and algae from acute and chronic NMP releases to surface water. The hazard characterization for all identified environmental hazard endpoints are summarized in Table 3-1. The environmental hazard data were reviewed for acute and chronic exposure duration related endpoints (*e.g.*, mortality, growth, immobility, reproduction). No ecotoxicity studies were identified for sediment-dwelling organisms.

3.1.2.1 Toxicity Data for Aquatic Organisms

EPA evaluated four studies for NMP acute exposures for fish. The acute 96-hour LC_{50} values reported for fish range from >500 mg/L for the freshwater rainbow trout (*Oncorhynchus mykiss*) to 4,030 mg/L for the freshwater orfe (*Leuciscus idus*).

For NMP acute toxicity data were evaluated for aquatic invertebrates for four species including the freshwater water flea (*Daphnia magna*), the saltwater grass shrimp (*Palaemonetes vulgaris*), the saltwater mud crab (*Neopanope texana sayi*), and the freshwater scud (*Gammarus sp.*) (GAF, 1979). The results of these studies are summarized in Table 3-1 with more detail provided in Appendix H. The 48-hour EC_{50} for NMP and *D. magna* is reported as 4,897 mg/L. The 96-hour LC_{50}'s for grass shrimp, mud crab, and scud are reported as 1,107, 1,585 and 4,655 mg/L, respectively (GAF, 1979).

For the fresh water green algae (*Scenedesmus subspicatus*), the 72-hour EC_{50} values were 600 mg/L (Biomass) and 673 mg/L (Growth rate) (BASF, 1989).

EPA evaluated one chronic toxicity study for NMP exposures for freshwater invertebrates (*D. magna*). A 21-day study with *D. magna* reported reproductive effects for NMP with a No Observed Effect

Concentration (NOEC) of 12.5 mg/L and a Lowest Observed Effect Concentration (LOEC) of 25 mg/L, resulting in a calculated chronic toxicity value of 17.68 mg/L (geometric mean of NOEC and LOEC) (BASF, 2001).

Chronic aquatic toxicity data are not reasonably available for NMP for fish. EPA estimated a chronic fish toxicity value based on an acute to chronic ratio (ACR) approach extrapolating from the acute fish toxicity data. The acute 96-hour LC_{50} value for rainbow trout of >500 mg/L was divided by 10 resulting in an estimated chronic fish toxicity value for NMP of >50 mg/L.

EPA evaluated one chronic aquatic toxicity study for aquatic plants. The green algae (*Scenedesmus subspicatus*) was exposed to NMP for 72-hours. The NOEC value for NMP was reported at 125 mg/L and the LOEC at 250 mg/L. EPA calculated a chronic toxicity value of 177 mg/L (geometric mean of NOEC and LOEC) (BASF, 1989).

Table 3-1. Aquatic Toxicity Data for NMP

Duration	Test Taxa	Endpoint	Hazard Value [a]	Units	Effect Endpoint	Reference
Acute	Fish	96-hour LC_{50}	>**500-4,030**	mg/L	Mortality	BASF (1983) (High); BASF (1986)
	Aquatic invertebrates	48/96 hour EC_{50}/LC_{50}	**1,107 – 4,897**	mg/L	Immobilization/ Mortality	GAF (1979)
	Algae	72-hour EC_{50}	**600** (Biomass) **673** (Growth rate)	mg/L	Growth	BASF (1989)
	Acute COC		>100	mg/L	Estimated by dividing lowest reported acute value across test organisms (<500) by an Application Factor (AF) of 5	

Duration	Test Taxa	Endpoint	Hazard Value [a]	Units	Effect Endpoint	Reference
Chronic	Fish	Chronic Value (ChV)	>50	mg/L	Estimated by dividing lowest reported acute value for fish (>500) by an acute to chronic ratio of 10.	
	Aquatic invertebrates	NOEC LOEC	**12.5 (Reported) 25 (Reported)**	mg/L	Reproduction	BASF (2001) [b]
		Chronic Value	17.7	mg/L	Estimated by calculating the geometric mean of the NOEC and LOEC.	
	Algae	NOEC LOEC	**125 (Reported) 250 (Reported)**	mg/L	Growth	BASF (1989)
		Chronic Value	177	mg/L	Estimated by calculating the geometric mean of the NOEC and LOEC	
	Chronic COC		1.77	mg/L	Lowest calculated or reported chronic value across taxa divided by an AF of 10.	

[a] Values in the table are presented as reported by the study authors; **Bold** = experimental data

[b] Reservation of Rights: BASF has agreed to share this toxicity study report ("Study Report") with US EPA, at its written request, for EPA 's use in implementing a statutory requirement of TSCA. Every other use, exploitation, reproduction, distribution, publication or submission to any other party requires BASF's written permission, except as otherwise provided by law. The submission of this Study Report to a public docket maintained by the United States Environmental Protection Agency is not a waiver of BASF's ownership rights. No consent is granted for any other third-party use of this Study Report for any purpose, in any jurisdiction. Specifically, and by example, no consent is granted allowing the use of this Study Report by a private entity in requesting any regulatory status, registration or other approval or benefit, whether international, national, state or local, including but not limited to the Registration, Evaluation, Authorisation and Restriction of Chemicals ("REACH") regulation administered by European Chemicals Agency ("ECHA"), an agency of the European Union.

3.1.2.2 Concentrations of Concern Calculation

Acute and chronic COCs were calculated for environmental toxicity of NMP using assessment factors (AFs). EPA applied an assessment factor (AF) according to EPA methods (U.S. EPA, 2013a, 2012d). The application of AFs provides a lower bound effect level that would likely encompass more sensitive species not specifically represented by the available experimental data. AFs can also account for differences in inter- and intra-species variability, as well as laboratory-to-field variability. These AFs are dependent on the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group. However, they are often standardized in risk assessments conducted under TSCA, since the data reasonably available for most industrial chemicals are limited. For fish and aquatic invertebrates (*e.g.*, daphnia) the acute toxicity values are divided by an AF of 5. For chronic COCs, an AF of 10 is used. The COC for the aquatic plant endpoint is determined based on the lowest value in the dataset and application of an AF of 10 (U.S. EPA, 2013a, 2012d).

After applying AFs, EPA converts COC units from mg/L to µg/L (or ppb) in order to more easily compare COCs to surface water concentrations during risk characterization.

Acute COC

To derive an acute COC for NMP, EPA used the lowest reported acute toxicity value across taxa (>500 mg/L) and divided by the AF of 5 and multiplied by 1,000 to convert from mg/L to µg/L, or ppb.

The acute COC = (>500 mg/L) / AF of 5 = 100 mg/L x 1,000 = 100,000 µg/L or ppb.

- The acute COC for NMP is 100,000 ppb.

Chronic COC

The chronic COC for NMP was derived by EPA by dividing the aquatic invertebrate 21-day chronic toxicity value of 17.7 mg/L (1,768 µg/L) by an AF of 10.

The chronic COC = (17.7 mg/L) / AF of 10 = 1.77 mg/L x 1,000 = 1,770 µg/L or ppb.

- The chronic COC for NMP is 1,770 ppb.

3.1.2.3 Toxicity to Soil/Sediment and Terrestrial Organisms

EPA did not further evaluate in this RE exposure pathways (and hazards) associated with NMP in sediments and soils based on analyses completed as part of the NMP Problem Formulation (U.S. EPA, 2018c).

3.1.3 Weight of the Scientific Evidence

During the data integration stage of EPA's systematic review for risk evaluation, EPA analyzed, synthesized, and integrated the data/information. This involved weighing scientific evidence for quality and relevance, using a Weight of the Scientific Evidence (WOE) approach (U.S. EPA, 2016c). In the June 2018 Problem Formulation for NMP (U.S. EPA, 2018c), seven studies were used to conduct a basic screening-level characterization the environmental hazards of NMP. At the time of the problem formulation, none of these studies identified during the literature search or ECHA summaries had been evaluated according to the systematic review criteria. Since the NMP Problem Formulation (U.S. EPA, 2018c) these studies have been evaluated according to the systematic review criteria in *The Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). The acceptable aquatic studies that were evaluated for NMP are summarized in Table_Apx H-1.

While EPA determined that there were enough environmental hazard data to characterize environmental hazards of NMP, there are uncertainties. First, some uncertainty may be associated with the use of the specific AFs used in the hazard assessment. Second, more acute duration data were reasonably available in the literature than chronic duration data. Therefore, EPA is less certain of chronic hazard values than the acute hazard values. The most sensitive taxonomic group from the acute duration data, aquatic invertebrates, has chronic duration data reasonably available in the literature. Because the chronic fish data were not reasonably available, the chronic fish endpoint was addressed using the acute to chronic ratio (ACR=10). The fish chronic toxicity value was estimated to be >50 mg/L.

3.1.4 Summary of Environmental Hazard

The acute 96-hour LC_{50} values for fish range from >500 mg/L to 4,030 mg/L. The acute EC_{50}/LC_{50} for aquatic invertebrates range from 1,107 mg/L to 4,897 mg/L. For fresh water green algae, the 72-hour EC_{50} values were 600 mg/L (Biomass) and 673 mg/L (Growth rate). EPA calculated the acute COC to be 100,000 µg/L (10 mg/L).

For the chronic fish endpoint, an acute to chronic ratio (ACR) approach was used to extrapolate a chronic toxicity value for NMP for fish based on the reported acute values. EPA calculated a chronic fish toxicity value for NMP of >50 mg/L using an ACR of 10 and the lowest reported acute toxicity value of >500 mg/L. For the aquatic invertebrate endpoint, a 21-day chronic toxicity value of 17.68 mg/L was calculated for NMP based on reproduction (geometric mean of the reported NOEC of 12.5 mg/L and LOEC of 25 mg/L). For the chronic aquatic plant endpoint, a 72-hour chronic toxicity value of 177 mg/L was calculated for NMP based on growth inhibition (geometric mean of the reported NOEC of 125 mg/L and the LOEC of 250 mg/L). EPA calculated the chronic COC 1,770 µg/L (1.77 mg/L).

The aquatic toxicity studies used to characterize the effects of acute and chronic NMP exposure to aquatic invertebrates are summarized in Table 3-1.

3.2 Human Health Hazards

3.2.1 Approach and Methodology

EPA identified hazard data for NMP through an extensive literature search as described in EPA's *Strategy for Conducting Literature Searches for NMP: Supplemental Document to the TSCA Scope Document* (U.S. EPA, 2017c). Only the identified "on-topic" references (as explained in the *n-Methylpyrrolidone (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017b) obtained from the human health hazard literature search were considered as relevant data/information sources for consideration in this risk evaluation of NMP. EPA's inclusion criteria were used to screen the initial literature search results (n = 1,397); 1,361 references were excluded based on PECO. In addition, seven key/supporting studies were identified outside of this process and included in the current evaluation. The remaining hazard studies (n = 40) were then evaluated using the data quality evaluation criteria for human health hazard studies as outlined in *The Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). The hazard data determined to be acceptable based on this data quality review were extracted and integrated. This systematic review process is summarized in Figure 3-1.

The human health hazard of NMP has been examined in several publications (EC, 2016; Danish Ministry of the Environment, 2015; U.S. EPA, 2015c; NICNAS, 2013; OECD, 2009; U.S. EPA, 2006b; WHO, 2001). EPA relied heavily on the hazard information presented in these documents to inform the human health hazard identification and the dose-response analysis. EPA also evaluated studies that were published since these reviews during the analysis phase of the risk evaluation, as identified in the literature search conducted by the Agency for NMP (*NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017d).

Brief summaries for each hazard endpoint are presented in Section 3.2.3. Detailed information about study quality review for study selection is provided in Section 1.5.1. Developmental and reproductive toxicity endpoints were evaluated for consistency, sensitivity and relevance (Section 3.2.3). Based on the conclusions of previous assessments and a review of reasonably available studies, EPA narrowed the focus of the NMP hazard characterization to specific reproductive and developmental toxicity endpoints, reduced fertility, including fetal resorptions (mortality) and growth retardation. EPA conducted a dose-response assessment for these endpoints (Section 3.2.5), using benchmark dose analysis and PBPK model estimates of internal doses (Section 3.2.5.6) to select points of departure (POD) for use in the risk evaluation (Section 4.2).

EPA considered new (on-topic) studies with information on acute and non-cancer endpoints for hazard identification and dose-response analysis if the study received an overall data quality rating of high, medium, or low as described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). EPA has not developed data quality criteria for all types of relevant information (*e.g.*, toxicokinetic data); however, this information was used to support the risk evaluation. Information that was rated unacceptable was not included in the risk evaluation. The human health hazard data used to characterize the effects of acute and chronic NMP exposure to humans are summarized in Table 3-2 and Table 3-3. Additional information on the human health hazard endpoints considered during hazard identification, are provided in Appendix I. The comprehensive results of the study evaluations can be

found in the systematic review supplemental files for animal and in vitro studies (U.S. EPA, 2020l) and epidemiological studies (U.S. EPA, 2020m).

The human health hazard information was integrated using a strategy that includes consideration of the weight of the scientific evidence for each hazard endpoint to select the data used for dose-response assessment. The weight of the scientific evidence analysis included integrating information from toxicokinetics and toxicodynamics in relation to the key hazard endpoints which include reproductive and developmental toxicity. Dose-response analyses were performed on key hazard endpoints using benchmark dose modeling (see Section 3.2.5).

Studies that met the evaluation criteria and were rated low, medium, or high were considered for hazard identification and dose-response analysis as described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

Studies considered PECO relevant that scored acceptable in the systematic review data quality evaluation and contained adequate dose-response information were considered for derivation of points of departure (PODs). EPA defines a POD as the dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on the extrapolated dose for an estimated incidence, a change in response level from a dose-response model (*e.g.*, benchmark dose or BMD), a no observed adverse effect level (NOAEL), a lowest observed adverse effect level (LOAEL) for an observed incidence, or a change in the level (*i.e.*, severity) of a given response. PODs were adjusted as appropriate to conform to the specific exposure scenarios evaluated.

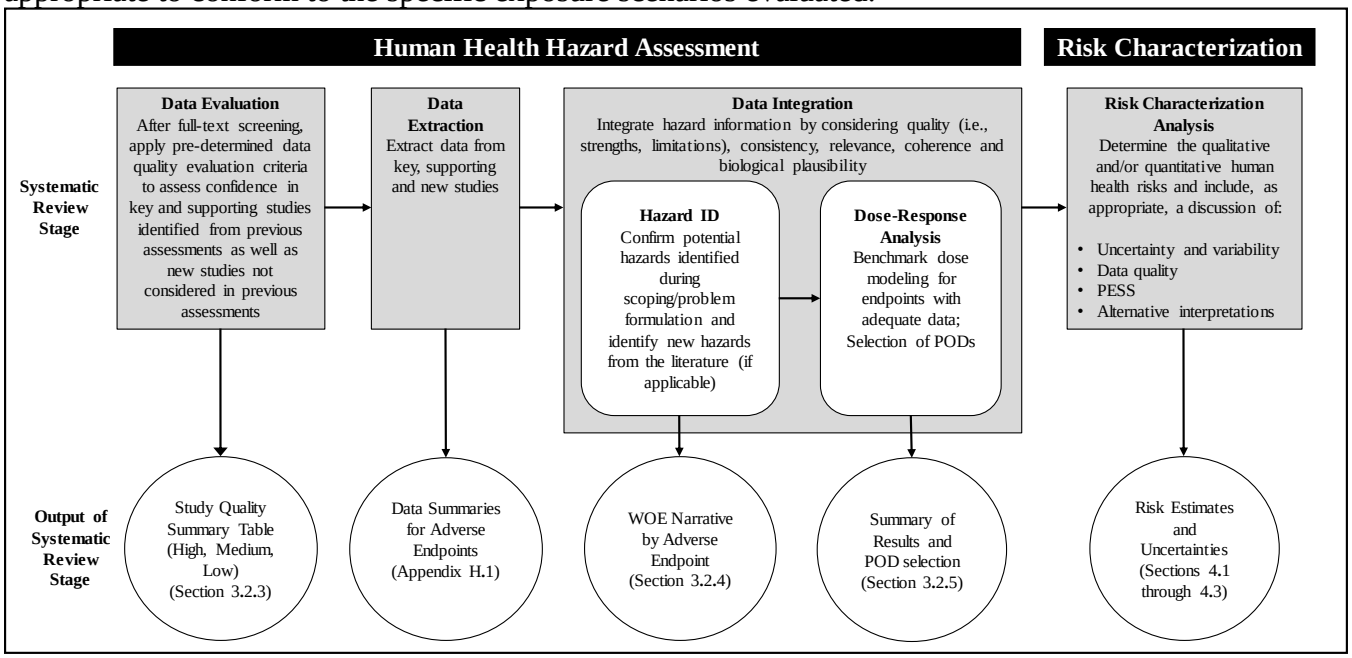


Figure 3-1. Summary of NMP Systematic Review

3.2.2 Toxicokinetics

NMP is readily absorbed by all exposure routes with widespread distribution via the systemic circulation and extensive first pass metabolism to polar compounds that are excreted primarily in urine (Akesson et al., 2004; Ligocka et al., 2003; Akesson and Paulsson, 1997). In rats administered a single intravenous dose, NMP was distributed to all major organs with the highest concentrations detected in the liver and intestines (Wells and Digenis, 1988). The major metabolites of NMP in humans are 5-hydroxy-N-methyl-2-pyrrolidone (5-HNMP) and 2-hydroxy-N-methylsuccinimide (2-HMSI); minor metabolites

include N-methylsuccinimide (MSI). Over 80% of the administered dose is excreted within 24 hours (WHO, 2001).

Dermal contact with NMP liquids generally presents the greatest potential for human exposure; however, vapor-through skin uptake has also been demonstrated in humans (Akesson et al., 2004; Jönsson and Akesson, 2003). Bader et al. (2008) exposed human volunteers to an NMP air concentration of 80 mg/m^3 for 8 hours and estimated peak concentrations following dermal-only exposure to be in the range of 36 to 42% of the results obtained after whole-body exposure based on NMP equivalents in urine (see Section 3.2.5.5).

It is not known whether NMP or its metabolites enter human breast milk. In addition, is not possible to predict human lactational transfer to the infant with the available PBPK model for NMP. NMP is a water-miscible (O'Neil et al., 2006) organic solvent that is distributed throughout the organism and eliminated mainly by hydroxylation to polar compounds, which are excreted via urine. Water soluble chemicals also may partition into the aqueous phase and be excreted via human milk (See EPA's Exposure Factors Handbook (2011), Chapter 15). The rapid excretion and water solubility suggest that NMP may be less likely to be detected in breast milk following exposure to the mother. However, there are animal studies with maternal exposures that continued throughout the postnatal period that found significant decreases in pup body weights, and therefore, postnatal exposure to NMP to the pups via lactation may contribute to these effects (Exxon, 1991; NMP Producers Group, 1999b and 1999c; Sitarek et al., 2012).

3.2.3 Hazard Identification

Previous assessments (EC, 2016; Danish Ministry of the Environment, 2015; U.S. EPA, 2015c; NICNAS, 2013; OECD, 2007; U.S. EPA, 2006b; WHO, 2001) have identified reproductive and developmental toxicity as the most sensitive effects of NMP. EPA therefore focused this risk evaluation on reproductive and developmental effects. This section summarizes evidence for reproductive and developmental hazards as well as a broader range of potential non-cancer and cancer health hazards.

A comprehensive set of summary tables which includes all endpoints considered for this assessment may be found in Appendix I. EPA reviewed the reasonably available data and key and supporting studies were evaluated for consistency and relevance to humans, according to the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). The results of the data quality evaluation for the non-cancer studies (key and supporting studies and new studies) are described below in Section 3.2.3.1 and included in the data quality evaluation tables in the *Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020l).

3.2.3.1 Non-Cancer Hazards

Toxicity Following Acute Exposure

The acute toxicity of NMP is low based on results from studies conducted via oral, dermal, inhalation, intraperitoneal and intravenous exposure in rats and mice WHO (2001). Oral LD_{50} values reported by reasonably available studies in rats and mice ranged from 3,914 to 7,725 mg/kg-bw (Ansell and Fowler, 1988; Bartsch et al., 1976). Dermal LD_{50} values in rats were reported as >5,000 mg/kg-bw (Clark et al., 1984). Following inhalation exposure, secondary sources report 4 hour LC_{50} was >5,100 mg/m^3 (OECD, 2007). Sublethal effects observed in response to single high doses include ataxia and diuresis in rats exposed orally to one-eighth of the LD_{50} (Ansell and Fowler, 1988).

The American Industrial Hygiene Association (AIHA) reports odor thresholds for NMP ranging from 4 to 10 ppm (AIHA, 1989). This is above the current California OSHA PEL of 1 ppm, suggesting that NMP has poor chemosensory warning properties.

Irritation and Sensitization

Evidence in animal studies indicates that NMP is a skin, eye and respiratory irritant. For example, rabbits receiving a single application of 0.1 ml NMP to one eye experienced corneal opacity, iritis, and conjunctivitis. Effects were reversible within 14 days (Ansell and Fowler, 1988). Secondary sources describe a 28-day dermal exposure study with rabbits exposed to 413, 826, or 1653 mg/kg/day once a day, five days a week for four weeks which resulted in local skin irritation at all doses tested (GAF Corp, 1986 as reported in the OECD SIAR (2007) and WHO (2001)). Secondary sources also describe nasal irritation (crust formation on nasal edges) reported in rats exposed to 1 or 3 mg/L for 6 hours a day, five days a week for three months. The inhalation study identified a NOAEC of 0.5 mg/L (BASF AG, 1994, as cited in the OECD SIAR document (2007)).

Human volunteer chamber studies revealed some discomfort during exposure but are otherwise suggestive of humans being less sensitive to respiratory irritation than rodents. No respiratory or eye irritation was reported in six volunteers exposed via inhalation to up to 50 mg/m^3 for 8 hours (Akesson and Paulsson, 1997). A study that is only available as a secondary source reported no dermal irritation following the first 24 hours of exposure in a patch test in 50 human volunteers (GAF 1974 as cited by Lee et al. (1987)). In contrast, an occupational case study reported skin irritation in 10 out of 12 workers exposed to NMP dermally over a two day period (Leira et al., 1992).

NMP is not corrosive. Limited data from secondary sources suggesting that NMP is not a sensitizer (RIVM, 2013; Lee et al., 1987) are insufficient to support conclusions on sensitization with a high degree of confidence.

Neurotoxicity

Two cross-sectional human occupational studies evaluated a range of neurological endpoints. While neither study reported a significant association between NMP exposure and neurological endpoints, very small sample sizes and limitations in study design (including reliance on self-reported effects for some endpoints) make it difficult to interpret these results (Haufroid et al., 2014; Nishimura et al., 2009).

Animal studies have noted effects related to neurotoxicity. A 90-day oral repeat dose study with a neurotoxicity screening panel in rats identified NOAELs of 169 and 217 mg/kg-bw/day for males and females, respectively, based on decreased body weight in both males and females and reversible neurological effects (including increased foot splay and low arousal) in males only (Malley et al., 1999).

In a rat study, whole body exposure to 0.1, 0.5, and 1.0 mg/L (25, 125, or 250 ppm, aerosol) 6 hours/day, five times a week for four weeks was associated with lethargy and irregular respiration at all concentrations. These signs were reversible within 30-45 minutes following exposure at the two lower concentrations. Rats in the highest dose group had excessive mortality. Lethargy and irregular respiration were not reversed in most surviving animals in the high dose group 18 hours after exposure had ceased (Lee et al., 1987). The actual exposure concentrations in this study cannot be determined due to aerosol formation and condensation.

In a gestational exposure study by Lee et al. (1987) rats were exposed to an NMP aerosol concentration of 100 and 360 mg/m^3 (analytical) for six hours/day from GD 6 through 15. Sporadic lethargy and irregular respiration were observed in treated dams at both exposure levels during the first three days of

exposure. These effects were not seen during the remainder of the exposure period or during the 10-day recovery period.

Developmental neurotoxicity endpoints have also been evaluated. Hass et al. (1994) investigated the effects of NMP on postnatal development and behavior in rats exposed during gestation. Dams were exposed by whole-body inhalation to measured levels of 151 ppm (612 mg/m^3) for six hrs/day from GD 7 to 20 and offspring were evaluated for a range of growth, development, and neurobehavioral endpoints from postnatal day (PND) 1 through 7 months of age. Performance was impaired in certain more complex tasks (*i.e.*, reversal procedure in Morris water maze and operant delayed spatial alternation). The impaired performance may be associated with decreased body weight at weaning. As the authors noted, the effect appeared most pronounced in offspring with the lowest body weights in the litter at weaning. Since only one dose was used, a NOAEL could not be established. This study was excluded by the systematic review process and did not go through data quality evaluation because it only used a single dose. It is discussed here because it was cited as a supporting study in a previous EPA assessment (U.S. EPA, 2015c), and it provides information about neurodevelopmental endpoints that have not been evaluated in any other studies.

Liver Toxicity

A chronic oral exposure study reported effects on the liver following oral exposure to NMP in rats and mice. Chronic oral exposure in rats was associated with centrilobular fatty change in the liver in males but not in females. This study identified a LOAEL of 678 mg/kg/day and a NOAEL of 207 mg/kg/day for liver toxicity in male rats (Malley et al., 2001). In mice, significantly increased liver weights as well as cellular alterations in the liver were reported in both male and female mice following oral exposure. The authors reported a LOAEL of 173 mg/kg/day and NOAEL of 89 mg/kg/day for liver toxicity in male mice (Malley et al., 2001). A sub-chronic 90-day oral exposure study in rats and mice at higher doses found no effect on the liver (Malley et al., 1999), while a four-week oral exposure study found increased incidence of centrilobular hepatocellular hypertrophy in addition to increase serum total protein and albumin in female rats exposed to 2,268 mg/kg/day (Malek et al., 1997).

Kidney Toxicity

Chronic progressive nephropathy was reported in male but not female rats following chronic oral exposure to 678 mg/kg-bw/day (Malley et al., 2001). No kidney toxicity was observed in male or female mice in this study (Malley et al., 2001). The study identified a NOAEL of 207 mg/kg/day based on kidney toxicity in male rats. Another study evaluated renal endpoints following four weeks of oral exposure in mice. Dark yellow urine was observed in all animals at 2,970 and 4,060 mg/kg-bw/day. Cloudy swelling of the distal renal tubule was observed in 3/5 females at 4,060 mg/kg-bw/day. This study identified a NOAEL for renal effects of 920 mg/kg-bw/day in females and 720 in males (NMP Producers Group, 1994). A separate oral exposure study in which male rats received 500 mg/kg/day five days a week for five weeks reported decreased creatinine. The NOAEL for decreased creatinine in male rats this study was 250 mg/kg/day (Gopinathan et al., 2013). This study also reported observations of mottled kidneys in treated rats at all doses, but a lack of incidence data for this endpoint in each dose group prevents identification of a NOAEL or LOAEL for renal effects.

Immune Toxicity

A four-week whole-body inhalation study in rats, which likely included dermal and oral uptake through grooming, identified bone marrow hypoplasia, necrosis of lymphoid tissue in the thymus, spleen and lymph nodes, as well as mortality at the highest dose. The NOAEC for immune effects and for other systemic effects in this study was 500 mg/m^3 (Lee et al., 1987). In a four-week oral exposure study,

thymic atrophy was observed in female rats exposed to 2,268 mg/kg-bw/day. The NOAEL for thymus effects in this study was 1,548 mg/kg/day (Malek et al., 1997).

Developmental Toxicity

There is robust evidence of developmental toxicity in animals exposed to NMP. Developmental inhalation, oral and dermal exposures to NMP have been linked to a range of developmental effects, including decreased fetal and pup weights and increased embryo/fetal and pup mortality (Sitarek et al., 2012; NMP Producers Group, 1999b, c; Hass et al., 1994; Exxon, 1991), skeletal malformations, and incomplete skeletal ossification (Saillenfait et al., 2002; E. I. Dupont De Nemours & Co, 1990; Becci et al., 1982). One study indicates that paternal exposures prior to mating contribute to decreased offspring viability (Sitarek and Stetkiewicz, 2008). Most of the reasonably available developmental toxicity studies for NMP were performed in rats. Secondary sources also describe rabbit developmental studies that reported developmental toxicity, including increased resorptions and fetal malformations following gestational exposure to NMP (RIVM, 2013; OECD, 2007).

Effects on postnatal neurological behavior were reported following whole-body inhalation exposure to 151 ppm (612 mg/m^3) NMP during gestation (Hass et al., 1994). However, because behavioral effects were only evaluated at this single exposure level, no NOAEL has been identified for developmental neurotoxicity and dose-response for this endpoint cannot be characterized.

Evidence of developmental toxicity and dose-response information from studies identified as acceptable in the systematic review process is summarized in Table 3-2 and discussed in depth in Sections 3.2.4 and 3.2.5.

Reproductive Toxicity

Reproductive toxicity endpoints that have been observed following repeated exposure to NMP include reduced male fertility and female fecundity and testicular histopathology. Evidence of reproductive toxicity is inconsistent across studies. Three oral exposure studies in rats, including a paternal exposure study, a maternal exposure study, and a two-generation study in both sexes (Sitarek et al., 2012; Sitarek and Stetkiewicz, 2008; Exxon, 1991) report reduced male and/or female fertility in response to NMP. Three other two-generation studies in rats reported no significant effect on fertility. Two of these studies are two-generation dietary exposure studies in rats (NMP Producers Group, 1999b, c) with dose levels and study designs similar to the Exxon (1991) study. The third study is a two-generation whole-body inhalation exposure study (Solomon et al., 1995) that deviates substantially from EPA and OECD guidelines. In addition, several oral exposure studies have reported effects on testicular size or histopathology in male rats (Sitarek and Stetkiewicz, 2008; Malley et al., 2001; Malek et al., 1997), while several others find no effect (Malley et al., 1999; Becci et al., 1983; DuPont, 1982).

Evidence of reproductive toxicity is summarized in Table 3-3 and discussed in depth in Sections 3.2.4 and 3.2.5. Reproductive toxicity findings are challenging to interpret due to the wide-ranging effect levels and the lack of consistency in findings across studies. While developmental effects are more consistently reported across studies, reductions in fertility have been reported at lower doses than developmental effects following repeated exposures.

Table 3-2. Acceptable Studies Evaluated for Developmental Effects

Data Source	Study Description	Effects Reported; POD	Data Quality Rating
Oral Exposure Studies			
Sitarek et al. (2012)	Oral gavage exposure (0, 150, 450, 1,000 mg/kg-bw/day) for 5 days/week for 2 weeks in female rats prior to mating, during mating, gestation and lactation	Number of live pups was reduced and number of stillbirths increased at 1,000 mg/kg-bw/day; Pup survival and body weights decreased in all exposure groups; LOAEL for pup survival = 150 mg/kg-bw/day	High
Sitarek and Stetkiewicz (2008)	Oral gavage exposure (0, 100, 300, 1,000 mg/kg-bw/day) 5 days/week for 10 weeks in male rats before mating and for one week during mating	Reduced viability of offspring in first four days of life following paternal exposure to 300 mg/kg/day; NOAEL = 100 mg/kg-bw/day	High
Saillenfait et al. (2002)	Oral gavage exposure (0, 125, 250, 500, 750 mg/kg-bw/day) through gestational days (GD) 6-20 in rats	Increased resorptions/ post-implantation losses, increased skeletal malformations, and decreased fetal body weights; NOAEL for developmental effects = 125 mg/kg-bw/day; NOAEL for maternal toxicity = 250 mg/kg-bw/day	High
NMP Producers Group (1999b)	Two-generation oral dietary exposure (50, 160, 350/500 mg/kg-bw/day) in male and female SD rats exposed prior to mating, throughout gestation and lactation. High dose reduced to 350 after the first litter.	Significant decrease in pup survival through PND4 and decrease in pup body weights in both generations in the high dose group; significant decrease in pup body weights at PND 7-21 in the second litter of the second generation in the 160 mg/kg/day dose group; significant increase in stillborn pups in the first litter of the first generation in the high dose group. NOAEL for developmental effects = 50 mg/kg-bw/day	High
NMP Producers Group (1999c)	Two-generation oral dietary exposure (50, 160, 500 mg/kg-bw/day) in male and female Wistar rats exposed prior to mating, throughout gestation and lactation. High dose reduced to 350 after the first litter.	Significant increase in the number of stillborn pups in the first generation high dose group; decrease in pup survival through PND4 and decrease in pup body weight in both generations in the high dose group; NOAEL for developmental effects = 160 mg/kg-bw/day	High
ISP (1992)	Oral gavage exposure (40, 125, 400 mg/kg-bw/day) through GD 6-15 in rats	Reduced fetal body weights, reduced ossification sites in proximal phalanges of the hindpaw, and reduced maternal body weight gain at 400 mg/kg-bw/day; NOAEL for maternal and developmental effects = 125 mg/kg-bw/day	High
Exxon (1991)	Two-generation oral dietary exposure (50, 160, 500 mg/kg-bw/day) in male and female rats	Significant decrease in offspring survival indices and growth rates and increase in the number of stillborn pups in both	High

Data Source	Study Description	Effects Reported; POD	Data Quality Rating
	exposed prior to mating, throughout gestation and lactation	generations in the high dose group; NOAEL for developmental effects = 160 mg/kg-bw/day	
Inhalation Exposure Studies			
Saillenfait et al. (2003)	Inhalation exposure (0, 122, 243, 487 mg/m^3) for 6 hours/day on GD 6-20 in rats	Reduced maternal weight gain and food consumption at 243 mg/m^3; Reduced fetal weight at 487 mg/m^3 exposure; NOAEL for maternal effects = 122 mg/m^3; NOAEL for developmental effects = 243 mg/m^3	High
Solomon et al. (1995); E. I. Dupont De Nemours & Co (1990)	Inhalation exposure (0, 42, 206, 472 mg/m^3) for 6 hours/day throughout mating period (100 exposure days) in male rats, and throughout gestation and weaning, except GD 20 – PND 4 (143 exposure days) in females	Decreased fetal body weights and pup body weights; decreased maternal response to auditory stimulus at the highest dose; NOAEL for maternal and developmental effects = 206 mg/m^3	High
Lee et al. (1987)	Inhalation exposure (100 or 360 mg/m^3) for 6 hours/day on gestational days 6-15 in rats	No effects reported on uterine or litter parameters, fetal weight or length, or incidence of gross, soft tissue, or skeletal anomalies; NOAEL for maternal and developmental effects = 360 mg/m^3	Medium
Dermal Exposure Studies			
Becci et al. (1982)	Dermal exposure (75, 237, 750 mg/kg-bw/day) on gestational days 6-15 in rats	Decreased number of live fetuses per dam, increased percentage of resorption sites, skeletal abnormalities, and decreased mean fetal body weight as well as maternal toxicity indicated by reduced body weight gain at the highest dose; NOAEL = 237 mg/kg-bw/day	Medium

Table 3-3. Acceptable Studies Evaluated for Reproductive Effects

Data Source	Study Description	Effects Reported; POD	Data Quality Rating
Oral Exposure Studies			
Sitarek et al. (2012)	Oral gavage exposure (0, 150, 450, 1,000 mg/kg-bw/day) for 5 days/week for 2 weeks in female rats prior to mating, during mating, gestation and lactation	Significant reduction in female fertility index at 450 or 1,000 mg/kg-bw/day; NOAEL for female fertility = 150 mg/kg-bw/day	High

Data Source	Study Description	Effects Reported; POD	Data Quality Rating
Sitarek and Stetkiewicz (2008)	Oral gavage exposure in male rats (0, 100, 300, 1,000 mg/kg-bw/day) 5 days/week for 10 weeks prior to mating and for one week during mating	Male infertility, damage to seminiferous epithelium and significant reduction in thyroid weight at 1,000 mg/kg-bw/day; NOAEL for male reproductive effects = 300 mg/kg-bw/day	High
Malley et al. (2001)	Chronic dietary oral exposure in rats (0, 1,600, 5,000 or 15,000 ppm) for two years (0, 66.4, 207, 678 mg/kg-bw/day in male rats), (0, 87.8, 283, 939 mg/kg-bw/day in female rats) and dietary exposure (0, 600, 1,200 or 7,200 ppm) for 18 months in mice (0, 89, 173, 1,089 mg/kg-bw/day in male mice) and (0, 115, 221, 1,399 mg/kg-bw/day in female mice)	In male rats only, bilateral degeneration/atrophy of seminiferous tubules in the testes, and bilateral oligospermia/germ cell debris in the epididymis at the highest dose; NOAEL for male reproductive effects = 207 mg/kg-bw/day	High
Malley et al. (1999)	Oral dietary exposure (0, 3,000, 7,500 or 18,000 ppm) for 90 days in male rats (0, 169, 433, 1,057 mg/kg-bw/day) and female rats (0, 217, 565, 1,344 mg/kg-bw/day); oral dietary exposure (0, 1,000, 2,500, or 7,500 ppm) for 90 days in mice (0, 277, 619, 1,931 mg/kg-bw/day)	No effect on reproductive organ weights. NOAEL in rats = 1,057 mg/kg-bw/day; NOAEL in mice = 1,931 mg/kg-bw/day	High
NMP Producers Group (1999b)	Two-generation oral dietary exposure (50, 160, 350/500 mg/kg-bw/day) in male and female SD rats exposed prior to mating, throughout gestation and lactation. High dose reduced to 350 after the first litter.	No significant reduction reported in male or female fertility; no significant difference from controls reported on estrous cycles, sperm parameters, reproductive organ weights or histopathological findings in ovaries or testes; NOAEL = 350 mg/kg-bw/day	High
NMP Producers Group (1999c)	Two-generation oral dietary exposure (50, 160, 500 mg/kg-bw/day) in male and female Wistar rats exposed prior to mating, throughout gestation and lactation. High dose reduced to 350 after the first litter.	No significant reduction reported in male or female fertility; no significant difference from controls reported on estrous cycles, sperm parameters, or histopathological findings in ovaries or testes; Significant change in testes weights relative to body weight in mid and high dose groups. NOAEL for fertility = 350 mg/kg-bw/day; NOAEL for testes weight = 50 mg/kg-bw/day	High

Data Source	Study Description	Effects Reported; POD	Data Quality Rating
Malek et al. (1997)	Oral dietary exposure (0, 2,000, 6,000, 18,000 or 30,000 ppm; 0, 149, 429, 1,234, 2,019 mg/kg-bw/day) for four weeks in male rats	Decreased body weight and altered testes and liver weights observed at 1,234 mg/kg-bw/day and above. Degeneration/atrophy of testicular seminiferous tubules were observed 1/5 males at 1,234 mg/kg-bw/day and in 5/5 at 2,019 mg/kg-bw/day; NOAEL for reproductive effects = 429 mg/kg-bw/day	High
NMP Producers Group (1994)	Oral dietary exposure (0, 500, 2,500, 7,500 or 10,000 ppm; 130, 720, 2,130, 2,670 mg/kg-bw/day) for four weeks in male mice	No exposure related reproductive organ effects reported; NOAEL for reproductive effects in mice = 2670 mg/kg-bw/day	High
Exxon (1991)	Two-generation oral dietary exposure (50, 160, 500 mg/kg-bw/day) in male and female Sprague-Dawley rats exposed prior to mating, throughout gestation and lactation	Reduced male fertility and female fecundity in second generation rats (exposed throughout development and prior to mating) at all doses; increased numbers of second generation females with microscopic changes in the uterus and ovaries, including decreased numbers of corpora lutea and decreased implantation sites in the high dose group; increased incidence of smaller than normal testes in second generation parental males in the high dose group; LOAEL= 50 mg/kg-bw/day; NOAEL not identified	High
Becci et al. (1983)	Oral dietary exposure (0, 24, 75, 246 mg/kg-bw/day in males; 0, 24, 76, 246 mg/kg-bw/day in females) for 13 weeks in male and female beagle dogs	No effects on reproductive organ weights; NOAEL for reproductive effects = 246 mg/kg-bw/day	High
Inhalation Exposure Studies			
Solomon et al. (1995); E. I. Dupont De Nemours & Co (1990)	Two generation whole body inhalation exposure (0, 42, 206, 472 mg/m^3) for 6 hours/day, 7 days/week throughout mating period, gestation, and weaning in male and female rats	No significant change in indices of reproductive performance (fertility and fecundity); NOAEL for reproductive effects = 472 mg/m^3	High
DuPont (1982)	Chronic whole-body inhalation exposure (0, 41, 405 mg/m^3) 6 hours/day, 5 days/week for two years in male and female rats	Mammary gland hyperplasia; No adverse effects reported based on histopathology of the epididymis and prostate. NOAEL for mammary gland effects = 10 ppm (41 mg/m^3); NOAEL for male reproductive effects = 100 ppm (405 mg/m^3))	Medium

3.2.3.2 Genotoxicity and Cancer Hazards

3.2.3.2.1 Genotoxicity and Other Mechanistic Data

EPA reviewed reasonably available information from genotoxicity studies on NMP. EPA obtained and evaluated three genotoxicity and mechanistic studies using data quality criteria presented in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). EPA also reviewed summaries of unpublished genotoxicity studies, as presented at the international OECD meeting (SIAM 24) and published in the Screening Information Assessment Report and Dossier (OECD, 2007). Results of additional studies as summarized by OECD are generally consistent with the reasonably available studies evaluated here, but the final risk evaluation does not rely on studies for which EPA does not have access to the full study.

In Vivo Genotoxicity Studies

EPA obtained access to one study that evaluated potential genotoxicity of NMP *in vivo*, the results of which are summarized in Table 3-4. Engelhardt and Fleig (1993) examined NMP for its clastogenic/genotoxic potential *in vivo* in the Chinese hamster bone marrow test for chromosomal aberrations and in a mouse micronucleus test.

In the Chinese hamster bone marrow assay, NMP dissolved in distilled water was administered once daily by gavage in doses of 1,900 and 3,800 mg/kg bw/day. NMP treatment led to signs of systemic toxicity but did not result in increased numbers of mitotic cells containing structural or numerical chromosomal aberrations in bone marrow (Engelhardt and Fleig, 1993).

In the mouse bone marrow micronucleus test, NMP dissolved in distilled water was administered to NMRI mice once daily by gavage at 950, 1,900 and 3,800 mg/kg bw/day. NMP treatment led to clinical signs of toxicity, including irregular respiration, abdominal position and poor general state. NMP did not induce micronuclei in the polychromatic erythrocytes of mice treated up to a dose showing clinical signs of toxicity and bone marrow toxicity (Engelhardt and Fleig, 1993).

In both assays, positive control responses demonstrate the assays were competent to detect genotoxic effects. The study authors conclude that the results of these two assays show no evidence of a clastogenic, aneugenic, or spindle poisoning effect (Engelhardt and Fleig, 1993).

The reasonably available *in vivo* data do not indicate that NMP has genotoxic effects.

Table 3-4. Summary of Reasonably Available *In Vivo* Genotoxicity Studies

Study Type	Dose Level/ Concentration	Result	Remark	Reference	Data Quality Rating
Cytogenetic assay, Chinese hamster	0, 1,900, 3,800 mg/kg bw/day oral (gavage), single application	Negative	Signs of systemic toxicity	Engelhardt and Fleig (1993)	High
Micronucleus assay, Mouse (NMRI)	0, 950, 1,900, 3,800 mg/kg bw/day oral (gavage), single application	Negative, no indication of a spindle poisoning effect	Signs of systemic and bone marrow toxicity	Engelhardt and Fleig (1993)	High

In Vitro Genotoxicity Studies

In vitro studies evaluating potential genotoxicity of NMP are summarized in Table 3-5. Several studies evaluated the potential mutagenicity of NMP using the Ames assay. Mortelmans et al. (1986) tested NMP in several *S. typhimurium* strains both with and without metabolic activation by S9 mix from rats or hamsters. NMP was determined to be negative in all strains, with and without metabolic activation (Mortelmans et al., 1986).

Wells (1988) also evaluated NMP in an Ames assay using several *S. typhimurium* strains both with and without metabolic activation. The panel of strains evaluated include strains capable of detecting base-pair substitutions, frameshift mutations, and excision repair effects. NMP had no clear mutagenic effect in these strains. In the assay without activation, increased revertants were observed for strains TA 102 and TA 104 but the increases were not greater than two times background and showed no clear dose-response relationship. In both studies, positive control responses demonstrated that the assay was able to detect mutagenic effects.

For genetic endpoints examined in reasonably available *in vitro* studies (*e.g.*, point mutations, DNA damage and repair), NMP showed negative responses in bacterial test systems.

Table 3-5. Summary of Reasonably Available *In Vitro* Genotoxicity Studies

Bioassay Test System	Concentration With/Without Metabolic Activation (± S9 Mix)	Result	Assay Description	Reference	Data Quality
Ames test, *S. typhimurium* (TA97, TA98, TA100, TA1535, TA1537)	0, 100, 333, 1,000, 3,333, 10,000 µg/plate (± S9 mix)	Negative	Preincubation assay, comparative study within NTP testing	Mortelmans et al. (1986)	High
Ames test, *S. typhimurium* (TA97, TA98, TA100, TA102, TA104, TA2638, UTH8413, UHT8414)	0.01 – 1,000 µM/plate (± S9 mix)	Negative	Standard plate test	Wells et al. (1988)	High
Ames test, *S. typhimurium* (TA98, TA104)	0.01 – 1,000 µM/plate (± S9 mix)	Negative	Preincubation assay	Wells et al. (1988)	High

Conclusions

NMP has been evaluated in several *in vitro* and *in vivo* genotoxicity assays that cover a range of endpoints, including chromosomal aberration, DNA damage and repair, and point mutations. While the set of genotoxicity studies reasonably available to EPA is limited, negative results in reasonably available mammalian and bacterial test systems indicate that NMP is unlikely to be genotoxic.

3.2.3.2.2 Carcinogenicity

In a 2-year inhalation cancer bioassay, Sprague-Dawley rats (120 per sex per concentration) were exposed in a whole-body experiment to NMP vapor concentrations of 41 and 405 mg/m^3 (0, 10 and 100 ppm) for 6 hours per day, 5 days per week. Survival of treated rats did not differ from controls. Other than an increase in pituitary adenocarcinomas at 41 mg/m^3 at 18 months but not at 405 mg/m^3 or at 24 months, there were no increases in incidence of benign or malignant tumors at any concentration (Lee et al., 1987; DuPont, 1982).

In an oral dietary study, NMP was examined for its chronic toxicity and carcinogenic potential in groups of 62 male and 62 female Sprague-Dawley rats at concentrations of 0, 1,600, 5,000 or 15,000 ppm (about 66/88, 207/283, 678/939 mg/kg bw/day, males/females) in food for two years. The survival of female rats was not affected, but males in the high dose group had lower survival due to increased severe chronic-progressive nephropathy. The incidence of benign or malignant tumors was not increased among rats (Malley et al., 2001; NMP Producers Group, 1997).

NMP was also administered to groups of 50 male and 50 female B6C3F1 mice receiving dietary concentrations of 0, 600, 1,200 and 7,200 ppm (about 89/115, 173/221, 1,089/1,399 mg/kg-bw/day, males/females) in an 18-month study. There was no difference in survival of treated mice compared with controls. Among the 7,200 ppm males, incidences of liver carcinomas were increased, whereas the incidence in females was within the historical control range. Increased incidences of liver adenomas were also noted at 7,200 ppm; these occurred in both sexes. NMP also caused other substance-related effects in the liver at 1,200 and 7,200 ppm. For example, increased metabolic activity was observed. In addition, mice exhibited increased liver weights and incidences of foci of cellular alteration in the liver at 7,200 ppm in both sexes. In the 1,200 ppm group, increased liver weights were also observed among males and 3/50 of the mice exhibited centrilobular liver cell hypertrophy (Malley et al., 2001) and NMP Producers Group, 1999a, as cited in OECD (2007). Results of cancer bioassays for NMP are summarized in Table 3-6.

Table 3-6. Summary of Tumor Incidence Data from Cancer Bioassays

Species/Strain/ Sex (Number/ Group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
Rat/Crj: CD(SD)/ Both (120)	Inhalation, whole body	0, 41, 405 mg/m^3	6 hrs/day 5 days/ week for 2 years	Summary data not presented	Increased pituitary adenocarcin-omas at 41 but not 405 mg/m^3 and at 18 but not 24 months	Lee et al. (1987); DuPont (1982) [a]	Medium
Rat/Other/ Female (62)	Oral, dietary	0, 87.8, 283, 939 mg/kg-bw/day (0, 1,600, 5,000, 15,000 ppm)	2 years	0, 2, 3, 3	At least one mammary neoplasm	Malley et al. (2001) [b]	High
Mouse/ B6C3F1/ Male (50)		0, 89, 173, 1,089 mg/kg-bw/day (0, 600, 1,200, 7,200 ppm)	18 months	5, 2, 4, 12[c]	Increased incidence of hepatocellular adenoma		
				4, 1, 3, 13[c]	Increased incidence of hepatocellular carcinoma		
Mouse/ B6C3F1/ Female (50)		0, 115, 221, 1,399 mg/kg-bw/day (0, 600, 1,200, 7,200 ppm)		2, 2, 1, 7[c]	Increased hepatocellular adenoma and carcinoma		
				0, 0, 0, 3[c]	Increased hepatocellular carcinoma		

[a] The publicly available study published as Lee et al. (1987) corresponds to the unpublished study DuPont (1982).
[b] This published study corresponds to unpublished results in rats presented in NMP Producers Group (1997).
[c] $p < 0.05$ by Cochran-Armitage trend test.

Conclusions

There is insufficient evidence of cancer risk from NMP to support a quantitative cancer risk characterization for inhalation and dermal exposures. The oral dietary exposure study in rats found no significant increase in tumor incidence. The oral dietary study in mice reported a small but significant increase in liver tumor incidence in males in the high dose group. In the inhalation study, a small but significant increase in incidence of pituitary adenocarcinomas was observed at the middle dose after 18 months of exposure, but the effect does not follow a clear dose-response relationship and was not significant after 24 months of exposure.

3.2.4 Weight of the Scientific Evidence

The best reasonably available human health hazard science was selected for dose-response modeling based on integrating the results of the data evaluation and weight of the scientific evidence. Other recent assessments (EC, 2016; Danish Ministry of the Environment, 2015; U.S. EPA, 2015c; NICNAS, 2013; OECD, 2009; U.S. EPA, 2006b; WHO, 2001) have previously evaluated the weight of scientific

evidence and identified reproductive and developmental toxicity as the most sensitive health effects associated with exposure to NMP. This section therefore focuses on the weight of the scientific evidence for reproductive and developmental toxicity for both short-term and chronic exposures.

3.2.4.1 Weight of the Scientific Evidence for Developmental Toxicity

A review of the reasonably available information shows evidence for developmental toxicity following oral, dermal, and inhalation exposures. Effect levels for developmental toxicity are similar across studies, with NOAELs reported in oral exposure studies typically ranging from 100-200 mg/kg-bw/day and NOAECs reported in inhalation exposure studies ranging 206-360 mg/m^3. EPA identified sensitive and biologically relevant effects that occur along a continuum of reproductive and developmental toxicity, including decreased fetal and pup body weight, delayed ossification, skeletal malformations, post-implantation loss, and increased fetal and pup mortality. These endpoints are discussed in more detail below.

There is very limited human evidence reasonably available to evaluate developmental effects of NMP exposure. A well-documented case report provides qualitative support for evidence in laboratory animals that NMP may be detrimental to mammalian development. In this case report, a pregnant woman who was exposed to NMP at work via dermal and inhalation exposure aborted at week 31 of pregnancy. Although the precise exposure levels are unknown, she reportedly cleaned up an NMP spill that dissolved her latex gloves during week 16 of the pregnancy. She was ill for the next four days and experienced malaise, headache, nausea and vomiting (Solomon et al., 1996). Although this case report provides some evidence that NMP may harm the developing conceptus, the lack of quantitative exposure data precludes its use for quantitative risk estimation.

In Sprague-Dawley rats, Becci et al. (1982) reported adverse developmental effects following NMP exposure via dermal administration. Dams were exposed to NMP at 0, 75, 237 or 750 mg/kg-bw on gestation days (GD) 6-15. All animals were killed and subjected to uterine examination on day 20 of gestation. Treatment at 750 mg/kg-bw was associated with significant decreases in maternal body weight gain, and live litter size, as well as an increased incidence of resorptions and skeletal anomalies. No evidence of teratogenic or maternal effects was observed at 75 or 237 mg/kg-bw; the NOAEL for maternal and developmental toxicity was 237 mg/kg-bw.

Developmental toxicity was also reported in Sprague-Dawley rats after NMP exposure via gavage administration (Saillenfait et al., 2002). Pregnant rats were dosed at 0, 125, 250, 500, or 750 mg/kg-bw on GD 6-20. All animals were killed and subjected to uterine examination on day 21 of gestation. A dose-related decrease in fetal body weights (males and females) was observed at all doses, reaching statistical significance at 250 mg/kg-bw. Significantly decreased maternal body weight gain/food consumption and increased incidence of post implantation loss/fetal resorption and fetal malformations were reported at doses ≥500 mg/kg-bw. Observed treatment-related anomalies included imperforate anus, the absence of a tail, and malformation of the spinal column, heart and/or great vessels. The NOAELs for maternal and developmental toxicity were 250 and 125 mg/kg/day, respectively.

Other oral gavage studies reported reduced offspring viability following maternal (Sitarek et al., 2012) or paternal (Sitarek and Stetkiewicz, 2008) exposure in rats. Maternal oral gavage exposure to 150, 450, or 1,000 mg/kg-bw/day for two weeks prior to mating and throughout gestation and lactation was associated with significantly decreased pup survival at PND4 and PND21 and decreased pup body weights at all doses tested and a significant increase in stillbirths in the high dose group (Sitarek et al., 2012). These exposure levels were also associated with significant reductions in maternal body weight during gestation. The LOAEL for both maternal and developmental toxicity in this study was 150

mg/kg-bw/day. No NOAEL was identified. Paternal oral gavage exposure to 300 or 1000 mg/kg-bw/day for ten weeks prior to mating was associated with decreased pup survival at PND4 (Sitarek and Stetkiewicz, 2008). The NOAEL for developmental effects following paternal exposure was 100 mg/kg-bw/day. Results of the (Sitarek and Stetkiewicz, 2008) study suggest that some developmental effects observed following NMP exposure may be paternally-mediated. Though paternally-mediated effects on offspring are a well-recognized phenomenon (see *EPA's Guidelines for Reproductive Toxicity Risk Assessment* (U.S. EPA, 1996), this is the only reasonably available study on NMP that evaluates the developmental effects of paternal exposure alone. In studies where both maternal and paternal rats are exposed, it is difficult to determine whether reduced offspring survival and other developmental effects are due to maternal or paternal exposures, or a combination of the two.

Three two-generation reproduction studies also reported developmental toxicity following dietary exposure to NMP in Sprague-Dawley (NMP Producers Group, 1999b; Exxon, 1991) or Wistar rats (NMP Producers Group, 1999c). The studies had similar study designs, with animals exposed to 50, 160 or 500 mg/kg-bw/day prior to mating, throughout gestation, lactation, post-weaning, and development for two-generations. In the 1999 studies, the high dose groups were reduced to 350 mg/kg-bw/day after the first litter. All three studies reported a significant increase in stillbirth following maternal exposure to 500 mg/kg-bw/day NMP prior to mating and throughout gestation. They also reported a significant decrease in pup survival to PND4 and PND21 following 350 mg/kg-bw/day (NMP Producers Group, 1999b, c) or 500 mg/kg-bw/day (Exxon, 1991) and a significant decrease in fetal or pup body weights following 160 mg/kg-bw/day (NMP Producers Group, 1999b), 350 mg/kg-bw/day (NMP Producers Group, 1999c), or 500 mg/kg-bw/day (Exxon, 1991). All three studies also reported decreased maternal body weight gain during gestation in the high dose groups. EPA identified NOAELs for developmental toxicity of 50 (NMP Producers Group, 1999b) or 160 mg/kg-bw/day (NMP Producers Group, 1999c; Exxon, 1991) and NOAELs for maternal effects of 160 mg/kg-bw/day (NMP Producers Group, 1999c; Exxon, 1991) or 350 mg/kg-bw/day (NMP Producers Group, 1999b).

The developmental toxicity of NMP was also studied in Sprague-Dawley rats after whole body inhalation exposure (Saillenfait et al., 2003). Pregnant rats were exposed to NMP vapor at 0, 30, 60 or 120 ppm (0, 122, 243 and 487 mg/m^3 nominal concentration) for 6 hours per day on GD 6-20. Maternal body weight gain was significantly decreased at 60 and 120 ppm during the first half of exposure (GD 6–13) and maternal food consumption was reduced at 120 ppm on GD 13–21; however, no significant difference in the gestational weight change of treated dams was observed when maternal body weight was corrected for gravid uterine weight. No evidence of teratogenicity was observed at any concentration tested. Fetal toxicity, as evidenced by dose-related decreases in fetal body weight (males, females) was observed at all doses tested, reaching statistical significance at 120 ppm (5-6% reduction in body weight relative to controls). The NOAEC for maternal and developmental toxicity were 30 and 60 ppm, respectively.

These findings are consistent with reports of fetal growth retardation and the absence of teratogenic effects in previous inhalation exposure studies. In a two-generation reproduction study, Sprague-Dawley rats were exposed to NMP via (whole body) inhalation at 116 ppm, 6 hours per day, prior to mating and throughout gestation and lactation (Solomon et al., 1995). Half of the dams were subjected to cesarean section on GD 21 and the remaining litters were evaluated up to weaning. No adverse effects on offspring viability or morphology were reported other than a decrease in fetal and pup body weights. Hass et al. (1995) exposed pregnant rats via (whole body) inhalation to 165 ppm NMP, 6 hours per day, from GD 4-20. Delayed skeletal ossification and decreased fetal body weights were reported in offspring of treated dams following NMP exposure. In a previous study, (whole body) inhalation exposure to Wistar rats at 150 ppm NMP on GD 7–20 resulted in significantly decreased pup body weights that

persisted from birth until 5 weeks of age (Hass et al., 1994). No signs of maternal toxicity were observed in either study. Hass et al. (1994) also reported neurodevelopmental effects following inhalation exposure during gestation. The effect was evaluated at a single dose and has not been evaluated in other studies, resulting in a lack of information about potential neurodevelopmental effects at lower exposure concentrations.

Mortality and structural malformations have been detected in rats following high levels of NMP exposure via dermal (Becci et al., 1982) and gavage administration (Saillenfait et al., 2002). Differences in the developmental response to NMP may be ascribed in part, to quantitative and/or qualitative differences in the exposure of the embryo/fetus by route of administration. Studies in humans and rats indicate that NMP is readily absorbed by all routes of exposure and extensively metabolized prior to excretion in urine; however, the peak concentration and residence time of the parent compound may vary depending on the route of exposure and the metabolic "status" of the exposed individual (Jönsson and Akesson, 2001; 2000; Anundi et al., 2000; Akesson and Jönsson, 1997; Ursin et al., 1995; Midgley et al., 1992).

NMP and its metabolites were evaluated for potential embryotoxicity using the rat whole embryo culture (WEC) and the BALB/c 3T3 cytotoxicity test (Flick et al., 2009). The resulting data were evaluated using two strategies; one based on all endpoints evaluated in the WEC and the other included endpoints from both the WEC and a cytotoxicity test. Based on the reported results, the substance with the highest embryotoxic potential was NMP, followed by 5-hydroxy-N-methyl-pyrrolidone (5-HNMP), 2-hydroxy-N-methylsuccinimide (2-HMSI) and N-methylsuccinimide (MSI). Developmental anomalies induced by NMP and 5-HNMP include aberrations in the head region of the embryos, abnormal development of the second branchial arches and open neural pores. Only NMP and 5-HNMP induced specific embryotoxic effects, whereas the other two metabolites, 2-HMSI and MSI, were determined to be non-embryotoxic.

EPA assessed risks for adverse developmental effects within the context of the exposure scenarios identified in the exposure assessment, as summarized in Table 3-7.

3.2.4.2 Weight of the Scientific Evidence for Reproductive Toxicity

A review of the reasonably available scientific information identified decreased male and female fertility and testicular lesions and atrophy as potential reproductive effects of NMP exposure. Effects on fertility have been reported at doses lower than those associated with developmental effects, but are less consistently observed across studies than developmental effects.

Three oral exposure reproductive studies reported reduced fertility or reproductive success. Sitarek et al. (2012) reported a decrease in the number of pregnant female rats following maternal oral gavage exposure to 450 mg/kg-bw/day five days a week for two weeks prior to mating. This study identified a NOAEL of 150 mg/kg-bw/day for reproductive toxicity. Another study focused on effects of paternal exposure via oral gavage. Paternal NMP exposure for ten weeks prior to mating and during mating was associated with reduced male fertility (NOAEL = 300 mg/kg-bw/day) and decreased viability of offspring in the first four days of life (NOAEL = 100 mg/kg-bw/day) (Sitarek and Stetkiewicz, 2008).

In a two-generation study, Exxon Biomedical Sciences (1991) reported significant decreases in male fertility and female fecundity as well as reduced survival and growth rates in offspring following oral dietary exposure to 500 mg/kg/day beginning ten days prior to conception and throughout gestation and lactation. In the second generation (rats exposed throughout development and as adults during mating), significant reductions in male fertility and female fecundity were reported at all doses. In the high dose group, there was also increased incidence of smaller than normal testes and an increase in the number of

females with macroscopic changes in the uterus and ovaries, including decreased numbers of corpora lutea and decreased numbers of implantation sites. At 50 mg/kg-bw/day, the lowest dose tested, male fertility decreased 18-28% and female fecundity decreased 18-20% relative to controls. Study authors concluded that these statistically significant effects were not biologically significant at low and mid-range doses because they were "within or close to historical control ranges" and identified a NOAEL of 160 mg/kg-bw/day for reproductive effects. However, historical control data from the performing laboratory were not provided. EPA considered these significant reductions in male fertility and female fecundity relative to concurrent controls biologically relevant and identified the lowest dose tested, 50 mg/kg/day, as the LOAEL for reproductive effects.

In reviewing the findings from Exxon (1991), EPA also considered limited published historical control data (HCD) for fertility data for male and female Sprague-Dawley rats in reproductive toxicity studies, as well as reasonably available online information from a contract research laboratory (CRO) (Charles River, 2018). These sources reported mean male HCD fertility indices of 86.4% in second generation males from 27 reproduction studies (Marty et al., 2009) and 94.1% from 208 studies (4359 rats) assessed by the CRO (Charles River, 2018). Mean female HCD fertility indices were 87.5% in second generation females from 27 studies reported by Marty et al. (2009), and 93.9% from 211 studies (4854 rats) evaluated by the CRO. These data support EPA's interpretation of the Exxon (1991) fertility data, although it is acknowledged that appropriate HCD data from the performing laboratory are preferred for use in data interpretation (U.S. EPA, 1991c).

Other two-generation studies in rats did not replicate effects on reduced fertility. Two two-generation guideline dietary exposure studies in Sprague-Dawley and Wistar rats reported developmental toxicity but no significant reduction in fertility at the highest doses tested (500 mg/kg/bw/day, subsequently reduced to 350 mg/kg-bw/day due to pup mortality) (NMP Producers Group, 1999b, c). The study in Wistar rats reported changes in adult male testes weights following exposure to 160 and 350 mg/kg-bw/day, but no corresponding histopathological changes in the testes or sperm parameters (NMP Producers Group, 1999c).

A two-generation whole body inhalation exposure study in rats also found no effects on fertility or fecundity following exposure to 10, 51, or 116 ppm NMP for 6 hours per day, 7 days per week prior to mating, and during mating, gestation, and lactation (Solomon et al., 1995). However, the second-generation rats were not exposed from weaning to mating, and the F1 adults were mated with a cohort of untreated rats. In addition, there were uncertainties related to actual exposures achieved in this study.

Several oral repeated-dose studies detected testicular lesions and smaller testes (atrophy). A four-week oral exposure study identified a NOAEL of 429 mg/kg-bw/day for testicular lesions and atrophy (Malek et al., 1997) while a two-year oral exposure study in rats identified a NOAEL of 207 mg/kg/day for testicular lesions and atrophy (Malley et al., 2001). The same study observed no effect on testicular atrophy in mice. In a third oral exposure study, male rats were exposed to NMP for ten weeks prior to mating and during mating. This study reported cellular depletion of seminiferous tubule epithelium and reduced male fertility at 1,000 mg/kg-bw/day, but not at 300 mg/kg-bw/day (Sitarek and Stetkiewicz, 2008).

Other studies reported no effect on male reproductive endpoints, including a three month oral exposure in beagle dogs (NOAEL = 246 mg/kg-bw/day) (Becci et al., 1983) and a 90 day oral exposure study in rats (NOAEL = 1,057 mg/kg-bw/day) and mice (NOAEL = 1,931 mg/kg-bw/day) (Malley et al., 1999) and a chronic inhalation study in rats (NOAEL = 405 mg/m^3) (DuPont, 1982).

The biological plausibility for effects of NMP on male fertility is supported by mechanistic data. NMP is a bromodomain inhibitor (Gjoksi et al., 2016; Gjoksi et al., 2015b) that has been shown to bind the BRDT (bromodomain testis-specific) protein (Shortt et al., 2014). BRDT, a member of the highly conserved bromo and extra-terminal (BET) family, is a unique and essential regulator of male germ cell differentiation in mammals (Berkovits and Wolgemuth, 2013; Jonathan Gaucher, 2012). BET proteins contain two bromodomains and function as scaffolding modules that recruit transcription regulatory factors to chromatin, forming protein complexes that regulate gene transcription in response to signal transduction (Gjoksi et al., 2016). The loss of the first bromodomain of BDRT, BD1, results in incomplete or improper spermatid elongation, as well as morphologically abnormal sperm (Berkovits and Wolgemuth, 2013), and sometimes complete sterility (Enyuan Shang, 2007). Single nucleotide BDRT mutations have been associated with sterility in mice and infertility in humans (Berkovits and Wolgemuth, 2013). Because BRDT is not expressed in mitotically dividing spermatogonia, the stem cell population is not affected, and the outcomes are presumed to be reversible. The BRDT-inhibitor JQ1 has been studied as a candidate male contraceptive pharmaceutical (Matzuk et al., 2012). JQI has been shown to interfere with sperm maturation in mice by binding to BRDT, thus interfering with the reorganization of hyperacetylated histones (Berkovits and Wolgemuth, 2013). Apical results of JQ1 identified by Matzuk et al. (Matzuk et al., 2012) included dose- and duration-dependent reductions in sperm production and quality, testis size, and fertility. Notably, NMP has likewise been shown to bind BRDT, although with less affinity than JQ1 (Shortt et al., 2014). In other tissues, NMP has been explored for pharmaceutical applications related to its role as a bromodomain inhibitor exhibiting antineoplastic and immunomodulatory activity (Shortt et al., 2014), antiadiposity (Gjoksi et al., 2016), and osteogenic modulation (Siegenthaler et al., 2018). At this time, there is no direct evidence for the effect of NMP-mediated inhibition of this testis-specific bromodomain protein; however, competitive binding to such an important epigenetic mediator of sperm development suggests the plausible potential for NMP to influence epigenetic regulation during spermatogenesis.

The critical role of BRDT in mediating chromatin remodeling in sperm also suggests a potential mechanism for the developmental toxicity reported following paternal exposure in (Sitarek and Stetkiewicz, 2008). Developmental effects resulting from paternal exposures have long been recognized for a range of developmental toxicants (U.S. EPA, 1996) and epigenetic programming in sperm is proposed as an important mediator of such effects (Estill and Krawetz, 2016; Wu et al., 2015; Cordier, 2008).

The biological plausibility of male reproductive effects is additionally supported by the fact that NMP crosses the blood:testis barrier. This was demonstrated in a metabolism study in rats (Wells and Digenis, 1988) in which NMP was identified in the testes 6 hours following a single intravenous dose.

EPA assessed risks for adverse reproductive effects within the context of the exposure scenarios identified in the exposure assessment, as summarized in Table 3-7.

Table 3-7. Summary of Exposure Pathways and Toxicity Endpoints used for Risk Evaluation

Receptors	Exposure Pathway and Analytical Approach	
	Acute Dermal and Inhalation Exposures	**Chronic Dermal and Inhalation Exposures**
Worker Users and Nearby Worker Non-Users	Toxic endpoint: Developmental toxicity [a] Risk approach: Margin of Exposure (MOE)	Toxic Endpoint: Reproductive toxicity (fertility/developmental) Risk approach: Margin of Exposure (MOE)
Consumer Users and Nearby Residential Non-Users		Chronic risks were not evaluated. This pathway was not expected to occur in consumer users or bystanders.

[a] Acute dermal and inhalation toxicity studies were not used because they typically measure lethality at high doses and do not provide the level of analysis to assess non-effect levels from single exposures.

3.2.4.3 Weight of the Scientific Evidence for Cancer Hazard

The reasonably available scientific information does not provide strong evidence for carcinogenicity. Inhalation exposure studies are more relevant to human exposure scenarios than oral exposure studies. The inhalation cancer bioassay reported a significant increase in pituitary adenocarcinoma incidence in rats at the middle dose after 18 months of exposure, but no significant effect after 24 months of exposure and no effect at the highest dose. The lack of dose-response relationship makes it difficult to determine that effects are related to exposure and prevents quantitative dose-response analysis. In oral dietary studies, there was no significant association between NMP exposure and increased tumor incidence in rats. There was a small but significant increase in liver tumor incidence in male, but not female mice. While some evidence is suggestive of a potential cancer risk at maximally tolerated doses, the data are inconsistent and do not demonstrate a clear dose-response relationship. In addition, available *in vivo* and *in vitro* studies report no evidence of genotoxicity. The reasonably available data is insufficient to support a quantitative evaluation of cancer risks from NMP. EPA did not further evaluate cancer risks in the dose-response assessment or risk characterization.

3.2.5 Dose-Response Assessment

This section identifies the endpoints EPA selected for risk estimation. Reasonably available studies were reviewed based on study design, analysis and reporting quality to evaluate their individual strengths and weaknesses as summarized in Section 1.5. Guideline studies and other protocols that utilized good laboratory practices were considered if they met PECO and study quality criteria. The selected studies were then evaluated in the dose-response assessment.

Effects observed in multiple studies that were determined to be sensitive and biologically relevant, were considered for points of departure (POD) and dose-response analysis. These endpoints include:

- Decreased fetal/pup weight, PND 0, 4, 21
- Increased post-implantation loss or pup mortality, PND 0, 4, 21
- Skeletal malformations and incomplete skeletal ossification
- Reduced male and female fertility

Although there are no available studies that clarify the contribution of maternal toxicity to observed fetal effects, direct fetal exposure to NMP is supported by data demonstrating that it can cross the placenta

(RIVM, 2013). Therefore, EPA considers that the fetal effects observed following NMP exposure are biologically relevant and might not have resulted solely as a secondary effect of maternal toxicity.

Numerous studies are reasonably available to assess the developmental effects of NMP exposure in rats. Most are based on oral exposure, although some administered NMP via the inhalation route. One study evaluated the developmental effects following dermal exposure to rats. Table 3-8 presents the developmental endpoints evaluated in the studies reviewed for this assessment. Although developmental outcomes may vary due to temporal variations in vulnerability, EPA considers the general consistency of outcomes observed across different species, routes, durations and windows of exposure to be supportive of the robustness of this treatment effect.

Several studies are available to assess the reproductive effects of NMP exposure. Reproductive effects are less consistently reported across studies than developmental effects, but significant reductions in fertility were reported in three studies. The reduced male fertility and female fecundity observed in the second generation of the Exxon study (1991) are particularly sensitive endpoints. These significant reductions in male fertility and female fecundity occurred in the second generation following exposure throughout gestation, lactation, growth, puberty, and prior to mating. Other studies with shorter exposure periods limited to the weeks prior to mating, also reported reduced fertility in male and female rats (Sitarek et al., 2012; Sitarek and Stetkiewicz, 2008), although NOAELs in these studies were higher than the LOAEL for reproductive effects identified in the Exxon study. Table 3-9 summarizes the effects on fertility observed in the reasonably available studies.

Table 3-8. Evidence for NMP-induced Developmental Toxicity

	Study	Data Quality Score	Fetal Weight GD 20-PND 1	Pup Weight PND 4	Pup Weight PND 21	Embryonic or Fetal Loss [a]	Pup Mortality PND 4	Pup Mortality PND 21	Incomplete Ossification	Skeletal Malformations
ORAL STUDIES	Sitarek et al. (2012)	High	--	↓	↓	↑	↑	↑	NA	NA
	Sitarek and Stetkiewicz (2008)	High	NA	NA	NA	--	↑	--	NA	NA
	Saillenfait et al. (2002)	High	↓	NA	NA	↑	NA	NA	↑	↑
	NMP Producers Group (1999b)	High	↓	↓	↓	↑	↑	↑	--	--
	NMP Producers Group (1999c)	High	↓	↓	↓	↑	↑	↑	--	--
	ISP (1992)	High	↓	NA	NA	--	NA	NA	↑	--
	Exxon (1991)	High	↓	↓	↓	↑	↑	↑	--	--
INHALATION STUDIES	Saillenfait et al. (2003)	High	↓	NA	NA	--	NA	NA	--	--
	Hass et al. (1995) [c]	Not rated	↓	NA	NA	↑	NA	NA	↑	--
	Hass et al. (1994) [c]	Not rated	↓	↓	↓	--	--	--	NA	NA
	Solomon et al. (1995); E. I. Dupont De Nemours & Co (1990)	High	↓	↓	↓	↑ [b]	--	--	↑ [b]	↑ [b]
	Lee et al. (1987)	High	--	NA	NA	--	NA		--	--
DERMAL STUDIES	Becci et al. (1982)	Medium	↓	NA	NA	↑	NA	NA	↑	↑

	Study	Data Quality Score	Fetal Weight GD 20-PND 1	Pup Weight PND 4	Pup Weight PND 21	Embryonic or Fetal Loss [a]	Pup Mortality PND 4	Pup Mortality PND 21	Incomplete Ossification	Skeletal Malformations

↓ indicates decrease, ↑ indicates increase, -- indicates no statistically significant difference from controls reported by study authors

[a] May be based on resorptions, post-implantation loss, dead pups at birth or decreased live pups at birth

[b] Considered biologically, but not statistically significant; the increase in embryonic loss (resorptions) in DuPont (1990) was statistically significant at p = 0.1.

[c] Studies not rated because they were excluded by the PECO statement in the systematic review process due to the lack of dose-response information (the study used a single high dose). These studies are included here because previous assessments have cited them as supporting studies and they contribute to overall weight of the scientific evidence.

NA = Not Assessed

Table 3-9. Evidence for NMP-induced Reproductive Toxicity

Study		Data Quality Score	Effects Following Adult Exposure		Effects Following Exposure Throughout Development [a]	
			Male Fertility	Female Fecundity	Male Fertility	Female Fecundity
ORAL STUDIES	Sitarek et al. (2012)	High	**NA**	↓	**NA**	**NA**
	Sitarek and Stetkiewicz (2008)	High	↓	**NA**	**NA**	**NA**
	NMP Producers Group (1999b)	High	--	--	--	--
	NMP Producers Group (1999c)	High	--	--	--	--
	Exxon (1991)	High	--	--	↓	↓
INHALATION STUDIES	Solomon et al. (1995; E. I. Dupont De Nemours & Co (1990)	High	--	--	--	--

↓ indicates decrease, ↑ indicates increase, -- indicates no change

[a] In Exxon (1991) and the NMP Producers Group (1999b; 1999c) studies, reproductive effects in the second generation were evaluated following exposures throughout gestation, lactation, growth, puberty and adulthood prior to mating. In the Solomon et al 1995/Dupont (1990) study, second generation rats were not exposed after weaning and exposed rats were mated with unexposed controls.

NA = Not Assessed

3.2.5.1 Selection of Endpoints for Dose-Response Assessment

EPA selected endpoints for dose-response assessment based on the relative potency of effects and the weight of the scientific evidence. The reproductive and developmental effects described in Table 3-8 and Table 3-9 were plotted graphically in exposure-response arrays for oral (Figure 3-2, Figure 3-3) inhalation (Figure 3-4) and dermal (Figure 3-5) studies. Exposure-response arrays are a graphical representation of reasonably available dose-response data for significant effects. The exposure-response arrays include LOAELs and NOAELs, based on applied doses. The graphical display allows the reader to quickly compare study outcomes, based on the same or groups of related endpoints for fertility, growth, and development.

Decreased fetal/pup weights

Decreased fetal and/or postnatal body weights were consistently observed across oral, inhalation, and dermal studies despite variations in dosing time and exposure routes. The exposure –response arrays in Figure 3-2, Figure 3-4 and Figure 3-5 illustrate the concordance and consistency of these effects,– meaning that the effects were present in multiple studies and the NOAELs and LOAELs occurred within a narrow dose range.

As illustrated in Figure 3-2, fetal and pup body weights were decreased with oral gavage or dietary exposures in several rat studies. Saillenfait (2002) reported fetal body weights decreased by 10% at 250 mg/kg-bw/day and by 47% at the highest dose, 750 mg/kg-bw/day. In the Exxon (1992) study, fetal body weights decreased by 10-11% at 400 mg/kg-bw/day, the highest dose tested. Sitarek et al. (2012) observed 25-30% decrements in pup body weight (PND 4) following maternal exposure to concentrations >150 mg/kg-bw/day. Three dietary two-generation reproduction studies consistently reported decreased pup body weights through PND21, with LOAELs of 160 mg/kg-bw/day (NMP Producers Group, 1999b), 350mg/kg-bw/day (NMP Producers Group, 1999c), and 500 mg/kg-bw/day (Exxon, 1991). Because the Sitarek, Exxon, and NMP Producers Group studies involved maternal exposures that continued through the postnatal period, the significant decreases in pup body weights might have been due to toxicity resulting from prenatal exposure to NMP and/or as a result of postnatal transfer of NMP to the pups via lactation.

Figure 3-4 presents the exposure-response array for the inhalation studies in rats. Statistically significant decreases in body weights were observed following inhalation exposure at concentrations ranging from 479 to 612 mg/m^3 in multiple studies (Saillenfait et al., 2003; Hass et al., 1995; Hass et al., 1994; E. I. Dupont De Nemours & Co, 1990). Saillenfait et al. (2003) observed 5-6% decrements in fetal body weights at 486 mg/m^3 and DuPont (1990) observed 7% decrements in fetal body weights at 479 mg/m^3. Two studies by Hass et al. (1995; 1994) also indicated that fetal body weights were decreased in both Wistar and Sprague-Dawley rats; however, both of the Hass studies were excluded by the systematic review process for selection of candidate PODs for this risk evaluation because only one dose level (612 mg/m^3) was used in each study. They are included here because they are used as supporting studies in several previous assessments (U.S. EPA, 2015c; RIVM, 2013), and they contribute to the overall weight of the scientific evidence. In contrast, no changes in fetal body weight were observed in an inhalation study by Lee et al. (1987).

The DuPont and Hass inhalation studies also noted decreased pup body weights (Hass et al., 1994; E. I. Dupont De Nemours & Co, 1990). In the DuPont study, exposures were suspended from GD 20 through PND 4, but the weight decrement remained, lending support to the notion that decreased body weight is a persistent, adverse effect.

The dermal developmental exposure study (Becci et al., 1982) also reports significant reductions in fetal body weight at 750 mg/kg-bw/day, the highest dose tested, following gestational exposures (Figure 3-5).

Based on the observations of decreased fetal and postnatal body weights, EPA considered decreased fetal body weights as a potential key endpoint for use in the risk calculation for chronic exposure. These effects were consistent among multiple studies with different dosing regimens and across exposure routes. Reduced fetal body weight is a sensitive endpoint that is considered a marker for fetal growth restriction which is often assumed to be representative of repeated dose rather than acute exposures (van Raaij et al., 2003). Decreases in fetal and postnatal body weights occur at similar dose levels. Decreased fetal body weight was assumed to be the proximate event. In a previous risk assessment, EPA used this endpoint as the basis for evaluating chronic risks (U.S. EPA, 2015c)

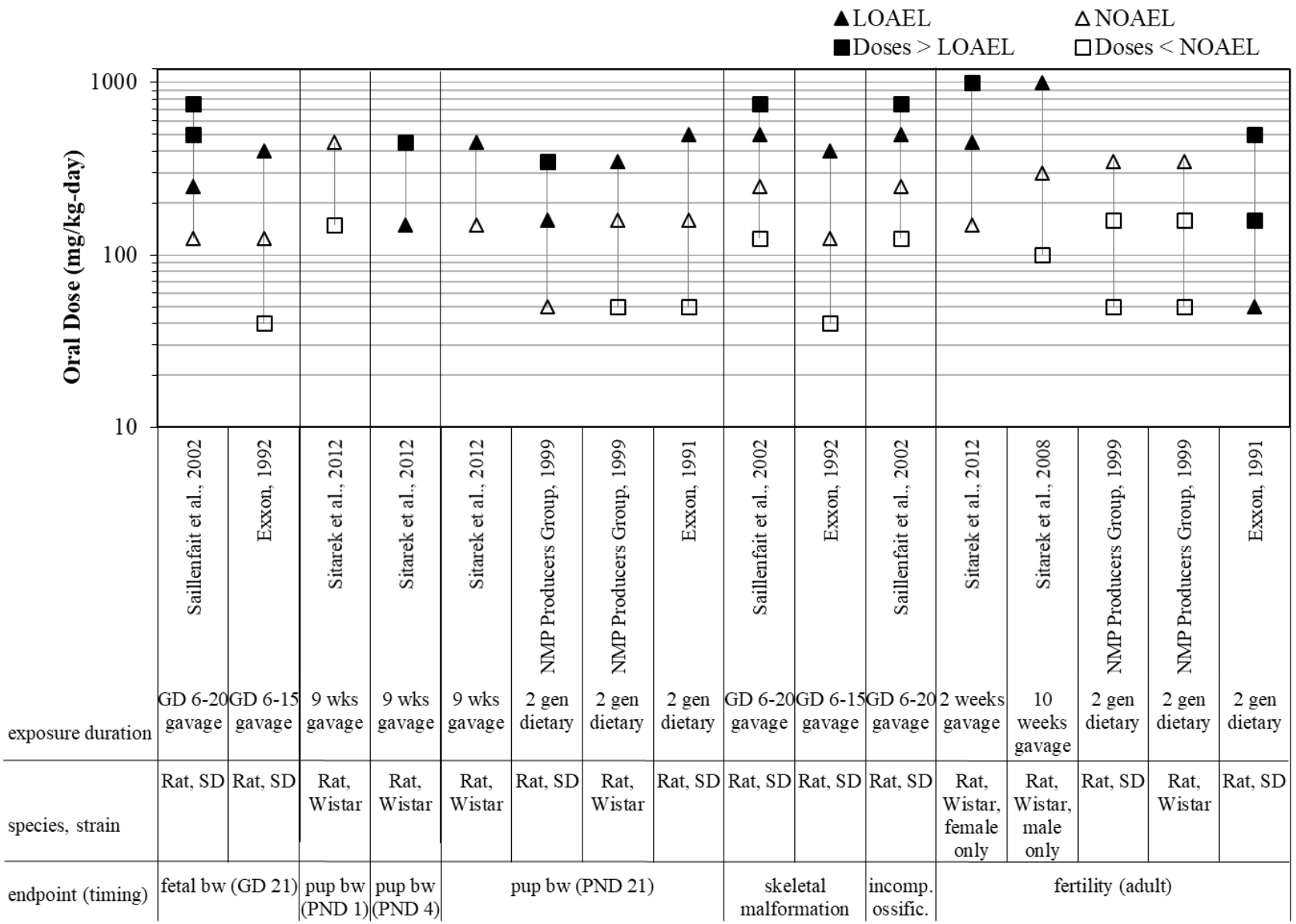


Figure 3-2. Oral Doses Resulting in Sublethal Reproductive and Developmental Effects.

Bw = body weight; incomp. ossific. = incomplete ossification; GD = gestational day; PND = postnatal day

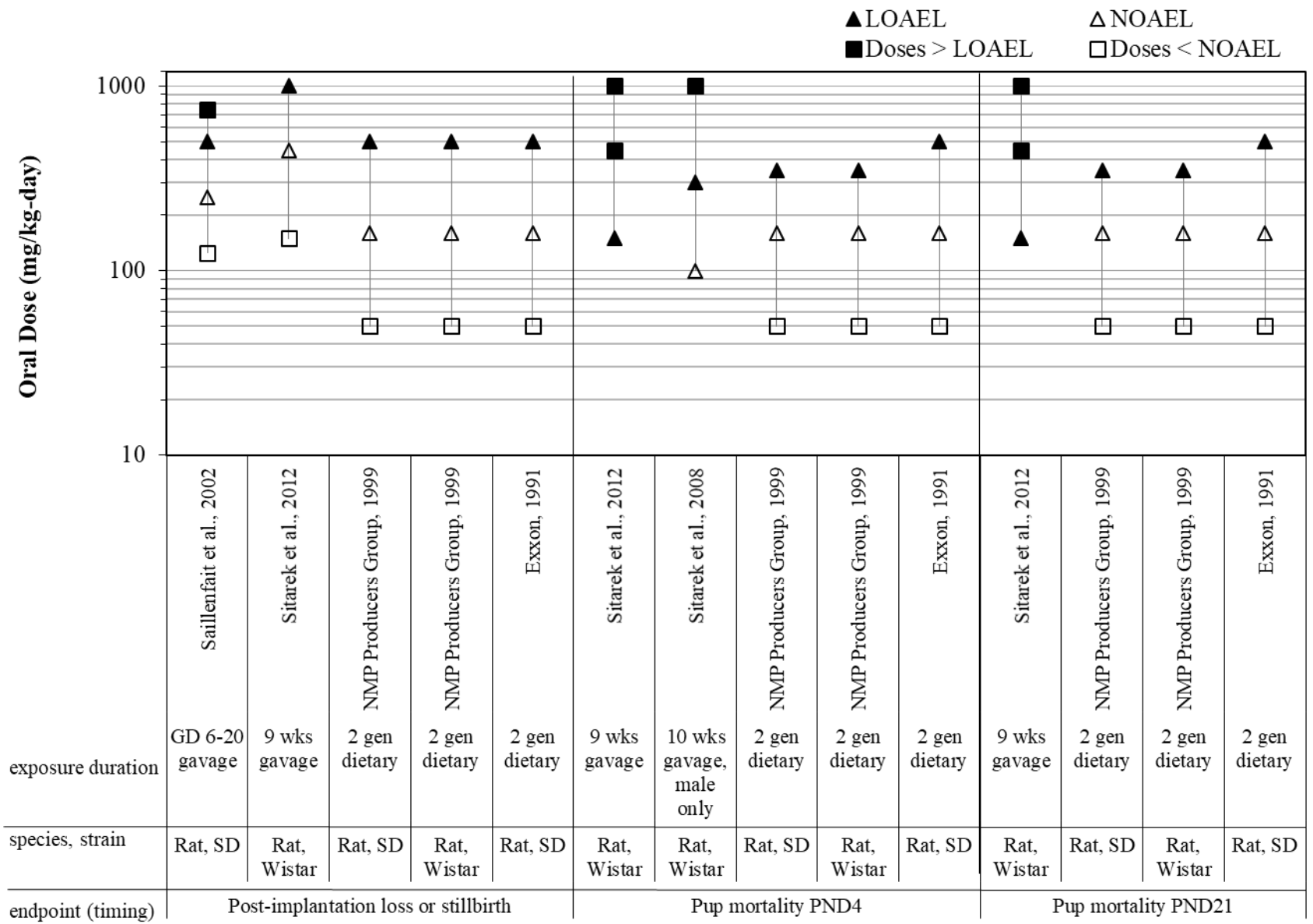


Figure 3-3. Oral Doses Resulting in Reduced Offspring Viability

PND = postnatal day

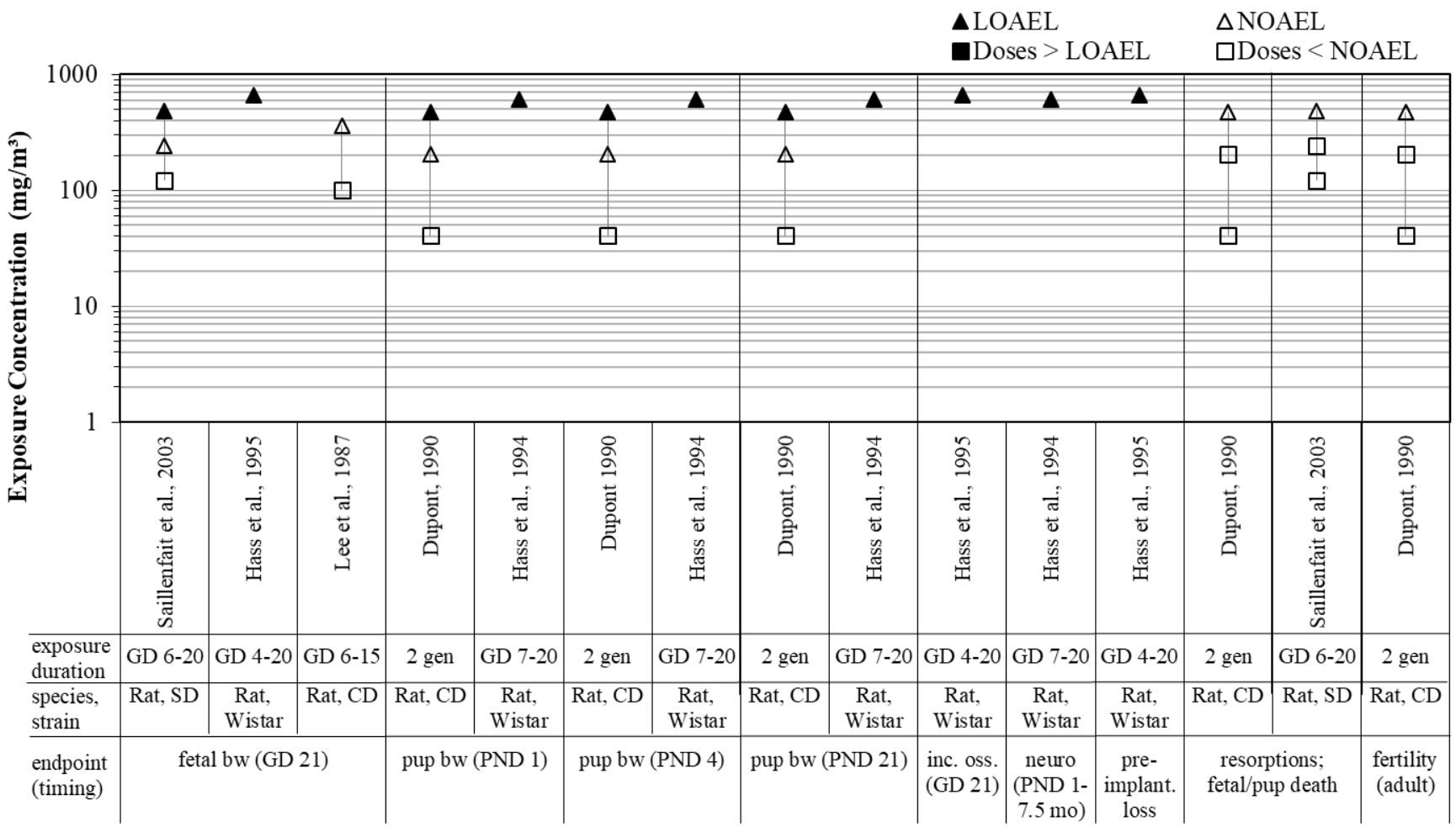


Figure 3-4. Inhalation Concentrations Resulting in Reproductive and Developmental Effects.

The Hass 1994 and Hass 1995 studies were screened out in systematic review because they evaluated effects of a single dose. They were not evaluated for study quality, but they are included here as part of the weight of the scientific evidence. The Dupont 1990 study (Solomon et al., 1995; E. I. Dupont De Nemours & Co, 1990) was rated a high-quality study, but it is not consistent with guidelines for 2 generation studies and there were uncertainties about the actual doses achieved at the highest exposure.

Bw = body weight; inc. oss. = incomplete ossification; neuro = developmental neurotoxicity; pre-implant. = pre-implantation loss; GD = gestational day; PND = postnatal day

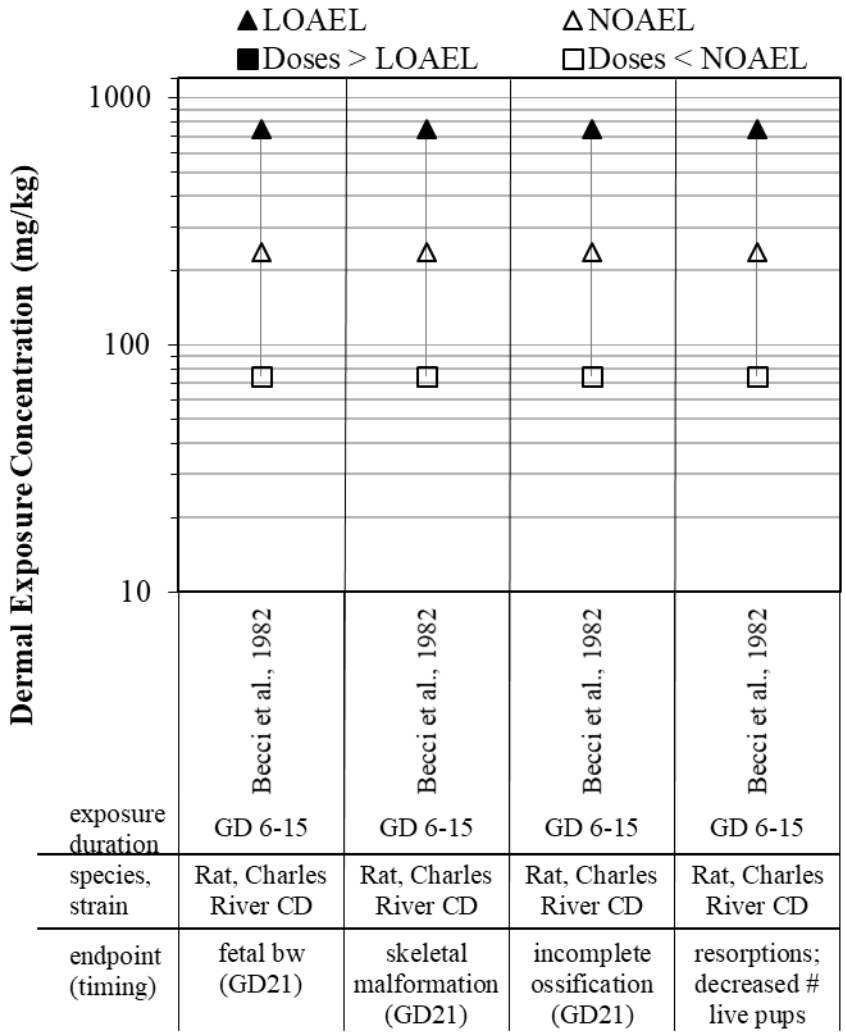


Figure 3-5. Dermal Doses Resulting in Reproductive and Developmental Effects
Bw = body weight; GD = gestational day

Post-implantation loss and pup mortality
Resorptions have been observed in oral, inhalation, and dermal studies (Saillenfait et al., 2002; E. I. Dupont De Nemours & Co, 1990; Becci et al., 1982). Embryo/fetal and postnatal mortality have also been observed in oral studies (Sitarek et al., 2012; NMP Producers Group, 1999b, c; Exxon, 1991). Statistically significant increases in resorptions or mortality were seen consistently at administered doses of 500-1,000 mg/kg-bw/day in all studies at the tested doses. Dose levels resulting in post-implantation loss (including resorptions and fetal mortality) or reduced pup viability in oral exposure studies are summarized in Figure 3-3.

In the single dermal study (Becci et al., 1982), resorptions significantly increased and the number of live pups significantly decreased at 750 mg/kg-bw/day (Figure 3-5). In inhalation studies with exposures up to the air saturating concentration, there were no statistically significant increases in resorptions or fetal and postnatal pup mortality reported (Figure 3-4), possibly due to the limited NMP exposure concentration.

Resorptions can occur following a single exposure during a sensitive developmental stage (van Raaij et al., 2003). As such, resorptions and fetal mortality are considered a relevant endpoint for acute effects.

There is more uncertainty around the relevance of acute exposures for stillbirths. While stillbirths may plausibly be the result of a single exposure during a critical period of development, they may also be the result of repeated-dose exposures. In the reasonably available studies, stillbirths occurred following repeated-dose exposures in a similar dose range as post-implantation loss (see Figure 3-3).

EPA also considered the relevance of increased postnatal mortality. Sitarek et al. (2012) observed increased pup mortality at 150 mg/kg-bw/day following maternal gavage exposure for two weeks prior to mating and throughout gestation and lactation. Sitarek et al. (2008) observed increased pup mortality at PND4 following paternal oral gavage exposure to 300 mg/kg-bw/day for ten weeks prior to mating, indicating that paternal exposure alone may reduce pup viability. In addition, all three two-generation dietary studies reported decreased pup survival to PND4 and PND21 at the highest doses tested (350 or 500 mg/kg-bw/day) but not at the lower doses (50 and 160 mg/kg-bw/day) (NMP Producers Group, 1999b, c; Exxon, 1991). No increase in pup mortality was observed in DuPont (1990). When increased post-natal mortality was observed, the NOAELs were generally within the same range as other sensitive endpoints relevant to repeated-dose exposures, such as reduced fetal body weight (*e.g.*, see Figure 3-2 and Figure 3-3).

EPA selected increased post-implantation loss (including resorptions and fetal mortality) as a key endpoint for the calculation of risks associated with acute exposures. Embryonic and fetal resorptions may result from a single exposure at a developmentally critical period (Davis et al, 2009; van Raaij et al., 2003; U.S. EPA, 1991b). In the studies reviewed, post-implantation loss occurred at relatively low exposures, suggesting that this was a sensitive and relevant endpoint, suitable for use in the risk assessment.

Other Fetal Effects

Incomplete ossification was observed following exposures to NMP via oral, inhalation and dermal routes. Incomplete ossification is a decrease in the amount of mineralized bone expected for developmental age and is one of the most common findings in developmental toxicity studies (Carney and Kimmel, 2007). Saillenfait et al. (2002) reported statistically significant increases in incidences of incomplete ossification of sternebrae, skull and thoracic vertebral centra at GD 20 for oral doses of 500 and 750 mg/kg-bw/day (Figure 3-2). Hass et al. (1995) reported statistically significant increases in delayed ossification of cervical vertebrae 4 through 7 and digital bones following an inhalation exposure at a concentration of 669 mg/m³ (Figure 3-4). Becci et al. (1982) reported a statistically significant increase in incidences of incomplete ossification of vertebrae at 750 mg/kg-bw/day dermal application (Figure 3-5). Several inhalation exposure studies found no increased incidence of incomplete or delayed ossification (Saillenfait et al., 2003; E. I. Dupont De Nemours & Co, 1990; Lee et al., 1987).

The areas of increased incomplete ossification that were observed in fetuses at GD 20 or 21 were in bones that are undergoing rapid ossification during the period of observation, but there are a number of hormones considered to be important for regulating skeletal development (Carney and Kimmel, 2007). There are several clues that may be indicative of effects due to something other than generalized delay, including: delays in the presence of specific skeletal malformations, teratogenesis or unusual patterns of delayed ossification (Carney and Kimmel, 2007; van Raaij et al., 2003). Based on the absence of such observations EPA considered NMP-associated delayed ossification to represent a continuum of effects related to delays in fetal growth and development, associated with decreased fetal and/or pup body weight.

Skeletal malformations are considered permanent structural changes that are likely to adversely affect the survival or health of the species (Daston and Seed, 2007) and were observed in some NMP studies

via oral exposure. The Saillenfait et al. (2002) study reported aggregated skeletal malformations (including ribs, vertebrae and others) at GD 20 for oral doses of 500 and 750 mg/kg-bw/day. Skeletal malformations were also reported at the highest dose tested in the dermal exposure study (Becci et al., 1982). In contrast, skeletal malformations were not observed in inhalation studies conducted up to the air-saturating concentration. Increased skeletal malformations may not have been observed in the inhalation studies because the vapor pressure of NMP limited the attainment of toxic concentrations in air.

Reduced fertility

Reduced fertility was reported in three oral exposure studies. Reduced male fertility and female fecundity in the second generation of rats in a two-generation dietary reproductive study (Exxon, 1991) were among the most sensitive reproductive and developmental effects reported in the repeated dose studies reviewed for this risk evaluation (Figure 3-2). Evidence of reduced fertility in this study is supported by coinciding observations of reduced litter size. Microscopic changes in the uterus and ovaries (including decreased numbers of corpora lutea and decreased implantation sites) and increased incidence of smaller than normal testes in the high dose group of the second generation provide further support for reproductive toxicity in this study. It is unknown whether the fertility effects were initiated during gestational, lactational, pubertal, growth, or adult exposures. The other two dietary two-generation studies reported no significant reduction in fertility index at any dose (NMP Producers Group, 1999b, c), though both studies report significant reductions in offspring viability at the high dose and one reported significant reductions in testes weights at the high dose.

Evidence of reduced male and female fertility following pre-mating exposures in male (Sitarek and Stetkiewicz, 2008) or female rats (Sitarek et al., 2012) provides further indication that NMP may be reproductively toxic. In females, oral gavage exposure to 450 mg/kg-bw/day for two weeks prior to mating significantly reduced fertility. In males, oral gavage exposure to 1,000 mg/kg-bw/day for ten weeks prior to mating resulted in extensive damage to the seminiferous epithelium and seminal tubules of the testes as well as reduced fertility (Sitarek and Stetkiewicz, 2008). Reductions in offspring survival reported following paternal pre-mating exposure to 300 mg/kg-bw/day (Sitarek and Stetkiewicz, 2008) indicate that male reproductive effects may include changes in gametes that impair offspring health and survival.

While effects of NMP on fertility are not consistent across all reasonably available studies, mechanistic evidence suggests s a plausible mechanism through which NMP may impair male fertility and reduce offspring viability (see discussion in Section 3.2.4.2). Considered in combination with evidence for testicular toxicity (Sitarek and Stetkiewicz, 2008; Exxon, 1991), increased pre-implantation loss (Hass et al., 1995), increased post-implantation loss (Sitarek et al., 2012; Saillenfait et al., 2002; Becci et al., 1982), and reduced pup viability following pre-conception exposure and/or gestational exposure (Sitarek et al., 2012; Sitarek and Stetkiewicz, 2008; NMP Producers Group, 1999b, c; Exxon, 1991), the reduced fertility reported following NMP exposure in several studies may be considered part of a continuum of effects that contribute to reduced reproductive success in males and females.

EPA considered decreased fertility a potential key endpoint for use in the risk calculation for chronic exposures. Reduced male fertility and female fecundity were the most sensitive endpoints reported. Observations from the two-generation exposure study are supported by effects on male and female fertility following adult exposures at higher doses. The previous EPA assessment (U.S. EPA, 2015c) did not characterize dose-response for these fertility endpoints because the effect observed in the Exxon (1991) study was not replicated in more recent two-generation studies and was initially dismissed as not biologically significant due to historical control data. However, re-evaluation of the Exxon study

demonstrates that the study shows a statistically and biologically significant effect in the most sensitive reproductive and developmental endpoints identified in the reasonably available literature.

Key Endpoints

Developmental effects have consistently been reported following NMP exposure in laboratory animals and a case report provides limited evidence of developmental toxicity in humans. In addition, reproductive effects following NMP exposure have been reported in several animal studies. Collectively the reported effects on reproduction and development, which include reduced male and female fertility, decreased fetal and postnatal body weight, incomplete ossification, skeletal malformations and fetal or postnatal mortality, represent a continuum of biologically relevant outcomes that provide important insights for hazard characterization. The developmental effects reported in different studies following NMP exposure occur within a narrow dose range (*i.e.*, 100 to 1,000 mg/kg-bw/day for oral and 470 to 669 mg/m^3 for inhalation exposures) and appear to persist based on clinical observations reported through PND 21. EPA considers the general consistency of the NMP treatment effects reported across studies to be supportive of the robustness of the developmental endpoints used for risk evaluation, which exist along a continuum of adverse treatment effects. While reproductive effects are less consistent across studies, reduced fertility is the most sensitive endpoint reported and reasonably available evidence for NMP suggests a plausible mechanism (see Section 3.2.4.2) for reduced male fertility.

EPA has selected post-implantation loss as the basis of the dose-response analysis for acute exposures. Acute toxicity studies observing other effects (*e.g.*, LD50 values for acute toxicity or lethality) were not used for the acute POD because the doses at which these effects were observed are higher than those that caused toxic effects in developmental studies. Developmental studies involve multiple exposures (*i.e.*, test substance is administered for 10-15 days); however, they are relevant to single exposures because some developmental effects, such as embryonic resorptions and fetal mortality, may result from a single exposure at a developmentally critical period (Davis et al., 2009; van Raaij et al., 2003; U.S. EPA, 1991b). In an analysis of the utility of developmental toxicity repeat dose studies for use in the assessment of risks following acute exposures, van Raaij et al. compared the potency (NOAELs and LOAELs) of developmental toxicity reported in repeated dose studies and single dose studies (van Raaij et al., 2003). Van Raaij et al. found that for most chemicals there is a relatively small difference between repeated and single dose studies in the NOAELs and LOAELs reported for embryonic and fetal resorptions. While the difference in potency of single and repeated doses varied across chemicals, for some chemicals the potencies of single and repeated doses were equal and for many other chemicals there was only a 2-4 fold difference in potency. The authors concluded that "resorptions observed in standard guideline-based developmental toxicity studies are considered to be relevant endpoints for setting limits for acute exposure." Consequently, EPA determined that these endpoints are most applicable to assessing risks from acute exposures, where the risk of their occurrence is assumed to depend on exceedance of a threshold value for even a single day (*i.e.*, peak concentration) rather than a time weighted average value and the magnitude of the exposure is considered more important for these effects under these study conditions.

EPA selected reduced male fertility, female fecundity and reduced fetal body weights as the basis for the dose-response analysis for chronic exposures. Reduced fertility in male and female rats exposed throughout development and prior to mating in a two-generation reproductive study was the most sensitive reproductive and developmental endpoint identified in the reasonably available literature following chronic exposures. Because NMP exposure in this study occurred throughout gestation, post-weaning, growth, and prior to mating, it is unknown whether effects represent a developmental effect or whether they are a result of subsequent exposures. Evidence for sensitive effects on fertility is complemented by robust evidence of developmental toxicity. As documented above, reduced fetal body

weight was observed consistently across multiple studies with different dosing regimens and across exposure routes. Reduced fetal body weight is a sensitive endpoint that is considered a marker for fetal growth restriction typically resulting from repeated dosing during gestation rather than a single acute dose (van Raaij et al., 2003). Together, these observations indicate a continuum of reproductive and developmental effects associated with NMP exposure. EPA therefore performed dose-response analysis on all three of these reproductive and developmental endpoints (male fertility, female fecundity, and fetal body weight) for consideration as the chronic POD.

3.2.5.2 Dose Metrics Selected

The selection of the internal dose metric, used to establish "equivalent" exposures, is an important decision in the use of the PBPK model for extrapolation of doses across routes and from rats to humans. Internal dose metric selection is endpoint specific (U.S. EPA, 2006a). For example, the dose metric area-under-the curve (AUC) of the average blood concentration is generally considered appropriate for endpoints associated with repeat dose exposures, assuming that a sustained internal dose of NMP is needed to induce the effects. Endpoints that are associated with a single or short-term acute exposure, assuming that a single dose effect is needed to induce these effects, are generally best evaluated by a metric that captures peak exposure, such as C_{max}.

Reduced fertility following chronic exposure throughout several lifestages is best represented by the AUC of average blood concentration. Similarly, as described above in Section 3.2.4.1, the endpoint of decreased fetal body weight was presumed to be a marker of reduced fetal growth resulting from repeated dose exposure during gestation. Therefore, decreased fetal body weight is expected to be better represented by the AUC of average maternal blood concentration during the vulnerable period of fetal development.

EPA evaluated average daily AUC (total AUC divided by the number of days, starting from the first day of exposure until the day of measurement), *e.g.*, GD 6-20 for Becci et al., (1982) or GD 5-21 for Saillenfait et al. (2003) with decreased fetal body weights for oral, inhalation and dermal routes of exposure to confirm the metric is consistent in its estimation of a toxic response across routes. Seven studies that measured fetal body weights were used for evaluating consistency between the internal dose and the response expressed as percent change from control in body weight. The data points were fit to a line and the correlation coefficient (R^2) was used to evaluate linearity, shown in Figure 3-6. The Average Daily AUC metric had a reasonable correlation with fetal body weight changes. Varying the period of averaging for the daily AUC metric may provide higher correlations with fetal body weights.

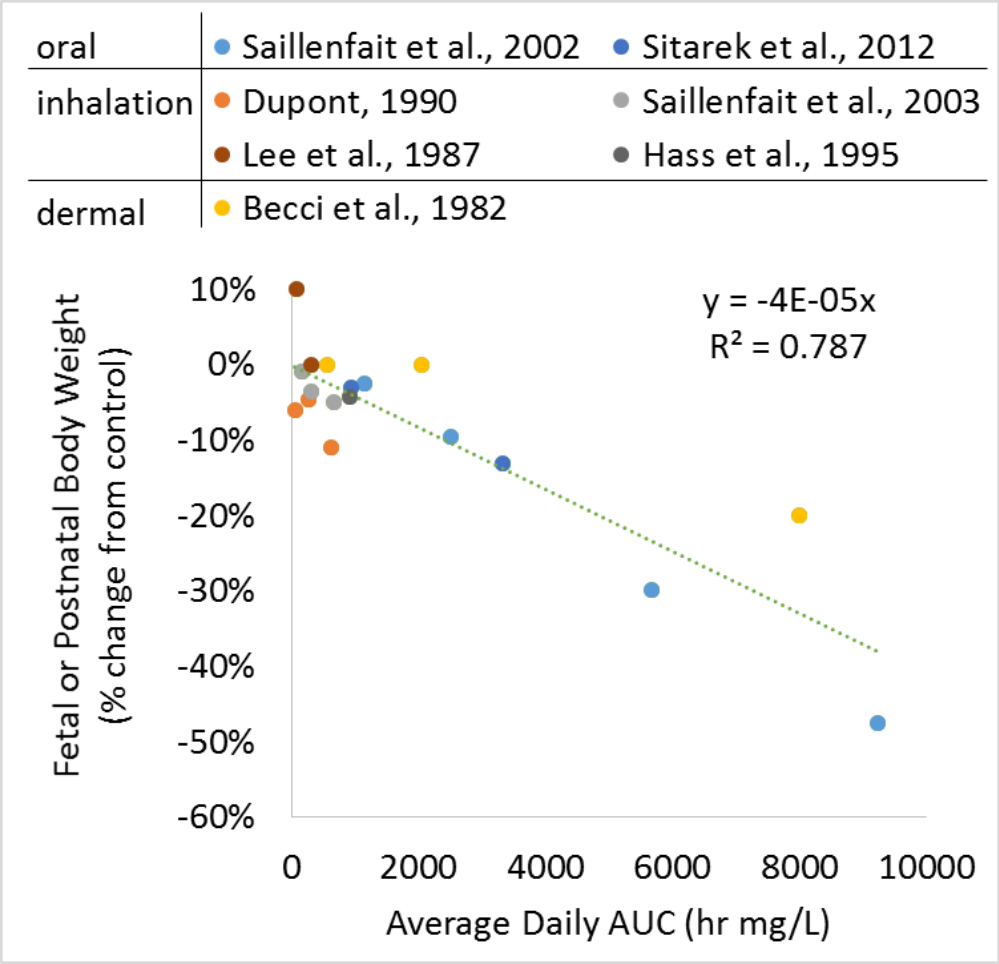


Figure 3-6. Analysis of Fit: Average Daily AUC vs. Fetal or Postnatal Body Weight

As described in Section 3.2.5.1, fetal resorptions and fetal mortality are assumed to be associated with acute exposures during fetal development; however, lacking a clear understanding of the possible mode of action, the best dose metric for the evaluation of fetal resorptions and mortality is unclear. Per EPA guidance (U.S. EPA, 2006a), both average daily AUC and peak blood dose (C_{max}) were used to evaluate this endpoint.

Developmental effects such as fetal mortality and reduced fetal body weight occur following maternal exposure. To identify C_{max} or AUC for developmental effects, BMD modeling was based on internal doses predicted by the PBPK model for adult females. Reproductive effects in the key study were observed following exposure throughout gestation, lactation, puberty, and mating and it is unknown which periods of exposure contributed to reduced fertility. Therefore, internal doses for fertility endpoints were calculated based on internal exposure levels in young post-weaning rats, the life stage at which calculated internal doses are the lowest. EPA performed a sensitivity analysis to determine the effect of this assumption on the POD. BMDLs calculated based on lower internal exposures in young post-weaning rats were up to 2-fold lower than BMDLs calculated based on internal exposures at other life stages. The predicted difference in internal doses at lower body weights is shown in Section 5.2 of *Risk Evaluation for n-Methylpyrrolidone (NMP), Benchmark Dose Modeling Supplemental File. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020e).

3.2.5.3 Potentially Exposed and Susceptible Subpopulation

Based on the weight of the scientific evidence, reduced fertility and developmental toxicity are the most sensitive effects of NMP exposure. The lifestages of greatest concern for developmental effects are pregnant women, the developing fetus, and women of childbearing age who may become pregnant. Lifestages of concern for effects on reproductive health and fertility include men and women of reproductive age as well as infants, children and adolescents. The results of one two-generation study in rats (Exxon, 1991) indicate that *in utero* and postnatal developmental exposure to NMP may contribute to risk of reduced fertility in adulthood. Other potential hazards of NMP identified in Section 3.2.3 may be of concern for other lifestages.

Certain human subpopulations may be more susceptible to exposure to NMP than others. One basis for this concern is that the enzyme CYP2E1 is partially involved in metabolism of NMP in humans and there are large variations in CYP2E1 expression and functionality in humans (Ligocka et al., 2003). The variability in CYP2E1 in pregnant women could affect how much NMP reaches the fetus, which typically does not express CYP2E1 (Hines, 2007). Newborns and very young infants are particularly susceptible to NMP exposure because they are metabolically immature. CYP2E1 is not fully expressed in children until about 90-days of age (Johnsrud et al., 2003). The variability in CYP2E1 was identified as an important uncertainty that was reflected in the calculation of the intraspecies uncertainty factor (human variability). Pre-existing conditions affecting the liver may also impair metabolism of NMP in some individuals. For example, fatty liver disease has been associated with reduced CYP function (Fisher et al., 2009).

Genetic variations or pre-existing conditions that increase susceptibility of the reproductive system, the hepatic, renal, nervous, immune, and other systems targeted by NMP could also make some individuals more susceptible to adverse health outcomes following consumer or workplace exposures. In addition, people simultaneously exposed to other chemicals targeting these systems may also be more susceptible to effects of NMP exposure.

While an uncertainty factor for interindividual variability provides some additional protection for susceptible subpopulations, a lack of quantitative information on the extent to which any of these specific factors increases risk precludes direct incorporation of these factors in the risk characterization.

3.2.5.4 Selection of Studies for Dose Response Assessment

EPA evaluated data from studies described above (Section 3.2.5.1) to characterize NMP's dose-response relationships and select studies to quantify risks for specific exposure scenarios.

In order to select the most appropriate key studies for this analysis, EPA considered the relative merits of the oral, inhalation and dermal animal studies, with respect to: (1) the availability of primary data for statistical analysis; (2) the robustness of the dose-response analysis; and (3) the exposure levels at which adverse effects were observed.

The selected key studies provided the dose-response information for the selection of points of departure (PODs). EPA defines a POD as the dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on the dose for an estimated incidence or a change in response level from a dose-response model (*i.e.*, benchmark dose or BMD), a NOAEL or a LOAEL for an observed incidence or change in level of response. PODs were adjusted as appropriate to conform to the exposure scenarios derived in Section 2.4.
The key studies and endpoints selected for BMD modeling in support of POD derivation are listed below. EPA performed additional BMD modeling on alternate endpoints that is described in more detail

in the supplemental file, *Risk Evaluation for n-Methylpyrrolidone (NMP), Benchmark Dose Modeling Supplemental File. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020e).

Studies Selected for BMD Modeling

For reduced fertility EPA selected the following study for dose response analysis:

- Exxon (1991); high quality oral dietary study

For reduced fetal body weights EPA selected the following studies for dose-response analysis:

- Becci (1982); medium quality dermal study
- DuPont (1990); high quality inhalation study
- Saillenfait (2002); high quality oral gavage study
- Saillenfait (2003); high quality inhalation study

For fetal resorptions and increased fetal mortality EPA selected the following studies for dose-response analysis:

- Becci (1982); medium quality dermal study
- Saillenfait (2002); high quality oral gavage study
- Saillenfait (Saillenfait et al. 2003; Saillenfait et al., 2002); combined dose-response data from a high quality oral gavage study and a high quality inhalation study
- Sitarek et al. (2012); high quality oral gavage study

For stillbirth, EPA selected the following studies for dose-response analysis:

- NMP Producers Group (1999b); high quality dietary study
- NMP Producers Group (1999c); high quality dietary study
- Exxon (1991); high quality dietary study

The Saillenfait et al. (2002) and Saillenfait et al. (2003) studies administered NMP via different routes but were otherwise similar in study design, using the same exposure duration (GD 6-20) and the same strain of rat (Sprague-Dawley); therefore, these studies were combined based on PBPK-derived internal dose metrics. This expands the range of doses covered by the dose-response model. Also, a more robust BMDL is likely, by virtue of using a model that is based on more data.

The relevance of reasonably available stillbirth data for acute versus chronic exposure scenarios is unknown. While stillbirths could plausibly result from a single exposure, stillbirths in reasonably available studies occur following repeated dietary exposures throughout gestation. EPA modeled dose-response information for stillbirths in reasonably available studies as a reference point for derivation of PODs for both acute and chronic exposures.

EPA guidance recommends a hierarchy of approaches for deriving PODs from data in laboratory animals, with the preferred approach being PBPK modeling (U.S. EPA, 2012a). When data were amenable, benchmark dose (BMD) modeling was used in conjunction with the PBPK models to estimate PODs. For the studies for which BMD modeling was not possible (Sitarek et al., 2012; Becci et al., 1982), the NOAEL was used for the POD. Details regarding BMD modeling were described in the supplemental file, *Risk Evaluation for n-Methylpyrrolidone (NMP), Benchmark Dose Modeling Supplemental File. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020e). Details regarding the PBPK model can be found in Appendix J.

Studies with only one exposure group (Hass et al., 1995; Hass et al., 1994) provide limited information about the shape of the dose-response curve and could not be used for BMD modeling. Given the concordance of effect levels in these studies with effect levels in other studies that had multiple exposure groups, they were still seen as supportive of the dose-response relationship. Studies that did not report a statistically significant effect for the endpoint being considered (Lee et al., 1987) may help with dose metric selection, but provide only limited information about the shape of the dose-response curve and were not included in the dose-response assessment of that endpoint.

3.2.5.5 Derivation of Internal Doses

PBPK models for NMP in rats and humans (Appendix J) facilitate cross-species extrapolation of hazard information. In this risk evaluation, EPA used a rat PBPK model to derive PODs based on internal doses associated with health hazards in rats and used a human PBPK model to estimate internal doses (blood concentrations) of NMP that may occur in humans under specific conditions of use. EPA calculated risks by comparing internal doses predicted by the model in humans to PODs in units of internal doses in rats. Internal doses are assumed to have consistent effects regardless of exposure route. EPA therefore used the PBPK model to derive internal dose PODs based on the weight of the scientific evidence from studies using different exposure routes. This section summarizes the toxicokinetics of NMP, the PBPK models and dose metrics used to estimate internal doses in rats.

Toxicokinetic Parameters used in PBPK Modeling

NMP is well absorbed following inhalation, oral and dermal exposures (NMP Producers Group, 1995b). In rats, NMP is distributed throughout the organism and eliminated mainly by hydroxylation to polar compounds, which are excreted via urine. About 80% of the administered dose is excreted as NMP and NMP metabolites within 24 hrs (WHO, 2001). The major metabolite is 5-hydroxy-N-methyl-2-pyrrolidone (5-HNMP). Studies in humans show that NMP is rapidly biotransformed by hydroxylation to 5-HNMP, which is further oxidized to N-methyl-succinimide (MSI); this intermediate is further hydroxylated to 2-hydroxy-N-methylsuccinimide (2-HMSI). The excreted amounts of NMP metabolites in the urine after inhalation or oral intake represented about 100% and 65% of the administered doses, respectively (Akesson and Jönsson, 1997).

Dermal absorption of NMP has been extensively studied as it typically poses the greatest potential for human exposure. Dermal penetration through human skin has been shown to be very rapid and the absorption rate is in the range of 1-2 mg/cm^2-hr. These values are 2- to 3-fold lower than those observed in the rat. Prolonged exposures to neat NMP were shown to increase the permeability of the skin. Water reduces the amount of dermal absorption (Payan et al., 2003) while other organic solvents (*e.g.*, d-limonene) can increase it (Huntingdon Life, 1998). The dermal penetration of 10% NMP in water is 100-fold lower than that of neat NMP, while dilution of NMP with d-limonene can increase the absorption of NMP by as much as 10-fold. The dermal absorption of neat NMP under different occlusion conditions indicated that dermal absorption 1 hour post-exposure was greatest under un-occluded conditions (69%), followed by semi-occluded (57%) and occluded (50%t) conditions (OECD, 2007).

Dermal uptake of vapor NMP has been reported in toxicokinetic studies in humans. Bader et al. (2008) exposed volunteers for 8 hrs to 80 mg/m^3 of NMP. Exposure was whole body or dermal-only (*i.e.*, with a respirator). Excretion of NMP and metabolites was used to estimate absorption under different conditions. The authors found that dermal-only exposures resulted in the excretion of 71 mg NMP equivalents whereas whole-body exposures in resting individuals resulted in the excretion of 169 mg NMP equivalents. Under a moderate workload, the excretion increased to 238 mg NMP equivalents.

Thus, the authors estimated that the dermal absorption component of exposure from the air will be in the range of 30% to 42% under whole-body exposure conditions to vapor.

Previously published PBPK models for NMP in rats and humans were adapted for use by EPA (see Appendix J and U.S. EPA (2015c) for details of the PBPK model). The rat version of the model allows for estimation of NMP time-courses in rat blood from inhalation, oral and dermal exposures. The human version of the model, based on non-pregnant and pregnant women, also includes skin compartments for portions of the skin in contact with NMP vapor and liquid and some of those details are described here because it is an important component of human risk.

Analyzing the experimental studies of Akesson et al. (2004), the model yielded an average uptake of 2.1 mg/cm^2-hr of neat NMP, but only 0.24 mg/cm^2-hr of aqueous NMP (1:1 dilution in water). Therefore, distinct values of the liquid permeability constant (PVL), 2.05×10^{-3} cm/h and 4.78×10^{-4} cm/h, were identified from the experimental data. The appropriate value of PVL for neat versus diluted NMP was used in the respective exposure scenarios in this assessment. Absorption also depends on the partition coefficient (PC) skin:liquid equilibrium, PSKL, which was taken to be the skin:saline PC reported by Poet et al. (2010), PSKL = 0.42 [no units] and assumed not to vary with dilution.

Predicted dermal uptake from liquid exposure is then a function of the liquid concentration, skin surface exposed and duration of contact. The thickness of the liquid film does not factor directly into the estimate. As a conservative estimate for user scenarios it is assumed that fresh material is constantly depositing over the time of use such that the concentration on the skin remains essentially constant at the formulation concentration. This is in contrast to simulations of experimental studies where the volume placed on the skin at the start of the experiment is not replenished (Akesson et al., 2004), in which case the model tracks the amount of NMP remaining in the film and hence the changing concentration for absorption from diluted NMP.

Penetration from vapor was estimated as part of model calibration using the Bader and van Thriel (2006) inhalation data set. This report does not state how the subjects were dressed but the exposures were conducted between late May and mid-June in Germany, so EPA assumed they wore short-sleeved shirts and long pants. While there is no reason to expect that NMP vapors do not penetrate clothing, clothing likely reduces uptake compared to open areas of skin. Since the fitted penetration constant (PV) is multiplied by the skin surface area assumed to be exposed when calculating the penetration rate, these cannot be uniquely determined from the toxicokinetic data. For the purpose of calibration and subsequent modeling, it is assumed that the head, arms and hands are entirely exposed unless PPE is worn. Together the fractional skin area exposed to vapor (SAVC) is 25% of the total skin surface area in the absence of PPE or liquid dermal contact.

The skin:air PC, PSKA, was calculated from the measured skin:saline and blood:saline PCs reported by Poet et al. (2010) and the blood:air PC specified in their model code: PSKA = 44.5. With these values of SAVC and PSKA, the average permeation constant for vapor-skin transport was estimated as PV = 16.4 cm/h. These assumptions and the value of PV resulted in a prediction of 20% of a total uptake from air (vapor) exposure via the dermal route. In contrast, Bader et al. (2008) measured 42% of total urinary excretion occurring after only dermal exposure to vapors compared to combined inhalation and dermal exposure under resting conditions. The discrepancy between the Bader et al. (2008) data and the current model predictions could be because the subjects in Bader and van Thriel (2006), on which this model is based, wore long-sleeved shirts, thereby reducing dermal absorption or due to the use of an idealized model of inhalation uptake which could over-predict uptake by that route.

For use scenarios in this assessment the air concentration in contact with the skin is assumed to be the same as that available for inhalation with SAVC kept at 25% for consistency, except as specified in the sections below when PPE is worn.

Rat Internal Doses for BMD

EPA used the validated PBPK models for extrapolating NMP doses across routes of exposure and from animals to humans based on NMP-specific data (U.S. EPA, 2015c). An internal dose metric such as a measure of toxicant concentration in the blood is expected to be a better predictor of response than the applied dose (*e.g.*, concentration in air) since it is closer to the site of the toxic effect (McLanahan et al., 2012). Further, a good internal dose metric should correlate with or be predictive of toxicity irrespective of the route of exposure by which it occurs. However, this is only true if the metric is in fact a measure of the likelihood of a toxic response or intensity of a toxic effect.

For NMP the existing toxicity data identified the parent (NMP) rather than the metabolites 5-hydroxy-N-methyl-2-pyrrolidone (5-HNMP), N-methylsuccinimide (MSI) or 2-hydroxy-N-methylsuccinimide (2-HMSI) as the proximate toxicant (Saillenfait et al., 2007). Therefore, PBPK model-derived blood concentrations of NMP were considered a better basis than applied dose for the dose-metric used in extrapolation of health effects.

3.2.5.6 Points of Departure for Human Health Hazard Endpoints

PODs for Acute Exposure

Acute exposure was defined for workers as the exposure that occurs over the course of a single day. For consumers, the acute exposure scenario was defined based on completion of a single project on a given day. EPA selected increased post-implantation losses (including resorptions and fetal mortality) as the most relevant endpoint for evaluating risks associated with acute exposure to workers and consumers. For reference, EPA also modeled dose-response information for stillbirths in reasonably available studies. While stillbirths could plausibly result from a single exposure, the relevance of the reasonably available stillbirth data for acute exposure scenarios is not known. Since repeated dose studies were used to investigate these hazard endpoints and the mode of action for NMP is uncertain, EPA assessed dose-response with both the internal dose metrics of C_{max} and AUC. Dose-response for these developmental endpoints is based on C_{max} and AUC maternal blood concentrations predicted by the PBPK model.

The Saillenfait et al. (2002); Saillenfait et al. (2003); Becci et al. (1982); Sitarek et al. (2012); Exxon Exxon (1991) and NMP Producers Group (1999b, c) studies were selected for dose-response analysis. The Saillenfait et al. studies measured post-implantation losses (*i.e.*, resorptions and fetal mortality) following oral (Saillenfait et al., 2002) and inhalation (Saillenfait et al., 2003) exposure to NMP. The Saillenfait et al. oral and inhalation studies were similar in design and used the same exposure duration (GD 6-20) and the same strain of rat (Sprague-Dawley). Higher internal serum doses of NMP (ranging from 120 to 831 mg/L based on C_{max}) were achieved in the oral study compared to the inhalation study (internal doses ranged from 15 to 62 mg/L based on C_{max}). Importantly, the dose-response relationship between internal serum dose and post-implantation losses was comparable for both the oral and inhalation studies conducted by Saillenfait et al. There was no significant evidence of a dose-response relationship between the internal serum dose and post-implantation loss in the inhalation study or at doses at the lower end of the dose-response in the oral exposure study. For these reasons, dose-response data from the two Saillenfait et al. studies were combined to provide additional statistical power and enhance confidence in the BMD modeling results, particularly in the low dose region of the response curve. In addition to the combined analysis, dose-response data for post-implantation losses from the Saillenfait et al. (2002) oral and inhalation (2003) studies were also modeled independently. However, given the lack of a clear dose-response relationship for post-implantation loss in the inhalation study,

EPA determined that it would be inappropriate to choose a BMDL from this study for use as a POD. For the Saillenfait studies, EPA characterized dose-response for both post-implantation loss (including resorptions and fetal mortality) and resorptions alone. While post-implantation loss in these studies is driven primarily by resorptions, resorptions were not amenable to modeling whereas post-implantation loss could be modeled as a dichotomous variable. A BMR of 1% for increased post-implantation losses was used to address the relative severity of this endpoint (U.S. EPA, 2012a).

Table 3-10 summarizes the derivation of PODs for acute exposure based on post-implantation loss and stillbirth in each of the studies selected for dose-response analysis. The PODs based on internal dose (AUC and C_{max}) were converted to an equivalent applied dose using the PBPK model. The calculated equivalent administered doses are nearly the same as the NOAELs identified in each study demonstrating consistency between the two methods for deriving PODs.

Table 3-10. Summary of Derivation of the PODs for Post-implantation Losses (Resorptions and Fetal Mortality) Following Acute Exposure to NMP

Endpoint and Reference (Exposure Duration/Route)	Dose Metric	Model [a]	BMR	BMD Internal Dose	BMDL Internal Dose	POD	
						Internal Dose [b]	Equivalent Oral Dose [a]
Post-implantation loss (GD 6-20, oral, post-implantation loss) Saillenfait et al. (2002)	C_{max} (mg/L blood)	Log-Probit	1% RD	474	437	**437**	418 mg/kg bw/day
	AUC (hr mg/L blood)	Log-Probit	1% RD	5010	4592	4592	419 mg/kg bw/day
Post-implantation loss (GD 6-20, oral and inhalation) (Saillenfait et al., (2003); Saillenfait et al. (2002)	C_{max} (mg/L blood)	Log-probit	1% RD	470	437	**437**	418 mg/kg bw/day
	AUC (hr mg/L blood)	Log-probit	1% RD	4990	4590	4590	419 mg/kg bw/day
Resorptions (GD 6-20, oral, post-implantation loss) Saillenfait et al. (2002)	NOAEL (C_{max}, mg/L blood)	N/A	N/A	N/A	N/A	250 [c]	250 mg/kg bw/day
Resorptions (GD 6-15, dermal) Becci et al. (1982)	NOAEL (C_{max}, mg/L blood)	N/A	N/A	N/A	N/A	662 [d]	612 mg/kg bw/day (oral) 237 mg/kg bw/day (dermal)
Embryo/fetal mortality (GD1-PND1, oral) Sitarek et al. (2012)	NOAEL (C_{max}, mg/L blood)	N/A	N/A	N/A	N/A	265 [e]	264 mg/kg bw/day
Stillbirth [f] (SD rats, dietary exposure throughout	NOAEL (C_{max}, mg/L blood)	N/A	N/A	N/A	N/A	142	147 mg/kg bw/day

Endpoint and Reference (Exposure Duration/Route)	Dose Metric	Model [a]	BMR	BMD Internal Dose	BMDL Internal Dose	POD	
						Internal Dose [b]	Equivalent Oral Dose [a]
gestation, lactation, growth, pre-mating) NMP Producers Group (1999b)	NOAEL (AUC, mg/L blood)	N/A	N/A	N/A	N/A	2120	216 mg/kg bw/day
Stillbirth [f] (Wistar rats, dietary exposure throughout gestation, lactation, growth, pre-mating) NMP Producers Group (1999c)	C_{max} (mg/L blood)	Nlogistic – ICC	1% ER	429	58	58	62 mg/kg bw/day
	AUC (hr mg/L blood)	Nlogistic – ICC	1% ER	6440	855	855	96 mg/kg bw/day
Stillbirth [f] (SD Rats, dietary exposure throughout gestation, lactation, growth, pre-mating) Exxon (1991)	AUC (hr mg/L blood)	Nlogistic – ICC	1% ER	6744	1183	1183	129 mg/kg bw/day

ER = extra risk; RD = relative deviation

Complete documentation of BMD modeling is available in *Risk Evaluation for n-Methylpyrrolidone (NMP), Benchmark Dose Modeling Supplemental File. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020e).

a Assuming daily oral gavage and initial BW 0.259 kg (*i.e.*, the same experimental conditions as the Saillenfait et al. (2002) study) for the purposes of comparison across the studies.

b Internal doses refer to maternal blood concentrations (as opposed to fetal blood concentrations which are not predicted by the PBPK model).

[c] BMD models were considered unacceptable due to uncertainty caused by lack of model fit; the internal serum dose is based on a NOAEL of 250 mg/kg-bw/day.

[d] Dose-response data were not considered amenable to BMD modeling. The internal serum dose is based on a NOAEL of 237 mg/kg bw/day dermal exposure. An oral dose of 612 mg/kg bw/day, given on GD 6-20, is predicted to yield the same peak concentration (662 mg/L).

[e] Dose-response data were not considered amenable to BMD modeling. The internal serum dose is based on a NOAEL of 450 mg/kg bw/day.

[f] The relevance of stillbirth for acute exposure is unclear, as these effects were only observed following exposure to NMP throughout gestation. In addition, the effect was reported in dietary studies in which exposure occurs throughout the day rather than through a single bolus (which would result in a greater peak exposure).

Post-implantation loss data from the Saillenfait et al. (2002) oral study and the pooled dataset from the Saillenfait et al. oral and inhalation studies were amenable to BMD modeling, and BMDLs based on the internal serum dose of NMP were calculated for both C_{max} and AUC dose metrics. The calculated BMDL for both the combined Saillenfait et al. studies and the Saillenfait et al. oral study alone was 437 mg/L (based on C_{max}).

Neither the Becci study nor the Sitarek study were suitable for BMD modeling, hence the NOAEL was used to derive PODs for these studies. The Becci et al. (1982) dermal study supports a NOAEL of 662 mg/L NMP based on increased resorptions, while the Sitarek et al. (2012) oral study supports a NOAEL of 265 mg/L based on embryo/fetal mortality.

Stillbirth data from several two-generation reproductive studies were amenable to BMD modeling (NMP Producers Group, 1999b, c; Exxon, 1991). BMD modeling for stillbirths identified at PND0 was

conducted using both C_{max} and AUC dose metrics, as it is unknown whether this effect is the result of a single dose at a critical stage of development or is a result of repeated exposure to NMP. For the two-generation reproductive study conducted with Sprague-Dawley rats (NMP Producers Group, 1999b), no BMD models adequately fit the dataset and the NOAEL (*i.e.*, 142 mg/L based on C_{max} and 2,120 hr mg/L based on AUC) was chosen as the POD. Alternatively, BMDLs of 58 mg/L (based on C_{max}) and 855 hr mg/L (based on AUC) were derived for stillbirths from the NMP Producers Group (1999c) study with Wistar rats, while a BMDL of 1,183 hr mg/L (based on AUC) was derived from the Exxon (1991) study.

EPA selected the BMDL for post-implantation losses from the pooled dataset from the Saillenfait et al. oral and inhalation studies as the basis for the acute POD. The BMDL of 437 mg/L for post-implantation losses was considered more appropriate for use as the acute POD than the highest NOAEL of 265 mg/L from the Sitarek et al. (2012) study for several reasons. First, as outlined in EPA guidance, the BMD approach overcomes many of the limitations inherently associated with the NOAEL/LOAEL approach, and thus is the preferred method for establishing a POD for use in risk assessment (U.S. EPA, 2012a). Furthermore, dose-response data from the Saillenfait et al. oral and inhalation studies was combined to provide additional statistical power and enhance confidence in the BMD modeling results, particularly in the low dose region of the response curve. Finally, embryo/fetal mortality in the study by Sitarek et al. occurred in a similar dose-range as post-implantation losses in the combined Saillenfait et al. oral and inhalation studies (*i.e.*, NOAELs for post-implantation losses and fetal mortality were 250 and 265 mg/L, respectively, and LOAELs were 669 and 531 mg/L, respectively).

Similarly, the BMDL of 437 mg/L for post-implantation losses was considered to be more appropriate as the basis for the acute POD than the BMDL of 58 mg/L based on stillbirths identified at PND0 in the two-generation reproductive study (NMP Producers Group, 1999c) for several reasons. First, the cause of the stillbirths was not determined and it is unknown whether stillbirths are the result of a single dose at a critical stage of development or a result of repeated exposure to NMP throughout development, and therefore it unknown whether stillbirths should be considered most relevant for acute or chronic exposures. Additionally, stillbirths were reported in dietary studies in which exposure to NMP occurred throughout the day rather than through a single bolus, which would result in a greater peak serum dose, and thus AUC may be a more appropriate dose metric for stillbirths reported in dietary studies. Finally, in reasonably available studies where it was reported, stillbirths occurred in a similar dose range as post-implantation loss (LOAELs for stillbirths in dietary two-generation studies were all 500 mg/kg/day, the same as the LOAEL for post-implantation loss in Saillenfait et al. (2002). Accordingly, EPA selected the BMDL from the pooled Saillenfait et al. (2003; 2002) oral and inhalation studies as the POD for use as the basis for calculating risk for acute NMP exposures.

The selected POD may be considered broadly relevant to both male and female exposures. As described in Section 3.2.4, evidence from (Sitarek and Stetkiewicz, 2008) indicates that paternal exposure prior to mating may decrease offspring viability. Though paternally-mediated effects on offspring are a well-recognized phenomenon (U.S. EPA, 1996), this is the only reasonably available study that evaluates the developmental effects of paternal NMP exposure alone. Several additional two-generation reproductive studies reported increased stillbirths and decreased pup survival following both maternal and paternal exposure to NMP; however, the relative contribution of each parental exposure was not determined. No other studies have specifically explored the paternal contribution to developmental toxicity of NMP, and the duration of paternal exposure required to have this effect is unknown. In the absence of further characterization of the paternally-mediated effects of NMP, it is prudent to assume that the POD for acute exposure may be relevant for males of reproductive age as well as pregnant women.

EPA applied a composite uncertainty factor (UF) of 30 for the acute exposure benchmark MOE, based on the following considerations:

- An interspecies uncertainty/variability factor of 3 (UF_A) was applied for animal-to-human extrapolation to account for toxicodynamic differences between species. This uncertainty factor is comprised of two separate areas of uncertainty to account for differences in the toxicokinetics and toxicodynamics of animals and humans. In this assessment, the toxicokinetic uncertainty was accounted for by the PBPK model as outlined in the RfC methodology (U.S. EPA, 1994b). As the toxicokinetic differences are accounted for, only the toxicodynamic uncertainties remain, and an UF_A of 3 is retained to account for this uncertainty.
- A default intraspecies uncertainty/variability factor (UF_H) of 10 was applied to account for variation in sensitivity within human populations. The PBPK model did not account for human toxicokinetic variability. Due to limited information on the degree that humans of varying gender, age, health status, or genetic makeup might vary in the disposition of, or response to, NMP a factor of 10 was applied.

PODs for Chronic Exposure

Chronic worker exposure was defined as exposure of 10% or more of a lifetime (U.S. EPA, 2011). Repeated exposures over the course of a work week are anticipated during chronic worker exposure. The most sensitive chronic endpoints were selected based on reproductive and developmental studies on NMP. Adverse developmental outcomes from exposure during critical windows of development during pregnancy can occur any time during the defined chronic worker exposure period. Reproductive toxicity may be of concern for all workers of reproductive age. In addition to the reproductive and developmental endpoints that serve as the basis for the POD, the POD is expected to be protective of pregnant women and children as well as men and women of childbearing age.

Decreased male fertility, decreased female fecundity, decreased fetal body weight, and increased stillbirths were selected as the endpoints of concern for chronic exposures. The Exxon (1991), Becci et al. (1982), E. I. Dupont De Nemours & Co (1990), Saillenfait et al. (2002), Saillenfait et al. (2003), and NMP Producers Group (1999b, 1999c) studies were selected for dose-response analysis. The PBPK model and BMD modeling were applied to these studies to calculate the BMDLs and PODs and BMD modeling results are described in *Risk Evaluation for n-Methylpyrrolidone (NMP), Benchmark Dose Modeling Supplemental File. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020e). Per BMD Technical Guidance (U.S. EPA, 2012a), an extra risk of 10% is recommended as the standard benchmark response (BMR) for quantal data, because the 10% response is at or near the limit of sensitivity in most cancer bioassays and in some non-cancer bioassays. For some endpoints, biological and statistical considerations may warrant the use of a BMR lower than 10%. For reduced fertility, a BMR of 10% was used because there is no biological basis for lowering the BMR. A BMR of 5% relative deviation was used for decreased fetal body weight because in the absence of knowledge as to what level of response to consider adverse, it has been observed that 5% change relative to the control mean is similar to statistically derived NOAELs in developmental studies (Kavlock et al., 1995). A BMR of 1% extra risk was used for stillbirths to account for the severity of this endpoint (U.S. EPA, 2012a). For studies where data were not amenable to modeling, EPA applied NOAELs (in units of internal dose) instead.

EPA considered combining fetal body weight data from the Saillenfait et al. (2002) and Saillenfait et al. (2003) studies to provide a more extensive characterization of the dose-response curve across exposure route. The Saillenfait et al. (2003) inhalation study observed a statistically significant decrease in fetal body weights at an internal dose that corresponds to an oral dose lower than the NOAEL in the Saillenfait et al. (2002) oral study. This implies that fetal body weights were more sensitive to inhalation

exposures and this was not fully accounted for in the PBPK model. Therefore, datasets from the two studies were not combined for this endpoint.

The results of benchmark dose modeling for fetal body weight and fertility endpoints are summarized in Table 3-11. Internal doses for fetal body weight reflect maternal blood concentrations during gestation and internal doses for fertility reflect blood concentrations in pups post-weaning. The PODs based on internal dose (AUC) were converted to an equivalent applied dose using the PBPK model. The calculated equivalent administered doses are nearly the same as the NOAELs identified in each study (where reasonably available) demonstrating consistency between the two methods for deriving PODs.

Table 3-11. Summary of Derivation of the PODs for Reproductive and Developmental Effects Following Chronic Exposure to NMP

Endpoint and Reference Exposure Duration/Route)	Selected Model or NOAEL	BMR	BMD Internal Dose AUC (hr mg/L blood)	BMDL Internal Dose AUC (hr mg/L blood)	POD	
					Internal Dose AUC (hr mg/L blood) [a]	Equivalent Applied Oral Dose [b]
Fetal Body Weight						
Saillenfait et al. (2002) (GD 6-20, oral)	Exponential 3 [c,d]	5% RD	1400	981	981	109 mg/kg bw/day
Saillenfait et al. (2003) (GD 6-20, inhalation)	Exponential 3 [c]	5% RD	654	414	414	48 mg/kg bw/day
E. I. Dupont De Nemours & Co (1990) (preconception exposure, GD 1–20, inhalation)	Exponential 3 [c]	5% RD	315	223	223	27 mg/kg bw/day
Becci et al. (1982) (GD 6-15, dermal)	NOAEL= 237 mg/kg/day [e]	NA	NA	NA	2052	210 mg/kg bw/day
Reduced Male Fertility						
Exxon (1991) (Dietary exposure throughout gestation, lactation, growth, pre-mating)	Log-logistic	10% ER	492[f1] 341[f2]	262 [f1] 183 [f2]	**183**	28 mg/kg bw/day
Reduced Female Fecundity						
Exxon (1991) (Dietary exposure throughout gestation, lactation, growth, pre-mating)	Log-logistic	10% ER	862 [f1] 420 [f2]	401 [f1] 202 [f2]	202	31 mg/kg bw/day
Stillbirth						

Endpoint and Reference Exposure Duration/Route)	Selected Model or NOAEL	BMR	BMD Internal Dose AUC (hr mg/L blood)	BMDL Internal Dose AUC (hr mg/L blood)	POD	
					Internal Dose AUC (hr mg/L blood) [a]	Equivalent Applied Oral Dose [b]
Stillbirth (SD rats, dietary exposure throughout gestation, lactation, growth, pre-mating) NMP Producers Group (1999b)	NOAEL = 160 mg/kg-day [g]	N/A	N/A	N/A	2120	216 mg/kg bw/day
Stillbirth (Wistar rats, dietary exposure throughout gestation, lactation, growth, pre-mating) NMP Producers Group (1999c)	Nlogistic - ICC	1% ER	6440	855	855	96 mg/kg bw/day
Stillbirth (SD Rats, dietary exposure throughout gestation, lactation, growth, pre-mating) Exxon (1991)	Nlogistic - ICC	1% ER	6744	1183	1183	129 mg/kg bw/day

RD = relative deviation; ER = extra risk

The POD selected for calculating risk of chronic NMP exposures is highlighted in bold. Complete documentation of BMD modeling is available in *Risk Evaluation for n-Methylpyrrolidone (NMP), Benchmark Dose Modeling Supplemental File. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020e).

[a] Internal doses for fetal body weight reflect maternal blood concentrations during gestation and internal doses for fertility reflect blood concentrations in pups post-weaning (see discussion in Section 3.2.5.2).

[b] Assuming daily oral gavage GDs 6-20 and initial BW 0.259 kg (*i.e.*, the same experimental conditions as the Saillenfait et al. (2002) study) for the purposes of comparison across the studies.

[c] Since standard models gave adequate results for all endpoints, non-standard models were not considered. Since fits to the means were obtained using normal distribution models, lognormal models were not applied

[d] For Saillenfait et al. (2002), the BMD and BMDL reported are from modeling the data with all the standard deviations set equal to the maximum standard deviation across the groups.

[e] The data in Becci (Becci et al., 1982) were not amenable to BMD modeling. The mean weight increased gradually from the control to the middle dose group and then decreased significantly at the high dose group. This dose-response pattern is essentially equivalent to one where only the highest dose has a response and thus the model estimates of the parameters and BMDs would not be reliable. The internal serum dose is based on a NOAEL of 237 mg/kg bw/day dermal exposure.

[f] In the Exxon (1991) study, each dam had two sets of mating periods. Each mating period was analyzed separately; d1 indicates results for the first mating period and d2 indicates results from the second mating period. PODs for male fertility and female fecundity in this study are calculated based on exposure levels in 50g rats immediately post-weaning.

[g] BMD modeling was attempted for stillbirth data reported in the NMP Producers Group (1999b) study with Sprague-Dawley rats; however, no models adequately fit the dataset.

EPA selected the POD derived from decreased male fertility (183 hr mg/L) in a two-generation reproductive study (Exxon, 1991) to be used in the calculation of risk estimates associated with chronic exposures. This high-quality study identified the most sensitive reproductive endpoints and had a significant dose-response relationship that was adequately modeled by the BMD model. The POD for effects on reduced female fecundity in this study was very similar (202 hr mg/L) to the POD for effects

on male fertility, making it highly relevant to both male and female reproductive endpoints. The broad relevance of this endpoint for males and females ensures that this POD is directly applicable for all chronic exposure scenarios considered in risk characterization. This POD selection is consistent with EPA's Guidelines for Reproductive Toxicity Risk Assessment (U.S. EPA, 1996).

While reduced fertility was not consistently observed across all reasonably available studies, significant reductions in fertility were reported in three high quality studies. The reduced male fertility and female fecundity observed in the second generation of the Exxon study (1991) are particularly sensitive endpoints. The biological plausibility of effects on male fertility and reproductive success is supported by mechanistic evidence (discussed in Section 3.2.4.2) demonstrating that NMP competitively binds to the testis-specific BRDT protein (Shortt et al., 2014), a master regulator of epigenetic reprograming during spermatogenesis (Jonathan Gaucher, 2012).

The selected chronic POD may be considered protective of reduced fetal body weight. The PODs derived from effects on fetal body weight in two developmental inhalation exposure studies (Saillenfait et al., 2003; E. I. Dupont De Nemours & Co, 1990) fall in an internal dose range (223 and 414 hr mg/L), similar to the POD based on reduced fertility (183 hr mg/L), lending further support for the selected POD. Both inhalation studies used whole body exposures where dermal absorption of NMP vapors likely contributed to the toxicity. This is similar to human exposure scenarios; however, the unknown differences between human and rat dermal absorption of NMP vapor adds uncertainty to values derived from either of these studies alone. While the POD for the DuPont study was lower than the Saillenfait study, the dose-response relationship in the DuPont study was not as robust as the Saillenfait study. Lower variability in body weights was observed in the Saillenfait study than in the DuPont study. In the DuPont study, statistically significant differences only occurred in the lowest and highest dose groups, not the middle dose group. The Becci et al. (1982) study contributes to the weight of the scientific evidence for developmental toxicity across exposure routes, but there are limitations in the dose-response analysis for this study. The duration of dosing was shorter than for the Saillenfait studies and the uncertainty regarding exposure duration and sampling time leads to uncertainty about recovery and compensation. Furthermore, the dose-response data in Becci et al. (1982) were not amenable to BMD modeling.

The selected chronic POD may also be considered protective of stillbirths associated with repeated-dose exposure. Dose-response analysis of stillbirths reported following repeated-dose exposures throughout gestation in the three two generation dietary studies identified PODs for chronic exposure ranging from internal doses of 855-2,120 hr mg/L.

Dose-response modeling for alternate developmental endpoints show PODs in a similar internal dose range to the key endpoints presented here. For example, BMD modeling of pup body weights at PND 21 reported by the NMP Producers Group (1999b) identified a BMDL of 100 hr mg/L. This endpoint was not selected as the basis for POD derivation because there is uncertainty around the level of post-natal exposure that occurs through lactation. Effects on post-natal body weight were reported at similar dose levels as effects on fetal body weight. Other developmental endpoints, including reduced pup survival, and delayed ossification were reported also at similar doses ranges as changes in fetal body weight following repeated dose exposures. Dose-response modeling for several of these alternate endpoints is described in more detail in the supplemental file, *Risk Evaluation for n-Methylpyrrolidone (NMP), Benchmark Dose Modeling Supplemental File. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020e).

EPA applied a composite uncertainty factor (UF) of 30 for the chronic exposure benchmark MOE, based on the following considerations:

- An interspecies uncertainty/variability factor of 3 (UF_A) was applied for animal-to-human extrapolation to account for toxicodynamic differences between species. This uncertainty factor is comprised of two separate areas of uncertainty to account for differences in the toxicokinetics and toxicodynamics of animals and humans. In this assessment, the toxicokinetic uncertainty was accounted for by the PBPK model as outlined in the RfC methodology (U.S. EPA, 1994b). As the toxicokinetic differences are thus accounted for, only the toxicodynamic uncertainties remain, and an UF_A of 3 is retained to account for this uncertainty.
- A default intraspecies uncertainty/variability factor (UF_H) of 10 was applied to account for variation in sensitivity within human populations. The PBPK model did not account for human toxicokinetic variability. Due to limited information on the degree of humans of varying gender, age, health status, or genetic makeup might vary in the disposition of, or response to, NMP a factor of 10 was applied.

3.2.6 Summary of Human Health Hazards

Table 3-12 summarizes the hazard studies, health endpoints and UFs that are used for risk characterization in this risk evaluation. The reported PODs reflect internal dose estimates (blood concentrations) for comparison with internal dose estimates of human exposures from multiple routes (*e.g.*, inhalation and/or dermal).

Table 3-12. PODs Selected for Non-Cancer Effects from NMP Exposures

Exposure Duration	Target System	Species	Dose Metric	BMR	POD	Effect	Uncertainty Factors (UFs) for Benchmark MOE	References	Data Quality Score
Acute	Developmental	Rat	C_{max} (mg/L blood)	1% RD	437 mg/L	Post-implantation loss (resorptions and fetal mortality)	UF_A = 3 UF_H = 10 Total UF = 30	Saillenfait et al. 2003; Saillenfait et al. (2002)	High
Chronic	Reproductive	Rat	AUC (hr-mg/L blood)	10% ER	183 hr-mg/L	Decreased Male Fertility	UF_A = 3 UF_H = 10 Total UF = 30	Exxon (1991)	High
RD = relative deviation; ER= extra risk; UF_A = interspecies UF; UF_H = intraspecies UF.									

Primary Strengths

There is a robust dataset for the critical reproductive and developmental effects that serve as the basis for the PODs used in this risk characterization. The reasonably available studies demonstrate clear, consistent effects on a continuum of reproductive and developmental endpoints following NMP exposure across oral, inhalation, and dermal exposure routes. Each of the critical endpoints supporting the PODs represents an adverse effect that is biologically relevant to humans. The acute POD based on post-implantation loss reflects consistent observations across multiple high-quality studies using multiple exposure routes. The chronic POD selected based on reduced fertility following exposure across lifestages in a high-quality study is supported by other high-quality studies demonstrating reduced fertility in males and females exposed only as adults. The biological plausibility of the effect on male fertility is further supported by toxicokinetic evidence demonstrating that NMP reaches the testes

and mechanistic evidence indicating that NMP competitively binds BRDT, a testis-specific regulator of epigenetic changes during spermatogenesis (discussed in Section 3.2.4.2). The POD derived from reduced fertility is within close range (approximately a factor of two) of PODs derived from a developmental endpoint (fetal body weight) that is consistently observed across studies, species, and routes of exposure. The quality of the studies, consistency of effects, relevance of effects for human health, coherence of the spectrum of reproductive and developmental effects observed and biological plausibility of the observed effects of NMP contribute to the overall confidence in the PODs identified based on reproductive and developmental endpoints.

The NMP PBPK models allow EPA to identify points of departure based on blood concentrations of NMP that are associated with effects in animal models. Because the effects of NMP at a specific blood concentration are independent of exposure route, a single internal dose POD can be applied to evaluate risk from all routes of exposure. This eliminates the need for extrapolating hazard information across exposure routes. The PBPK model also accounts for toxicokinetic information in rats and humans, reducing a source of uncertainty associated with cross-species extrapolation.

Primary Limitations

While there is a large amount of animal data on reproductive and developmental effects of NMP, there are not studies on reproductive and developmental toxicity of NMP in humans. Therefore, this risk evaluation relies on the assumption that reproductive and developmental toxicity observed in animal models is relevant to human health. It is unknown whether this assumption leads to an underestimation or overestimation of risk.

Some potentially sensitive endpoints remain poorly characterized. For example, neurodevelopmental effects were observed in response to a high dose exposure, but no NOAEL has been established for these effects. In addition, there are limited data on the effects of NMP on sensitization and immunotoxicity, endocrine effect, and cardiometabolic effects. If endpoints that are not well characterized are in fact more sensitive to NMP than the endpoints that serve as the basis for the POD, this could lead to an underestimation of risk.

For studies that identified developmental outcomes following pre- and/or postnatal exposures, maternal toxicity was often also present. Although it has been demonstrated that NMP crosses the placenta, so direct prenatal exposure to the offspring was likely, there were no studies that characterized the interrelationship or contribution of maternal toxicity to offspring toxicity.

There is some uncertainty around which dose metrics are most appropriate for specific endpoints. For example, there is uncertainty around whether stillbirths should be considered most relevant for acute or chronic exposures. Stillbirths were reported in several of the reasonably available studies following repeated-dose exposures (discussed in Section 3.2.4.1). It is unknown whether this effect was the result of a single dose at a critical stage of development or a result of repeated exposure to NMP. In reasonably available studies where it was reported, stillbirth occurred in a similar dose range as post-implantation loss.

There are also some uncertainties associated with the specific endpoint used as the basis for the chronic POD. The chronic POD is based on sensitive reproductive endpoints observed in a two-generation reproductive study. Two of the subsequent studies that evaluated fertility in two-generation reproductive studies reported developmental toxicity but found no significant effect on fertility at any dose tested. Another two-generation study via inhalation deviated substantially from EPA and OECD guidelines and had serious limitations due to uncertainties about the actual doses achieved, making it difficult to draw

clear conclusions from the results. Although the critical effect is only observed in a single two-generation study, it is supported by evidence in other high-quality studies of reduced fertility in male and female rats exposed as adults. It is unclear whether this data limitation leads to an overestimation or underestimation of risk.

In addition, because exposure in the key study occurred throughout gestation, lactation, post-weaning, puberty and pre-mating, it is not possible to determine which exposure periods contributed to reduced fertility. EPA therefore established a POD based on lifestage at which the lowest level of exposure relative to body weight occurred. This assumption could result in up to a two-fold overestimation of risk (see discussion in Section 3.2.5.2).

In inhalation studies, there is some uncertainty around the techniques used to generate NMP air concentrations for animal exposures in some supporting studies considered in the weight of the scientific evidence. Experimental conditions may have inadvertently resulted in the inclusion of aerosolized particles in the exposure chamber in some inhalation exposure studies. NMP is hygroscopic; therefore, variations in temperature, humidity and/or test protocol (*e.g.*, the number of air changes, use of a spray or nebulization technique to generate test atmospheres) may impact the NMP air saturation concentration, resulting in condensation of NMP. Aerosol formation would result in increased dermal and/or oral exposures (from grooming behavior) in addition to the intended inhalation exposure. The two-generation inhalation study (Solomon et al., 1995; E. I. Dupont De Nemours & Co, 1990) noted that condensation observed on the chamber walls at the highest dose indicates that the actual air concentrations of NMP were lower than the intended exposure. Nonetheless, higher test concentrations and total body exposures to NMP were associated with adverse developmental effects in rats.

Overall Confidence

EPA has high confidence in the POD identified for evaluating risk from acute NMP exposure. The POD is derived from developmental endpoints that are consistently observed in response to NMP across oral, dermal and inhalation exposure routes. Application of the PBPK model reduces uncertainties associated with extrapolation across species and exposure routes, further contributing to overall confidence in the PODs.

EPA has medium confidence in the POD identified for evaluating risk from chronic NMP exposure. The POD is informed by multiple endpoints that fall along a continuum of reproductive and developmental effects. The fertility endpoint that serves as the quantitative basis for the POD is supported by evidence from multiple studies, but is not consistently replicated across studies. Application of the PBPK model reduces uncertainties associated with extrapolation across species and exposure routes, further contributing to overall confidence in the PODs.

4 RISK CHARACTERIZATION

4.1 Environmental Risk

4.1.1 Risk Estimation Approach

The environmental risk of NMP is characterized by calculating risk quotients or RQs (U.S. EPA, 1998; Barnthouse et al., 1982). The RQ is defined as:

RQ = Environmental Concentration / Effect Level

An RQ equal to 1 indicates that the exposures are the same as the concentration that causes effects. If the RQ is above 1, the exposure is greater than the effect concentration. If the RQ is below 1, the exposure is less than the effect concentration. The Effect Levels and COCs used to calculated RQs are identified in Section 3.1.2 and in Table 4-1, respectively.

Frequency and duration of exposure also affects the potential for adverse effects in aquatic organisms. Therefore, the number of days that the chronic COC was exceeded was also calculated using E-FAST as described in Section 2.3.2. The days of exceedance modeled in E-FAST are not necessarily consecutive and may occur sporadically throughout the year. Facilities with an RQ ≥ 1 for the acute exposure scenario or an RQ ≥ 1 and 20 days or more of exceedance for the chronic exposure scenario would suggest the potential for environmental risks posed by NMP. The 20-day exceedance time frame was derived from partial life cycle tests (*e.g.*, daphnid chronic and fish early life stage tests) that typically range from 21 to 28 days in duration.

Table 4-1. Concentrations of Concern (COCs) for Environmental Toxicity

Environmental Toxicity	Most Sensitive Species	COCs
Acute Toxicity, aquatic organisms	48-Hour aquatic invertebrates	100,000 µg/L
Chronic Toxicity, aquatic organisms	21-Day aquatic invertebrates	1,770 µg/L

EPA used estimated acute and chronic exposure concentrations of NMP in surface water (Section 2.3.2) and acute and chronic COCs (Section 3.1.2) to evaluate the risk of NMP to aquatic species. Table 4-2 and Table 4-3 summarize the RQs and days of exceedance used to characterize risk to aquatic organisms from acute and chronic exposures to NMP. In Table 4-2 RQ values are reported for the top ten direct and indirect dischargers reporting to the TRI in 2015. Table 4-3 shows RQ values to the nine direct dischargers and top ten indirect dischargers reporting to the TRI in 2018. Based on these values (acute RQs all < 1, and chronic RQs < 1 or RQ > 1 but < 20 days of exceedance) risk to aquatic organisms from acute or chronic exposure pathways was not indicated. As previously stated, an RQ below 1 indicates that the exposure concentrations of NMP is less than the concentration that would cause an effect to organisms in aquatic exposure pathways. The chronic COC was exceeded in 2015 at one location in Oregon (RQ = 1.1), but exceedance was predicted to occur for less than 20 days.

Table 4-2. Calculated Risk Quotients (RQs) for NMP Based Top Facility Dischargers Reported in 2015 TRI data

		Acute Exposure Scenario		Chronic Exposure Scenario		
Facility	**State**	**Stream NMP Concentration (µg/L)**	**RQ**	**Stream NMP Concentration (µg/L)**	**RQ**	**# Days Chronic COC Exceeded**
Direct Discharger Facilities						
Fortron Industries	NC	2.2E+02	2.2E-03	1.1E+01	6.1E-03	0
Spruance Plant	VA	1.2E+02	1.2E-03	5.8E+00	3.2E-03	0
GlobalFoundries	VT	4.4E+01	4.4E-04	2.1E+00	1.2E-03	0
American Refining Group	PA	8.5E+00	8.5E-05	4.0E-01	2.3E-04	0
Essex Group, Fort Wayne	IN	5.6E+00	5.6E-05	2.7E-01	1.5E-04	0
BASF Corp	MI	1.1E-03	1.1E-08	4.9E-04	2.8E-07	0
Indirect Discharger Facilities						
Koch Membrane	MA	N/A	N/A	6.0E+01	3.4E-02	0
Pall Corp.	FL	N/A	N/A	8.8E+02	5.0E-01	0
Air Products	MO	N/A	N/A	6.4E+02	3.6E-01	0
GVS; GE Healthcare: Westborough POTW	MA	N/A	N/A	8.6E+02	4.9E-01	0
Intel, Aloha; Intel, Ronler Acres: Rock Creek STP, Hillsboro POTW	OR	N/A	N/A	2.0E+03	**1.1E+00**	2

Table 4-3. Calculated Risk Quotients (RQs) for NMP Based on Top Facility Dischargers Reported in 2018 TRI data

		Acute Exposure Scenario		Chronic Exposure Scenario		
Facility	**State**	**Stream NMP Concentration (µg/L)**	**RQ**	**Stream NMP Concentration (µg/L)**	**RQ**	**# Days Chronic COC Exceeded**
Direct Discharger Facilities						
Fortron Industries,	NC	6.2E+00	6.2E-05	2.5E-01	1.4E-04	0
Spruance Plant,	VA	1.2E+02	1.2E-03	4.9E+00	2.8E-03	0
GlobalFoundries	VT	7.3E+01	7.3E-04	3.4E+00	1.9E-03	0
BASF, McIntosh	AL	7.6E+00	7.6E-05	2.9E-01	1.6E-04	0
American Refining Group	PA	4.2E+00	4.2E-05	1.7E-01	9.6E-05	0
Essex Group, Fort Wayne	IN	2.3E+02	2.3E-03	9.2E+00	5.2E-03	0
GlobalFoundries	NY	4.9E+01	4.9E-04	2.3E+00	1.3E-03	0
BASF Corp	MI	6.2E-03	6.2E-08	5.4E-04	3.1E-07	0
Essex Group Franklin	IN	3.0E+01	3.0E-04	1.4E+00	7.9E-04	0
Indirect Discharger Facilities						
Koch Membrane	MA	N/A	N/A	9.0E+01	5.1E-02	0
Pall Corp.	FL	N/A	N/A	8.1E+02	4.6E-01	0
Air Products	MO	N/A	N/A	4.3E+02	2.4E-01	0
GVS; GE Healthcare: Westborough POTW	MA	N/A	N/A	1.0E+03	5.7E-01	0
Intel, Aloha; Intel, Ronler Acres: Rock Creek STP, Hillsboro	OR	N/A	N/A	1.0E+03	5.8E-01	0
Veolia ES Technical Solutions, LLC	NJ	N/A	N/A	2.8E+01	1.6E-02	0
Intel Corp	AZ	N/A	N/A	0.0E+00	0.0E+00	0
Caterpillar, Inc	IL	N/A	N/A	8.6E-01	4.9E-04	0
Cree, Inc	NC	N/A	N/A	2.2E+01	1.2E-02	0
Pall Filtration	CA	N/A	N/A	3.6E+01	2.0E-02	0

4.1.2 Assumptions and Key Uncertainties for the Environment

In the NMP Problem Formulation (U.S. EPA, 2018c) and this RE, EPA completed a screening level evaluation of environmental risk using inherently conservative assumptions. The analysis was completed using estimated concentrations of NMP in the aquatic environment as described in Section 2.3.2 and compared those acute and chronic exposure estimates to conservative measures of acute and chronic hazard (COCs) as described in Section 3.1.2. However, there is uncertainty associated with the acute and chronic COCs identified for aquatic receptors. First, more acute duration toxicity data were reasonably available in the literature compared to chronic duration data. For the chronic fish endpoint, an acute to chronic ratio (ACR) approach was used to extrapolate a chronic toxicity value for NMP based on the reported acute values. Using a single value of 10 to extrapolate from acute to chronic hazard for species in the aquatic compartment is consistent with existing EPA methodology for the screening and analysis of industrial chemicals (U.S. EPA, 2012e). While this value is routinely used by EPA to assess the hazard of new industrial chemicals, there is uncertainty regarding using a single ACR value to estimate chronic hazards across species and chemicals. Therefore, EPA is less certain of chronic hazard values than the acute hazard values. Second, AFs were used to calculate the acute and chronic COCs for NMP. AFs account for differences in inter- and intra-species variability, as well as laboratory-to-field variability and are routinely used within TSCA for assessing the hazard of new industrial chemicals (with very limited environmental test data). There is some uncertainty associated with the use of standardized AFs used the hazard assessment. EPA in the NMP Problem Formulation (U.S. EPA, 2018c) did not conduct any further analyses on pathways of exposure for terrestrial receptors as described in Section 2.5.3.1 of the NMP Problem Formulation and further described in Section 2.2 and 2.3 of this risk evaluation.

4.2 Human Health Risk

The human health risks associated with NMP conditions of use identified in Section 1.4 are discussed below. Specific information regarding the methodologies used to derive exposure estimates, including related assumptions and data limitations or uncertainties can be found in Section 2.4; an overview of the potential human health hazards, including key and supporting studies is presented in Section 3.2.

4.2.1 Risk Estimation Approach

An overview of the approach to quantifying occupational and consumer risks for the evaluated conditions of use for NMP is shown in Figure 4-1. To evaluate the human health risks of NMP, EPA first evaluated acute and chronic exposures to NMP for workers and ONUs (Section 2.4.1), and acute exposures to NMP for consumer users and consumer bystanders (Section 2.4.2). For workers and ONUs, EPA evaluated the dermal (worker only), inhalation, and vapor-through-skin exposure routes. For consumers and bystanders, EPA evaluated dermal (user only), inhalation, vapor-through-skin, and oral (child users only) exposure routes. As discussed in Section 2.4, EPA used reasonably available exposure data from models and measured concentrations to estimate occupational and consumer exposure to NMP for all conditions of use. Dermal and inhalation exposure parameters and concentrations of NMP were used as input parameters for a validated human PBPK model, which was used to predict the human internal serum dose (*i.e.*, C_{max} (mg/L) or AUC (hr mg/L)) of NMP for combined routes of exposure (*i.e.*, inhalation, dermal, vapor-through-skin). The internal human serum dose for each condition of use was then compared to the rat internal serum dose point of departure (POD), which was calculated using a validated rat PBPK model and benchmark dose modeling as described in Section 3.2.

To evaluate non-cancer risks, margins of exposure (MOEs) for acute and chronic exposure were calculated using Equation 4-1. The MOE is the ratio of the non-cancer POD divided by a human exposure dose. MOEs allow for the presentation of a range of risk estimates.

EPA interpreted the MOE risk estimates for each use scenario in reference to benchmark MOEs. Benchmark MOEs are the total UF for each non-cancer POD. The MOE estimate was interpreted as a human health risk if the MOE estimate was less than the benchmark MOE (*i.e.*, the total UF). On the other hand, the MOE estimate indicated negligible concerns for adverse human health effects if the MOE estimate was equal to or exceeded the benchmark MOE. Typically, the larger MOE, the more unlikely it is that a non-cancer adverse effect would occur.

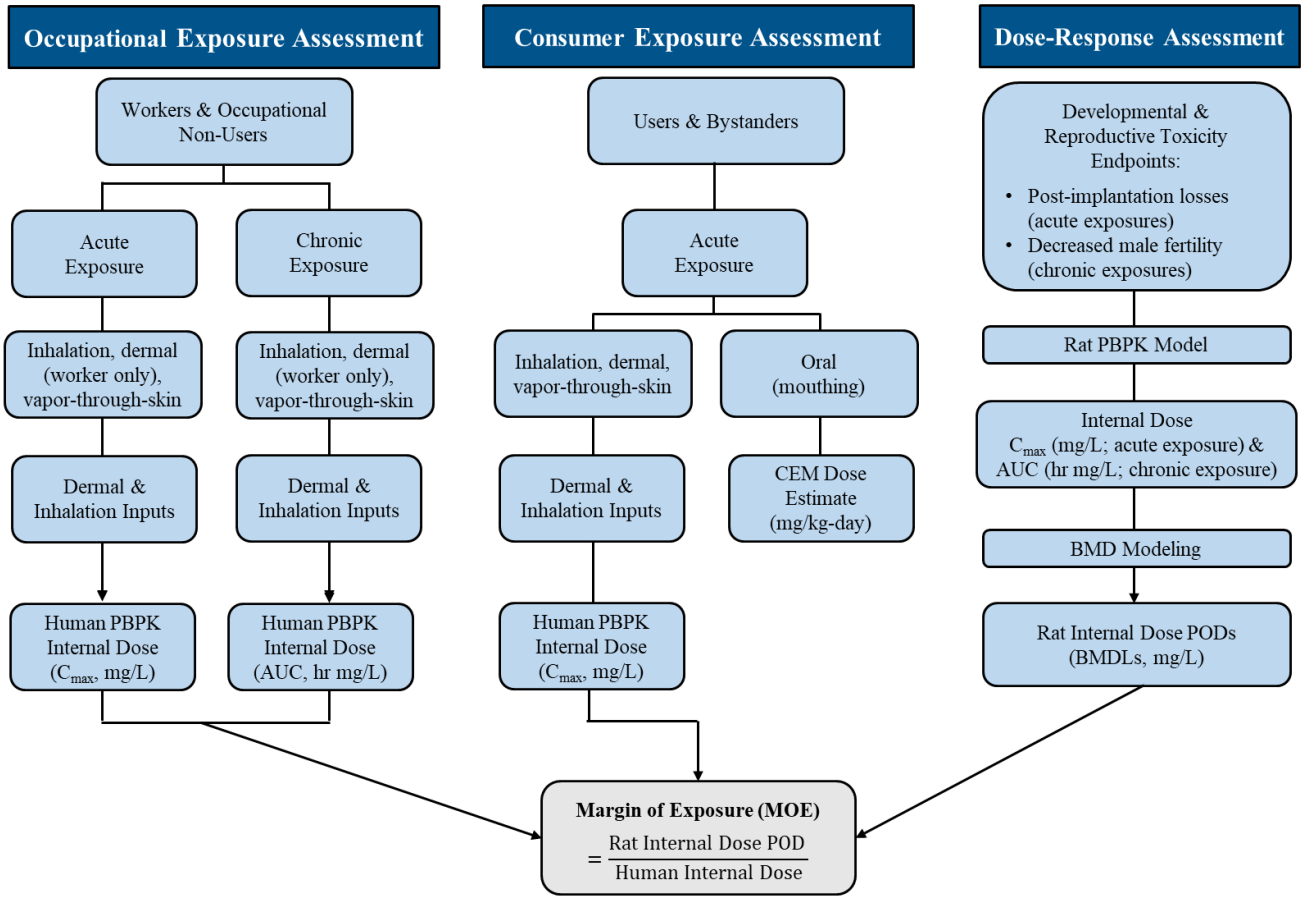


Figure 4-1. Schematic of Analysis Plan for Quantifying Occupational and Consumer Risks of NMP.

Equation 4-1. Equation to Calculate Non-Cancer Risks Following Acute or Chronic Exposures Using Margin of Exposures

$$\boldsymbol{MOE = \frac{Non-cancer\ Hazard\ value\ (POD)}{Human\ Exposure}}$$

Where:

MOE = Margin of exposure (unitless)
(POD) = internal dose (C_{max}, mg/L or AUC hr mg/L)
Human Exposure = internal dose exposure estimate (C_{max}, mg/L or AUC hr mg/L) from occupational or consumer exposure assessment. C_{max} was used for acute exposure scenarios and the AUC was used for chronic exposure scenarios.

In this risk characterization, peer-reviewed PBPK models for NMP in rats and humans (Appendix J) allow EPA to estimate internal doses (blood concentrations) that may occur in humans and compare these to PODs based on internal doses associated with health hazards in rats. MOEs are calculated by dividing PODs in units of internal blood concentrations in rats by human blood concentrations expected for specific exposure scenarios. For characterization of risks from acute exposures, PODs and human exposure estimates are in terms of maximum blood concentrations (C_{max}) while for risks from chronic exposures, they are in terms of average daily exposure (AUC).

The PBPK models facilitate integration of exposure and hazard information across exposure routes. For each exposure scenario, the PBPK model is used to aggregate simultaneous inhalation and dermal exposures into a single human internal dose. The relative contribution of inhalation and dermal exposure routes varies across exposure scenario. The PBPK models also allow the risk characterization to incorporate information about toxicokinetics. Internal doses predicted by the model account for internal exposure that remains after external exposure has ceased, reflecting the rate of metabolism and elimination. Toxicokinetic information captured in rat and human models reduces toxicokinetic uncertainty associated with interspecies extrapolation.

Table 4-4 and Table 4-5 summarize the use scenarios, populations of interest and toxicological endpoints used to evaluate risk for acute and chronic exposures for workers and acute exposure for consumers, respectively.

Table 4-4. Use Scenarios, Populations of Interest and Toxicological Endpoints for Assessing Occupational Risks Following Acute and Chronic Exposures to NMP

Populations and Toxicological Approach	Occupational Use Scenarios of NMP	
Population of Interest and Exposure Scenario:	***Users:*** Adults and youth of both sexes (>16 years old) exposed to NMP during product use in a workday, typically 8 or 12 hours [a,b] ***Occupational Non-users:*** Adults and youth of both sexes (>16 years old) indirectly exposed to NMP while in the vicinity of product use.	
Health Effects of Concern, Concentration and Time Duration	***Acute Non-Cancer Health Effects:*** Developmental toxicity (post-implantation loss) ***Hazard Values (POD):*** 437 mg/L (C_{max} blood concentration)	***Chronic Non-Cancer Health Effects:*** Reproductive toxicity (reduced fertility) ***Hazard Values (POD):*** 183 hr mg/L (AUC blood concentration)
Uncertainty Factors (UF) used in Non-Cancer Margin of Exposure (MOE) Calculations	UFs for Acute Hazard: Total UF = 30 (10X UF_H * 3X UF_A) [c]	UFs for Chronic Hazard: Total UF = 30 (10X UF_H * 3X UF_A) [c]

[a] It is assumed that there is no substantial buildup of NMP in the body between exposure events due to NMP's short biological half-life (~2.5 hours).
[b] EPA expects that the users of NMP-based products and exposed non-users are generally adults, but younger individuals may be users and exposed non-users.
[c] UF_H = intraspecies UF; UF_A = interspecies UF

Table 4-5. Use Scenarios, Populations of Interest and Toxicological Endpoints for Assessing Consumer Risks Following Acute Exposures to NMP

Populations and Toxicological Approach	Consumer Use Scenarios of NMP
Population of Interest and Exposure Scenario:	***Users:*** Adults of both sexes (>16 years old) typically exposed to NMP [a,b] ***Bystanders:*** Individuals of any age indirectly exposed to NMP while being in the rest of the house during product use (see Section 2.4.2 for more information).
Health Effects of Concern, Concentration and Time Duration	***Non-Cancer Health Effects:*** Developmental toxicity (post-implantation loss). ***Hazard Values (POD):*** 437 mg/L (C_{max} blood concentration)
Uncertainty Factors (UF) used in Non-Cancer Margin of Exposure (MOE) Calculations	Total UF = 30 (10X UF_H * 3X UF_A) [c]

[a] It is assumed that there is no substantial buildup of NMP in the body between exposure events due to NMP's short biological half-life (~2.5 hours).
[b] EPA expects that the users of these products are generally adults, but younger individuals may be users of NMP-based paint strippers.
[c] UF_H = intraspecies UF; UF_A = interspecies UF

4.2.2 Risk Estimation for Worker Exposures for Occupational Use of NMP

The risk characterization was performed using internal dose estimates derived from PBPK modeling of occupational exposures based on reasonably available monitoring data. PBPK modeling allowed EPA to estimate internal doses integrating inhalation, dermal, and vapor through skin exposures, which further allowed EPA to evaluate acute and chronic risks from aggregate exposure to NMP for each condition of use. The following sections (Sections 4.2.2.1 through 4.2.2.17) present risk estimates of acute and chronic inhalation, dermal, and vapor through skin exposures for workers following occupational use of NMP in each condition of use. Risk estimates for occupational non-users are shown in Section 4.2.3.

Risks shown in this section are calculated based on occupational exposure estimates summarized in Table 2-73 and hazard points of departure summarized in Table 3-12. MOEs calculated for acute and chronic occupational exposures for each condition of use are summarized in Table 4-6 through Table 4-39. MOE values below the benchmark MOE of 30 (described in Section 3.2.5.6) are indicated with bold and shaded grey.

For each occupational exposure scenario, EPA calculated risk based on a glove protection factor of 1, which corresponds to no glove usage or use of gloves that are not protective against NMP. EPA also calculated risks based on glove protection factors of 5, 10, and 20 based on exposure modeling described in Section 2.4.1 and in the *Supplemental Excel File on Occupational Risk Calculations* (U.S. EPA, 2020s). As indicated in Table 2-3, use of protection factors above 1 is valid only for glove materials that have been tested for permeation against the NMP-containing liquids associated with the condition of use. More information on glove materials for protection against NMP is in Appendix F. For each

occupational exposure scenario, EPA also calculated risk based on use of a half mask air-purifying respirator (APF of 10). For most occupational exposure scenarios the primary route of exposure to NMP was via the dermal route, and respirator use had minimal impact on internal dose estimates and subsequent risk calculations (see Table 4-55 for a comparison of MOEs with and without respirator use). For this reason, risk calculations for respirator use are not shown in Sections 4.2.2.1 - 4.2.2.17, but are shown for select occupational exposure scenarios in Table 4-55 and are fully summarized in the *Supplemental Excel File on Occupational Risk Calculations* (U.S. EPA, 2020s).

As described in Section 2.4.1, EPA calculated alternate exposure estimates for some occupational exposure scenarios based on alternate assumptions about contact durations, monitoring times, or other input parameters. Risks calculated for these alternate "what-if" exposure scenarios are shown in the *Supplemental Excel File on Occupational Risk Calculations* (U.S. EPA, 2020s).

4.2.2.1 Manufacturing of NMP

Table 4-6. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Manufacturing

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**5.3**	32	65	133	30
		High-End	**1.1**	**10**	**23**	49	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

Table 4-7. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Manufacturing

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.4**	**2.8**	**6.0**	**12**	30
		High-End	**0.04**	**0.6**	**1.3**	**2.9**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. Modeling, in the middle of the approach hierarchy, was used to estimate

occupational air concentrations for both the loading of NMP into bulk containers and into drums. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, for modeling of air concentrations during the loading of drums, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic for loading activities, as these durations are based on the length of time required to load NMP into specific container sizes (*i.e.*, tank trucks, rail cars, and drums).

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the loading activities toward the true distribution of durations for all worker activities in this occupational exposure scenario is uncertain. NMP concentration is reported to CDR as a range and EPA assessed only the upper end of the range since a central value cannot be ascertained for this scenario. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. EPA is uncertain of the accuracy of emission factors used to estimate fugitive NMP emissions and thereby model NMP air concentrations. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.2 Repackaging

Table 4-8. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Importation and Repackaging

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**5.3**	32	65	133	30
		High-End	**1.1**	**10**	**23**	49	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

Table 4-9. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Importation and Repackaging

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.4**	**2.8**	**6.0**	**12**	30
		High-End	**0.04**	**0.6**	**1.3**	**2.9**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations for both the unloading of NMP from bulk containers and from drums. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, for modeling of air concentrations during the loading of drums, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic, as the durations are based on the length of time to load NMP into specific container sizes (*i.e.*, tank trucks, rail cars, and drums).

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the unloading activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. NMP concentration is reported to CDR as a range and EPA assessed only the upper end of the range since a central value cannot be ascertained for this scenario. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. EPA is uncertain of the accuracy of the emission factors used to estimate fugitive NMP emissions and thereby to model NMP air concentrations. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.3 Chemical Processing, Excluding Formulation

Table 4-10. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Chemical Processing (Excluding Formulation)

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**5.3**	32	65	133	30
		High-End	**1.1**	**10**	**23**	49	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

Table 4-11. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Chemical Processing (Excluding Formulation)

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.4**	**2.8**	**6.0**	**12**	30
		High-End	**0.04**	**0.6**	**1.3**	**2.9**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations for both the unloading of NMP from bulk containers and from drums. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic, as the duration is based on the length of time to load NMP into drums.

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the unloading activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. NMP concentration is reported to CDR as a range and EPA assessed only the upper end of the range since a central value cannot be ascertained for this scenario. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model

as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. EPA is uncertain of the accuracy of the emission factors used to estimate fugitive NMP emissions and thereby to model NMP air concentrations. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.4 Incorporation into Formulation, Mixture, or Reaction Product

Table 4-12. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Formulations, Mixtures, or Reaction Products

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Liquid – Unloading drums							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**5.3**	32	65	133	30
		High-End	**1.1**	**10**	**23**	49	
Liquid – Miscellaneous (Maintenance, analytical, loading)							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	91	459	906	1,757	30
		High-End	**1.1**	**10**	**23**	49	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

Table 4-13. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Formulations, Mixtures, or Reaction Products

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Liquid – Unloading drums							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.4**	**2.8**	**6.0**	**12**	30
		High-End	**0.04**	**0.6**	**1.3**	**2.9**	
Liquid – Miscellaneous (Maintenance, analytical, loading)							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**8.4**	43	84	163	30
		High-End	**0.04**	**0.6**	**1.4**	**2.9**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations for the unloading of NMP from drums. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic, as the duration is based on the length of time to load NMP into drums. EPA assessed worker inhalation exposure during maintenance, bottling, shipping, and loading of NMP using directly applicable monitoring data, which is the highest of the approach hierarchy, taken at an adhesive formulation facility. The data quality rating for the monitoring data used by EPA is high. EPA expects the duration of inhalation and dermal exposure to be realistic for the unloading of drums, as the duration is based on the length of time to load NMP into drums.

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. NMP concentration is reported to CDR as a range and EPA assessed only the upper end of the range since a central value cannot be ascertained for this scenario (NMP concentration is lower in the formulated products). Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. EPA estimated worker inhalation exposure concentration during the loading of NMP in solid formulations using EPA's OSHA PEL for PNOR model (U.S. EPA, 2015a), which is the lowest approach on the hierarchy. EPA did not use these inhalation exposure concentrations

for the PBPK modeling because the PBPK model does not account for solids and because both the inhalation and dermal exposure potential are captured within other occupational exposure scenarios. EPA is uncertain of the accuracy of the emission factors used to estimate fugitive NMP emissions and thereby to model NMP air concentrations. For the maintenance, bottling, shipping, and loading of liquid NMP, the monitoring data consists of only 7 data points from 1 source. The representativeness of the modeling and the monitoring data toward the true distribution of inhalation concentrations for these occupational exposure scenarios is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.5 Metal Finishing

Table 4-14. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Metal Finishing

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Spray application							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**2.7**	143	288	573	30
		High-End	**1.7**	**14**	31	64	
Dip application							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**27**	142	281	550	30
		High-End	**1.7**	**14**	31	65	
Brush application							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**27**	135	258	466	30
		High-End	**1.7**	**14**	31	64	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration (unless specified otherwise), 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration (unless specified otherwise), 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-15. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Metal Finishing

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Spray application							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**2.4**	**13**	**27**	53	30
		High-End	**0.1**	**0.8**	**1.8**	**3.8**	
Dip application							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**2.4**	**13**	**26**	51	30
		High-End	**0.1**	**0.8**	**1.8**	**3.8**	
Brush application							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**2.4**	**12**	**24**	43	30
		High-End	**0.1**	**0.8**	**1.8**	**3.8**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration (unless specified otherwise), 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration (unless specified otherwise), 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to liquids using the most recent CDR data for concentration provided by industry submitters. To estimate inhalation exposure during spray application, EPA used surrogate monitoring data, which is in the middle of the approach hierarchy, including 26 data points. These data have a data quality rating of high. To estimate inhalation exposure during dip application, EPA used surrogate monitoring data for dip cleaning, which is in the middle of the approach hierarchy, including data from 5 sources. These data have data quality ratings of medium to high. To estimate inhalation exposure during brush application, EPA used modeled data from the RIVM report (RIVM, 2013), which has a data quality rating of high. The use of modeling is in the middle of the approach hierarchy. EPA used durations associated with inhalation monitoring data to estimate duration of inhalation and dermal exposure during spray application.

Primary Limitations

For occupational exposure scenarios other than spray application, EPA did not find exposure duration data and assumed a high-end of 8 hours because the surrogate data or modeled values are 8-hour TWA values. EPA assumed a mid-range of 4 hours for central tendency exposure duration. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Due to lack of data, EPA could not calculate central tendency and high-end NMP concentration in metal finishing products and used the low-end and high-end of the NMP

concentration range reported in 2016 CDR. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. The reasonably available monitoring data for spray application is from 1996. The extent to which these data are representative of current worker inhalation exposure potential is uncertain. The worker activities associated with the surrogate data used to assess worker inhalation exposure during dip application are not detailed for all sample points. The modeled inhalation exposure concentration during roller/brush application was obtained from RIVM (2013) and not generated by EPA. For all occupational exposure scenarios, representativeness of the monitoring data, surrogate monitoring data, or modeled data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.6 Application of Paints, Coatings, Adhesives and Sealants

Table 4-16. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Application of Paints, Coatings, Adhesives and Sealants

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Spray application							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	1,395	6,070	10,424	16,249	30
		High-End	**14**	81	161	311	
Roll / curtain application							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	1,445	7,110	13,919	26,699	30
		High-End	**14**	83	169	342	
Dip application							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	1,261	4,182	5,872	7,359	30
		High-End	**14**	81	164	323	
Roller / brush and syringe / bead application							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	890	1,780	2,030	2,182	30
		High-End	**14**	81	162	313	

MOEs < 30 are indicated in bold and shaded grey2,182

[a] Central tendency means: typical air concentration (unless specified otherwise), 1-hand dermal (445 cm^2 surface area

exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration (unless specified otherwise), 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-17. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Application of Paints, Coatings, Adhesives and Sealants

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Spray application							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	130	567	976	1,530	30
		High-End	**0.8**	**4.8**	**9.6**	**19**	
Roll / curtain application							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	134	661	1,294	2,485	30
		High-End	**0.8**	**4.9**	**10**	**20**	
Dip application							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	118	394	556	700	30
		High-End	**0.8**	**4.8**	**9.8**	**19**	
Roller / brush and syringe / bead application							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	84	169	194	209	30
		High-End	**0.8**	**4.8**	**9.6**	**19**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration (unless specified otherwise), 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration (unless specified otherwise), 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from 79 values from a variety of data sources with data quality ratings ranging from medium to high. The spread of the 79 values of weight fraction was more pronounced than other OESs, leading to a larger than average difference of central tendency and high-end exposures; however, this data set is stronger than average and reduces uncertainties. To estimate inhalation exposure during spray application, EPA used directly applicable personal monitoring data, the highest of the approach hierarchy, including 26 data points. These data have a data quality rating of high. To estimate inhalation exposure during roll/curtain application, EPA used modeling, which is in the middle of the approach hierarchy. To estimate inhalation exposure during dip application, EPA used surrogate monitoring data for dip cleaning, which is in the middle of the approach hierarchy, including data from 5 sources. These data have data quality ratings of medium to high. To estimate inhalation

exposure during roller / brush and syringe/bead application, EPA used modeled data from the RIVM report (RIVM, 2013), which has a data quality rating of high. The use of modeling is in the middle of the approach hierarchy. EPA used durations associated with short-term inhalation monitoring data to estimate duration of inhalation and dermal exposure during spray application.

Primary Limitations

For occupational exposure scenarios other than spray application, EPA did not find exposure duration data and assumed a high-end of 8 hours because the surrogate data or modeled values are 8-hour TWA values. EPA assumed a mid-range of 4 hours for central tendency exposure duration. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. The reasonably available monitoring data for spray application is from 1996 and the surrogate monitoring data used in the model for roll / curtain application is from 1994 or earlier. The extent to which these data are representative of current worker inhalation exposure potential is uncertain. The worker activities associated with the surrogate data used to assess worker inhalation exposure during dip application are not detailed for all sample points. The modeled inhalation exposure concentration during roller / brush application was obtained from RIVM (2013) and not generated by EPA. For all occupational exposure scenarios, representativeness of the monitoring data, surrogate monitoring data, or modeled data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.7 Recycling and Disposal

Table 4-18. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Recycling and Disposal of NMP

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**6.8**	40	82	165	30
		High-End	**1.1**	**10**	**23**	49	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-19. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Recycling and Disposal of NMP

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.5**	**3.6**	**7.5**	**15**	30
		High-End	**0.04**	**0.6**	**1.3**	**2.9**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations for both the unloading of NMP from bulk containers and from drums. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, for modeling of air concentrations during the unloading of drums, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic for the unloading activities, as the durations are based on the length of time to unload NMP from specific container sizes (*i.e.*, tank trucks, rail cars, and drums).

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the unloading activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. EPA did not find NMP concentration data and assumed waste NMP may contain very little impurities and be up to 100% NMP. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. For the modeling of NMP air concentrations, EPA

is uncertain of the accuracy of the emission factors used to estimate fugitive NMP emissions and thereby estimate worker inhalation exposure concentration. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.8 Removal of Paints, Coatings, Adhesives and Sealants

Table 4-20. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in the Removal of Paints, Coatings, Adhesives and Sealants

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Miscellaneous removal							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	70	182	226	257	30
		High-End	**4.4**	**27**	51	85	
Graffiti removal							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	55	280	546	1,036	30
		High-End	**7.7**	49	99	196	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: mid-range or mean air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means high-end air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-21. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in the Removal of Paints, Coatings, Adhesives and Sealants

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Miscellaneous removal							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**6.4**	**17**	**21**	**24**	30
		High-End	**0.2**	**1.6**	**3.0**	**5.1**	
Graffiti removal							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**5.0**	**26**	51	96	30
		High-End	**0.4**	**2.9**	**5.9**	**12**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: mid-range or mean air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means high-end air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50^{th} and 95^{th} percentiles, respectively, from a variety of data sources with data quality ratings ranging from medium to high. To estimate inhalation exposure during miscellaneous paint and coating removal, EPA used directly applicable personal monitoring data, the highest of the approach hierarchy, including data from three studies. These data have a data quality rating of high. To estimate inhalation exposure during graffiti removal, EPA used directly applicable personal monitoring data, the highest of the approach hierarchy, including 25 data points. These data have a data quality rating of high. EPA used durations associated with inhalation monitoring data to estimate duration of inhalation and dermal exposure during miscellaneous paint and coating removal.

Primary Limitations

For graffiti removal, EPA did not find data other than 8-hour TWA values. EPA assumed a high-end exposure duration equal to 8 hours and a central tendency exposure duration of 4 hours, which is the mid-range of a full shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. The short-term inhalation exposure concentrations for miscellaneous removal are based on data from 1993 and the extent to which these data are representative of current worker inhalation exposure potential is uncertain. For graffiti removal, EPA used the minimum, mean, and maximum air concentrations reported by one literature source for 25 datapoints. EPA did not have these 25 data points with which to calculate 50^{th} and 95^{th} percentile values. The representativeness of the monitoring data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.9 Other Electronics Manufacturing

Table 4-22. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Other Electronics Manufacturing

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**27**	137	266	494	30
		High-End	**1.1**	**9.6**	**21**	42	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

Table 4-23. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Other Electronics Manufacturing

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**2.4**	**13**	**25**	46	30
		High-End	**0.04**	**0.5**	**1.2**	**2.5**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from OSHA data (OSHA, 2017), which has a data quality rating of high. EPA used directly applicable inhalation monitoring data, which is the highest of the approach hierarchy, to estimate worker inhalation exposure during one electronics manufacturing operation. These data have a data quality rating of high.

Primary Limitations

The OSHA data (OSHA, 2017) monitoring data were provided as 8-hour TWA values. EPA assumed 8 hours as the high-end duration of liquid contact and mid-range of 4 hours as the central tendency duration of liquid contact. The representativeness of the estimates of duration of inhalation and dermal exposure for the assessed activity toward the true distribution of duration for all worker activities in this occupational exposure scenario beyond capacitor, resistor, coil, transformer, and other inductor manufacturing is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The OSHA data (OSHA, 2017) monitoring data only include capacitor, resistor, coil, transformer, and other inductor manufacturing. The representativeness of the monitoring data for capacitor, resistor, coil, transformer, and other inductor manufacturing toward the true distribution of inhalation concentrations for all worker activities in this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.10 Semiconductor Manufacturing

Table 4-24. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Semiconductor Manufacturing

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Container handling, small containers							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**23**	125	252	504	30
		High-End	**2.3**	**21**	47	98	
Container handling, drums							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	48	253	508	1,020	30
		High-End	**2.3**	**21**	46	97	
Fab worker (75% body coverage)							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	1,013	4,916	9,461	17,586	30
		High-End	198	988	1,925	3,646	
Maintenance							

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	48	252	508	1,020	30
		High-End	**0.6**	**7.9**	**19**	43	
Virgin NMP truck unloading							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**5.3**	31	63	125	30
		High-End	**1.1**	**10**	**23**	48	
Waste truck loading							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**6.8**	40	81	165	30
		High-End	**1.5**	**13**	**29**	61	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

Table 4-25. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Semiconductor Manufacturing

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Container handling, small containers							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**1.5**	**8.7**	**18**	35	30
		High-End	**0.1**	**0.9**	**2.1**	**4.3**	
Container handling, drums							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**3.3**	**18**	36	72	30
		High-End	**0.1**	**0.9**	**2.0**	**4.3**	
Fab worker (75% body coverage)							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	71	346	667	1,242	30
		High-End	**8.7**	44	85	161	
Maintenance							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**3.3**	**18**	36	72	30
		High-End	**0.02**	**0.3**	**0.8**	**1.9**	

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Virgin NMP truck unloading							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.4**	**2.8**	**5.8**	**11**	30
		High-End	**0.04**	**0.6**	**1.3**	**2.8**	
Waste truck loading							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.5**	**3.6**	**7.4**	**15**	30
		High-End	**0.1**	**0.7**	**1.7**	**3.6**	

MOEs < 30 are indicated in bold and shaded grey2,182

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction (EPA expects 100% NMP for this condition of use). High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction (EPA expects 100% NMP for this condition of use).

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from the data provided by SIA (2019c), which has a data quality rating of high. EPA used directly applicable inhalation monitoring data, which is the highest of the approach hierarchy, to estimate worker inhalation exposure during a variety of semiconductor manufacturing tasks. These data have a data quality rating of high.

Primary Limitations

The SIA (2019c) monitoring data were provided as 8-hour or 12-hour TWA values. EPA assumed 8 or 12 hours as the high-end duration of liquid contact and mid-range of 4 or 6 hours as the central tendency duration of liquid contact. The representativeness of the estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The majority of the data points in SIA (2019c) were non-detect for NMP and, for these samples, EPA used the LOD/2 to calculate central tendency and high-end inhalation exposure concentration values (U.S. EPA, 1994). The extent to which the use of LOD/2 accurately represents the actual inhalation concentrations is uncertain. The representativeness of the SIA monitoring data for semiconductor manufacturing toward the true distribution of inhalation concentrations for all worker activities in this occupational exposure scenario is uncertain. The uncertainty in the representativeness of the data may result in either overestimation or underestimation of exposures, depending on the true distribution of inhalation concentrations.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.11 Printing and Writing

Table 4-26. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Printing and Writing

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a,b]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Printing [a]							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	575	2,812	5,452	10,267	30
		High-End	158	802	1,598	3,164	
Writing [b]							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	470,210	2,357,126	NA	NA	30
		High-End	470,210	2,357,126	NA	NA	

MOEs < 30 are indicated in bold and shaded grey

[a] For printing, central tendency means: central tendency (50th percentile) air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case (95th percentile) air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

[b] For writing, central tendency means: dermal exposure over 1 cm^2 surface area exposed [incidental contact] and central tendency NMP weight fraction. High-end means dermal over 1 cm^2 surface area exposed [incidental contact], and high-end weight NMP fraction. EPA expects inhalation exposure to NMP during writing is negligible.

Table 4-27. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Printing and Writing

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a,b]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Printing [a]							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	53	261	507	957	30
		High-End	**9.4**	48	95	188	
Writing [b]							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	116,016	578,404	NA	NA	30
		High-End	116,016	578,404	NA	NA	

MOEs < 30 are indicated in bold and shaded grey

[a] For printing, central tendency means: central tendency (50th percentile) air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case (95th percentile) air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

[b] For writing, central tendency means: dermal exposure over 1 cm^2 surface area exposed [incidental contact] and central tendency NMP weight fraction. High-end means dermal over 1 cm^2 surface area exposed [incidental contact], and high-end weight NMP fraction. EPA expects inhalation exposure to NMP during writing is negligible.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

For printing activities, EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from a variety of data sources with data quality ratings of high. For writing activities, EPA assessed dermal exposure to 1 to 2% NMP based on one writing product identified in the *Use and Market Profile for n-Methylpyrrolidone* (ABT, 2017). For worker dermal exposure during writing, EPA determined the skin surface area dermally exposed to writing ink using a literature source with a data quality rating of high. To estimate worker inhalation exposure during printing, EPA used surrogate monitoring data, which is in the middle of the approach hierarchy. These data include 48 samples and have a data quality rating of high. EPA used durations associated with inhalation monitoring data to estimate duration of inhalation and dermal exposure during printing activities.

Primary Limitations

For writing, EPA did not find exposure duration data and assumed a high-end of 8 hours based on the length of a full shift and a central tendency of 4 hours based on the mid-range of a shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed printing and writing activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. For printing, skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. The surrogate monitoring data used to estimate occupational inhalation exposure during printing is from 1983. The extent to which these data are representative of current worker inhalation exposure potential is uncertain. The representativeness of

the surrogate monitoring data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.12 Soldering

Table 4-28. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Soldering

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	1,285	2,030	2,182	2,268	30
		High-End	400	1,398	2,024	2,608	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-29. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Soldering

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	122	194	209	217	30
		High-End	**24**	84	123	159	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed worker dermal exposure to 1 – 2.5% NMP based on one soldering product identified in the Use and Market Profile for NMP (ABT, 2017).

Primary Limitations

EPA did not find inhalation monitoring data specific to this use and used modeled data for the bush application of a substance containing NMP as surrogate. The representativeness of this modeled data towards this use is uncertain. EPA did not find reasonably available data on actual duration of liquid contact and assumed a high-end of 8 hours based on the length of a full shift and a central tendency of 4 hours based on the mid-range of a shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.13 Commercial Automotive Servicing

Table 4-30. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Commercial Automotive Servicing

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	651	1,207	1,347	1,430	30
		High-End	**28**	111	169	227	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: central tendency (50th percentile) air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means high-end (95th percentile) air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-31. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Commercial Automotive Servicing

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	62	115	129	137	30
		High-End	**1.6**	**6.7**	**10**	**14**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: central tendency (50th percentile) air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means high-end (95th percentile) air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from a variety of data sources with data quality ratings of high. Modeling, in the middle of the approach hierarchy, was used to estimate occupational inhalation exposure concentrations. For modeling of these air concentrations, EPA attempted to address variability in input parameters by estimating both central tendency and high-end parameter values. Additionally, EPA used Monte Carlo simulation to capture variability in input parameters. EPA expects the duration of inhalation and dermal exposure to be realistic, as the duration is based on the length of time to conduct aerosol degreasing of automotive brakes.

Primary Limitations

The representativeness of the estimates of duration of inhalation and dermal exposure for the aerosol brake degreasing activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. For the modeling of NMP air concentrations, EPA used aerosol product use rate and application frequency from one literature source (CARB, 2000) on brake servicing. The extent to which this is representative of other aerosol degreasing applications involving NMP is uncertain. The representativeness of the modeling results toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.14 Laboratory Use

Table 4-32. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Laboratories

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**5.3**	32	65	133	30
		High-End	**1.1**	**10**	**23**	48	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-33. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Laboratories

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.4**	**2.8**	**6.0**	**12**	30
		High-End	**0.04**	**0.6**	**1.3**	**2.9**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed occupational inhalation exposure using directly applicable personal monitoring data, which is the highest of the approach hierarchy, from one source with a data quality rating of medium. EPA also used a modeled inhalation exposure concentration value, which is in the middle of the approach hierarchy, from RIVM (2013). This data has a data quality rating of high. EPA determined central tendency exposure duration from the inhalation monitoring data. EPA expects the central tendency duration of inhalation and dermal exposure to be realistic, as the duration is task-based.

Primary Limitations

EPA assumed a high-end duration of liquid contact of 8 hours based on the length of a full shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. EPA did not find NMP concentration data and assumed workers may be exposed to up to 100% NMP since NMP is a carrier chemical, and carrier chemical concentrations may be very high. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The monitoring data used for central tendency worker inhalation exposure is only one data point from a 1996 industrial hygiene report. The extent to which these data are representative of current worker inhalation exposure potential is uncertain. The modeled high-end inhalation exposure concentration was obtained from RIVM (2013) and not generated by EPA. The representativeness of the monitoring data and modeled exposure toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the

health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.15 Lithium Ion Cell Manufacturing

Table 4-34. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Lithium Ion Cell Manufacturing

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Container handling, small containers							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**4.1**	**27**	58	119	30
		High-End	**0.6**	**8.0**	**19**	43	
Container handling, drums							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**23**	125	254	511	30
		High-End	**0.6**	**7.9**	**19**	43	
Cathode coating							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**27**	134	253	450	30
		High-End	**8.1**	46	84	139	
Cathode mixing							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**27**	139	272	514	30
		High-End	**8.3**	51	102	195	
Research and development							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**27**	143	287	570	30
		High-End	**1.1**	**10**	**23**	48	
Miscellaneous additional activities							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**26**	131	245	426	30
		High-End	**1.1**	**10**	**22**	48	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: central tendency (50th percentile) air concentration (for virgin NMP truck unloading and waste truck loading, EPA scaled a single 8-hour TWA value to a 4-hour TWA values), 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means high-end (95th percentile) air concentration (for virgin NMP truck unloading and waste truck loading, EPA used a single 8-hour TWA value), 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-35. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Lithium Ion Cell Manufacturing

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Container handling, small containers							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.2**	**1.9**	**4.0**	**8.3**	30
		High-End	**0.02**	**0.3**	**0.8**	**1.9**	
Container handling, drums							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**1.5**	**8.8**	**18**	36	30
		High-End	**0.02**	**0.3**	**0.8**	**1.9**	
Cathode coating							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**2.4**	**12**	**23**	42	30
		High-End	**0.4**	**2.7**	**5.0**	**8.4**	
Cathode mixing							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**2.4**	**13**	**25**	48	30
		High-End	**0.5**	**3.0**	**6.1**	**12**	
Research and development							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**2.4**	**13**	**27**	53	30
		High-End	**0.04**	**0.6**	**1.3**	**2.9**	
Miscellaneous additional activities							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**2.3**	**12**	**23**	40	30
		High-End	**0.04**	**0.6**	**1.3**	**2.8**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: central tendency (50^{th} percentile) air concentration (for virgin NMP truck unloading and waste truck loading, EPA scaled a single 8-hour TWA value to a 4-hour TWA values), 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means high-end (95^{th} percentile) air concentration (for virgin NMP truck unloading and waste truck loading, EPA used a single 8-hour TWA value), 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50^{th} and 95^{th} percentiles, respectively, from the data provided by Lithium Ion Cell Manufacturers'

Coalition (LICM, 2020a) which has a data quality rating of high. EPA used directly applicable inhalation monitoring data, which is the highest of the approach hierarchy, to estimate worker inhalation exposure during a variety of lithium ion cell manufacturing tasks. These data have a data quality rating of high.

Primary Limitations

The Lithium Ion Cell Manufacturers' Coalition (LICM, 2020a) monitoring data were provided as 8-hour or 12-hour TWA values. EPA assumed 8 or 12 hours as the high-end duration of liquid contact and mid-range of 4 or 6 hours as the central tendency duration of liquid contact. The representativeness of the estimates of duration of inhalation and dermal exposure for the assessed activities toward the true distribution of duration for all worker activities in this occupational exposure scenario beyond semiconductor manufacturing is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The representativeness of the monitoring data for lithium ion cell manufacturing toward the true distribution of inhalation concentrations for all worker activities in this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.16 Cleaning

Table 4-36. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Cleaning

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Dip cleaning							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	**8.8**	50	102	206	30
		High-End	**1.1**	**10**	**23**	49	
Spray / wipe cleaning							
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	90	451	885	1,697	30
		High-End	**1.1**	**10**	**23**	50	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: central tendency (50th percentile) air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means high-end (95th percentile) air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-37. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Cleaning

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
Dip cleaning							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**0.7**	**4.5**	**9.4**	**19**	30
		High-End	**0.04**	**0.6**	**1.3**	**2.9**	
Spray / wipe cleaning							
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	**8.3**	42	82	158	30
		High-End	**0.04**	**0.6**	**1.4**	**3.0**	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: central tendency (50th percentile) air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means high-end (95th percentile) air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to central tendency and high-end NMP weight fractions, calculated as the 50th and 95th percentiles, respectively, from a variety of data sources with data quality ratings ranging from medium to high. To estimate inhalation exposure during dip cleaning, EPA used directly

applicable monitoring data, which is in the highest of the approach hierarchy, including data from 5 sources. These data have data quality ratings ranging from medium to high. To estimate inhalation exposure during spray / wipe application, EPA used directly applicable monitoring data, which is in the highest of the approach hierarchy, including data from 4 sources. These data have data quality ratings ranging from medium to high.

Primary Limitations

EPA did not find reasonably available data on actual duration of liquid contact and assumed a high-end of 8 hours based on the length of a full shift and a central tendency of 4 hours based on the mid-range of a shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure for the assessed cleaning activities toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain.

The worker activities associated with the monitoring data used to assess inhalation exposure during dip cleaning and spray/wipe cleaning were not detailed for all samples. Where EPA could not determine the type of cleaning activities associated with a data point, EPA used the data in the estimates for both dip and spray/wipe cleaning. For both occupational exposure scenarios, the representativeness of the monitoring data toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.2.17 Fertilizer Application

Table 4-38. Non-Cancer Risk Estimates for Acute Worker Exposures Following Occupational Use of NMP in Fertilizer Application

Health Endpoint	Acute POD, C_{max} (mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
DEVELOPMENTAL EFFECTS Post-implantation Loss	437	Central Tendency	2,892	3,210	3,246	3,264	30
		High-End	149	628	1,032	1,519	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

Table 4-39. Non-Cancer Risk Estimates for Chronic Worker Exposures Following Occupational Use of NMP in Fertilizer Application

Health Endpoint	Chronic POD, AUC (hr mg/L)	Exposure Level [a]	MOE				Benchmark MOE (Total UF)
			No Gloves	Gloves PF 5	Gloves PF 10	Gloves PF 20	
REPRODUCTIVE EFFECTS Decreased Fertility	183	Central Tendency	279	307	311	313	30
		High-End	**8.9**	38	62	92	

MOEs < 30 are indicated in bold and shaded grey

[a] Central tendency means: typical air concentration, 1-hand dermal (445 cm^2 surface area exposed), and central tendency NMP weight fraction. High-end means worst-case air concentration, 2-hand dermal (890 cm^2 surface area exposed), and high-end weight NMP fraction.

EPA considered the assessment approach, the quality of the data, and uncertainties to determine the level of confidence.

Primary Strengths

EPA assessed dermal exposure to 0.1 to 7% NMP, based on data from public comments and literature, which have data quality ratings of high. EPA assessed occupational inhalation exposure during fertilizer application using a modeled inhalation exposure concentration value, which is in the middle of the approach hierarchy, from RIVM (2013). This data has a data quality rating of high.

Primary Limitations

EPA did not find reasonably available data on actual duration of liquid contact and assumed a high-end of 8 hours based on the length of a full shift and a central tendency of 4 hours based on the mid-range of a shift. The representativeness of the assumed estimates of duration of inhalation and dermal exposure toward the true distribution of duration for all worker activities in this occupational exposure scenario is uncertain. Skin surface areas for actual dermal contact are uncertain. The glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. The modeled inhalation exposure concentration was obtained from RIVM (2013) and not generated by EPA. The representativeness of the modeled exposure toward the true distribution of inhalation concentrations for this occupational exposure scenario is uncertain.

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for this occupational exposure scenario is medium. The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.3 Risk Estimation for Exposures to NMP for Occupational Non-Users (ONUs)

Table 4-40 presents the risk estimates for chronic inhalation exposures to ONUs for reproductive effects. A human PBPK model (described in Appendix J) was used to calculate internal NMP exposure estimates for ONUs. Duration-based NMP air concentrations, which are used for worker and ONU exposure estimates, assure that the PBPK model accounts for the full amount of inhalation and vapor-through-skin exposure. Unlike workers, ONUs are not assumed to be exposed via dermal contact with

liquid NMP because they do not have direct dermal contact with liquid chemicals, see Section 2.4.1.1. ONUs are not assumed to be wearing a respirator. EPA expects that ONUs are exposed to lower air concentrations than workers since they may be further from the emission source than workers. Examples of ONUs include supervisors, managers, and other employees that may be in the production areas but do not perform tasks that result in direct dermal contact with NMP.

Calculated MOE values that are below the benchmark MOE (30), indicate a risk concern (shown in bold and shaded grey). EPA analyzed the highest acute exposure scenario for ONUs, paint removers – miscellaneous stripping, calculating an 8 hr TWA air concentration of 64 mg/m^3, resulting in a peak blood concentration of 1.53 mg/L. Based on an acute POD of 437 mg/L, the acute MOE for the ONUs with the highest acute exposure is 285, well above the benchmark MOE of 30. Therefore, EPA did not further analyze ONU risks from acute exposure for additional COUs.

Table 4-40. ONU Risk Estimates based on Adverse Reproductive Effects (Decreased Fertility) from Chronic NMP Exposures

Occupational Exposure Scenario [a]	Exposure Level [b]	Chronic Exposure [c] AUC (hr mg/L)	MOEs [d]
Manufacturing of NMP	Central Tendency	0.064	2,870
	High-End	0.41	443
Repackaging	Central Tendency	0.064	2,870
	High-End	0.41	443
Chemical Processing, Excluding Formulation	Central Tendency	0.069	2,642
	High-End	0.16	1,130
Incorporation into Formulation, Mixture, or Reaction Product (Liquid – Unloading Drums)	Central Tendency	0.069	2,642
	High-End	0.16	1,130
Incorporation into Formulation, Mixture, or Reaction Product (Liquid – Miscellaneous)	Central Tendency	0.074	2,487
	High-End	1.38	133
Metal Finishing (Spray Application)	Central Tendency	0.066	2,763
	High-End	1.00	184
Metal Finishing (Dip Application)	Central Tendency	0.21	859
	High-End	0.64	286
Metal Finishing (Brush Application)	Central Tendency	0.85	215
	High-End	0.92	199
Application of Paints, Coatings, Adhesives, and Sealants (Spray Application)	Central Tendency	0.054	3,394
	High-End	0.93	197
	Central Tendency	0.0063	28,925

Occupational Exposure Scenario [a]	Exposure Level [b]	Chronic Exposure [c] AUC (hr mg/L)	MOEs [d]
Application of Paints, Coatings, Adhesives, and Sealants (Roll / Curtain)	High-End	0.055	3,329
Application of Paints, Coatings, Adhesives, and Sealants (Dip Application)	Central Tendency	0.20	911
	High-End	0.57	319
Application of Paints, Coatings, Adhesives, and Sealants (Brush Application)	Central Tendency	0.84	218
	High-End	0.85	214
Recycling and Disposal	Central Tendency	0.053	3,432
	High-End	0.20	926
Paint and Coating Removal (Miscellaneous Removal)	Central Tendency	6.67	**27**
	High-End	13.24	**14**
Paint and Coating Removal (Graffiti Removal)	Central Tendency	0.21	868
	High-End	0.94	194
Other Electronics Manufacturing (Capacitor, Resistor, Coil, Transformer, and Other Inductor Manufacturing)	Central Tendency	0.61	299
	High-End	9.18	**20**
Semiconductor Manufacturing (Container Handling, Small Containers)	Central Tendency	0.096	1,909
	High-End	0.26	704
Semiconductor Manufacturing (Container Handling, Drums)	Central Tendency	0.011	15,989
	High-End	0.54	336
Semiconductor Manufacturing (Fab Worker - 75% Body Coverage)	Central Tendency	0.021	8,540
	High-End	0.12	1,465
Semiconductor Manufacturing (Maintenance)	Central Tendency	0.013	14,630
	High-End	0.37	492
Semiconductor Manufacturing (Virgin NMP Truck Unloading)	Central Tendency	1.02	179
	High-End	1.08	170
Semiconductor Manufacturing (Waste Truck Loading)	Central Tendency	0.12	1,584
	High-End	0.23	792
Printing	Central Tendency	0.023	7,888
	High-End	0.024	7,520

Occupational Exposure Scenario [a]	Exposure Level [b]	Chronic Exposure [c] AUC (hr mg/L)	MOEs [d]
Writing	Central Tendency	0.00016	1,159,299
	High-End	0.00032	580,042
Soldering	Central Tendency	0.84	218
	High-End	0.84	218
Commercial Automotive Servicing	Central Tendency	1.30	141
	High-End	8.91	**21**
Laboratory Use	Central Tendency	0.064	2,847
	High-End	0.95	193
Lithium Ion Cell Manufacturing (Container Handling, Small Containers)	Central Tendency	0.16	1,172
	High-End	0.35	527
Lithium Ion Cell Manufacturing (Container Handling, Drums)	Central Tendency	0.021	8,792
	High-End	0.63	290
Lithium Ion Cell Manufacturing (Cathode Coating)	Central Tendency	1.00	183
	High-End	8.16	**22**
Lithium Ion Cell Manufacturing (Cathode Mixing)	Central Tendency	0.46	401
	High-End	1.98	93
Lithium Ion Cell Manufacturing (Research and Development)	Central Tendency	0.088	2,077
	High-End	0.93	197
Lithium Ion Cell Manufacturing (Miscellaneous Additional Activities)	Central Tendency	1.25	147
	High-End	1.59	115
Dip cleaning	Central Tendency	0.15	1,217
	High-End	0.65	281
Spray / Wipe Cleaning	Central Tendency	0.10	1,774
	High-End	0.65	280
Fertilizer Application	Central Tendency	0.60	304
	High-End	1.07	171

[a] Use of PPE is not assumed for ONUs.
[b] Central tendency means: typical air concentration for most scenarios. High-end means worst-case air concentration for most scenarios. ONUs are not expected to have direct contact with NMP-containing liquids (see Section 2.4.1.1).
[c] POD blood concentration = 183 hr mg/L (AUC)
[d] Benchmark MOE = 30; MOEs < 30 are indicated in bold and shaded grey

Overall Confidence

Considering the overall strengths and limitations, the overall confidence of the PBPK input parameters for all of the occupational exposure scenarios for ONUs is medium. EPA assigns the same confidence level for PBPK inputs for both workers and ONUs because lower surface areas for liquid contact for ONUs have higher certainty, but air concentrations experienced by ONUs have lower certainty. These factors cannot be quantified and are assumed to offset one another in determining ONU confidence level using worker confidence level as a starting point.

The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure and medium confidence in the health endpoint and POD selected for risk characterization of chronic exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.4 Risk Estimation for Acute Exposures from Consumer Use of NMP

The following sections present the risk estimates for acute dermal and inhalation exposures following consumer use of NMP in each condition of use. Risk estimates that indicate risk relative to the benchmark MOE (*i.e.*, non-cancer MOEs that are below the benchmark MOE of 30) are highlighted by shading the cell.

4.2.4.1 Adhesives and Sealants

Table 4-41. Non-Cancer Risk Estimates for Acute Exposures Following Consumer Use of NMP in Adhesives and Sealants

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
Low Weight Fraction Adhesives and Sealants Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.011	38,758	30
Low Weight Fraction Adhesives and Sealants High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.070	6,248	30
High Weight Fraction Adhesives and Sealants Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	4.084	107	30
High Weight Fraction Adhesives and Sealants High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	18.628	**23**	30

One MOE calculated using a high-end estimate for acute exposure to consumers from the use of NMP-containing adhesives is below the benchmark MOE (30); MOE High Intensity Use = 23.

Overall Confidence

The adhesives scenarios and the sealants scenarios are based on corresponding publicly available consumer product data, specifically the weight fractions and the amount of product used and duration of use from consumer survey data. EPA has a high confidence in these parameters for representing the adhesives and sealants consumer use scenarios.

EPA has a high confidence in the Consumer Exposure Model (CEM), its appropriate use for semi-volatile chemicals such as NMP in estimating air concentrations based on the consumer use, activity patterns, and NMP physical and chemical properties. The emission rate used in CEM for the adhesives scenario and sealants scenario was estimated since product-specific emission from chamber studies was not reasonably available. EPA has high confidence in the emission rate estimate based on physical and chemical properties.

The input parameters for estimating the consumer's internal dose using the PBPK model are: the estimated air concentration resulting from product use as predicted by CEM, the dermal contact time (based on the duration of product use) and the weight fraction of the product.

EPA has a high confidence in the input parameters estimating the adhesive scenario and the sealants scenario.

The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure described above in Section 3.2. Section 3.2.6 describes the justification for this confidence rating.

4.2.4.2 Adhesives Removers

Table 4-42. Non-Cancer Risk Estimates for Acute Exposures Following Consumer Use of NMP in the Removal of Adhesives

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
Adhesives Removers Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	1.292	338	30
Adhesives Removers High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	5.957	73	30

All MOEs calculated using high-end estimates for acute exposure to consumers from use of NMP-containing adhesive removal products are above the benchmark MOE (30).

Overall Confidence

The adhesives remover scenario is based on corresponding publicly available consumer product data, specifically the weight fractions and the amount of product used and duration of use from consumer

survey data. EPA has a high confidence in these parameters for representing the adhesives remover consumer use scenarios.

EPA has a high confidence in the Consumer Exposure Model (CEM), its appropriate use for semi-volatile chemicals such as NMP in estimating air concentrations based on the consumer use, activity patterns, and NMP physical and chemical properties. The emission rate used in CEM for the adhesive remover scenario was estimated since product-specific emission from chamber studies was not reasonably available. EPA has high confidence in the emission rate estimate based on physical and chemical properties.

The input parameters for estimating the consumer's internal dose using the PBPK model are: the estimated air concentration resulting from product use as predicted by CEM, the dermal contact time (based on the duration of product use) and the weight fraction of the product.

EPA has a high confidence in the input parameters estimating the adhesives remover scenario.

The studies that support the health concerns for adverse developmental effects following acute exposure described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.4.3 Auto Interior Liquid and Spray Cleaners

Table 4-43. Non-Cancer Risk Estimates for Acute Exposures Following Consumer Use of NMP in Auto Interior Liquid and Spray Cleaners

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
Auto Interior Liquid Cleaner Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.256	1,710	30
Auto Interior Liquid Cleaner High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	4.356	100	30
Auto Interior Spray Cleaner Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.093	4,676	30
Auto Interior Spray Cleaner High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.184	2,381	30

All MOEs calculated using high-end estimates for acute exposure to consumers from the use of NMP-containing auto interior (liquid and spray) cleaners are above the benchmark MOE (30).

Overall Confidence

The auto interior liquid cleaner scenario and the auto interior spray cleaner scenario are based on corresponding publicly available consumer product data, specifically the weight fractions and the amount of product used and duration of use from consumer cleaner/degreaser survey data. EPA has a medium to high confidence in these parameters for representing the auto interior liquid cleaner scenario and the auto interior spray cleaner consumer use scenarios.

EPA has a high confidence in the Consumer Exposure Model (CEM), its appropriate use for semi-volatile chemicals such as NMP in estimating air concentrations based on the consumer use, activity patterns, and NMP physical and chemical properties. The emission rate used in CEM for the auto interior liquid cleaner scenario and the auto interior spray cleaner scenario was estimated since product-

specific emission from chamber studies was not reasonably available. EPA has high confidence in the emission rate estimate based on physical and chemical properties.

The input parameters for estimating the consumer's internal dose using the PBPK model are: the estimated air concentration resulting from product use as predicted by CEM, the dermal contact time (based on the duration of product use) and the weight fraction of the product.

EPA has a medium to high confidence in the input parameters estimating the auto interior liquid cleaner scenario and the auto interior spray cleaner scenario.

The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure described above in Section 3.2. Section 3.2.6 describes the justification for this confidence rating.

4.2.4.4 Cleaners/Degreasers, Engine Cleaner/Degreaser and Spray Lubricant

Table 4-44. Non-Cancer Risk Estimates for Acute Exposures Following Consumer Use of NMP in Cleaners/Degreasers, Engine Cleaner/Degreaser and Spray Lubricant

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
Cleaners/Degreasers Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	1.034	423	30
Cleaners/Degreasers High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	13.40	33	30
Engine Cleaner/Degreaser Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	1.682	260	30
Engine Cleaner/Degreaser High Intensity Use	DEVELOPMENTAL EFFECTS	437	16.46	**27**	30

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
	Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)				
Spray Lubricant Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.332	1,316	30
Spray Lubricant High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	2.853	153	30

One MOE calculated using a high-end estimate for acute exposure to consumers from the use of NMP-containing engine cleaners/degreasers is below the benchmark MOE (30); MOE High Intensity Use = 27.

Overall Confidence
The cleaner/degreaser scenario and the engine cleaner/degreaser scenario are based on corresponding publicly available consumer product data, specifically the weight fractions and the amount of product used and duration of use from consumer survey data. EPA has a high confidence in these parameters for representing the cleaner/degreaser and engine cleaner/degreaser consumer use scenarios.

EPA has a high confidence in the Consumer Exposure Model (CEM), its appropriate use for semi-volatile chemicals such as NMP in estimating air concentrations based on the consumer use, activity patterns, and NMP physical and chemical properties. The emission rate used in CEM for the cleaner/degreaser scenario and engine cleaner/degreaser scenario was estimated since product-specific emission from chamber studies was not reasonably available. EPA has high confidence in the emission rate estimate based on physical and chemical properties.

The difference in MOE between the medium-intensity and high-intensity use scenarios for the engine cleaner/degreaser is the result of the unique combination of longer duration of use, higher weight fraction, and greater mass used that results in significantly higher NMP air concentration. The inhalation exposure combined with the dermal exposure results in the high-intensity use MOE below 30.

The input parameters for estimating the consumer's internal dose using the PBPK model are: the estimated air concentration resulting from product use as predicted by CEM, the dermal contact time (based on the duration of product use) and the weight fraction of the product.

EPA has a high confidence in the input parameters estimating the cleaner/degreaser scenario and the sealants scenario.

The studies that support the health concerns for adverse developmental effects following acute exposure described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.4.5 Paints and Arts and Craft Paint

Table 4-45. Non-Cancer Risk Estimates for Acute Exposures Following Consumer Use of NMP in Paint and Arts and Craft Paint

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
Paints Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.374	1,169	30
Paints High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	1.422	307	30
Arts and Crafts Paints Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.071	6,139	30
Arts and Crafts Paints High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.222	1,970	30

All MOEs calculated using high-end estimates of acute exposure to consumers from the use of NMP-containing paints (including those used in arts and crafts) are above the benchmark MOE (30).

Overall Confidence
The paint and the arts and crafts paint scenarios are based on corresponding publicly available consumer product data, specifically the weight fractions and the amount of product used and duration of use from consumer survey data. EPA has a high confidence in these parameters for representing the paint and arts and crafts paint scenarios.

EPA has a high confidence in the Consumer Exposure Model (CEM), its appropriate use for semi-volatile chemicals such as NMP in estimating air concentrations based on the consumer use, activity patterns, and NMP physical and chemical properties. The emission rate used in CEM for the paint and arts and crafts paint scenarios was estimated since product-specific emission from chamber studies was not reasonably available. EPA has high confidence in the emission rate estimate based on physical and chemical properties.

The input parameters for estimating the consumer's internal dose using the PBPK model are: the estimated air concentration resulting from product use as predicted by CEM, the dermal contact time (based on the duration of product use) and the weight fraction of the product.

EPA has a high confidence in the input parameters estimating the paint and arts and crafts paint scenarios.

The studies that support the health concerns for adverse developmental effects following acute exposure described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.4.6 Stains, Varnishes, Finishes (Coatings)

Table 4-46. Non-Cancer Risk Estimates for Acute Exposures Following Consumer Use of NMP in Stains, Varnishes, Finishes (Coatings)

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.341	1,283	30
High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	1.947	224	30

All MOEs calculated using high-end estimates of acute exposure to consumers from the use of NMP-containing stains, varnishes and finishes (coatings) are above the benchmark MOE (30).

Overall Confidence
The stains, varnishes and finishes (coatings) scenarios are based on corresponding publicly available consumer product data, specifically the weight fractions and the amount of product used and duration of use from consumer survey data. EPA has a high confidence in these parameters for representing the stains, varnishes and finishes (coatings) scenarios.

EPA has a high confidence in the Consumer Exposure Model (CEM), its appropriate use for semi-volatile chemicals such as NMP in estimating air concentrations based on the consumer use, activity patterns, and NMP physical and chemical properties. The emission rate used in CEM for the stains, varnishes and finishes (coatings) scenarios was estimated since product-specific emission from chamber studies was not reasonably available. EPA has high confidence in the emission rate estimate based on physical and chemical properties.

The input parameters for estimating the consumer's internal dose using the PBPK model are: the estimated air concentration resulting from product use as predicted by CEM, the dermal contact time (based on the duration of product use) and the weight fraction of the product.

EPA has a high confidence in the input parameters estimating the stains, varnishes and finishes (coatings) scenarios.

The studies that support the health concerns for adverse developmental effects following acute exposure described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.4.7 Paint Removers

Table 4-47. Non-Cancer Risk Estimates for Acute Exposures Following Consumer Use of NMP in Paint Removers

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
Medium Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	2.014	217	30
High Intensity Use	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	15.13	**29**	30

One MOE calculated using a high-end estimate for acute exposure to consumers from the use of NMP-containing paint removers is below the benchmark MOE (30); MOE High Intensity Use = 29.

Overall Confidence
The paint removers scenario is based on corresponding publicly available consumer product data, specifically the weight fractions and the amount of product used and duration of use from consumer survey data. EPA has a high confidence in these parameters for representing the paint removers scenario.

EPA has a high confidence in the Multi-Chamber Concentration and Exposure Model (MCCEM), its appropriate use for semi-volatile chemicals such as NMP in estimating air concentrations based on the consumer use, activity patterns, and NMP physical and chemical properties. The emission rate used in MCCEM for the paint removers scenario was based on emission data from a chamber study for a product containing NMP. EPA has high confidence in the emission rate estimate based on peer-reviewed study data.

The input parameters for estimating the consumer's internal dose using the PBPK model are: the estimated air concentration resulting from product use as predicted by MCCEM, the dermal contact time (based on the duration of product use) and the weight fraction of the product.

EPA has a high confidence in the input parameters estimating the paint removers scenarios.

The studies that support the health concerns for adverse developmental effects following acute exposure and adverse reproductive effects following chronic exposure are described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.4.8 Risks to Bystanders

EPA evaluated bystander exposure to NMP for all COUs where risk estimates below the benchmark were found for consumers, including use of NMP-containing paint removers, high weight fraction adhesives and sealants, and engine cleaner/ degreasers. Bystander exposures and risks were not further evaluated for scenarios that do not pose a risk to consumer users because bystander exposures are expected to be lower than consumer user exposures. Risk estimates for adult bystanders are summarized in Table 4-48. Risk estimates for child bystanders are summarized in Table 4-49. All MOEs calculated using high-end estimates of acute exposure to bystanders are above the benchmark MOE (30).

Table 4-48. Risk Estimates for Acute Exposure to Adult Bystanders Following Consumer Use of NMP

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
Paint Removers High Intensity Use (In room of use) [a]	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses	437	9.812	45	30

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Women Childbearing Age Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
	Saillenfait et al. (2003); Saillenfait et al. (2002)				
Paint Removers High Intensity Use (In rest of house)	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	3.561	123	30
High Weight Fraction Adhesives and Sealants High Intensity Use (In room of use) [a]	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.156	2,806	30
High Weight Fraction Adhesives and Sealants High Intensity Use (In rest of house)	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.000 [b]	N/A	30
Engine Cleaner/ Degreaser High Intensity Use (In room of use) [a]	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	8.150	54	30
Engine Cleaner/ Degreaser High Intensity Use (In rest of house)	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	5.552	79	30

[a] Bystander C_{max} estimates in room of use assume exposure to the same NMP air concentrations as the user.
[b] C_{max} is assumed to be zero for bystanders in the rest of house, as outdoor use of the product is not expected to result in NMP in indoor air.
N/A = not applicable

Table 4-49. Risk Estimates for Acute Exposure to Child Bystanders via Consumer Use of NMP

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Child (3-5yrs) Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
Paint Removers High Intensity Use (In room of use) [a]	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	11.44	38	30
Paint Removers High Intensity Use (In rest of house)	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	3.609	121	30
High Weight Fraction Adhesives and Sealants High Intensity Use (In room of use) [a]	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.200	2,187	30
High Weight Fraction Adhesives and Sealants High Intensity Use (In rest of house)	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	0.000 [b]	N/A	30
Engine Cleaner/ Degreaser High Intensity Use (In room of use) [a]	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	10.56	41	30
Engine Cleaner/ Degreaser High Intensity Use (In rest of house)	DEVELOPMENTAL EFFECTS Increased Post-implantation Losses Saillenfait et al. (2003); Saillenfait et al. (2002)	437	6.512	67	30

[a] Bystander C_{max} estimates in room of use assume exposure to the same NMP air concentrations as the user.

Exposure Scenario	Health Effect, Endpoint and Study	POD (peak blood concentration, mg/L)	Child (3-5yrs) Exposure, Peak Blood Concentration, C_{max} (mg/L)	MOE	Benchmark MOE (Total UF)
[b] C_{max} is assumed to be zero for bystanders in the rest of house, as outdoor use of the product is not expected to result in NMP in indoor air. N/A = not applicable					

Overall Confidence

The estimate of bystander exposures is based on the air concentration estimates developed in the corresponding exposure scenarios: paint removers, high weight fraction adhesives and sealants, and engine cleaner/degreaser. The overall confidence of these scenarios is found in Sections 4.2.4.1, 4.2.4.4, and 4.2.4.7, respectively.

The studies that support the health concerns for adverse developmental effects following acute exposure described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure. Section 3.2.6 describes the justification for this confidence rating.

4.2.5 Risk Estimation for General Population Exposures to NMP

During problem formulation, EPA considered general population exposures to NMP through ambient water, sediment, land-applied biosolids, and ambient air. Based on fate properties and screening level analyses, EPA concluded that no further analysis of these pathways is required.

EPA has since updated the screening level analysis of risks from incidental exposure to NMP in surface water based on more recent TRI release information from 2018. This updated exposure analysis is described in Section 2.4.3 and updated release information is in Appendix E.

Table 4-50 and Table 4-51 show risk estimates for NMP exposure from incidental ingestion and dermal contact with surface water. Calculated MOEs below the benchmark MOE of 30 would indicate a risk concern. All MOEs calculated using high-end estimates of acute exposure to swimmers are above the benchmark MOE (30).

Table 4-50. Risk Estimates for Acute Oral Exposure Through Incidental Ingestion of Water; Benchmark MOE = 30

OES	Facility/Data Source [a]	Surface Water Concentration (µg/L)	Drinking Water Acute Dose, Female (mg/kg/day) [b]	MOE (Oral POD 418 mg/kg/day)
Chemical Processing, Excluding Formulation	Spruance Plant	3.4E+00	1.3E-05	3.3E+07
Chemical Processing, Excluding Formulation	BASF Corp., Alabama	2.2E-01	8.2E-07	5.1E+08
Chemical Processing, Excluding Formulation	Fortron Industries LLC	1.7E+00	6.5E-06	6.4E+07
Chemical Processing, Excluding Formulation	American Refining Group, Inc.	1.1E-01	4.1E-07	1.0E+09
Chemical Processing, Excluding Formulation	BASF Corp, Michigan	1.3E-04	4.7E-10	8.9E+11
Electronics Manufacturing	GlobalFoundries, Vermont	2.3E+00	8.6E-06	4.9E+07
Electronics Manufacturing	GlobalFoundries, New York	1.4E+00	5.2E-06	8.1E+07
Formulation	Essex Group Inc. Chemical Processing Plant	5.4E+00	2.0E-05	2.1E+07
Metal Finishing	Essex Group LLC	7.7E-01	2.9E-06	1.5E+08

[a] Site specific modeling to estimate surface water concentrations.
[b] Dose is based on high-end incidental intake rate for adult females.

Table 4-51. Risk from Acute Dermal Exposure from Swimming; Benchmark MOE = 30

OES	Facility/Data Source [a]	Surface Water Concentration (µg/L)	Dermal Acute Dose, Adult [b] (mg/kg/day)	MOE (Dermal POD 418 mg/kg/day)
Chemical Processing, Excluding Formulation	Spruance Plant	3.4E+00	1.3E+00	3.3E+02
Chemical Processing, Excluding Formulation	BASF Corp., Alabama	2.2E-01	8.3E-02	5.0E+03

OES	Facility/Data Source [a]	Surface Water Concentration (µg/L)	Dermal Acute Dose, Adult [b] (mg/kg/day)	MOE (Dermal POD 418 mg/kg/day)
Chemical Processing, Excluding Formulation	Fortron Industries LLC	1.7E+00	6.6E-01	6.4E+02
Chemical Processing, Excluding Formulation	American Refining Group, Inc.	1.1E-01	4.2E-02	1.0E+04
Chemical Processing, Excluding Formulation	BASF Corp., Michigan	1.3E-04	4.8E-05	8.8E+06
Electronics Manufacturing	GlobalFoundries, Vermont	2.3E+00	8.7E-01	4.8E+02
Electronics Manufacturing	GlobalFoundries, New York	1.4E+00	5.2E-01	8.0E+02
Formulation	Essex Group Inc. Chemical Processing Plant	5.4E+00	2.0E+00	2.1E+02
Metal Finishing	Essex Group LLC	7.7E-01	2.9E-01	1.4E+03

[a] Site specific modeling to estimate surface water concentrations.
[b] Dose is based on high-end competitive swimmer (3 hrs/day).

Overall Confidence
Confidence ratings for general population ambient water exposure scenarios are informed by uncertainties surrounding inputs and approaches used in modeling surface water concentrations and estimating incidental oral and dermal doses. Estimated daily releases (kg/site-day) on a per occupational exposure scenario (OES) basis reflect moderate confidence.

Other considerations that impact confidence in the ambient water exposure scenarios include the model used (E-FAST 2014) and its associated default and user-selected values and related uncertainties. As described, there are uncertainties related to the ability of E-FAST 2014 to incorporate downstream fate and transport. Of note, as stated on EPA's E-FAST 2014 website, "modeled estimates of concentrations and doses are designed to reasonably overestimate exposures, for use in an exposure assessment in the absence of or with reliable monitoring data." Regarding the assumption that members of the general population could reasonably be expected to swim at or near the point of release, there is relatively low confidence.

There are no readily available NMP surface water monitoring data available that reflect ambient water exposure levels in the United States thus, EPA relied on facility submitted data as reported in TRI.

Based on the above considerations, the general population ambient water exposure assessment scenarios have an overall low to moderate confidence

The studies that support the health concerns for adverse developmental effects following acute exposure described above in Section 3.2. Overall, EPA has high confidence in the health endpoint and POD selected for risk characterization of acute exposure. Section 3.2.6 describes the justification for this confidence rating.

4.3 Assumptions and Key Sources of Uncertainty

4.3.1 Assumptions and Uncertainties in Occupational Exposure Assessment

Assumptions and sources of uncertainty for occupational exposure estimates are described in greater detail in Section 2.4.1.4. Sources of uncertainty and overall confidence in occupational exposure estimates vary across occupational exposure scenarios. Overall confidence in exposure estimates for specific conditions of use are described in Section 4.2.2.

A peer-reviewed PBPK model allows EPA to estimate aggregate exposures from simultaneous dermal and inhalation and vapor-through-skin exposures with relatively high confidence. The body weight parameter is related to all of these three routes. The assumed values for human body weight have relatively lower uncertainties, and the median values used may underestimate exposures at the high-end of PBPK exposure results.

Estimates of dermal exposure rely on a set of assumptions that introduce uncertainty because no data are reasonably available for many parameters. The types of data and assumptions used to estimate exposure for each exposure scenario is summarized in Table 4-53. Parameters that rely on such assumptions include glove use and effectiveness, durations of contact with liquid, skin surface areas for contact with liquids. For many OESs, the high-end surface area assumption of contact over the full area of two hands likely overestimates exposures. EPA has more confidence in dermal exposure parameters that are supported by data, such as NMP concentrations in formulas. There is also uncertainty around the impact of vapors being trapped next to the skin during glove use. For most of the assumptions made for exposure parameters and other sources of uncertainty, EPA does not have enough information to determine whether most of these assumptions may overestimate or underestimate exposures. The NMP concentrations in liquid used in dermal exposure predictions are likely to have a relatively low impact (less than an order of magnitude, or factor of 10) on overestimation or underestimation of exposure.

Estimates of inhalation and vapor-through-skin exposures also rely on various assumptions that introduce uncertainty. The specific types of data sources used estimated air concentrations that are based on monitoring data where reasonably available and based on deterministic or probabilistic modeling for exposure scenarios lacking monitoring data. Table 4-52 summarizes the types of data used to estimate air concentrations for each occupational exposure scenario. The principal limitation of the air concentration monitoring data is the uncertainty in the representativeness of the data. EPA identified a limited number of exposure studies and data sets that provided data for facilities or job sites where NMP was used. Some of these studies primarily focused on single sites. This small sample pool introduces uncertainty as it is unclear how representative the data for a specific end use are for all sites and all workers across the US. Limited monitoring datasets precluded EPA from describing actual parameter distributions. In most scenarios where data were reasonably available, EPA did not find enough data to determine complete statistical distributions to identify 50^{th} and 95^{th} percentile exposures. In the absence of percentile data for monitoring, the means or midpoint of the range serve as substitutes for 50^{th} percentiles of the actual distributions and high ends of ranges serve as substitutes for 95^{th} percentiles of

the actual distributions. The effects of limited air monitoring datasets of unknown representativeness on the occupational exposure assessment are unknown. They may result in either over or underestimation of exposures depending on the actual distribution.

Where air monitoring data were not reasonably available, exposure was estimated based on deterministic or probabilistic modeling. Modeling approaches used to estimate air concentrations also have uncertainties. Parameter values used in models did not all have distributions known to represent the modeled scenario. It is also uncertain whether the model equations generate results that represent actual workplace air concentrations. Some activity-based modeling does not account for exposures from other activities. Additional model-specific uncertainties are included below. In general, the effects of model-specific uncertainties on the exposure estimates are unknown, as the uncertainties may result in either over or underestimation on exposures depending on the actual distributions of each of the model input parameters. Dermal exposures to NMP vapor that may penetrate clothing fabrics and the potential for associated direct skin contact with clothing saturated with NMP vapor are not included in quantifying exposures, which could potentially result in underestimation of exposures.

Table 4-52. Summary of Occupational Air Concentration Estimate Approaches

Exposure Scenario	Work Activity	Worker Personal Breathing Zone Monitoring Data	Modeling: Deterministic Worker [a]	Modeling: Probabilistic Worker (X) Near Field/ ONU Far Field (X [e])	Potential ONU-related Data
1. Manufacturing	Loading NMP into bulk containers		X		
	Loading NMP into drums			X	
2. Repackaging	Unloading NMP from bulk containers		X		
	Unloading NMP from drums			X	
3. Chemical Processing, Excluding Formulation	Unloading NMP from drums			X	
4. Incorporation into Formulation, Mixture, or Reaction Product	Unloading liquid NMP from drums			X	
	Maintenance, bottling, shipping, loading	X (23 samples)			^ (area monitoring) [c]
5. Metal finishing	Spray application	X (45 samples)			^ (area monitoring) [c]

Exposure Scenario	Work Activity	Worker Personal Breathing Zone Monitoring Data	Modeling: Deterministic Worker [a]	Modeling: Probabilistic Worker (X) Near Field/ ONU Far Field (X [e])	Potential ONU-related Data
	Dip application	X (103 samples)	X [b]		
	Brush application		X [b]		
6. Application of Paints, Coatings, Adhesives and Sealants	Spray application	X (45 samples)			X (area monitoring) [c]
	Roll/ curtain application		X		
	Dip application	X (103 samples)	X [b]		
	Roller/ brush and syringe/ bead application		X [b]		
7. Recycling and disposal	Unloading NMP from bulk containers		X		
	Unloading NMP from drums			X	
8. Removal of Paints, Coatings, Adhesives and Sealants	Miscellaneous paint, coating, adhesive, and sealant removal	X (unknown) [d]			
	Graffiti removal	X (25 samples)			
9. Other Electronics Manufacturing	Capacitor, resistor, coil, transformer, and other inductor manufacturing	X (4 samples)			
10. Semiconductor Manufacturing [e]	Container handling, small containers	X (19 samples)			
	Container handling, drums	X (15 samples)			
	Fab worker	X (28 samples)			^ (area monitoring) [c]
	Maintenance	X (45			

Exposure Scenario	Work Activity	Worker Personal Breathing Zone Monitoring Data	Modeling: Deterministic Worker [a]	Modeling: Probabilistic Worker (X) Near Field/ ONU Far Field (X [e])	Potential ONU-related Data
		samples)			
	Virgin NMP truck unloading	X (1 sample)			
	Waste truck loading	X (1 sample)			
11. Printing and Writing	Printing	X (6 samples)			
	Writing	Inhalation not assessed			
12. Soldering	Brush application		X [b]		
13. Commercial Automotive Servicing				X [f]	
14. Laboratory Use	Laboratory use	X (1 sample)	X [b]		
15. Lithium Ion Cell Manufacturing	Container handling, small containers	X (14 samples)			
	Container handling, drums	X (10 samples)			
	Cathode coating	X (5 samples)			
	Cathode mixing	X (8 samples)			
	Research and development	X (4 samples)			
	Miscellaneous additional activities	X (5 samples)			
16. Cleaning	Dip cleaning / degreasing	X (103 samples)	X [b]		
	Spray / wipe cleaning	X (73 samples)	X [b]		
17. Fertilizer application	Spray application		X [b]		

X = These data or modeling approaches were available and used to quantify air concentrations.
[a] The deterministic modeling approaches estimate worker exposures.
[b] These modeling estimates are from literature (Rivm, 2013). Other modeling estimates are from modeling performed by EPA.
[^c] While area monitoring data were identified, EPA does not expect that these data are representative of ONU exposures for these specific OESs because of the intended sample population and the selection of the specific monitoring location.

Exposure Scenario	Work Activity	Worker Personal Breathing Zone Monitoring Data	Modeling: Deterministic Worker [a]	Modeling: Probabilistic Worker (X) Near Field/ ONU Far Field (X [e])	Potential ONU-related Data

Therefore these data are not used.
[d] The number of samples is unknown. The data source only presented the range.
[e] The listed approaches for Semiconductor Manufacturing include EPA's approach and do not include industry-proposed PBPK runs.
[f] This modeling includes Near Field modeling for worker exposures and Far Field modeling for ONU exposures. Far Field modeling results are not included in the RE but are included in *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Occupational Exposure Assessment* (U.S. EPA, 2020f).

Table 4-53. Summary of Worker Dermal Parameter Estimate Approaches

Exposure Scenario	Work Activity	NMP weight fraction in the liquid product (data source(s) used if applicable)	Total skin surface area of hands in contact with the liquid product [b]	Duration of dermal contact with the liquid product [c]
1. Manufacturing	Loading NMP into bulk containers	Data (2016 CDR[a])	Default Assumption	Default Assumption
	Loading NMP into drums			
2. Repackaging	Unloading NMP from bulk containers	Data (2016 CDR[a])	Default Assumption	Default Assumption
	Unloading NMP from drums			
3. Chemical Processing, Excluding Formulation	Unloading NMP from drums	Data (2016 CDR[a], public comments, and Use and Market Profile for NMP[a])	Default Assumption	Default Assumption
4. Incorporation into Formulation, Mixture, or Reaction Product	Unloading liquid NMP from drums	Data (2016 CDR[a], public comments, literature, and Use and Market Profile for NMP[a])	Default Assumption	Default Assumption
	Maintenance, bottling, shipping, loading			
5. Metal finishing	Spray application	Data (2012 and 2016 CDR[a])	Default Assumption	Default Assumption
	Dip application			
	Brush application			
6. Application of Paints, Coatings,	Spray application	Data (public comments, literature, and Use and	Default Assumption	Default Assumption
	Roll/ curtain application			

Exposure Scenario	Work Activity	NMP weight fraction in the liquid product (data source(s) used if applicable)	Total skin surface area of hands in contact with the liquid product [b]	Duration of dermal contact with the liquid product [c]
Adhesives and Sealants	Dip application	Market Profile for n-Methylpyrrolidone[a])		
	Roller/ brush and syringe/ bead application			
7. Recycling and disposal	Unloading NMP from bulk containers	Data (SIA[a]) and Non-default Assumption	Default Assumption	Default Assumption
	Unloading NMP from drums			
8. Removal of Paints, Coatings, Adhesives and Sealants	Miscellaneous paint, coating, adhesive, and sealant removal	Data (public comments, literature, and Use and Market Profile for n-Methylpyrrolidone[a])	Default Assumption	Default Assumption
	Graffiti removal			
9. Other Electronics Manufacturing	Capacitor, resistor, coil, transformer, and other inductor manufacturing	Data (literature, public comments, and the Use and Market Profile for n-Methylpyrrolidone[a])	Default Assumption	Default Assumption
10. Semiconductor Manufacturing	Container handling (small containers);	Data (SIA, public comments, literature, and Use and Market Profile for n-Methylpyrrolidone[a])	Default Assumption	Default Assumption
	Container handling, drums			
	Fab worker			
	Maintenance			
	Virgin NMP truck unloading			
	Waste truck loading			
11. Printing and Writing	Printing	Data (public comments, and Use and Market Profile for n-Methylpyrrolidone[a])	Default Assumption	Default Assumption
	Writing		Data (Australian Government Department of Health, 2016)	Non-default Assumption

Exposure Scenario	Work Activity	NMP weight fraction in the liquid product (data source(s) used if applicable)	Total skin surface area of hands in contact with the liquid product [b]	Duration of dermal contact with the liquid product [c]
12. Soldering	Soldering	Data (Use and Market Profile for n-Methylpyrrolidone[a])	Default Assumption	Default Assumption
13. Commercial Automotive Servicing		Data (public comments and the Use and Market Profile for n-Methylpyrrolidone[a])	Default Assumption	Default Assumption
14. Laboratory Use	Laboratory use	Non-default Assumption	Default Assumption	Default Assumption
15. Lithium Ion Cell Manufacturing	Container handling, small containers	Data (literature, public comments, and the Use and Market Profile for n-Methylpyrrolidone[a])	Default Assumption	Default Assumption
	Container handling, drums			
	Cathode coating			
	Cathode mixing			
	Research and development			
	Miscellaneous additional activities			
16. Cleaning	Dip cleaning / degreasing	Data (public comments, literature sources, and the Use and Market Profile for n-Methylpyrrolidone[a])	Default Assumption	Default Assumption
	Spray / wipe cleaning			
17. Fertilizer application	Spray application	Data (literature, public comments, and the Use and Market Profile for n-Methylpyrrolidone[a])	Default Assumption	Default Assumption

[a] Sources for weight fractions: 2016 CDR (U.S. EPA, 2016a), Use and Market Profile for n-Methylpyrrolidone (ABT, 2017), 2012 CDR (U.S. EPA, 2012b), SIA (2019c), as well as various public comments and literature sources.

[b] Default assumption for "Total skin surface area of hands in contact with the liquid product" is: (1) high-end value, which represents two full hands in contact with a liquid: 890 cm2 (mean for females),1070 cm2 (mean for males); (2) central tendency value, which is half of two full hands (equivalent to one full hand) in contact with a liquid and represents only the palm-side of both hands exposed to a liquid: 445 cm2 (females), 535 (males).

[c] Default assumption for "Duration of dermal contact with the liquid product" is: (1) high-end value of a full-shift, usually 8 or 12 hours; central tendency value of value of half of a full-shift, usually 4 or 6 hours. For OES with available task durations, EPA assessed "what-if" scenarios using the task duration as the duration of dermal contact with the liquid product (in addition to the scenarios that use the default assumption).

4.3.2 Data Uncertainties in Consumer Exposure Assessment

Systematic review was conducted to identify chemical- and product-specific monitoring and use data for assessing consumer exposures. As no product-specific monitoring data were identified, exposure scenarios were assessed using a modeling approach that requires the input of various chemical parameters and exposure factors. When possible, default model input parameters were modified based on chemical and product specific inputs reasonably available in literature and product databases. Uncertainties related to these inputs are discussed below.

4.3.2.1 Product & Market Profile

The products and articles assessed in this risk evaluation are largely based on EPA's 2016-2017 Use and Market Profile for n-Methylpyrrolidone, which provides information on commercial and consumer products available in the US marketplace at that time (ABT, 2017). While it is possible that some products may have changed since 2017, EPA believes that the timeframe is recent enough to still represent the current market. Information on products from the Use and Market Profile was augmented with other sources such as the NIH Household Product Survey and EPA's Chemical and Products Database (CPDat), as well as reasonably available product labels and SDSs. However, it is still possible that the entire universe of products may not have been identified, due to market changes or research limitations.

4.3.2.2 Westat Survey

A number of product labels and/or technical fact sheets were identified for use in assessing consumer exposure. The identified information often did not contain product-specific use data, and/or represented only a small fraction of the product brands containing the chemical of interest. A comprehensive survey of consumer use patterns in the United States, called the Household Solvent Product: A National Usage Survey (U.S. EPA, 1987), was used to parameterize critical consumer modeling inputs, based on applicable product and use categories. This large survey of over 4,920 completed questionnaires, obtained through a randomized sampling technique, is highly relevant because the primary purpose was to provide statistics on the use of solvent-containing consumer products for the calculation of exposure estimates. The survey focused on 32 different common household product categories, generally associated with cleaning, painting, lubricating, and automotive care. Although there is uncertainty due to the age of the use pattern data, as specific products in the household product categories have likely changed over time, EPA assumes that the use pattern data presented in the Westat survey reflect reasonable estimates for current use patterns of similar product type. The Westat study aimed to answer the following key questions for each product category, some of which were used as key model inputs in this consumer assessment:

- room of product use (key input: environment of use);
- how much time was spent using the product (key input: duration of product use per event);
- how much of the product was used (key input: mass of product used per event);
- how often the products were used;
- when the product was last used;
- product formulation;
- brand names used; and
- degree of ventilation or other protective measures undertaken during product use.

The strengths and weakness of the Westat survey are discussed in more detail below with an emphasis on the key modeling inputs.

Product Use Category

A crosswalk was completed to assign consumer products in the current risk evaluation to one of the product or article scenarios in the CEM model, and then to an appropriate Westat survey category. Although detailed product descriptions were not provided in the Westat survey, a list of product brands and formulation type in each category was useful in pairing the Westat product categories to the scenarios being assessed. In most cases, the product categories in the Westat survey aligned well with the products being evaluated. For product scenarios without an obvious Westat scenario match, professional judgment was used to make an assignment. For a limited number of scenarios, technical fact sheets or labels with information on product use amounts were reasonably available, and this information was used in the assessment as needed.

Another limitation of the Westat data is that while the overall respondent size of the survey was large, the number of users in each product category varied, with some product categories having a much smaller pool of respondents than others. Product categories such as spot removers, cleaning fluids, glues and adhesives, lubricants, paints, wood stains, engine degreasers, and specialized electronic cleaners had sample sizes ranging from roughly 500 to 2,000 users; whereas, categories such as shoe polish, adhesive removers, rust removers, and brake cleaners had sample sizes of less than 500 users.

The survey was conducted for adults and adolescents ages 18 and older. Most consumer products are targeted to this age category, and thus the respondent answers reflect the most representative age group. However, adolescents may also be direct users of some consumer products. It is unknown how the usage patterns compare between adult and adolescent users, but it is assumed that the product use patterns for adults will be very similar to, or more conservative (*i.e.*, longer use duration, higher frequency of use) than use patterns for adolescents.

Room of Use

The CEM model requires specification of a room of use, which results in the following default model assumptions (relevant for inhalation exposure only): ventilation rates, room volume, and the amount of time per day that a person resides in the room of use. The Westat survey provided the location of product use for the following room categories: basement, living room, other inside room, garage, and outside. The room with the highest percentage was selected as the room to model in CEM. For some specific product scenarios, however, professional judgement was used to assign the room of use; these selections are documented above in Table 2-78 of Section 2.4.2.4. For many scenarios in which "other inside room" was the highest percentage, the utility room was selected as the default room of use. The utility room is a smaller room, and therefore may provide a more conservative assumption for peak concentrations. In cases where outside was identified as the "room of use," but it was deemed reasonable to assume the product could be used inside (such as for auto care products), the garage was typically selected as the room of use.

Amount of Product Used and Duration of Product Use

The Westat survey reported the number of ounces per use, derived from the fluid ounces of product used per year (based on can size and number of cans used), divided by the number of reported uses per year. The duration of use (in minutes) reported in Westat was a direct survey question. An advantage to these parameters is that the results are reported in percentile rankings and were used to develop profiles of high intensity, moderate intensity, and low intensity users of the products (95^{th}, 50^{th}, and 10^{th} percentile values, respectively). In cases where a product was not crosswalked to a CEM scenario, the amount of product used was tailored to those specific products instead of depending on Westat data.

Ventilation and Protection

For most scenarios, the CEM model was run using median air exchange rates from EPA's Exposure Factors Handbook (2011), and interzone ventilation rates derived from the air exchange rates and the default median building volume from EPA's Exposure Factors Handbook (2011). These inputs do not incorporate any measures that would serve to increase air exchange. The Westat survey questions indicated that most respondents did not have an exhaust fan on when using these products, most respondents kept the door to the room open when using these products, and most people reported reading the directions on the label. The modeling conducted by EPA did not account for specific product instructions or warning labels. For example, some product labels might indicate that PPE (chemical resistant gloves or respirator) should be worn, which would lower estimated exposures.

4.3.2.3 Other Parameters and Data Sources

Activity Patterns

EPA assumed that a consumer product would be used only once per day. This is a realistic assumption for most scenarios, but a high-intensity user could use the same product multiple times in one day. Additionally, CEM allows for selection of activity patterns based on a "stay-at-home" resident or a part-time or full-time "out-of-the home" resident. The activity patterns were developed based on Consolidated Human Activity Database (CHAD) data of activity patterns, which is an EPA database that includes more than 54,000 individual study days of detailed human behavior. It was assumed that the user followed a "stay-at-home" activity pattern that would place them in various rooms as well as outside of the home and room of use for more time than a part-time or full-time "out-of-the home" resident. Therefore, applying an "out-of-the home" resident activity pattern would reduce estimated exposures.

Product Density

If reasonably available, product-specific densities were obtained from SDS information, and used to convert the ounces of the product used from Westat, to grams of product used. If product-specific densities were not reasonably available, default product densities from the CEM User Guide were used.

Outdoor Scenario

The CEM model does not currently accommodate outdoor scenarios. For products that are solely intended to be used outdoors, modifications to the CEM inputs were made to simulate an outdoor scenario by adjusting Zone 1 parameters (which represents the room of use, or outside). The garage was selected as the room of use, but the room volume was changed to 16 m^3 to represent a half dome chemical cloud around the person using the product. Additionally, the air exchange rate for Zone 1 was set to 100 to reflect the high rate between the cloud and the rest of outside. The interzone ventilation rate was set to 0, which effectively blocks the exchange of air between Zone 1 and the rest of the house. Thus, the concentrations users are exposed to inside the home after product use is zero. In the outside scenario, non-users are assumed to have zero exposures. These assumptions may be either an underestimation of exposures given outdoor conditions such as high temperatures in summer which could increase volatilization of NMP in the product but could also be an overestimation of exposures if outdoor conditions could include wind that effectively disperses the NMP in air.

4.3.3 Approach and Methodology for Uncertainties in Consumer Exposure Assessment

EPA's approach recognizes the need to include an uncertainty analysis. An important distinction for such an analysis concerns variability versus uncertainty – both aspects need to be addressed. Variability refers to the inherent heterogeneity or diversity of data in an assessment. It is "a quantitative description of the range or spread of a set of values" and is often expressed through statistical metrics, such as

variance or standard deviation, that reflect the underlying variability of the data. Uncertainty refers to a lack of data or an incomplete understanding of the context of the risk assessment decision.

Variability cannot be reduced, but it can be better characterized. Uncertainty can be reduced by collecting more or better data. Quantitative methods to address uncertainty include non-probabilistic approaches such as sensitivity analysis and probabilistic methods such as Monte Carlo analysis. Uncertainty can also be addressed qualitatively, by including a discussion of factors such as data gaps and subjective decisions or instances where professional judgment was used.

4.3.3.1 Deterministic vs. Stochastic Approaches

With deterministic approaches, the output of the model is fully determined by the choices of parameter values and initial conditions. Stochastic approaches feature inherent randomness, such that a given set of parameter values and initial conditions can lead to an ensemble of different model outputs. Because EPA's largely deterministic approach involves choices regarding low, medium, and high values for highly influential factors such as chemical mass and frequency/duration of product use, it likely captures the range of potential exposure levels although it does not necessarily enable characterization of the full probabilistic distribution of all possible outcomes.

4.3.3.2 Sensitive Inputs

Certain inputs to which model outputs are sensitive, such as zone volumes and airflow rates, were not varied across product-use scenarios. As a result, model outcomes for extreme circumstances such as a relatively large chemical mass in a relatively low-volume environment likely are not represented among the model outcomes. Such extreme outcomes are believed to lie near the upper end (*e.g.*, at or above the 90th percentile) of the exposure distribution.

4.3.4 Environmental Hazard and Exposure Assumptions Uncertainties

In the NMP Problem Formulation (U.S. EPA, 2018c) and this risk evaluation, EPA completed a screening level evaluation of environmental risk using inherently conservative assumptions. The analysis was completed using estimated concentrations of NMP in the aquatic environment as described in Section 2.3.2 and compared those acute and chronic exposure estimates to conservative measures of acute and chronic hazard (COCs) as described in Section 3.1.2. There is some uncertainty associated with the acute and chronic COCs calculated for aquatic receptors. First, more acute duration data were reasonably available in the literature than chronic duration data. Therefore, EPA is less certain of chronic hazard values compared to the acute hazard values. For the chronic fish endpoint, an ACR approach was used to extrapolate a chronic toxicity value for NMP based on the reported acute values. Utilizing a single value of 10 to extrapolate from acute to chronic hazard for species in the aquatic environment is consistent with existing EPA methodology for the screening and analysis of industrial chemicals (U.S. EPA, 2012e). While this value is routinely utilized by EPA to assess the hazard of new industrial chemicals, there is uncertainty regarding using a single ACR value to estimate chronic hazards across species and chemicals. Second, AFs were also used to calculate the acute and chronic COCs for NMP. AFs account for differences in inter- and intra-species variability, as well as laboratory-to-field variability and are routinely used within TSCA for assessing the hazard of new industrial chemicals (with very limited environmental test data). There is some uncertainty associated with the use of standardized AFs used the hazard assessment. EPA in the NMP Problem Formulation (U.S. EPA, 2018c) did not conduct any further analyses on pathways of exposure for terrestrial receptors as described in Section 2.5.3.1 of the NMP Problem Formulation and further described in Section 2.2 and 2.3 of this risk evaluation.

4.3.5 Human Health Hazard Assumptions and Uncertainties

There is a robust dataset for the critical reproductive and developmental effects that serve as the basis for the points of departure used in this risk characterization. High quality studies have consistently documented the developmental effects of NMP exposure across species and following dermal, oral, and inhalation exposures. The high quality of studies, consistency of effects, relevance of effects for human health, coherence of the spectrum of reproductive and developmental effects observed and biological plausibility of the observed effects of NMP contribute to the overall confidence in the PODs identified based on reproductive and developmental endpoints.

Data on the reproductive and developmental toxicity of NMP in humans are not reasonably available. Therefore, this risk evaluation relies on the assumption that reproductive and developmental toxicity observed in animal models is relevant to human health. It is unknown whether this assumption contributes to an overestimation or underestimation of risk.

The rat PBPK model used to derive PODs based on internal doses facilitates integration of dose-response information from multiple high-quality studies that assessed the effects of NMP exposure across multiple routes. This model incorporates toxicokinetic information, reducing a key source of uncertainty in animal-to-human extrapolation. Furthermore, the availability of this model in combination with studies directly evaluating developmental toxicity across multiple exposure routes eliminates the need for route-to-route extrapolation thereby eliminating another source of uncertainty.

There are several remaining sources of uncertainty around the identification of PODs. As discussed in Section 3.2.1, there is uncertainty associated with the reproductive endpoints selected as the basis for the POD used to evaluate risks from chronic NMP exposure. Because NMP exposures occurred throughout development and into adulthood in the key study, it is not known which period(s) of exposure contributed to the reduced fertility seen in adult rats. It is also unclear which life stages may be most sensitive to the adverse reproductive effects of NMP exposure in humans. Although effects on male fertility and female fecundity were not consistently observed across studies, the POD derived from the key study (183 hr mg/L), is within close range of other PODs (223 and 414 hr mg/L), derived from effects on fetal body weight that are consistently observed across studies, species, and routes of exposure. It is unknown whether the limited set of 2-generation studies contributed to an overestimation or underestimation of risk. The concordance of PODs across reproductive and developmental endpoints and consistency of developmental effects across species and exposure routes contributes to the overall confidence in the POD.

In developmental toxicity studies, there is inherent uncertainty around the potential contribution of maternal toxicity to observed developmental effects. The maternal effect reported in the Saillenfait et al. (2003) inhalation study (transient decrease in body weight gain and food consumption) has been cited as a confounding factor by some study authors. EPA does not concur with this assertion, specifically as it relates to the observed decrease in maternal body weight gain on GD 6-21 (minus gravid uterine weight). Although a decrease in maternal body weight gain was observed, it is not statistically significant. Dams weighed roughly 235 g at GD 0, and whereas the controls gained approximately 32 grams, the high dose dams gained slightly less, roughly 26 grams. Given the lack of significant change in maternal body weight gain, it is unlikely that the observed decreases in fetal and pup body weights reflect a secondary effect of maternal toxicity. In other key and supporting studies, including an inhalation study (Solomon et al., 1995; E. I. Dupont De Nemours & Co, 1990), and an oral gavage study (Saillenfait et al., 2002), similar decreases in pup body weight were observed at similar exposure levels, in the absence of any effects on maternal body weight. These findings support EPA's conclusion that this developmental effect is a direct consequence of NMP exposure.

In whole body inhalation studies, there is uncertainty around the techniques used to generate NMP air concentration. Experimental conditions may have inadvertently resulted in the inclusion of aerosolized particles in the exposure chamber in some inhalation exposure studies. In addition, because the partial pressure of NMP depends on the temperature and relative humidity of the test system, variations in test protocol can introduce uncertainty regarding the actual exposure concentrations achieved in some of the inhalation studies used for hazard characterization. Aerosol formation would result in increased dermal and/or oral exposures (from grooming behavior) in addition to the intended inhalation exposure. The PODs that were ultimately selected as the basis for risk calculations did not rely on studies with this source of uncertainty, making it unlikely that this uncertainty contributes to an overall over or under-estimate of risk.

Another important source of uncertainty around POD selection is the lack of complete information on potentially sensitive endpoints, including endocrine effects, sensitization, immunotoxicity, cardiometabolic effects, and developmental neurotoxicity. Though the database for developmental toxicity is robust, some endpoints have not been fully characterized. For example, as described in Section 3.2.3.1, there is evidence of neurodevelopmental effects following gestational exposure to a relatively high dose of NMP, but a NOAEL for neurodevelopmental endpoints has not been identified. Incomplete information on potentially sensitive endpoints could lead to an underestimation of risk.

Overall, EPA has high confidence in the acute and chronic PODs identified for evaluating risk from NMP. The PODs are derived from endpoints that fall along a continuum of reproductive and developmental effects that are consistently observed in response to NMP across oral, dermal and inhalation exposure routes. Application of the PBPK model reduces uncertainties associated with extrapolation across species and exposure routes, further contributing to overall confidence in the PODs.

4.3.6 PBPK Model Assumptions and Uncertainties

There are several assumptions and sources of uncertainty associated with the PBPK model used to convert exposure estimates and hazard PODs to internal dose metrics.

While parameters for the rates of dermal and oral uptake, metabolism, and urinary elimination have been fit to the PK data it should be recognized that the physiological parameters that define the tissue volumes, blood flow rates, and respiration rate, as well as the chemical-specific parameter that define tissue-blood and tissue-air partitioning, but are measured independently (*in vitro*) have not been adjusted to fit the data. Hence there has not been any compromise in the model's biological realism or "correctness." Further, the partition coefficient values are obtained in a manner that is unambiguous and does not confound them with other parameters. Given this solid physiological and biochemical underpinning, the fitting of the remaining chemical-specific parameters to the available data allows for interpolation of internal doses between the specific levels used in those experiments, some extrapolation beyond them, and for an analysis of the internal doses when exposure via both inhalation and dermal absorption occurs.

More specifically, the fact that several data sets are available for rats provides reasonable confidence in the model's ability to predict dosimetry in the test animals. The carefully controlled human PK data provide data of a quality that is rarely available for humans, providing fairly good confidence in the ability to predict inhalation dosimetry in humans, although the modest number of subjects (8) gives some uncertainty as to how well it represents the population as a whole. When compared to worker and observer data from Xiaofei et al. (2000), the model did under-predict the measured blood concentrations by a factor of 1.5 to 6, depending on the particular comparison. Some of this discrepancy could be due to

underestimation of exposure, but the result suggests that blood concentrations may be underestimated for some groups. There is also uncertainty with respect to how dermal absorption might vary with dilution and matrix, but the fact that data are available for neat vs. 50% dilution provides a measure of the impact of dilution.

Importantly, the PBPK model is being used to estimate the dosimetry in an average adult human, and the question being addressed here is the degree of uncertainty in the estimation of that average, rather than an estimation of variability across the population. Hence the modeling does not evaluate the effect of variation in physiological and metabolic parameters. Instead the use of a MOE of 30 is intended to include a factor of 10 for inter-individual variability in both pharmacokinetics and in pharmacodynamic sensitivity. It also includes a factor of 3 for possible greater pharmacodynamic sensitivity of humans to an NMP exposure compared to the rats used in the bioassays.

One source of uncertainty is around the dose metric: it is assumed that the parent NMP is the primary toxicant, that average concentration (or AUC) is a measure of risk for BW effects, and peak concentration for skeletal abnormalities. However, one must recognize that under any exposure scenario, AUC and peak concentration are closely related: as peak concentration increases, so does AUC and vice-versa. For example, limiting exposure to limit the peak concentration to avoid skeletal abnormalities also limits the AUC. Because both metrics have been used to estimate toxicological limits, possible exposures will be limited in both dimensions: the peak concentration is limited, even if it is associated with a relatively low AUC, and AUC is limited even if it is from more continuous low-level exposure where the peak is less high. This limits the possible impact of this uncertainty on total risk.

Another uncertainty is uncertainty around the potential contribution of NMP metabolites to toxicity. Risk would be inversely correlated with metabolic rate if the parent compound is responsible, while it will be positively correlated with metabolic rate if risk is due to a metabolite. Here, the fact that human PK data are available to evaluate the metabolic rate strongly mitigates the uncertainty; within the bounds of the remaining modest uncertainty, limiting AUC also limits the total amount of metabolism occurring. Because metabolism is the primary route of elimination, the total amount of metabolism is not highly sensitive to the metabolic rate: if metabolism is 25% less than predicted, it takes longer to eliminate the NMP, allowing more to be eliminated by other routes, but the total metabolism might only be reduced 20%. AUC of parent NMP and the total amount metabolized will remain closely correlated despite uncertainty in the metabolic rate. The risk from continuous (24 h/d, 7 d/w) exposure is not being evaluated for the NMP uses under consideration, hence there is not a concern for that type of scenario leading to a cumulative effect not captured by this analysis.

The specific elements listed above are those aspects of the model for which uncertainty is the greatest. But for the reasons given, none of them is believed to create a high level of uncertainty. Toxicity was evaluated for exposure by oral gavage, feed, dermal exposure, and inhalation. The reduction in pup bodyweight response appears to be more sensitive to inhalation exposure than dermal exposure: all internal doses are lower for the inhalation LOAEL than the dermal LOAEL. But this means that a human MOE based on the inhalation response will be protective compared to the response after dermal exposure. For skeletal abnormalities the dose-response relationship was comparable for each route, which gives more confidence that the model is providing meaningful predictions and allows the data from both routes to be combined in the dose-response analysis, increasing the statistical power of the analysis. This benefit is obtained because the PBPK model is available for use. Hence, there is little uncertainty in applying the PBPK model to estimate risk for either or both dermal and inhalation exposure , thanks to the bioassay results for multiple routes of exposure.

4.3.7 Risk Characterization Assumptions and Uncertainties

This risk characterization uses peer-reviewed human and rat PBPK models for NMP to make a direct comparison of internal doses (blood concentrations) predicted in humans in specific exposure scenarios to internal concentrations that occurred in rats in toxicology studies. The human PBPK models allows EPA to estimate total human exposures from combined inhalation and dermal exposures associated with specific exposure scenarios. The rat PBPK model facilitates integration of data from studies using different routes of exposure. Both models incorporate information on toxicokinetics, providing more robust exposure estimates and reducing uncertainties about species differences. As described above in Section 4.3.6, there are several assumptions and sources of uncertainty associated with the PBPK models, but these uncertainties are expected to have limited impact overall risk estimates.

The peer-reviewed human PBPK models for NMP allow EPA to estimate total human exposures from combined inhalation and dermal exposures associated with specific exposure scenarios. While the PBPK models allowed EPA to consider aggregate exposure across exposure routes, EPA did not have sufficient information to consider aggregate exposure across conditions of use. This is a source of uncertainty that may underestimate risk.

The relative exposures from dermal, inhalation and vapor through skin can be deduced by comparing the internal exposure to workers due to inhalation, vapor through skin and dermal liquid contact with internal exposure to ONUs due to inhalation and vapor through skin exposure (a subtraction technique). The chronic exposures to workers assuming no protective glove use and ONUs and calculated percent exposure due to dermal contact with liquid are shown in Table 4-54.

Table 4-54. Comparison of NMP Exposures by Route Showing Percent Exposure Due to Dermal Contact with Liquid from Chronic NMP Exposures

Occupational Exposure Scenario [a]	Exposure Level [b]	Chronic Exposure Worker [c], AUC (hr mg/L) No protective gloves	Chronic Exposure ONU [d], AUC (hr mg/L)	Percent Exposure Due to Dermal Contact with Liquid [e]
Manufacturing of NMP	Central Tendency	470	0.064	100%
	High-End	4500	0.41	100%
	What-if (Central Tendency)	40	0.016	100%
	What-if (High-End)	510	0.33	100%
Repackaging	Central Tendency	470	0.064	100%
	High-End	4500	0.41	100%
	What-if (Central Tendency)	40	0.016	100%
	What-if (High-End)	510	0.33	100%
Chemical Processing, Excluding Formulation	Central Tendency	470	0.069	100%
	High-End	4500	0.16	100%

Occupational Exposure Scenario [a]	Exposure Level [b]	Chronic Exposure Worker [c], AUC (hr mg/L) No protective gloves	Chronic Exposure ONU [d], AUC (hr mg/L)	Percent Exposure Due to Dermal Contact with Liquid [e]
	What-if (Central Tendency)	28	0.020	100%
	What-if (High-End)	60	0.058	100%
Incorporation into Formulation, Mixture, or Reaction Product – Drum unloading	Central Tendency	470	0.069	100%
	High-End	4500	0.16	100%
	What-if (Central Tendency)	28	0.020	100%
	What-if (High-End)	60	0.058	100%
Incorporation into Formulation, Mixture, or Reaction Product – Maintenance, analytical, loading	Central Tendency	22	0.074	100%
	High-End	4300	1.4	100%
Metal Finishing - Spray application	Central Tendency	76	0.066	100%
	High-End	2700	1.0	100%
Metal Finishing – Dip application	Central Tendency	77	0.21	100%
	High-End	2700	0.64	100%
Metal Finishing – Brush application	Central Tendency	77	0.85	99%
	High-End	2700	0.92	100%
Application of Paints, Coatings, Adhesives, and Sealants – Spray application	Central Tendency	1.4	0.054	96%
	High-End	230	0.93	100%
Application of Paints, Coatings, Adhesives, and Sealants – Roll/curtain application	Central Tendency	1.4	0.0063	100%
	High-End	230	0.055	100%
Application of Paints, Coatings, Adhesives, and Sealants – Dip application	Central Tendency	1.6	0.20	88%
	High-End	230	0.57	100%
Application of Paints, Coatings, Adhesives, and Sealants – Brush application	Central Tendency	2.2	0.84	62%
	High-End	230	0.85	100%
Recycling and Disposal	Central Tendency	350	0.053	100%
	High-End	4500	0.20	100%
	What-if (Central Tendency)	32	0.015	100%
	What-if (High-End)	110	0.097	100%

Occupational Exposure Scenario [a]	Exposure Level [b]	Chronic Exposure Worker [c], AUC (hr mg/L) No protective gloves	Chronic Exposure ONU [d], AUC (hr mg/L)	Percent Exposure Due to Dermal Contact with Liquid [e]
Paint and Coating Removal – Misc. removal	Central Tendency	29	6.7	77%
	High-End	810	13	98%
	What-if (Central Tendency)	5.6	0.34	94%
	What-if (High-End)	70	7.2	90%
Paint and coating removal – Graffiti removal	Central Tendency	36	0.21	99%
	High-End	440	0.94	100%
Other Electronics Manufacturing – Capacitor, resistor, coil, transformer, and other inductor mfg.	Central Tendency	77	0.61	99%
	High-End	4500	9.2	100%
Semiconductor Manufacturing – Container handling, small containers	Central Tendency	120	0.096	100%
	High-End	2100	0.26	100%
	What-if (Central Tendency)	1.4	0.0013	100%
	What-if (High-End)	78	0.022	100%
	Industry-proposed (Central Tendency)	0.017 [f]	0.0053	69%
	Industry-proposed (High-End)	0.27 [f]	0.022	92%
Semiconductor Manufacturing – Container handling, drums	Central Tendency	55	0.011	100%
	High-End	2100	0.54	100%
	What-if (Central Tendency)	0.28	0.000063	100%
	What-if (High-End)	24	0.015	100%
	Industry-proposed (Central Tendency)	0.0064 [f]	0.00063	90%
	Industry-proposed (High-End)	0.29 [f]	0.046	84%
Semiconductor Manufacturing – Fab worker	Central Tendency	2.6	0.021	99%
	High-End	21	0.12	99%
	What-if (Central Tendency)	4.5	0.038	99%
	What-if (High-End)	18	0.11	99%

Occupational Exposure Scenario [a]	Exposure Level [b]	Chronic Exposure Worker [c], AUC (hr mg/L) No protective gloves	Chronic Exposure ONU [d], AUC (hr mg/L)	Percent Exposure Due to Dermal Contact with Liquid [e]
Semiconductor Manufacturing – Fab worker with container changeout	Industry-proposed (Central Tendency)	0.0014 [f]	0.0011[f]	21%
	Industry-proposed (High-End)	0.016 [f]	0.010[f]	38%
Semiconductor Manufacturing – Maintenance	Central Tendency	55	0.013	100%
	High-End	9200	0.37	100%
	What-if (Central Tendency)	0.98	0.00024	100%
	What-if (High-End)	7900	0.34	100%
	Industry-proposed (Central Tendency)	0.070 [f]	0.00069	99%
	Industry-proposed (High-End)	2.6 [f]	0.031	99%
Semiconductor Manufacturing – Virgin NMP truck unloading [f]	Central Tendency	470	1.0	100%
	High-End	4500	1.1	100%
	What-if (Central Tendency)	200	1.0	100%
	What-if (High-End)	500	1.0	100%
	Industry-proposed (Central Tendency)	0.22 [f]	0.045	80%
	Industry-proposed (High-End)	1.9 [f]	0.14	93%
Semiconductor Manufacturing – Waste truck unloading	Central Tendency	350	0.12	100%
	High-End	3000	0.23	100%
	What-if (Central Tendency)	150	0.058	100%
	What-if (High-End)	370	0.058	100%
	Industry-proposed (Central Tendency)	0.15 [f]	0.010	93%
	Industry-proposed (High-End)	1.5 [f]	0.029	98%
Printing	Central Tendency	3.4	0.023	99%
	High-End	20	0.024	100%

Occupational Exposure Scenario [a]	Exposure Level [b]	Chronic Exposure Worker [c], AUC (hr mg/L) No protective gloves	Chronic Exposure ONU [d], AUC (hr mg/L)	Percent Exposure Due to Dermal Contact with Liquid [e]
	What-if (Central Tendency)	0.73	0.023	97%
	What-if (High-End)	2.0	0.023	99%
Writing	Central Tendency	0.0016	0.00016	90%
	High-End	0.0016	0.00032	80%
Soldering	Central Tendency	1.5	0.84	44%
	High-End	7.7	0.84	89%
Commercial Automotive Servicing	Central Tendency	3.0	1.3	57%
	High-End	110	8.9	92%
	What-if (Central Tendency)	0.92	0.51	45%
	What-if (High-End)	15	3.3	78%
Laboratory Use	Central Tendency	470	0.064	100%
	High-End	4500	0.95	100%
	What-if (Central Tendency)	190	0.037	100%
	What-if (High-End)	490	0.037	100%
Lithium Ion Cell Manufacturing – Container handling, small containers	Central Tendency	790	0.16	100%
	High-End	9200	0.35	100%
	What-if (Central Tendency)	39	0.013	100%
	What-if (High-End)	200	0.029	100%
Lithium Ion Cell Manufacturing – Container handling, drums	Central Tendency	120	0.021	100%
	High-End	9200	0.63	100%
	What-if (Central Tendency)	8.6	0.0017	100%
	What-if (High-End)	200	0.053	100%
Lithium Ion Cell Manufacturing – Cathode coating	Central Tendency	78	1.0	99%
	High-End	410	8.2	98%
	What-if (Central Tendency)	37	0.99	97%

Occupational Exposure Scenario [a]	Exposure Level [b]	Chronic Exposure Worker [c], AUC (hr mg/L) No protective gloves	Chronic Exposure ONU [d], AUC (hr mg/L)	Percent Exposure Due to Dermal Contact with Liquid [e]
	What-if (High-End)	290	8.2	97%
Lithium Ion Cell Manufacturing – Cathode slurry mixing	Central Tendency	77	0.46	99%
	High-End	400	2.0	100%
	What-if (Central Tendency)	9.0	0.45	95%
	What-if (High-End)	20	2.0	90%
Lithium Ion Cell Manufacturing – Research and development	Central Tendency	77	0.088	100%
	High-End	4500	0.93	100%
	What-if (Central Tendency)	46	0.083	100%
	What-if (High-End)	670	0.86	100%
Lithium Ion Cell Manufacturing – Miscellaneous additional activities	Central Tendency	78	1.2	98%
	High-End	4500	1.6	100%
	What-if (Central Tendency)	19	1.2	94%
	What-if (High-End)	1300	1.5	100%
Cleaning – Dip	Central Tendency	260	0.15	100%
	High-End	4400	0.65	100%
Cleaning – Spray / Wipe	Central Tendency	22	0.10	100%
	High-End	4200	0.65	100%
Fertilizer Application	Central Tendency	0.66	0.60	9%
	High-End	21	1.1	95%

[a] Use of PPE is not assumed for ONUs. Percent due to dermal liquid exposure is the worker exposure (inhalation, vapor through skin and dermal liquid contact) minus ONU exposure (inhalation and vapor through skin exposure) divided by worker exposure.

[b] Central tendency means: typical air concentration for most scenarios. High-end means worst-case air concentration for most scenarios. ONUs are not expected to have direct contact with NMP-containing liquids (see Section 2.4.1.1). These exposure scenarios do not assume glove use.

[c] See tables of exposure estimates in Section 4.2.2.

[d] See tables of exposure estimates in Section 4.2.3.

[e] Due to rounding 100% is shown when the inhalation and vapor through skin exposures are small relative to dermal liquid contact however inhalation and vapor through skin exposures are not zero, see the exposure estimates and MOEs calculation in Section 4.2.3.

[f] The SIA industry proposed PBPK runs assume all workers and fab ONUs always wear gloves with PF = 20.

Uncertainty factors used to generate benchmark MOEs used in the risk characterization account for various sources of uncertainty for each non-cancer POD. In this evaluation, benchmark MOEs for all scenarios are consistently low, reflecting the relatively low degree of overall uncertainty. As described in detail in Section 3.2.5.6, there are two uncertainty factors used in this risk characterization across both acute and chronic exposure scenarios:

- An interspecies uncertainty/variability factor of 3 (UF_A) was applied for animal-to-human extrapolation to account for toxicodynamic differences between species. Toxicokinetic differences are incorporated into PBPK models.
- A default intraspecies uncertainty/variability factor (UF_H) of 10 was applied to account for variation in sensitivity within human populations, including variation across gender, age, health status, or genetic makeup.

The human populations considered in this final risk evaluation include pregnant women and men and women of reproductive age in occupational and consumer settings. Although exposures to younger non-users may be possible, there is insufficient data regarding specific genetic and/or life stage differences that could impact NMP metabolism and toxicity for further refinement of quantitative risk estimates. EPA does not have sufficient information to determine whether these uncertainty factors may lead to an overestimation or underestimation of risk.

4.4 Potentially Exposed or Susceptible Subpopulations

TSCA Section 6(b)(4) requires that EPA conduct a risk evaluation to "*determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of cost or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use*." TSCA Section 3(12) states that "*the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly*."

As described in Section 3.2.5.3, certain biological characteristics may increase susceptibility to NMP exposure. The developmental effects identified as a critical human health endpoint for acute exposures in this risk evaluation are a major concern for pregnant women, the developing fetus, and women who may become pregnant. The reproductive effects identified as a critical human health endpoint for chronic exposures may be of concern for all males and females of reproductive age as well as for infants, children and adolescents whose reproductive systems are still developing. Other populations that may be more sensitive to the hazards of NMP exposure include people with pre-existing conditions, and people with lower metabolic capacity due to life stage, genetic variation, or impaired liver function. The magnitude of the effect of each of these factors alone or in combination on overall risk is unknown.

The acute and chronic PODs used in this risk characterization are based on studies that evaluated effects of exposure during sensitive life stages in rats. Toxicology data (Exxon, 1991) demonstrate early postnatal body weight decreases and early postnatal death increases at doses that are greater than the POD derived for decreased fertility from the same study. It is considered likely that these postnatal outcomes are the result of repeated exposures to NMP. These findings could be considered a surrogate for analysis of risks to newborns and young infants. Nonetheless , there is uncertainty around the impact of metabolic differences in newborns and young infants on susceptibility. There is also uncertainty around susceptibility of infants and young children to potential neurodevelopmental effects of NMP

which have been observed in animals exposed at a high dose, but have not been characterized at lower doses.

There is insufficient information to support a quantitative analysis of interindividual variability in other potentially susceptible populations. An uncertainty factor of 10 was applied to account for interindividual variability across gender, age, health status, genetic makeup, or other factors, but the actual effect of various factors contributing to biological susceptibility on overall risk is unknown.

As described in Section 2.5.1, EPA identified workers, occupational non-users, consumers of NMP-containing products and bystanders, including children, as potentially exposed populations. The exposure factors and hazard endpoints used in this risk evaluation are representative of the most sensitive subpopulations (*i.e.*, pregnant women or women who might become pregnant, male workers, and the fetus). The associated risk findings are expected to be protective of children and adolescents. In developing the risk evaluation, EPA analyzed the reasonably available information to ascertain whether some human receptor groups may have greater exposure than the general population to the hazard posed by a chemical. For example, EPA estimated acute exposures for children who may be located near the consumer user at the time of use and determined that these exposures were below levels that may pose a risk.

4.5 Aggregate and Sentinel Exposures

Section 2605(b)(4)(F)(ii) of TSCA requires EPA, as a part of the risk evaluation, to describe whether aggregate or sentinel exposures under the conditions of use were considered and the basis for their consideration. EPA has defined aggregate exposure as "*the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways* (40 CFR Section 702.33)."

In many exposure scenarios, NMP exposure occurs through multiple routes. Considering risk from a single exposure route at a time instead of evaluating total exposures could underestimate risk. This risk characterization therefore uses PBPK modeling to derive exposure estimates that account for multiple simultaneous routes of exposure to NMP. Exposure for each condition of use was evaluated by determining both the exposure to NMP vapor and dermal contact with the liquid. Time profiles of each type of exposure were estimated for a variety of job categories and household consumer uses, behaviors, and activity profiles. Vapor exposure is specified by the air concentration encountered as a function of time during the work day or for 24 h from the start of a household application. Dermal contact is characterized by the weight fraction (WF) of NMP in the product being used, the surface area of skin (hands) exposed, and the duration of the dermal exposure. For workplace exposures vapor and dermal exposures are assumed to be only simultaneous (both end at the end of the task, shift, or work day). For household exposures vapor exposure typically continues for some time after the application is complete due to slower air exchange but is lower for the rest of house than the location where the project is done, with movement of the individual between these zones included. Dermal exposure for consumers is also limited to the user's direct contact with the product as defined by the duration of use.

The availability of validated rat and human PBPK models that include a dermal compartment PBPK allowed EPA to integrate absorption from both vapor and liquid contact via three pathways: inhalation of vapors, absorption of liquid in contact with the skin, and absorption of vapor by exposed skin. Exhalation and desorption of vapor from skin are also post-exposure elimination pathways. Vapor absorption through the skin is a minor component of total exposure in most scenarios but is included for completeness and uses the same dermal resistance as liquid absorption to account for absorption from un-occluded areas of the face, neck, arms and hands. Use of a face mask is assumed to reduce

concentration inside the mask by a factor of 10 (*i.e.*, the mask has a protection factor, PF = 10) while use of gloves is assumed to reduce the surface area of the skin exposed to liquid NMP, where the PF was varied for different quality gloves.

While this assessment evaluates specific COUs based on exposure estimates that incorporate multiple routes of exposure, it does not consider the potential for aggregate exposures from multiple conditions of use. For example, it does not evaluate the aggregate risk to individuals exposed via occupational and consumer uses. This could result in an underestimation of risk.

EPA defines sentinel exposure as "*the exposure to a single chemical substance that represents the plausible upper bound of exposure relative to all other exposures within a broad category of similar or related exposures* (40 CFR Section 702.33)." In this risk evaluation, EPA considered sentinel exposure in the form of high-end estimates for consumer and occupational exposure scenarios which incorporate dermal and inhalation exposure, as these routes are expected to present the highest exposure potential based on details provided for the manufacturing, processing and use scenarios discussed in Section 2.4. The exposure calculation used to estimate dermal exposure to liquid is conservative for high-end occupational and consumer scenarios where it assumes full contact of both hands and no protective glove use.

4.6 Risk Conclusions

4.6.1 Environmental Risk Conclusions

EPA did not identify risks to fish, aquatic invertebrates or algae from NMP releases to ambient water. EPA used environmental release data from EPA's TRI and a "first-tier" exposure assessment to derive conservative estimates of NMP surface water concentrations near facilities reporting the highest NMP water releases. Using the 2015 and 2018 TRI data and EPA's Exposure and Fate Assessment Screening Tool (EFAST, Version 2014) EPA predicted NMP surface water concentrations for the acute and chronic scenarios, respectively. Table 4-2 and Table 4-3 summarize the RQs and days of exceedance used to characterize risk to aquatic organisms from acute and chronic exposures to NMP. Based on these values (acute RQs all < 1, and chronic RQs < 1 or RQ > 1 but < 20 days of exceedance) risk to aquatic organisms from acute or chronic exposure to NMP in surface water was not indicated.

During problem formulation, EPA also considered fate properties of NMP and performed first tier analysis of environmental risks from NMP exposure through sediment, land-applied biosolids, and ambient air. EPA did not identify environmental risks from these pathways. As described in problem formulation, NMP is not expected to adsorb to sediment due to its water solubility (>1000 g/L) and low partitioning to organic matter (Log K_{oc} = 0.9). No ecotoxicity studies were identified for sediment dwelling organisms; however, the reasonably available hazard data indicate a low concern for NMP toxicity to aquatic organisms and plants. Because NMP toxicity to sediment-dwelling invertebrates is expected to be comparable to that of aquatic invertebrates and NMP is unlikely to accumulate in sediment, a low risk concern is expected for this environmental compartment.

During problem formulation, EPA did not identify risks from land releases of NMP, including those that may result from land application of biosolids. NMP exhibits high water solubility and limited potential for adsorption to organic matter; therefore, land releases will ultimately partition to the aqueous phase (*i.e.*, biosolids associated wastewater and soil pore water) upon release into the environment. Because NMP readily biodegrades in environments with active microbial populations, NMP residues that remain following wastewater treatment are not expected to persist. NMP concentrations in biosolids-associated water are expected to decrease, primarily via aerobic degradation, during transport, processing

(including dewatering), handling, and land application of biosolids (which may include spraying). Migration of NMP between ground water and surface water has not been documented but may be mitigated by abiotic and biotic degradation in the water column.

In addition, the bioaccumulation potential for NMP are expected to be low (BCF = 3.16, BAF= 0.9; see Table 2-1). Negligible volatilization of NMP is expected from moist soil and wastewater. Because NMP exhibits low volatility and readily biodegrades under aerobic conditions, the concentration in ambient air is unlikely to reach levels that would present a risk concern for terrestrial organisms. In a quantitative analyses completed by EPA in support of the derivation of Ecological Screening Levels (Eco-SSLs) for soils exposures and risks associated with inhalation of chemical contamination in soils for terrestrial wildlife are negligible compared to oral exposures (incidental ingestion and dietary) (ranged from 0.0001% to 0.1022% of the oral risks, and averaged 0.0172% of oral risks) (U.S. EPA, 2005).

4.6.2 Human Health Risk Conclusions

4.6.1.1 Summary of Risk Estimates for Workers and ONUs

Table 4-55 summarizes the acute and chronic risks of combined inhalation, dermal and vapor-through-skin exposures for all occupational exposure scenarios. Exposure and risk estimates for each occupational exposure scenario are described in more detail in Section 2.4.1.2 and Section 4.2.2, respectively. Risk estimates for each condition of use are shown for use without gloves or respirators, with gloves or respirators alone, or with both gloves and respirators. For PPE use, risk estimates are primarily shown for glove PFs of 5 and respirator APFs of 10, unless otherwise indicated in footnotes. Risk estimates that indicate risk relative to the benchmark MOE (*i.e.*, non-cancer MOEs that are below the benchmark MOE) are highlighted by shading the cell.

In general, the conditions of use that present the lowest concern for human health risks include those that incorporate a high level of containment or small-scale use of NMP. The conditions of use which involve a lower level of containment, elevated temperatures or high intensity use show greater risk even when PPE is considered. For example, high-end occupational exposure estimates for NMP use in cleaning, metal finishing, electronic parts manufacturing, automotive servicing, and use in (or removal of) paints, coatings, adhesives and sealants show risks that are not mitigated via glove use.

Risk estimates for ONUs indicate risk relative to the benchmark MOEs for several conditions of use, including paint and coating removal, commercial automotive servicing, and some electronics parts manufacturing. ONUs are assumed not to wear respirators.

EPA has high confidence in the POD used to evaluate risks associated with acute exposure and medium confidence in the POD used to evaluate chronic NMP exposure. As discussed in Section 3.2.6, post-implantation loss (resorptions and fetal mortality) and reduced fertility were considered relevant hazards for evaluating risks following acute and chronic NMP exposure, respectively. While there is some uncertainty regarding temporal windows of vulnerability for developmental toxicity and whether the timing of a single exposure can produce a permanent adverse effect on human development, EPA considers the post-implantation loss endpoint associated with NMP exposure to be applicable to acute exposures. The reasonably available literature suggests that a single developmental exposure may have sustained effects on the conceptus. Fetal mortality represents the most severe endpoint associated with the developmental hazard profile for NMP. Reduced fertility in males is the most sensitive effect associated with chronic exposures. The chronic POD based on effects on reduced male fertility is supported by effects on female fecundity and developmental toxicity in a similar dose range.

Table 4-55. Summary of Risk Estimates for Aggregate Exposures to Workers by Condition of Use

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
Manufacture/ Domestic Manufacture	Domestic Manufacture [a]	Section 2.4.1.2.1 – Manufacturing	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	32	32	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
				Central Tendency	10	65	65	**6.0**	**6.0**
				High-End	10	**23**	**23**	**1.3**	**1.3**
			ONU	Central Tendency	1	--	--	2,870	NA
				High-End	1	--	--	443	NA
Manufacture/ Import	Import	Section 2.4.1.2.2 – Repackaging	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	32	32	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,870	NA
				High-End	1	--	--	443	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
Processing/ Processing as a reactant or intermediate	Intermediate in Plastic Material and Resin Manufacturing	Section 2.4.1.2.3 – Chemical Processing, Excluding Formulation	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
	Other Non-Incorporative Processing			Central Tendency	5	32	32	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,642	NA
				High-End	1	--	--	1,130	NA
Processing/ Incorporated into formulation, mixture or reaction product	Adhesives and sealant chemicals in Adhesive Manufacturing	Section 2.4.1.2.4 – Incorporation into Formulation, Mixture, or Reaction Product (unloading drums)	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
	Anti-adhesive agents in Printing and Related Support Activities			High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
	Paint additives and coating additives not described by other codes in Paint and Coating Manufacturing; and Print Ink Manufacturing			Central Tendency	5	32	32	**2.8**	**2.8**
	Processing aids not otherwise listed in Plastic Material and Resin Manufacturing			High-End	5	**10**	**10**	**0.6**	**0.6**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
	Solvents (for cleaning or degreasing) in Non-Metallic Mineral Product Manufacturing; Machinery Manufacturing; Plastic Material and Resin; Manufacturing; Primary Metal Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Preparation Manufacturing; Printing and Related Support Activities; Services; Wholesale and Retail Trade		ONU	Central Tendency	1	--	--	2,642	NA
	Surface active agents in Soap, Cleaning Compound and Toilet Preparation Manufacturing			High-End	1	--	--	1,130	NA
	Plating agents and surface treating agents in Fabricated Metal Product Manufacturing	Section 2.4.1.2.4 – Incorporation into Formulation, Mixture, or Reaction Product (miscellaneous)	Worker	Central Tendency	1	91	91	**8.4**	**8.4**
	Solvents (which become part of product formulation or mixture) in Electrical Equipment, Appliance and Component Manufacturing; Other Manufacturing; Paint and Coating Manufacturing; Print Ink Manufacturing;			High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	459	465	43	43
				High-End	5	**10**	**10**	**0.6**	**0.6**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
	Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Wholesale and Retail Trade								
	Other uses in Oil and Gas Drilling, Extraction and Support Activities; Plastic Material and Resin Manufacturing; Services		ONU	Central Tendency	1	--	--	2,487	NA
				High-End	1	--	--	133	NA
Processing/ Incorporated into article	Lubricants and lubricant additives in Machinery Manufacturing	Section 2.4.1.2.5 – Metal Finishing (Spray Application)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.7**	**1.7**	**0.1**	**0.1**
				Central Tendency	5	143	144	**13**	**13**
				High-End	5	**14**	**14**	**0.8**	**0.8**
			ONU	Central Tendency	1	--	--	2,763	NA
				High-End	1	--	--	184	NA
		Section 2.4.1.2.5 – Metal Finishing (Dip)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.7**	**1.7**	**0.1**	**0.1**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				Central Tendency	5	142	143	**13**	**13**
				High-End	5	**14**	**14**	**0.8**	**0.8**
			ONU	Central Tendency	1	--	--	859	NA
				High-End	1	--	--	286	NA
		Section 2.4.1.2.5 – Metal Finishing (Brush)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.7**	**1.7**	**0.1**	**0.1**
				Central Tendency	5	135	141	**12**	**13**
				High-End	5	**14**	**14**	**0.8**	**0.8**
			ONU	Central Tendency	1	--	--	215	NA
				High-End	1	--	--	199	NA
	Paint additives and coating additives not described by other codes in Transportation Equipment Manufacturing	Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Spray Application)	Worker	Central Tendency	1	1,395	1,436	130	134
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	6,070	6,929	567	645
				High-End	5	81	82	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	3,394	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	1	--	--	197	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Roll/Curtain)	Worker	Central Tendency	1	1,445	1,450	134	135
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	7,110	7,229	661	672
				High-End	5	83	83	**4.9**	**4.9**
			ONU	Central Tendency	1	--	--	28,925	NA
				High-End	1	--	--	3,329	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Dip)	Worker	Central Tendency	1	1,261	1,396	118	130
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	4,182	6,142	394	576
				High-End	5	81	83	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	911	NA
				High-End	1	--	--	319	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Brush)	Worker	Central Tendency	1	890	1,244	84	117
				High-End	1	**14**	**14**	**0.8**	**0.8**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				Central Tendency	5	1,780	4,118	169	393
				High-End	5	81	82	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	218	NA
				High-End	1	--	--	214	NA
	Solvents (which become part of product formulation or mixture), including in Textiles, Apparel and Leather Manufacturing	Section 2.4.1.2.4 – Incorporation into Formulation, Mixture, or Reaction Product (unloading drums)	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
			Worker	High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
			Worker	Central Tendency	5	32	32	**2.8**	**2.8**
			Worker	High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,642	NA
			ONU	High-End	1	--	--	1,130	NA
		Section 2.4.1.2.4 – Incorporation into Formulation, Mixture, or Reaction Product (miscellaneous)	Worker	Central Tendency	1	91	91	**8.4**	**8.4**
			Worker	High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
			Worker	Central Tendency	5	459	465	43	43
			Worker	High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,487	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
			ONU	High-End	1	--	--	133	NA
Processing/ Incorporated into article	Other, including in Plastic Product Manufacturing	Section 2.4.1.2.3 – Chemical Processing, Excluding Formulation	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	32	32	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,642	NA
				High-End	1	--	--	1,130	NA
Processing/ Recycling	Recycling	Section 2.4.1.2.7 – Recycling and Disposal	Worker	Central Tendency	1	**6.8**	**6.8**	**0.5**	**0.5**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	40	40	**3.6**	**3.6**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	3,432	NA
				High-End	1	--	--	926	NA
Processing/ Repackaging	Wholesale and Retail Trade	Section 2.4.1.2.2 – Repackaging	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				Central Tendency	5	32	32	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,870	NA
				High-End	1	--	--	443	NA
Distribution in Commerce/ Distribution	Distribution in commerce	Distribution in commerce	Worker	Central Tendency	N/A - Not Separately addressed; exposures/releases from distribution are considered within each condition of use				
Industrial, and commercial use/ Paint and coatings	Paint and coating removers	Section 2.4.1.2.8 - Removal of Paints, Coatings, Adhesives, and Sealants (Misc. Removal)	Worker	Central Tendency	1	70	85	**6.4**	**7.9**
	Adhesives removers			High-End	1	**4.4**	**4.6**	**0.2**	**0.2**
				Central Tendency	5	182	339	**17**	32
				High-End	5	**27**	31	**1.6**	**1.8**
			ONU	Central Tendency	1	--	--	**27**	NA
				High-End	1	--	--	**14**	NA
		Section 2.4.1.2.8 - Removal of Paints, Coatings, Adhesives, and Sealants (Graffiti Removal)	Worker	Central Tendency	1	55	56	**5.0**	**5.1**
				High-End	1	**7.7**	**7.7**	**0.4**	**0.4**
				Central Tendency	5	280	286	**26**	**26**
				High-	5	49	49	**2.9**	**2.9**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				End					
			ONU	Central Tendency	1	--	--	868	NA
				High-End	1	--	--	194	NA
	Lacquers, stains, varnishes, primers and floor finishes	Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Spray Application)	Worker	Central Tendency	1	1,395	1,436	130	134
	Powder coatings (surface preparation)			High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	6,070	6,929	567	645
				High-End	5	81	82	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	3,394	NA
				High-End	1	--	--	197	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Roll/Curtain)	Worker	Central Tendency	1	1,445	1,450	134	135
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	7,110	7,229	661	672
				High-End	5	83	83	**4.9**	**4.9**
			ONU	Central Tendency	1	--	--	28,925	NA
				High-End	1	--	--	3,329	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Dip)	Worker	Central Tendency	1	1,261	1,396	118	130
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	4,182	6,142	394	576
				High-End	5	81	83	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	911	NA
				High-End	1	--	--	319	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Brush)	Worker	Central Tendency	1	890	1,244	84	117
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	1,780	4,118	169	393
				High-End	5	81	82	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	218	NA
				High-End	1	--	--	214	NA
Industrial, and commercial use/ Paint additives and coating additives not	Use in Computer and Electronic Product Manufacturing in Electronic Parts Manufacturing [a]	Section 2.4.1.2.9 – Other Electronics Manufacturing (Capacitor, Resistor, Coil, Transformer, and Other Inductor Manufacturing)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	137	142	**13**	**13**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
described by other codes				High-End	5	**9.6**	**9.9**	**0.5**	**0.6**
				Central Tendency	10	266	284	**25**	**26**
				High-End	10	**21**	**22**	**1.2**	**1.3**
			ONU	Central Tendency	1	--	--	299	NA
				High-End	1	--	--	**20**	NA
	Use in Computer and Electronic Product Manufacturing in Semiconductor Manufacturing [a]	Section 2.4.1.2.10 – Semiconductor Manufacturing (Container Handling, Small Containers)	Worker	Central Tendency	1	**23**	**23**	**1.5**	**1.5**
				High-End	1	**2.3**	**2.3**	**0.1**	**0.1**
				Central Tendency	5	125	125	**8.7**	**8.8**
				High-End	5	**21**	**21**	**0.9**	**0.9**
				Central Tendency	10	252	253	**18**	**18**
				High-End	10	47	47	**2.1**	**2.1**
				Central Tendency	20	504	510	35	36
				High-End	20	98	98	**4.3**	**4.3**
			ONU	Central Tendency	1	--	--	1,909	NA
				High-End	1	--	--	704	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
		Section 2.4.1.2.10 – Semiconductor Manufacturing (Container Handling, Drums)	Worker	Central Tendency	1	48	48	**3.3**	**3.3**
				High-End	1	**2.3**	**2.3**	**0.1**	**0.1**
				Central Tendency	5	253	253	**18**	**18**
				High-End	5	**21**	**21**	**0.9**	**0.9**
				Central Tendency	10	508	509	36	36
				High-End	10	46	47	**2.0**	**2.1**
				Central Tendency	20	1,020	1,021	72	72
				High-End	20	97	98	**4.3**	**4.3**
			ONU	Central Tendency	1	--	--	15,989	NA
				High-End	1	--	--	336	NA
		Section 2.4.1.2.10 – Semiconductor Manufacturing (Fab Worker, 75% Body Coverage)	Worker	Central Tendency	1	1,013	1,019	71	72
				High-End	1	198	199	**8.7**	**8.8**
				Central Tendency	5	4,916	5,067	346	356
				High-End	5	988	1,011	44	44
				Central Tendency	10	9,461	10,037	667	707

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	10	1,925	2,012	85	89
				Central Tendency	20	17,586	19,683	1,242	1,387
				High-End	20	3,646	3,971	161	175
			ONU	Central Tendency	1	--	--	8,540	NA
				High-End	1	--	--	1,465	NA
		Section 2.4.1.2.10 – Semiconductor Manufacturing (Maintenance)	Worker	Central Tendency	1	48	48	**3.3**	**3.3**
				High-End	1	**0.6**	**0.6**	**0.02**	**0.02**
				Central Tendency	5	252	253	**18**	**18**
				High-End	5	**7.9**	**8.0**	**0.3**	**0.3**
				Central Tendency	10	508	509	36	36
				High-End	10	**19**	**19**	**0.8**	**0.8**
				Central Tendency	20	1,020	1,021	72	72
				High-End	20	43	43	**1.9**	**1.9**
			ONU	Central Tendency	1	--	--	14,630	NA
				High-End	1	--	--	492	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
		Section 2.4.1.2.10 – Semiconductor Manufacturing (Waste Truck Loading)	Worker	Central Tendency	1	**6.8**	**6.8**	**0.5**	**0.5**
				High-End	1	**1.5**	**1.5**	**0.1**	**0.1**
				Central Tendency	5	40	40	**3.6**	**3.6**
				High-End	5	**13**	**13**	**0.7**	**0.7**
				Central Tendency	10	81	82	**7.4**	**7.5**
				High-End	10	**29**	**29**	**1.7**	**1.7**
				Central Tendency	20	165	165	**15**	**15**
				High-End	20	61	62	**3.6**	**3.6**
			ONU	Central Tendency	1	--	--	1,584	NA
				High-End	1	--	--	792	NA
	Use in Construction, Fabricated Metal Product Manufacturing, Machinery Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Primary Metal Manufacturing, Transportation Equipment Manufacturing, Wholesale and Retail Trade	Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Spray Application)	Worker	Central Tendency	1	1,395	1,436	130	134
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	6,070	6,929	567	645
				High-End	5	81	82	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	3,394	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	1	--	--	197	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Roll/Curtain)	Worker	Central Tendency	1	1,445	1,450	134	135
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	7,110	7,229	661	672
				High-End	5	83	83	**4.9**	**4.9**
			ONU	Central Tendency	1	--	--	28,925	NA
				High-End	1	--	--	3,329	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Dip)	Worker	Central Tendency	1	1,261	1,396	118	130
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	4,182	6,142	394	576
				High-End	5	81	83	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	911	NA
				High-End	1	--	--	319	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Brush)	Worker	Central Tendency	1	890	1,244	84	117
				High-End	1	**14**	**14**	**0.8**	**0.8**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				Central Tendency	5	1,780	4,118	169	393
				High-End	5	81	82	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	218	NA
				High-End	1	--	--	214	NA
Industrial, and commercial use/ Solvents (for cleaning or degreasing)	Use in Electrical Equipment Appliance and Component Manufacturing [a]	Section 2.4.1.2.9 – Other Electronics Manufacturing (Capacitor, Resistor, Coil, Transformer, and Other Inductor Manufacturing)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	137	142	**13**	**13**
				High-End	5	**9.6**	**9.9**	**0.5**	**0.6**
				Central Tendency	10	266	284	**25**	**26**
				High-End	10	**21**	**22**	**1.2**	**1.3**
			ONU	Central Tendency	1	--	--	299	NA
				High-End	1	--	--	**20**	NA
	Use in Electrical Equipment Appliance and Component Manufacturing in Semiconductor Manufacturing [a]	Section 2.4.1.2.10 – Semiconductor Manufacturing (Container Handling, Small Containers)	Worker	Central Tendency	1	**23**	**23**	**1.5**	**1.5**
				High -End	1	**2.3**	**2.3**	**0.1**	**0.1**
				Central Tendency	5	125	125	**8.7**	**8.8**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	5	**21**	**21**	**0.9**	**0.9**
				Central Tendency	10	252	253	**18**	**18**
				High-End	10	47	47	**2.1**	**2.1**
				Central Tendency	20	504	510	35	36
				High-End	20	98	98	**4.3**	**4.3**
			ONU	Central Tendency	1	--	--	1,909	NA
				High-End	1	--	--	704	NA
		Section 2.4.1.2.10 – Semiconductor Manufacturing (Container Handling, Drums)	Worker	Central Tendency	1	48	48	**3.3**	**3.3**
				High-End	1	**2.3**	**2.3**	**0.1**	**0.1**
				Central Tendency	5	253	253	**18**	**18**
				High-End	5	**21**	**21**	**0.9**	**0.9**
				Central Tendency	10	508	509	36	36
				High-End	10	46	47	**2.0**	**2.1**
				Central Tendency	20	1,020	1,021	72	72
				High-End	20	97	98	**4.3**	**4.3**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
			ONU	Central Tendency	1	--	--	15,989	NA
				High-End	1	--	--	336	NA
		Section 2.4.1.2.10 – Semiconductor Manufacturing (Fab Worker, 75% Body Coverage)	Worker	Central Tendency	1	1,013	1,019	71	72
				High-End	1	198	199	**8.7**	**8.8**
				Central Tendency	5	4,916	5,067	346	356
				High-End	5	988	1,011	44	44
				Central Tendency	10	9,461	10,037	667	707
				High-End	10	1,925	2,012	85	89
				Central Tendency	20	17,586	19,683	1,242	1,387
				High-End	20	3,646	3,971	161	175
			ONU	Central Tendency	1	--	--	8,540	NA
				High-End	1	--	--	1,465	NA
		Section 2.4.1.2.10 – Semiconductor Manufacturing (Maintenance)	Worker	Central Tendency	1	48	48	**3.3**	**3.3**
				High-End	1	**0.6**	**0.6**	**0.02**	**0.02**
				Central Tendency	5	252	253	**18**	**18**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	5	**7.9**	**8.0**	**0.3**	**0.3**
				Central Tendency	10	508	509	36	36
				High-End	10	**19**	**19**	**0.8**	**0.8**
				Central Tendency	20	1,020	1,021	72	72
				High-End	20	43	43	**1.9**	**1.9**
			ONU	Central Tendency	1	--	--	14,630	NA
				High-End	1	--	--	492	NA
		Section 2.4.1.2.10 – Semiconductor Manufacturing (Virgin NMP Truck Unloading)	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	31	31	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
				Central Tendency	10	63	65	**5.8**	**5.9**
				High-End	10	**23**	**23**	**1.3**	**1.3**
				Central Tendency	20	125	131	**11**	**12**
				High-End	20	48	49	**2.8**	**2.9**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
			ONU	Central Tendency	1	--	--	179	NA
				High-End	1	--	--	170	NA
		Section 2.4.1.2.10 – Semiconductor Manufacturing (Waste Truck Loading)	Worker	Central Tendency	1	**6.8**	**6.8**	**0.5**	**0.5**
				High-End	1	**1.5**	**1.5**	**0.1**	**0.1**
				Central Tendency	5	40	40	**3.6**	**3.6**
				High-End	5	**13**	**13**	**0.7**	**0.7**
				Central Tendency	10	81	82	**7.4**	**7.5**
				High-End	10	**29**	**29**	**1.7**	**1.7**
				Central Tendency	20	165	165	**15**	**15**
				High-End	20	61	62	**3.6**	**3.6**
			ONU	Central Tendency	1	--	--	1,584	NA
				High-End	1	--	--	792	NA
Industrial, and commercial use/ Ink, toner, and colorant products	Printer Ink	Section 2.4.1.2.11 - Printing and Writing: Printing	Worker	Central Tendency	1	575	578	53	54
				High-End	1	158	158	**9.4**	**9.4**
				Central Tendency	5	2,812	2,882	261	268

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	5	802	805	48	48
			ONU	Central Tendency	1	--	--	7,888	NA
				High-End	1	--	--	7,520	NA
	Inks in writing equipment	Section 2.4.1.2.11 - Printing and Writing: Writing	Worker	Central Tendency	1	470,210	470,210	116,016	116,016
				High-End	1	470,210	470,210	116,016	116,016
				Central Tendency	5	2,357,126	2,357,126	578,404	578,404
				High-End	5	2,357,126	2,357,126	578,404	578,404
			ONU	Central Tendency	1	--	--	1,159,299	NA
				High-End	1	--	--	580,042	NA
Industrial, and commercial use/ Processing aids, specific to petroleum production	Petrochemical Manufacturing	Section 2.4.1.2.3 - Chemical Processing, Excluding Formulation	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	32	32	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,642	NA
				High-End	1	--	--	1,130	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
Industrial, and commercial use/ Other Uses	Other uses in Oil and Gas Drilling, Extraction and Support Activities	Section 2.4.1.2.3 - Chemical Processing, Excluding Formulation	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	32	32	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,642	NA
				High-End	1	--	--	1,130	NA
	Functional Fluids (closed systems)	Section 2.4.1.2.3 - Chemical Processing, Excluding Formulation	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	32	32	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,642	NA
				High-End	1	--	--	1,130	NA
Industrial, and commercial use/ Adhesives and sealants	Adhesives and sealant chemicals including binding agents	Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Spray Application)	Worker	Central Tendency	1	1,395	1,436	130	134
				High-End	1	**14**	**14**	**0.8**	**0.8**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
	Single component glues and adhesives, including lubricant adhesives			Central Tendency	5	6,070	6,929	567	645
	Two-component glues and adhesives, including some resins			High-End	5	81	82	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	3,394	NA
				High-End	1	--	--	197	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Roll/Curtain)	Worker	Central Tendency	1	1,445	1,450	134	135
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	7,110	7,229	661	672
				High-End	5	83	83	**4.9**	**4.9**
			ONU	Central Tendency	1	--	--	28,925	NA
				High-End	1	--	--	3,329	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Dip)	Worker	Central Tendency	1	1,261	1,396	118	130
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	4,182	6,142	394	576
				High-End	5	81	83	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	911	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	1	--	--	319	NA
		Section 2.4.1.2.6 – Application of Paints, Coatings, Adhesives, and Sealants (Brush)	Worker	Central Tendency	1	890	1,244	84	117
				High-End	1	**14**	**14**	**0.8**	**0.8**
				Central Tendency	5	1,780	4,118	169	393
				High-End	5	81	82	**4.8**	**4.9**
			ONU	Central Tendency	1	--	--	218	NA
				High-End	1	--	--	214	NA
Industrial, and commercial use/ Other uses	Soldering materials	Section 2.4.1.2.12 – Soldering	Worker	Central Tendency	1	1,285	2,180	122	207
				High-End	1	400	436	**24**	**26**
				Central Tendency	5	2,030	5,747	194	555
				High-End	5	1,398	1,964	84	118
			ONU	Central Tendency	1	--	--	218	NA
				High-End	1	--	--	218	NA
	Anti-freeze and de-icing products	Section 2.4.1.2.13 - Commercial Automotive Servicing	Worker	Central Tendency	1	651	962	62	91
	Automotive care products			High-End	1	**28**	**29.8**	**1.6**	**1.8**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
	Lubricants and greases			Central Tendency	5	1,207	2,986	115	286
				High -End	5	111	149	**6.7**	**8.9**
			ONU	Central Tendency	1	--	--	141	NA
				High-End	1	--	--	**21**	NA
	Metal products not covered elsewhere	Section 2.4.1.2.5 – Metal Finishing (Spray Application)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.7**	**1.7**	**0.1**	**0.1**
				Central Tendency	5	143	144	**13**	**13**
				High-End	5	**14**	**14**	**0.8**	**0.8**
			ONU	Central Tendency	1	--	--	2,763	NA
				High-End	1	--	--	184	NA
		Section 2.4.1.2.5 – Metal Finishing (Dip)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.7**	**1.7**	**0.1**	**0.1**
				Central Tendency	5	142	143	**13**	**13**
				High-End	5	**14**	**14**	**0.8**	**0.8**
			ONU	Central Tendency	1	--	--	859	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	1	--	--	286	NA
		Section 2.4.1.2.5 – Metal Finishing (Brush)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.7**	**1.7**	**0.1**	**0.1**
				Central Tendency	5	135	141	**12**	**13**
				High-End	5	**14**	**14**	**0.8**	**0.8**
			ONU	Central Tendency	1	--	--	215	NA
				High-End	1	--	--	199	NA
	Lubricant and lubricant additives, including hydrophilic coatings	Section 2.4.1.2.5 – Metal Finishing (Spray Application)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.7**	**1.7**	**0.1**	**0.1**
				Central Tendency	5	143	144	**13**	**13**
				High-End	5	**14**	**14**	**0.8**	**0.8**
			ONU	Central Tendency	1	--	--	2,763	NA
				High-End	1	--	--	184	NA
		Section 2.4.1.2.5 – Metal Finishing (Dip)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.7**	**1.7**	**0.1**	**0.1**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				Central Tendency	5	142	143	**13**	**13**
				High-End	5	**14**	**14**	**0.8**	**0.8**
			ONU	Central Tendency	1	--	--	859	NA
				High-End	1	--	--	286	NA
		Section 2.4.1.2.5 – Metal Finishing (Brush)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.7**	**1.7**	**0.1**	**0.1**
				Central Tendency	5	135	141	**12**	**13**
				High-End	5	**14**	**14**	**0.8**	**0.8**
			ONU	Central Tendency	1	--	--	215	NA
				High-End	1	--	--	199	NA
	Laboratory chemicals	Section 2.4.1.2.14 - Laboratory Use	Worker	Central Tendency	1	**5.3**	**5.3**	**0.4**	**0.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	32	32	**2.8**	**2.8**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	2,847	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	1	--	--	193	NA
	Lithium Ion Battery Manufacturing [a]	Section 2.4.1.2.15 - Lithium Ion Cell Manufacturing (Small Container Handling)	Worker	Central Tendency	1	**4.1**	**4.1**	**0.2**	**0.2**
				High-End	1	**0.6**	**0.6**	**0.02**	**0.02**
				Central Tendency	5	**27**	**27**	**1.9**	**1.9**
				High-End	5	**8.0**	**8.0**	**0.3**	**0.3**
				Central Tendency	10	58	58	**4.0**	**4.0**
				High-End	10	**19**	**19**	**0.8**	**0.8**
				Central Tendency	20	119	119	**8.3**	**8.3**
				High-End	20	43	43	**1.9**	**1.9**
			ONU	Central Tendency	1	--	--	1,172	NA
				High-End	1	--	--	527	NA
		Section 2.4.1.2.15 - Lithium Ion Cell Manufacturing (Drum Handling)	Worker	Central Tendency	1	**23**	**23**	**1.5**	**1.5**
				High-End	1	**0.6**	**0.6**	**0.02**	**0.02**
				Central Tendency	5	125	125	**8.8**	**8.8**
				High-End	5	**7.9**	**8.0**	**0.3**	**0.3**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				Central Tendency	10	254	254	**18**	**18**
				High-End	10	**19**	**19**	**0.8**	**0.8**
				Central Tendency	20	511	511	36	36
				High-End	20	43	43	**1.9**	**1.9**
			ONU	Central Tendency	1	--	--	8,792	NA
				High-End	1	--	--	290	NA
		Section 2.4.1.2.15 - Lithium Ion Cell Manufacturing (Cathode Coating)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**8.1**	**8.3**	**0.4**	**0.5**
				Central Tendency	5	134	141	**12**	**13**
				High-End	5	46	51	**2.7**	**3.0**
				Central Tendency	10	253	280	**23**	**26**
				High-End	10	84	102	**5.0**	**6.1**
				Central Tendency	20	450	543	42	51
				High-End	20	139	195	**8.4**	**12**
			ONU	Central Tendency	1	--	--	183	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	1	--	--	**22**	NA
		Section 2.4.1.2.15 - Lithium Ion Cell Manufacturing (Cathode Slurry Mixing)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**8.3**	**8.4**	**0.5**	**0.5**
				Central Tendency	5	139	143	**13**	**13**
				High-End	5	51	53	**3.0**	**3.1**
				Central Tendency	10	272	285	**25**	**26**
				High-End	10	102	108	**6.1**	**6.4**
				Central Tendency	20	514	564	48	52
				High-End	20	195	216	**12**	**13**
			ONU	Central Tendency	1	--	--	401	NA
				High-End	1	--	--	93	NA
		Section 2.4.1.2.15 - Lithium Ion Cell Manufacturing (Research and Development)	Worker	Central Tendency	1	**27**	**27**	**2.4**	**2.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	143	143	**13**	**13**
				High-End	5	**10**	**10**	**0.6**	**0.6**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				Central Tendency	10	287	289	**27**	**27**
				High-End	10	**23**	**23**	**1.3**	**1.3**
				Central Tendency	20	570	579	53	54
				High-End	20	48	49	**2.9**	**2.9**
			ONU	Central Tendency	1	--	--	2,077	NA
				High-End	1	--	--	197	NA
		Section 2.4.1.2.15 - Lithium Ion Cell Manufacturing (Miscellaneous)	Worker	Central Tendency	1	**26**	**27**	**2.3**	**2.4**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	131	140	**12**	**13**
				High-End	5	**10**	**10**	**0.6**	**0.6**
				Central Tendency	10	245	277	**23**	**26**
				High-End	10	**22**	**23**	**1.3**	**1.3**
				Central Tendency	20	426	534	40	50
				High-End	20	48	49	**2.8**	**2.9**
			ONU	Central Tendency	1	--	--	147	NA

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				High-End	1	--	--	115	NA
	Cleaning and furniture care products, including wood cleaners, gasket removers	Section 2.4.1.2.16 – Cleaning (Dip Cleaning)	Worker	Central Tendency	1	**8.8**	**8.8**	**0.7**	**0.7**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	50	50	**4.5**	**4.5**
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	1,217	NA
				High-End	1	--	--	281	NA
		Section 2.4.1.2.16 – 2.4.1.2.16 (Spray/Wipe Cleaning)	Worker	Central Tendency	1	90	90	**8.3**	**8.3**
				High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
				Central Tendency	5	451	459	42	43
				High-End	5	**10**	**10**	**0.6**	**0.6**
			ONU	Central Tendency	1	--	--	1,774	NA
				High-End	1	--	--	280	NA
	Fertilizer and other agricultural chemical manufacturing-processing aids and solvents	Section 2.4.1.2.17 - Fertilizer Application	Worker	Central Tendency	1	2,892	8,571	279	849
				High-End	1	149	156	**8.9**	**9.3**

Life Cycle State/ Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Level	Glove PF (1 = no protective gloves)	Acute MOEs *Benchmark MOE = 30*		Chronic MOEs *Benchmark MOE = 30*	
						No Respirator	With Respirator (APF 10) [b]	No Respirator	With Respirator (APF 10) [b]
				Central Tendency	5	3,210	12,118	307	1,196
				High-End	5	628	754	38	45
			ONU	Central Tendency	1	--	--	304	NA
				High-End	1	--	--	171	NA
Disposal	Industrial pre-treatment	Section 2.4.1.2.7 – Recycling and Disposal	Worker	Central Tendency	1	**6.8**	**6.8**	**0.5**	**0.5**
	Industrial wastewater treatment			High-End	1	**1.1**	**1.1**	**0.04**	**0.04**
	Publicly owned treatment works (POTW)			Central Tendency	5	40	40	**3.6**	**3.6**
	Underground injection			High-End	5	**10**	**10**	**0.6**	**0.6**
	Landfill (municipal, hazardous or other land disposal)		ONU	Central Tendency	1	--	--	3,432	NA
	Incinerators (municipal and hazardous waste)			High-End	1	--	--	926	NA
	Emissions to air								

NA = not assessed because ONUs are not assumed to be wearing PPE; "--" = ONU risk from acute exposures are not expected to be below the MOE; see further explanation in Section 4.2.3

[a] Risks for glove PFs 10 and 20 are included for some COUs where appropriate based on glove use information described in Sections 2.4.1 and 2.4.1.2.

[b] To achieve an APF of 10, EPA assumes use of a half mask air-purifying respirator with organic vapor cartridges.

4.6.1.2 Summary of Risk Estimates for Consumers and Bystanders

Table 4-56 summarizes the acute risks of combined inhalation, dermal and vapor-through-skin exposures for all consumer exposure scenarios. For consumers, risk concerns are indicated for acute exposures associated with high intensity use of paint removers, high weight fraction adhesives and engine cleaners/degreasers. The main factors that impact consumer exposures during use of NMP-containing products include the NMP weight fraction, duration of product use and the actual amount of product used (see Table 2-85 and Table 2-91). In addition, specific factors related to the room of use (*e.g.*, room size, air exchange rate) may affect the estimated NMP air concentrations to which consumers may be exposed. For example, air concentrations can vary depending on whether windows or garage doors are open or closed during product use. Variations in individual activity patterns can also impact exposure potential (*e.g.*, risks associated with the engine degreasing activity may be underestimated if the product is used continuously).

EPA evaluated risks to child and adult bystanders for all COUs where risk was found for consumer users, including use of NMP-containing paint removers, high weight fraction adhesives and sealants, and engine cleaner/degreasers. (Section 4.2.4.8). These exposure scenarios did not present a risk concern to bystanders. Bystander risks were not further evaluated for scenarios that do not pose a risk to consumer users because bystander exposures are expected to be lower than consumer user exposures.

EPA has high confidence in the POD used to evaluate risks associated with acute exposure and medium confidence in the POD used to evaluate chronic NMP exposure. As discussed in Section 3.2.6, post-implantation loss (resorptions and fetal mortality) and reduced fertility were considered relevant hazards for evaluating risks following acute and chronic NMP exposure, respectively. While there is some uncertainty regarding temporal windows of vulnerability for developmental toxicity and whether the timing of a single exposure can produce a permanent adverse effect on human development, EPA considers the post-implantation loss endpoints associated with NMP exposure to be applicable to acute exposures. The reasonably available literature suggests that a single developmental exposure may have sustained effects on the conceptus. Fetal mortality represents the most severe endpoint associated with the developmental hazard profile for NMP. Reduced fertility in males is the most sensitive effect associated with chronic exposures. The chronic POD based on effects on reduced male fertility is supported by effects on female fecundity and developmental toxicity in a similar dose range.

Table 4-56. Summary of Risk Estimates from Acute Exposures to Consumers by Conditions of Use

Life Cycle Stage/ Category	Subcategory	Consumer Condition of Use/Exposure Scenario	Population	Exposure Level	Risk Estimate
					Acute Non-Cancer (Benchmark MOE = 30)
Consumer use/ Paints and coatings	Paint and coating removers	Section 2.4.2.5, Paint Removers	Consumer	Medium-Intensity User	217
				High-Intensity User	**29**
			Bystander [a] (In room of use)	Medium-Intensity User	N/A
				High-Intensity User	45
			Bystander (In rest of house)	Medium-Intensity User	N/A
				High-Intensity User	123
	Adhesive removers	Section 2.4.2.5, Adhesive Removers	Consumer	Medium-Intensity User	338
				High-Intensity User	73
			Bystander	Medium-Intensity User	N/A
				High-Intensity User	N/A
	Lacquer, stains, varnishes, primers and floor finishes	Section 2.4.2.5, Stains, Varnishes	Consumer	Medium-Intensity User	1,283
				High-Intensity User	224
			Bystander	Medium-Intensity User	N/A
				High-Intensity User	N/A
Consumer use/ Paint additives and coatings additives not described by other codes	Paints and Arts and Crafts Paints	Section 2.4.2.5, Paint	Consumer	Medium-Intensity User	1,169
				High-Intensity User	307
			Bystander	Medium-Intensity User	N/A
				High-Intensity User	N/A
		Section 2.4.2.5, Arts and Crafts	Consumer	Medium-Intensity User	6,139
				High-Intensity User	1,970
			Bystander	Medium-Intensity User	N/A
				High-Intensity User	N/A

Life Cycle Stage/ Category	Subcategory	Consumer Condition of Use/Exposure Scenario	Population	Exposure Level	Risk Estimate
					Acute Non-Cancer (Benchmark MOE = 30)
Consumer use/ adhesives and sealants	Glues and adhesives, including lubricant adhesives	Section 2.4.2.5, High Weight Fraction Adhesives and Sealants	Consumer	Medium-Intensity User	107
				High-Intensity User	**23**
			Bystander [a] (In room of use)	Medium-Intensity User	N/A
				High-Intensity User	2,806
			Bystander (In rest of house)	Medium-Intensity User	N/A
				High-Intensity User	N/A [b]
		Section 2.4.2.5, Low Weight Fraction Adhesives and Sealants	Consumer	Medium-Intensity User	38,758
				High-Intensity User	6,248
			Bystander	Medium-Intensity User	N/A
				High-Intensity User	N/A
Consumer use/ Other uses	Automotive care products	Section 2.4.2.5, Auto Interior Cleaner	Consumer	Medium-Intensity User	1,710
				High-Intensity User	100
			Bystander	Medium-Intensity User	N/A
				High-Intensity User	N/A
		Section 2.4.2.5, Auto Interior Spray Cleaner	Consumer	Medium-Intensity User	4,676
				High-Intensity User	2,381
			Bystander	Medium-Intensity User	N/A
				High-Intensity User	N/A
	Cleaning and furniture care products, including wood cleaners, gasket removers	Section 2.4.2.5, Cleaners/Degreaser	Consumer	Medium-Intensity User	423
				High-Intensity User	33
			Bystander	Medium-Intensity User	N/A
				High-Intensity User	N/A
		Section 2.4.2.5,	Consumer	Medium-Intensity User	260

Life Cycle Stage/ Category	Subcategory	Consumer Condition of Use/Exposure Scenario	Population	Exposure Level	Risk Estimate
					Acute Non-Cancer (Benchmark MOE = 30)
		Engine Cleaner/ Degreaser		High-Intensity User	**27**
			Bystander [a] (In room of use)	Medium-Intensity User	N/A
				High-Intensity User	54
			Bystander (In rest of house)	Medium-Intensity User	N/A
				High-Intensity User	79
Consumer use/ Other uses	Lubricant and lubricant additives, including hydrophilic coatings	Section 2.4.2.5, Spray Lubricant	Consumer	Medium-Intensity User	1,316
				High-Intensity User	153
			Bystander	Medium-Intensity User	N/A
				High-Intensity User	N/A

[a] Bystander risk (MOEs) estimates for bystanders in the room of use assume exposure to the same NMP air concentrations as the user.
[b] C_{max} is assumed to be zero for bystanders in the rest of house, as outdoor use of the product is not expected to result in NMP in indoor air. No MOE was calculated.
N/A = not assessed

4.6.1.3 Summary of Risk for the General Population

EPA considered reasonably available information to characterize general population exposure and risk. During problem formulation, EPA evaluated potentials exposures and risks to the general population through ambient water, land-applied biosolids, and ambient air. Based on environmental fate properties of NMP and first-tier screening level analyses, EPA did not identify risk to the general population from these pathways.

Surface water pathway

EPA did not identify risks from exposure to NMP through surface water pathways. Based on 2015 TRI reporting, an estimate 14,092 pounds of NMP was released to surface water from industrial and commercial sources. Although NMP exhibits high water solubility, it is not expected to persist in surface waters because it readily biodegrades under aerobic conditions. In this risk evaluation, EPA updated the screening level analysis of ambient water pathways using recent TRI reporting data from 2018 (Appendix E). A first-tier analysis used to estimate NMP surface water concentrations based on the highest water releases reported in 2018 did not identify risks from incidental ingestion of surface water or from dermal contact during swimming (Section 2.4.3 and 4.2.5).

Land-applied biosolids pathway

EPA did not identify risks from land releases of NMP, including those that may result from land application of biosolids. NMP exhibits high water solubility and limited potential for adsorption to organic matter; therefore, land releases will ultimately partition to the aqueous phase (*i.e.*, biosolids associated wastewater and soil pore water) upon release into the environment. Because NMP readily biodegrades in environments with active microbial populations, NMP residues that remain following waste water treatment are not expected to persist. NMP concentrations in biosolids-associated water are expected to decrease, primarily via aerobic degradation, during transport, processing (including dewatering), handling, and land application of biosolids (which may include spraying).

Migration of NMP between ground water and surface has not been documented, but may be mitigated by abiotic and biotic degradation in the water column. Overall, the NMP concentrations in surface water resulting from land application of biosolids are expected to be much less than those associated with direct release of waste water treatment plant effluents to surface water. During problem formulation, EPA's conservative assessment of this exposure scenario predicted NMP surface water concentrations that are well below the hazard benchmarks identified for humans and aquatic organisms; therefore, this exposure pathway is not expected to present a risk concern.

Ambient air pathway

EPA did not identify risks from human exposures that may result from inhalation of outdoor air containing NMP released from industrial and commercial facilities. During problem formulation, EPA performed a first-tier screening analysis to estimate the potential (near field) exposure to populations located downwind of facilities reporting the highest NMP air releases based on 2015 TRI data. Using EPA's SCREEN3 Model and the highest reported stack emissions, the estimated NMP concentration in ambient air was approximately 0.41 mg/m^3. EPA assessed the risks associated with chronic NMP exposure by comparing the estimated concentration of NMP in ambient air to hazard benchmarks. This resulted in a MOE that exceeded the benchmark.

5 UNREASONABLE RISK DETERMINATION

5.1 Overview

In each risk evaluation under TSCA Section 6(b), EPA determines whether a chemical substance presents an unreasonable risk of injury to health or the environment, under the conditions of use. These determinations do not consider costs or other non-risk factors. In making these determinations, EPA considers relevant risk-related factors, including, but not limited to: the effects of the chemical substance on health and human exposure to such substance under the conditions of use (including cancer and non-cancer risks); the effects of the chemical substance on the environment and environmental exposure under the conditions of use; the population exposed (including any PESS); the severity of hazard (including the nature of the hazard, the irreversibility of the hazard); and the uncertainties. EPA also takes into consideration the Agency's confidence in the data used in the risk estimates. This includes an evaluation of the strengths, limitations and uncertainties associated with the information used to inform the risk estimates and the risk characterization. This approach is in keeping with the Agency's final rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726).[8]

This section describes the final unreasonable risk determinations for the conditions of use in the scope of the risk evaluation. The final unreasonable risk determinations are based on the risk estimates and consideration of other risk-related factors in the final risk evaluation, which may differ from the draft risk evaluation due to peer review and public comments. The relevant risk-related factors for NMP are further explained in Section 5.1.1 below and in Section 4.3 and Section 4.4 of the risk characterization. In Section 5.1.1, the relevant risk-related factors are identified for each condition of use, such as the health effects considered, the use of high-end risk estimates to address PESS, and other uncertainties relevant to each condition of use. Therefore, the final unreasonable risk determinations of some conditions of use may differ from those in the draft risk evaluation.

5.1.1 Human Health

EPA's risk evaluation identified non-cancer adverse effects from acute (developmental) and chronic (reproductive) inhalation and dermal exposures to NMP. The health risk estimates for all conditions of use are in Section 4.6 (Table 4-55 and Table 4-56).

For the NMP risk evaluation, EPA identified as Potentially Exposed or Susceptible Subpopulations: workers and ONUs, consumers and bystanders, males and females of reproductive age, pregnant women and the developing fetus, infants, children and adolescents, people with pre-existing conditions and people with lower metabolic capacity due to life stage, genetic variation, or impaired liver function.

EPA evaluated exposures to workers, ONUs, consumer users, and bystanders using reasonably available monitoring and modeling data for inhalation and dermal exposures, as applicable. For example, EPA assumed that ONUs and bystanders do not have direct contact with NMP; therefore, non-cancer effects from dermal exposures to NMP are not expected and were not evaluated. Additionally, EPA did not evaluate chronic exposures for consumer users and bystanders because daily use intervals are not reasonably expected to occur for all consumer uses. The description of the data used for human health

[8] This risk determination is being issued under TSCA Section 6(b) and the terms used, such as unreasonable risk, and the considerations discussed are specific to TSCA. Other statutes have different authorities and mandates and may involve risk considerations other than those discussed here.

exposure is in Section 2.4. Uncertainties in the analysis are discussed in Section 4.3 and considered in the unreasonable risk determination for each condition of use presented below in Section 5.2.

EPA considered potential exposure pathways for the general population via ambient water, ambient air and land-applied biosolids. EPA evaluated environmental fate properties, reasonably available information and first-tier screening level analyses to characterize general population exposure from these pathways. EPA determined there is no general population risk for these pathways. The exposures to the general population via drinking water and disposal pathways fall under the jurisdiction of other environmental statutes administered by EPA, *i.e.*, CAA, SDWA, CWA, and CERCLA. EPA did not evaluate risks to the general population from drinking water or disposal pathways. Additional details regarding general population are found in Sections 1.4.2 and 4.6.1.3.

5.1.1.1 Non-Cancer Risk Estimates

The risk estimates of non-cancer effects (MOEs) refer to adverse health effects associated with health endpoints other than cancer, including to the body's organ systems, such as reproductive/developmental effects, cardiac and lung effects, and kidney and liver effects. The MOE is the POD (an approximation of the no-observed adverse effect level (NOAEL) or benchmark dose level (BMDL)) for a specific health endpoint divided by the exposure concentration for the specific scenario of concern. Section 3.2.5 presents the PODs for non-cancer effects for NMP and Section 4.2 presents the MOEs for non-cancer effects.

The MOEs are compared to a benchmark MOE. The benchmark MOE accounts for the total uncertainty in a POD, including, as appropriate: (1) the variation in sensitivity among the members of the human population (*i.e.*, intrahuman/intraspecies variability); (2) the uncertainty in extrapolating animal data to humans (*i.e.*, interspecies variability); (3) the uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure to lifetime exposure (*i.e.*, extrapolating from subchronic to chronic exposure); and (4) the uncertainty in extrapolating from a LOAEL rather than from a NOAEL. A lower benchmark MOE (*e.g.*, 30) indicates greater certainty in the data (because fewer of the default UFs relevant to a given POD as described above were applied). A higher benchmark MOE (*e.g.*, 1000) would indicate more uncertainty for specific endpoints and scenarios. However, these are often not the only uncertainties in a risk evaluation. The benchmark MOE for acute and chronic non-cancer risks for NMP is 30 (accounting for interspecies and intraspecies variability). Additional information regarding the benchmark MOE is in Section 4.2.1.

5.1.1.2 Cancer Risk Estimates

Cancer risk estimates represent the incremental increase in probability of an individual in an exposed population developing cancer over a lifetime (excess lifetime cancer risk) following exposure to the chemical. Standard cancer benchmarks used by EPA and other regulatory agencies are an increased cancer risk above benchmarks ranging from 1 in 1,000,000 to 1 in 10,000 (*i.e.*, $1x10^{-6}$ to $1x10^{-4}$) depending on the subpopulation exposed.[9]

[9] As an example, when EPA's Office of Water in 2017 updated the Human Health Benchmarks for Pesticides, the benchmark for a "theoretical upper-bound excess lifetime cancer risk" from pesticides in drinking water was identified as 1 in 1,000,000 to 1 in 10,000 over a lifetime of exposure (EPA. Human Health Benchmarks for Pesticides: Updated 2017 Technical Document (pp.5). (EPA 822-R -17 -001). Washington, DC: U.S. Environmental Protection Agency, Office of Water. January 2017. https://www.epa.gov/sites/production/files/2015-10/documents/hh-benchmarks-techdoc.pdf). Similarly, EPA's approach under the CAA to evaluate residual risk and to develop standards is a two-step approach that "includes a presumptive limit on maximum individual lifetime [cancer] risk (MIR) of approximately 1 in 10 thousand" and consideration of whether emissions standards provide an ample margin of safety to protect public health "in consideration of all health information, including the number of persons at risk levels higher than approximately 1 in 1 million, as well as other relevant factors" (54 FR 38044, 38045, September 14, 1989).

With respect to cancer risks, as discussed in Section 2.4.2.2 of the Problem Formulation of the Risk Evaluation for NMP, NMP is not mutagenic and is not considered carcinogenic so EPA did not conduct analysis of genotoxicity and cancer hazards during risk evaluation.

5.1.1.3 Determining Unreasonable Risk of Injury to Health

Calculated risk estimates (MOEs) can provide a risk profile by presenting a range of estimates for different health effects for different conditions of use. A calculated MOE that is less than the benchmark MOE supports a determination of unreasonable risk of injury to health, based on non-cancer effects. Similarly, a calculated cancer risk estimate that is greater than the cancer benchmark supports a determination of unreasonable risk of injury to health from cancer. Whether EPA makes a determination of unreasonable risk depends upon other risk-related factors, such as the endpoint under consideration, the reversibility of effect, exposure-related considerations (*e.g.*, duration, magnitude, or frequency of exposure, or population exposed), and the confidence in the information used to inform the hazard and exposure values. A calculated MOE greater than the benchmark MOE or a calculated cancer risk estimate less than the cancer benchmark alone do not support a determination of no unreasonable risk, since EPA may consider other risk-based factors when making an unreasonable risk determination.

When making an unreasonable risk determination based on injury to health of workers (who are one example of PESS), EPA also makes assumptions regarding workplace practices and the implementation of the required hierarchy of controls from OSHA. EPA assumes that feasible exposure controls, including engineering controls, or use of PPE are implemented in the workplace. EPA's decisions for unreasonable risk to workers are based on high-end exposure estimates, in order to capture not only exposures for PESS but also to account for the uncertainties related to whether or not workers are using PPE. However, EPA does not assume that ONUs use PPE. For each condition of use of NMP, depending on the information available and professional judgement, EPA assumes the use of appropriate respirators with APF 10. Based on peer review and public comments, EPA adjusted glove PF assumptions. Once EPA has applied the appropriate PPE assumption for a particular condition of use in each unreasonable risk determination, in those instances when EPA assumes PPE is used, EPA also assumes that the PPE is used in a manner that achieves the stated APF or PF.

In the NMP risk characterization, the best representative endpoints for non-cancer effects were from acute (reproductive toxicity) and chronic (developmental toxicity) inhalation and dermal exposures for all conditions of use. Additional risks associated with other adverse effects (*e.g.*, liver toxicity, kidney toxicity, immunotoxicity, neurotoxicity, irritation and sensitization) were identified for acute and chronic inhalation and dermal exposures.

The previous EPA assessment (U.S. EPA, 2015c), did not characterize dose-response for these fertility endpoints because the effect observed in one study (reduced fertility) was not replicated in more recent studies. However, together, the acute and chronic effects indicate a continuum of reproductive and developmental effects associated with NMP exposure. The complete basis for selection of endpoints is described in detail in Section 3.2.5.1 (Selection of Endpoints for Dose-Response Assessment) and Section 3.2.5.6 (Points of Departure for Human Health Hazard Endpoints).

When making a determination of unreasonable risk, the Agency has a higher degree of confidence where uncertainty is low. Similarly, EPA has high confidence in the hazard and exposure characterizations when, for example, the basis for characterizations is measured or monitoring data or a robust model and the hazards identified for risk estimation are relevant for conditions of use. Where EPA has made assumptions

in the scientific evaluation, whether or not those assumptions are protective is also a consideration. Additionally, EPA considers the central tendency and high-end exposure levels when determining the unreasonable risk. High-end risk estimates (*e.g.*, 95th percentile) are generally intended to cover individuals or sub-populations with greater exposure (PESS) as well as to capture individuals with sentinel exposure, and central tendency risk estimates are generally estimates of average or typical exposure.

EPA may make a determination of no unreasonable risk for conditions of use where the substance's hazard and exposure potential, or where the risk-related factors described previously, lead the Agency to determine that the risks are not unreasonable.

5.1.2 Environment

EPA calculated a RQ to compare environmental concentrations against an effect level. The environmental concentration is determined based on the levels of the chemical released to the environment (*e.g.*, surface water, sediment, soil, biota) under the conditions of use, based on the fate properties, release potential, and reasonably available environmental monitoring data. The effect level is calculated using COCs that represent hazard data for aquatic, sediment-dwelling, and terrestrial organisms. Section 4.1 provides more detail regarding the RQ for NMP.

5.1.2.1 Determining Unreasonable Risk of Injury to the Environment

An RQ equal to 1 indicates that the exposures are the same as the concentration that causes effects. An RQ less than 1, when the exposure is less than the effect concentration, supports a determination that there is no unreasonable risk of injury to the environment. An RQ greater than 1, when the exposure is greater than the effect concentration, supports a determination that there is unreasonable risk of injury to the environment. Consistent with EPA's human health evaluations, other risk-based factors may be considered (*e.g.*, confidence in the hazard and exposure characterization, duration, magnitude, uncertainty) for purposes of making an unreasonable risk determination.

EPA considered the effects on aquatic, sediment-dwelling, and terrestrial organisms. EPA provides estimates for environmental risk in Section 4.1, while the details for determining whether there is unreasonable risk to the environment are discussed in Section 5.2.2.

5.2 Detailed Unreasonable Risk Determinations by Conditions of Use

Table 5-1. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category [a]	Subcategory [b]	Unreasonable Risk	Detailed Risk Determination
Manufacturing	Domestic manufacture	Domestic manufacture	Yes	Section 5.2.1.1, Section 5.2.1.38 and Section 5.2.2
	Import	Import	Yes	Section 5.2.1.2, Section 5.2.1.38 and Section 5.2.2
Processing	Processing as a reactant or intermediate	Intermediate in Plastic Material and Resin Manufacturing	Yes	Section 5.2.1.3, Section 5.2.1.38 and Section 5.2.2
		Other Non-Incorporative Processing		

Life Cycle Stage	Category [a]	Subcategory [b]	Unreasonable Risk	Detailed Risk Determination
	Incorporation into formulation, mixture or reaction products	Adhesives and sealant chemicals in Adhesive Manufacturing	Yes	Section 5.2.1.4, Section 5.2.1.38 and Section 5.2.2
		Anti-adhesive agents in Printing and Related Support Activities		
		Paint additives and coating additives not described by other codes in Paint and Coating Manufacturing; and Print Ink Manufacturing		
		Processing aids not otherwise listed in Plastic Material and Resin Manufacturing		
		Solvents (for cleaning or degreasing) in Non-Metallic Mineral Product Manufacturing; Machinery Manufacturing; Plastic Material and Resin Manufacturing; Primary Metal Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Services; Wholesale and Retail Trade		
		Surface active agents in Soap, Cleaning Compound and Toilet Preparation Manufacturing		
		Plating agents and surface treating agents in Fabricated Metal Product Manufacturing		
		Solvents (which become part of product formulation or mixture) in Electrical Equipment, Appliance and Component Manufacturing; Other Manufacturing; Paint and Coating Manufacturing; Print Ink Manufacturing; Soap, Cleaning Compound and Toilet Preparation		

Life Cycle Stage	Category [a]	Subcategory [b]	Unreasonable Risk	Detailed Risk Determination
		Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Wholesale and Retail Trade		
		Other uses in Oil and Gas Drilling, Extraction and Support Activities; Plastic Material and Resin Manufacturing; Services		
Processing	Incorporation into articles	Lubricants and lubricant additives in Machinery Manufacturing	Yes	Section 5.2.1.5, Section 5.2.1.38 and Section 5.2.2
		Paint additives and coating additives not described by other codes in Transportation Equipment Manufacturing	Yes	Section 5.2.1.6, Section 5.2.1.38 and Section 5.2.2
		Solvents (which become part of product formulation or mixture), including in Textiles, Apparel and Leather Manufacturing	Yes	Section 5.2.1.7, Section 5.2.1.38 and Section 5.2.2
		Other, including in Plastic Product Manufacturing	Yes	Section 5.2.1.8, Section 5.2.1.38 and Section 5.2.2
Processing	Repackaging	Wholesale and Retail Trade	Yes	Section 5.2.1.9, Section 5.2.1.38 and Section 5.2.2
Processing	Recycling	Recycling	Yes	Section 5.2.1.10, Section 5.2.1.38 and Section 5.2.2
Distribution in commerce	Distribution	Distribution in commerce	No	Section 5.2.1.11, Section 5.2.1.38 and Section 5.2.2

Life Cycle Stage	Category [a]	Subcategory [b]	Unreasonable Risk	Detailed Risk Determination
Industrial and Commercial use	Paints and coatings	Paint and coating removers	Yes	Section 5.2.1.12, Section 5.2.1.38 and Section 5.2.2
		Adhesive removers		
		Lacquers, stains, varnishes, primers and floor finishes	Yes	Section 5.2.1.13, Section 5.2.1.38 and Section 5.2.2
		Powder coatings (surface preparation)		
	Paint additives and coating additives not described by other codes	Use in Computer and Electronic Product Manufacturing in Electronic Parts Manufacturing	Yes	Section 5.2.1.14, Section 5.2.1.38 and Section 5.2.2
		Use in Computer and Electronic Product Manufacturing in Semiconductor Manufacturing	Yes	Section 5.2.1.15, Section 5.2.1.38 and Section 5.2.2
		Use in Construction, Fabricated Metal Product Manufacturing, Machinery Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Primary Metal Manufacturing, Transportation Equipment Manufacturing, Wholesale and Retail Trade	Yes	Section 5.2.1.16, Section 5.2.1.38 and Section 5.2.2
	Solvent (for cleaning or degreasing)	Use in Electrical Equipment, Appliance and Component Manufacturing	Yes	Section 5.2.1.17, Section 5.2.1.38 and Section 5.2.2
		Use in Electrical Equipment Appliance and Component Manufacturing in Semiconductor Manufacturing	Yes	Section 5.2.1.18, Section 5.2.1.38 and Section 5.2.2
	Ink, toner, and colorant products	Printer Ink	No	Section 5.2.1.19, Section 5.2.1.38 and Section 5.2.2
		Inks in writing equipment		
	Processing aids, specific to petroleum production	Petrochemical Manufacturing	Yes	Section 5.2.1.20, Section 5.2.1.38 and Section 5.2.2
	Other uses	Other uses in Oil and Gas Drilling, Extraction and Support Activities		
		Functional fluids (closed systems)		
	Adhesives and sealants	Adhesives and sealant chemicals including binding agents	Yes	Section 5.2.1.21, Section 5.2.1.38 and Section 5.2.2

Life Cycle Stage	Category [a]	Subcategory [b]	Unreasonable Risk	Detailed Risk Determination
		Single component glues and adhesives, including lubricant adhesives		
		Two-component glues and adhesives, including some resins		
	Other uses	Soldering materials	No	Section 5.2.1.22, Section 5.2.1.38 and Section 5.2.2
		Anti-freeze and de-icing	Yes	Section 5.2.1.23, Section 5.2.1.38 and Section 5.2.2
		Automotive care products		
		Lubricants and greases		
		Metal products not covered elsewhere	Yes	Section 5.2.1.24, Section 5.2.1.38 and Section 5.2.2
		Lubricant and lubricant additives, including hydrophilic coatings		
		Laboratory chemicals	Yes	Section 5.2.1.25, Section 5.2.1.38 and Section 5.2.2
		Lithium Ion battery manufacturing	Yes	Section 5.2.1.26, Section 5.2.1.38 and Section 5.2.2
		Cleaning and furniture care products, including wood cleaners, gasket removers	Yes	Section 5.2.1.27, Section 5.2.1.38 and Section 5.2.2
		Fertilizer and other agricultural chemical manufacturing - processing aids and solvents	No	Section 5.2.1.28, Section 5.2.1.38 and Section 5.2.2
Consumer Uses	Paints and coatings	Paint and coating removers	No	Section 5.2.1.29, Section 5.2.1.38 and Section 5.2.2
		Adhesive removers	No	Section 5.2.1.30, Section 5.2.1.38 and Section 5.2.2
		Lacquers, stains, varnishes, primers and floor finishes	No	Section 5.2.1.31, Section 5.2.1.38 and Section 5.2.2
Consumer Uses	Paint additives and coating additives not described by other codes	Paints and Arts and Crafts Paints	No	Section 5.2.1.32, Section 5.2.1.38 and Section 5.2.2
Consumer Uses	Adhesives and sealants	Glues and adhesives, including lubricant adhesives	Yes	Section 5.2.1.33, Section 5.2.1.38 and Section 5.2.2
Consumer Uses	Other uses	Automotive care products	No	Section 5.2.1.34, Section 5.2.1.38 and Section 5.2.2
		Cleaning and furniture care products, including wood cleaners, gasket removers	No	Section 5.2.1.35, Section 5.2.1.38 and Section 5.2.2

Life Cycle Stage	Category [a]	Subcategory [b]	Unreasonable Risk	Detailed Risk Determination
		Lubricant and lubricant additives, including hydrophilic coatings	No	Section 5.2.1.36, Section 5.2.1.38 and Section 5.2.2
Disposal	Disposal	Industrial pre-treatment	Yes	Section 5.2.1.37, Section 5.2.1.38 and Section 5.2.2
		Industrial wastewater treatment		
		Publicly owned treatment works (POTW)		
		Underground injection		
		Landfill (municipal, hazardous or other land disposal)		
		Incinerators (municipal and hazardous waste)		
		Emissions to air		

[a] These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent conditions of use of NMP in industrial and/or commercial settings.
[b] These subcategories reflect more specific information regarding the conditions of use of NMP.

5.2.1 Human Health

5.2.1.1 Manufacture – Domestic manufacture (Domestic manufacture)

Section 6(b)(4)(A) unreasonable risk determination for domestic manufacture of NMP: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that domestic manufacture of NMP presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation

exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and-vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of loading of bulk storage containers and drums, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from domestic manufacturing of NMP.

5.2.1.2 Manufacture – Import (Import)

Section 6(b)(4)(A) unreasonable risk determination for import of NMP: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that import of NMP presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of unloading of various containers, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from import of NMP.

5.2.1.3 Processing – Processing as a reactant or intermediate – Intermediate in Plastic Material and Resin Manufacturing; Other Non-Incorporative Processing (Processing as a reactant or intermediate)

Section 6(b)(4)(A) unreasonable risk determination for the processing of NMP as a reactant or intermediate in plastic material and resin manufacturing and other non-incorporative processing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the processing of NMP as a reactant or intermediate in plastic material and resin manufacturing and other non-incorporative processing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of the unloading of various containers, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the processing of NMP as a reactant or intermediate in plastic material and resin manufacturing and other non-incorporative processing.

5.2.1.4 Processing – Incorporation into formulation, mixture or reaction product – in multiple industrial sectors (listed in Table 5-1) (Processing into a formulation, mixture, or reaction product)

Section 6(b)(4)(A) unreasonable risk determination for processing of NMP for incorporation into a formulation, mixture or reaction product in multiple industrial sectors: **Presents an unreasonable risk**

of injury to health (workers); does not present an unreasonable risk of injury to health (ONUs) at the central tendency.

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the processing of NMP for incorporation into a formulation, mixture or reaction product in multiple industrial sectors presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of unloading of various containers, and from maintenance, bottling, shipping, and loading of NMP in formulation, which EPA expects present the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from processing of NMP for incorporation into a formulation, mixture or reaction product in multiple industrial sectors.

5.2.1.5 Processing – Incorporation into articles – Lubricants and lubricant additives in Machinery Manufacturing (processing into articles in lubricant and lubricant additives)

Section 6(b)(4)(A) unreasonable risk determination for the processing of NMP for incorporation into articles in lubricants and lubricant additives in machinery manufacturing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects

from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the processing of NMP for incorporation into articles in lubricants and lubricant additives in machinery manufacturing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of metal finishing products containing NMP, including brush, spray, and dip applications, which EPA expects present the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from processing of NMP for incorporation into articles in lubricants and lubricant additives in machinery manufacturing.

5.2.1.6 Processing – Incorporation into articles – Paint additives and coating additives not described by other codes in Transportation Equipment Manufacturing (Processing into articles in paint and coating additives)

Section 6(b)(4)(A) unreasonable risk determination for the processing of NMP for incorporation into articles in paint additives and coating additives not described by other codes in transportation equipment manufacturing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from chronic (reproductive) inhalation and dermal exposures at the high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the processing of NMP for incorporation into articles in paint additives and coating additives not described by other codes in transportation equipment manufacturing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects (reproductive) to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also

considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the high-end support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of spray, roll/curtain, dip, and brush application exposures to paints, coatings, adhesives, and sealants containing NMP. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that application activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from processing of NMP for incorporation into articles in paint additives and coating additives not described by other codes in transportation equipment manufacturing.

5.2.1.7 Processing – Incorporation into articles – Solvents (which become part of product formulation or mixture), including in Textiles, Apparel and Leather Manufacturing (Processing as an article in solvents (which become part of product formulation or mixture))

Section 6(b)(4)(A) unreasonable risk determination for the processing of NMP for incorporation into articles as a solvent (which become part of product formulation or mixture) including in textiles, apparel and leather manufacturing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the processing of NMP for incorporation into articles as a solvent (which become part of product formulation or mixture) including in textiles, apparel and leather manufacturing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of unloading of various containers, and from maintenance, bottling, shipping, and loading of NMP in formulation, which EPA expects present the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from processing of NMP for incorporation into articles as a solvent (which become part of product formulation or mixture) including in textiles, apparel and leather manufacturing.

5.2.1.8 Processing – Incorporation into articles – Other, including in Plastic Product Manufacturing (Processing into articles in plastic product manufacturing)

Section 6(b)(4)(A) unreasonable risk determination for processing of NMP for incorporation into articles in other sectors, including in plastic product manufacturing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the processing of NMP for incorporation into articles in other sectors, including in plastic product manufacturing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty,

EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of the unloading of various containers, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from processing of NMP for incorporation into articles in other sectors, including plastic product manufacturing.

5.2.1.9 Processing – Repackaging – Wholesale and Retail Trade (Processing for repackaging)

Section 6(b)(4)(A) unreasonable risk determination for processing of NMP for repackaging in wholesale and retail trade: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the processing of NMP for repackaging in wholesale and retail trade presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of unloading of various containers, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the processing of NMP for repackaging in wholesale and retail trade.

5.2.1.10 Processing – Recycling – Recycling (processing as recycling)

Section 6(b)(4)(A) unreasonable risk determination for recycling of NMP: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the recycling of NMP presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of unloading of various containers containing waste NMP, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the recycling of NMP.

5.2.1.11 Distribution in Commerce

Section 6(b)(4)(A) unreasonable risk determination for distribution in commerce of NMP: Does not present an unreasonable risk of injury to health (workers and ONUs).

For the purposes of the unreasonable risk determination, distribution in commerce of NMP is the transportation associated with the moving of NMP in commerce. EPA is assuming that workers and ONUs will not be handling NMP because the loading and unloading activities are associated with other

conditions of use and EPA assumes transportation of NMP is in compliance with existing regulations for the transportation of hazardous materials (49 CFR 172). Emissions are therefore minimal during transportation, so there is limited exposure (with the exception of spills and leaks, which are outside the scope of the risk evaluation). Based on the limited emissions and exposures from the transportation of chemicals, EPA determined there is no unreasonable risk of injury to health (workers and ONUs) from the distribution in commerce of NMP.

5.2.1.12 Industrial and Commercial Use – Paints and coatings – Paint and Coating Removers; Adhesive Removers (paint, coating, and adhesive removers)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in paints, coatings, and adhesive removers: **Presents an unreasonable risk of injury to health (workers).**

For workers, EPA found that there was unreasonable risk of non-cancer effects from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects (reproductive) from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in paint, coating, and adhesive removers presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of application exposures to paints, coatings, adhesives, and sealant removal products containing NMP in miscellaneous paint and coating removal and graffiti removal. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that removal activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in paints, coatings, and adhesive removers.

5.2.1.13 Industrial and Commercial Use – Paints and coatings – Lacquers, stains, varnishes, primers and floor finishes; Powder coatings (surface preparation) (paints and coatings)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in paints and coatings in lacquers, stains, varnishes, primers and floor finishes, and powder coatings in surface preparation: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from chronic (reproductive) inhalation and dermal exposures at the high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in paints and coatings in lacquers, stains, varnishes, primers and floor finishes, and powder coatings in surface preparation presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the high-end support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of spray, roll/curtain, dip, and brush application exposures to paints, coatings, adhesives, and sealants containing NMP. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that application activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in paints and coatings in lacquers, stains, varnishes, primers and floor finishes, and powder coatings in surface preparation.

5.2.1.14 Industrial and Commercial Use – Paint additives and coating additives not described by other codes – Use in Computer and Electronic Product Manufacturing in Electronic Parts Manufacturing (Electronic Parts Manufacturing)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in paint additives and coating additives not described by other codes in computer and electronic product manufacturing in electronic parts manufacturing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in paint additives and coating additives not described by other codes in computer and electronic product manufacturing in electronic parts manufacturing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of capacitor, resistor, coil, transformer, and other inductor manufacturing, which EPA expects present the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in paint additives and coating additives not described by other codes in computer and electronic product manufacturing in electronic parts manufacturing.

5.2.1.15 Industrial and Commercial Use – Paint additives and coating additives not described by other codes – Use in Computer and Electronic Product Manufacturing in Semiconductor Manufacturing (Semiconductor Manufacturing)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in paint additives and coating additives not described by other codes in computer and electronic product manufacturing for use in semiconductor manufacturing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in paint additives and coating additives not described by other codes in computer and electronic product manufacturing for use in semiconductor manufacturing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the central tendency and high-end in container handling small container activities and waste truck loading support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the high-end in container handling drum activities support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute and chronic inhalation and dermal exposures at the high-end in maintenance activities support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high end in container handling small container, container handling drums, and waste truck loading activities do not support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute and chronic inhalation and dermal exposures at the high end in fab worker activities do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.

- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of activities in semiconductor manufacturing, including exposures from container handling small containers, container handling drums, fab workers, maintenance, and waste truck loading activities, which EPA expects present the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in paint additives and coating additives not described by other codes in computer and electronic product manufacturing for use in semiconductor manufacturing.

5.2.1.16 Industrial and Commercial Use –Paint additives and coating additives not described by other codes – Use in Construction, Fabricated Metal Product Manufacturing, Machinery Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Primary Metal Manufacturing, Transportation Equipment Manufacturing, Wholesale and Retail Trade (paint additives and coating additives not described by other codes, other manufacturing and trade)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in paint additives and coating additives not described by other codes in multiple manufacturing sectors: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from chronic (reproductive) inhalation and dermal exposures at the high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in paint additives and coating additives not described by other codes in multiple manufacturing sectors presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the high-end support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation and vapor-through-skin exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation exposures when determining ONUs' unreasonable risk.

- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of spray, roll/curtain, dip, and brush application exposures to paint additives and coating additives containing NMP. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that application activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP paint additives and coating additives not described by other codes in multiple manufacturing sectors.

5.2.1.17 Industrial and Commercial Use – Solvents (for cleaning or degreasing) – Use in Electrical Equipment, Appliance and Component Manufacturing (Solvents for electrical equipment, appliance and component manufacturing)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of capacitor, resistor, coil, transformer, and other inductor manufacturing, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing.

5.2.1.18 Industrial and Commercial Use – Solvents (for cleaning or degreasing) – Use in Electrical Equipment, Appliance and Component Manufacturing in Semiconductor Manufacturing (Solvents for electrical equipment, appliance and component manufacturing in semiconductor manufacturing)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing for use in semiconductor manufacturing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing for use in semiconductor manufacturing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the central tendency and high-end in container handling small container and waste truck loading activities support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the high-end in container handling drum activities support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute and chronic inhalation and dermal exposures at the high-end in maintenance activities support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end in virgin NMP truck unloading activities support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end in container handling small container, container handling drums, and waste truck loading activities do not support an unreasonable risk determination.

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute and chronic inhalation and dermal exposures at the high-end in fab worker activities do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of activities in semiconductor manufacturing, including exposures from container handling small containers, container handling drums, fab workers, maintenance, virgin NMP truck unloading, and waste truck loading activities, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing for use in semiconductor manufacturing.

5.2.1.19 Industrial and Commercial Use – Ink, toner, and colorant products – Printer ink; Inks in writing equipment (Ink, toner, and colorant products)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in ink, toner, and colorant products in printer ink and inks in writing equipment: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA did not identify an unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end when considering use of PPE. For ONUs, EPA did not identify an unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in ink, toner, and colorant products in printer ink and inks in writing equipment does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute and chronic inhalation and dermal exposures at the central tendency and high-end do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty,

EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.

- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of inhalation, vapor-through-skin, and dermal exposures to inks containing NMP during printing activities and dermal exposures to inks containing NMP during writing activities. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or maintenance activities, EPA expects that printing and writing activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (workers and ONUs) from the industrial and commercial use of NMP in ink, toner, and colorant products in printer ink and inks in writing equipment.

5.2.1.20 Industrial and Commercial Use – Processing aids, specific to petroleum production – Petrochemical Manufacturing; – Other uses – Other uses in Oil and Gas Drilling, Extraction and Support Activities; Functional fluids (closed systems) (petrochemical manufacturing and other uses in oil and gas drilling and as functional fluids (closed systems))

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in processing aids, specific to petroleum production in petrochemical manufacturing, in other uses in oil and gas drilling, extraction and support activities, and in functional fluids (closed systems): **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in processing aids, specific to petroleum production in petrochemical manufacturing, other uses in oil and gas drilling, extraction and support activities, and in functional fluids (closed systems) presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty,

EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of the unloading of various containers, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in processing aids, specific to petroleum production in petrochemical manufacturing, other uses in oil and gas drilling, extraction and support activities, and in functional fluids (closed systems).

5.2.1.21 Industrial and Commercial Use – Adhesives and Sealants – Adhesives and sealant chemicals including binding agents; Single component glues and adhesives, including lubricant adhesives; Two-component glues and adhesives, including some resins (Adhesives and Sealants)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in adhesives and sealants including binding agents, single component glues and adhesives, including lubricant adhesives, and two-component glues and adhesives including some resins: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from chronic (reproductive) inhalation and dermal exposures at the high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in adhesives and sealants including binding agents, single component glues and adhesives, including lubricant adhesives, and two-component glues and adhesives including some resins presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the high-end support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty,

EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.

- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of spray, roll/curtain, dip, and brush application exposures to paints, coatings, adhesives, and sealants containing NMP. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that application activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in adhesives and sealants including binding agents, single component glues and adhesives, including lubricant adhesives, and two-component glues and adhesives including some resins.

5.2.1.22 Industrial and Commercial Use – Other Uses – Soldering materials (soldering materials)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in other uses in soldering materials: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA did not identify an unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end when considering use of PPE. For ONUs, EPA did not identify an unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in other uses in soldering materials does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for occupational non-users:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute and chronic inhalation and dermal exposures at the high-end do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of inhalation, vapor-through-skin, and dermal exposures to NMP during soldering activities. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or maintenance activities, EPA expects that soldering activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (workers and ONUs) from the industrial and commercial use of NMP in other uses in soldering materials.

5.2.1.23 Industrial and Commercial Use – Other Uses – Anti-freeze and de-icing products; Automotive care products; Lubricants and greases (automotive products)

Section 6(b)(4)(A) unreasonable risk determination for industrial and commercial use of NMP in other uses in anti-freeze and de-icing products, automotive care products, and lubricants and greases: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA identified an unreasonable risk of non-cancer effects (reproductive) from chronic inhalation and dermal exposures at the high-end, even when considering use of PPE. For ONUs, EPA did not identify an unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in other uses in anti-freeze and de-icing products, automotive care products, and lubricants and greases presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the high-end support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of automotive servicing with products containing NMP. For this commercial exposure scenario, EPA assessed inhalation, vapor-through-skin, and dermal exposures to products containing NMP during aerosol degreasing of automotive brakes. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that aerosol degreasing activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in other uses in anti-freeze and de-icing products, automotive care products, and lubricants and greases.

5.2.1.24 Industrial and Commercial Use – Other Uses – Metal products not covered elsewhere; Lubricant and lubricant additives, including hydrophilic coatings (metal products and lubricant and lubricant additives)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in other uses in metal products not covered elsewhere, and lubricants and lubricant additives including hydrophilic coatings: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in other uses in metal products not covered elsewhere, and lubricants and lubricant additives including hydrophilic coatings presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of metal finishing products containing NMP, including brush, spray, and dip applications.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in other uses in metal products not covered elsewhere, and lubricants and lubricant additives including hydrophilic coatings.

5.2.1.25 Industrial and Commercial Use – Other Uses – Laboratory chemicals (laboratory chemicals)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in other uses in laboratory chemicals: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in other uses in laboratory chemicals presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of exposure to 100% NMP during laboratory activities. While EPA does expect that workers may perform additional activities during this scenario, such as unloading, EPA expects that laboratory use activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in other uses in laboratory chemicals.

5.2.1.26 Industrial and Commercial Use – Other Uses – Lithium Ion battery manufacturing (Lithium Ion battery manufacturing)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in other uses in lithium ion battery manufacturing: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in other uses in lithium ion battery manufacturing presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1,

EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end in small container handling, drum handling, research and development, and miscellaneous activities support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from chronic inhalation and dermal exposures at the high-end in cathode coating and cathode slurry mixing activities support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high end in cathode coating and cathode slurry mixing activities do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of activities in other uses in lithium ion battery manufacturing, including exposures from small container handling, drum handling, cathode coating, cathode slurry mixing, research and development, and miscellaneous activities, which EPA expects present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in other uses in lithium ion battery manufacturing.

5.2.1.27 Industrial and Commercial Use – Other Uses – Cleaning and furniture care products, including wood cleaners, gasket removers (cleaning and furniture care products)

Section 6(b)(4)(A) unreasonable risk determination for industrial and commercial use of NMP in other uses in cleaning and furniture care products, including wood cleaners and gasket removers: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in other uses in cleaning and furniture care products, including wood cleaners and gasket removers presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of exposure to cleaning products containing NMP from the following dip cleaning and degreasing, and spray and wipe cleaning. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or sampling, EPA expects that cleaning activities present the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from the industrial and commercial use of NMP in other uses in cleaning and furniture care products, including wood cleaners and gasket removers.

5.2.1.28 Industrial and Commercial Use – Other Uses – Fertilizer and other agricultural chemical manufacturing - processing aids and solvents (fertilizer manufacturing)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of NMP in other uses in fertilizer and other agricultural chemical manufacturing, processing aids and solvents: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA did not identify an unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end when considering use of PPE. For ONUs, EPA did not identify an unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that the industrial and commercial use of NMP in other uses in fertilizer and other agricultural chemical manufacturing, processing aids and solvents does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for occupational non-users:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute and chronic inhalation and dermal exposures at the high-end do not support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of exposures during application of fertilizers. While EPA does expect that workers may perform additional activities during this scenario, such as unloading or maintenance activities, EPA expects that fertilizer application presents the largest range of potential exposures.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (workers and ONUs) from the industrial and commercial use of NMP in other uses in fertilizer and other agricultural chemical manufacturing, processing aids and solvents.

5.2.1.29 Consumer Use – Paints and coatings – Paint and coating removers (paint and coating removers)

Section 6(b)(4)(A) unreasonable risk determination for consumer use of NMP in paint and coating removers: Does not present an unreasonable risk of injury to health (consumers and bystanders).

For consumers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation, dermal, and vapor-through-skin exposures at the moderate and high intensity use. For bystanders, EPA found there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation and vapor-through-skin exposures at the high intensity use.

EPA's determination that the consumer use of NMP in paint and coating removers presents no unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-56) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3):

- For consumers, the risk estimates of non-cancer effects from acute inhalation, dermal, and vapor-through-skin exposures do not support an unreasonable risk determination.
- Risk estimates for the consumer use of NMP in paint and coating removers were based on modeled risk estimates from 35 products.
- Consumer exposure resulting from inhalation, dermal and vapor through skin results were assessed using modeled data as inputs to the PBPK model.
- The PBPK model was used to derive internal exposure estimates for consumer and bystander acute exposures. The PBPK model required a set of input parameters related to exposure by the dermal and inhalations routes; NMP weight fraction in the liquid product, total skin surface area of hands in contact with the liquid product; duration of dermal contact with the liquid product; air concentration for inhalation and vapor-through-skin exposure; and body weight of the exposed consumer/user.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (consumers and bystanders) from the consumer use of NMP in paint and coating removers.

5.2.1.30 Consumer Use – Paints and coatings – Adhesive removers (adhesive removers)

Section 6(b)(4)(A) unreasonable risk determination for consumer use of NMP in adhesive removers: Does not present an unreasonable risk of injury to health (consumers and bystanders)**.**

For consumers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation, dermal, and vapor-through-skin exposures at the moderate and high intensity use. For bystanders, EPA found there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation and vapor-through-skin exposures.

EPA's determination that the consumer use of NMP in adhesive removers does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-56) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3):

- Risk estimates for the consumer use of NMP in adhesive removers were based on modeled risk estimates from five products.
- Consumer exposure resulting from inhalation, dermal and vapor through skin results were assessed using modeled data as inputs to the PBPK model.
- The PBPK model was used to derive internal exposure estimates for consumer acute exposures. The PBPK model required a set of input parameters related to exposure by the dermal and inhalations routes; NMP weight fraction in the liquid product, total skin surface area of hands in contact with the liquid product; duration of dermal contact with the liquid product; air concentration for inhalation and vapor-through-skin exposure; and body weight of the exposed consumer/user.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (consumers and bystanders) from the consumer use of NMP in adhesive removers.

5.2.1.31 Consumer Use – Paints and coatings – Lacquers, stains, varnishes, primers and floor finishes (lacquers, stains, varnishes, primers and floor finishes)

Section 6(b)(4)(A) unreasonable risk determination for consumer use of NMP in paints and coatings in lacquers, stains, varnishes, primers and floor finishes: Does not present an unreasonable risk of injury to health (consumers and bystanders).

For consumers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation, dermal, and vapor-through-skin exposures at the moderate and high intensity use. For bystanders, EPA found there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation and vapor-through-skin exposures.

EPA's determination that the consumer use of NMP in paints and coatings in lacquers, stains, varnishes, primers and floor finishes does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-56) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3):

- Risk estimates for the consumer use of NMP in lacquers, stains, varnishes, primers and floor finishes were based on modeled risk estimates from nine products.
- Consumer exposure resulting from inhalation, dermal and vapor through skin results were assessed using modeled data as inputs to the PBPK model.
- The PBPK model was used to derive internal exposure estimates for consumer acute exposures. The PBPK model required a set of input parameters related to exposure by the dermal and inhalations routes; NMP weight fraction in the liquid product, total skin surface area of hands in contact with the liquid product; duration of dermal contact with the liquid product; air concentration for inhalation and vapor-through-skin exposure; and body weight of the exposed consumer/user.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (consumers and bystanders) from the consumer use of NMP in paints and coatings in lacquers, stains, varnishes, primers and floor finishes.

5.2.1.32 Consumer Use – Paint additives and coating additives not described by other codes – Paints and Arts and Crafts Paints (paint additives and coating additives not described by other codes)

Section 6(b)(4)(A) unreasonable risk determination for consumer use of NMP in paint additives and coating additives not described by other codes in paints and arts and crafts paints: Does not present an unreasonable risk of injury to health (consumers and bystanders).

For consumers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation, dermal, and vapor-through-skin exposures at the moderate and high intensity use. For bystanders, EPA found there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation and vapor-through-skin exposures.

EPA's determination that the consumer use of NMP in paint additives and coating additives not described by other codes in paints and arts and crafts paints does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-56) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3):

- Risk estimates for the consumer use of NMP in paint additives and coating additives not described by other codes were based on modeled risk estimates from four products, and two consumer exposure scenarios, paint and arts and crafts.
- Consumer exposure resulting from inhalation, dermal and vapor through skin results were assessed using modeled data as inputs to the PBPK model.
- The PBPK model was used to derive internal exposure estimates for consumer acute exposures. The PBPK model required a set of input parameters related to exposure by the dermal and inhalations routes; NMP weight fraction in the liquid product, total skin surface area of hands in

contact with the liquid product; duration of dermal contact with the liquid product; air concentration for inhalation and vapor-through-skin exposure; and body weight of the exposed consumer/user.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (consumers and bystanders) from the consumer use of NMP in paint additives and coating additives not described by other codes in paints and arts and crafts paints.

5.2.1.33 Consumer Use – Adhesives and sealants – Glues and adhesives, including lubricant adhesives (adhesives and sealants)

Section 6(b)(4)(A) unreasonable risk determination for consumer use of NMP in adhesives and sealants in glues and adhesives, including lubricant adhesives and sealants: **Presents an unreasonable risk of injury to health (consumers);** does not present an unreasonable risk of injury to health (bystanders).

For consumers, EPA found there was unreasonable risk of non-cancer effects (development) from acute inhalation, dermal, and vapor-through-skin exposures at the high intensity use. For bystanders, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation and vapor-through-skin exposures at the high intensity use.

EPA's determination that the consumer use of NMP in adhesives and sealants in glues and adhesives, including lubricant adhesives and sealants presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-56) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3):

- Risk estimates for the consumer use of NMP in adhesives and sealants were based on modeled risk estimates from four products and two consumer exposure scenarios, high weight fraction adhesives and sealants and low weight fraction adhesives and sealants.
- Consumer exposure resulting from inhalation, dermal and vapor through skin results were assessed using modeled data as inputs to the PBPK model.
- The PBPK model was used to derive internal exposure estimates for consumer and bystander acute exposures. The PBPK model required a set of input parameters related to exposure by the dermal and inhalations routes; NMP weight fraction in the liquid product, total skin surface area of hands in contact with the liquid product; duration of dermal contact with the liquid product; air concentration for inhalation and vapor-through-skin exposure; and body weight of the exposed consumer/user.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (consumers) from the consumer use of NMP in adhesives and sealants in glues and adhesives, including lubricant adhesives and sealants.

5.2.1.34 Consumer Use – Other uses – Automotive care products (automotive care products)

Section 6(b)(4)(A) unreasonable risk determination for consumer use of NMP in other uses in automotive care products: Does not present an unreasonable risk of injury to health (consumers and bystanders).

For consumers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation, dermal and vapor-through-skin exposures at the moderate and high intensity use. For bystanders, EPA found there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation and vapor-through-skin exposures.

EPA's determination that the consumer use of NMP in other uses in automotive care products does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-56) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3):

- Risk estimates for the consumer use of NMP in automotive care products were based on modeled risk estimates from two products and two consumer exposure scenarios, auto interior cleaner and auto interior spray cleaner.
- Consumer exposure resulting from inhalation, dermal and vapor through skin results were assessed using modeled data as inputs to the PBPK model.
- The PBPK model was used to derive internal exposure estimates for consumer acute exposures. The PBPK model required a set of input parameters related to exposure by the dermal and inhalations routes; NMP weight fraction in the liquid product, total skin surface area of hands in contact with the liquid product; duration of dermal contact with the liquid product; air concentration for inhalation and vapor-through-skin exposure; and body weight of the exposed consumer/user.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (consumers and bystanders) for the consumer use of NMP in other uses in automotive care products.

5.2.1.35 Consumer Use – Other Uses – Cleaning and furniture care products, including wood cleaners, gasket removers (cleaning and furniture care products)

Section 6(b)(4)(A) unreasonable risk determination for consumer use of NMP in other uses in cleaning and furniture care products, including wood cleaners and gasket removers**:** Does not present an unreasonable risk of injury to health (consumers and bystanders).

For consumers, EPA found there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation, dermal and vapor-through-skin exposures at the moderate and high intensity use. For bystanders, EPA found there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation and vapor-through skin exposures at the high intensity use.

EPA's determination that the consumer use of NMP in other uses in cleaning and furniture care products, including wood cleaners and gasket removers does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-56) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3):

- For consumers, the risk estimates of non-cancer effects from acute inhalation, dermal and vapor-through skin exposures do not support an unreasonable risk determination.

- Risk estimates for the consumer use of NMP in cleaning and furniture care products were based on modeled risk estimates from 10 products and two consumer exposure scenarios, cleaners/degreasers and engine cleaner/degreaser.
- Consumer exposure resulting from inhalation, dermal and vapor through skin results were assessed using modeled data as inputs to the PBPK model.
- The PBPK model was used to derive internal exposure estimates for consumer and bystander acute exposures. The PBPK model required a set of input parameters related to exposure by the dermal and inhalations routes; NMP weight fraction in the liquid product, total skin surface area of hands in contact with the liquid product; duration of dermal contact with the liquid product; air concentration for inhalation and vapor-through-skin exposure; and body weight of the exposed consumer/user.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (consumers and bystanders) for the consumer use of NMP in other uses in cleaning and furniture care products, including wood cleaners and gasket removers.

5.2.1.36 Consumer Use – Other Uses – Lubricant and lubricant additives; including hydrophilic coatings (lubricant and lubricant additives, including hydrophilic coatings)

Section 6(b)(4)(A) unreasonable risk determination for consumer use of NMP in other uses in lubricant and lubricant additives, including hydrophilic coatings: Does not present an unreasonable risk of injury to health (consumers and bystanders).

For consumers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation, dermal and vapor-through-skin exposures at the moderate and high intensity use. For bystanders, EPA found there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation and vapor-through-skin exposures.

EPA's determination that the consumer use of NMP in other uses in lubricant and lubricant additives, including hydrophilic coatings does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-56) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3):

- Risk estimates for the consumer use of NMP in lubricant and lubricant additives, including hydrophilic coatings were based on modeled risk estimates from one spray product.
- Consumer exposure resulting from inhalation, dermal and vapor through skin results were assessed using modeled data as inputs to the PBPK model.
- The PBPK model was used to derive internal exposure estimates for consumer acute exposures. The PBPK model required a set of input parameters related to exposure by the dermal and inhalations routes; NMP weight fraction in the liquid product, total skin surface area of hands in contact with the liquid product; duration of dermal contact with the liquid product; air concentration for inhalation and vapor-through-skin exposure; and body weight of the exposed consumer/user.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (consumers and bystanders) for the consumer use of NMP in other uses in lubricant and lubricant additives, including hydrophilic coatings.

5.2.1.37 Disposal – Disposal – Industrial pre-treatment; industrial wastewater treatment; publicly owned treatment works (POTW); underground injection; landfill (municipal, hazardous or other land disposal); emissions to air; incinerators (municipal and hazardous waste) (disposal)

Section 6(b)(4)(A) unreasonable risk determination for disposal of NMP: **Presents an unreasonable risk of injury to health (workers);** does not present an unreasonable risk of injury to health (ONUs).

For workers, EPA found that there was unreasonable risk of non-cancer effects from acute (developmental) inhalation and dermal exposures at the high-end, and from chronic (reproductive) inhalation and dermal exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects from acute (developmental) and chronic (reproductive) inhalation and vapor-through-skin exposures at the central tendency.

EPA's determination that disposal of NMP presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-55) and other considerations. As explained in Section 5.1, EPA also considered the health effects of NMP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3), including uncertainties related to the exposures for ONUs:

- For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 5, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end support an unreasonable risk determination.
- Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and vapor-through-skin exposures when determining ONUs' unreasonable risk.
- Inhalation, vapor-through-skin, and dermal exposures were assessed by inputting exposure parameters into a PBPK model. The model is representative of waste NMP unloading activities, which EPA expects presents the largest range of potential exposures, though EPA does expect that workers may perform additional activities during this scenario, such as sampling or maintenance work.

In summary, the risk estimates, the health effects of NMP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers) from disposal of NMP.

5.2.1.38 General Population

Section 6(b)(4)(A) unreasonable risk determination for **all conditions of use** of NMP: Does not present an unreasonable risk of injury to health (general population). For all conditions of use, EPA determined

that exposures to ambient water, ambient air, and land-applied biosolids do not support an unreasonable risk determination. EPA based this determination on an evaluation of potential exposures to the general population during problem formulation, environmental fate properties, and first tier screening level analyses. EPA did not assess exposures from drinking water and disposal pathways because they fall under the jurisdiction of other environmental statutes administered by EPA, *i.e.*, CAA, SDWA, and RCRA, and CERCLA. EPA has not developed recommended ambient water quality criteria for the protection of human health for NMP. Exposure to the general population via surface water can occur through recreational activities (*e.g.*, swimming) and through consuming fish. EPA evaluated the human health risks of potential acute incidental exposures via oral and dermal routes from recreational swimming and determined that these risks are not unreasonable.

5.2.2 Environment

6(b)(4)(A) unreasonable risk determination **for all conditions** of use of NMP: Does not present an unreasonable risk of injury **to the environment** (aquatic, sediment dwelling and terrestrial organisms).

For all conditions of use in ambient water, the RQ values (Table 4-2) do not support an unreasonable risk determination for acute and chronic exposures to NMP for amphibians, fish, and aquatic invertebrates. To characterize the exposure to NMP by aquatic organisms, modeled data were used to represent surface water concentrations near facilities actively releasing NMP to surface water, and modeled concentrations were used to represent ambient water concentrations of NMP. EPA considered the biological relevance of the species to determine the COCs for the location of surface water concentration data to produce RQs, as well as frequency and duration of the exposure.

NMP is not expected to partition to or accumulate in soil; rather, based on its physical and chemical properties, it is expected to volatilize to air or migrate through soil into groundwater. Therefore, risk to terrestrial organisms is not expected.

In summary, the risk estimates, the environmental effects of NMP, the exposures, physical chemical properties of NMP and consideration of uncertainties support EPA's determination that there is no unreasonable risk to the environment from all conditions of use of NMP.

5.3 Changes to the Unreasonable Risk Determination from Draft Risk Evaluation to Final Risk Evaluation

In this final risk evaluation, EPA made changes to the unreasonable risk determinations for NMP following the publication of the draft risk evaluation (Table 5-2), as a result of the analysis following peer review and public comments. The changes are: an updated POD; removal of several processing and industrial/commercial uses of NMP because they are not conditions of use under TSCA; revisions to the subcategory of a consumer use; separating conditions of use to provide clearer unreasonable risk determinations for conditions of use evaluated with multiple exposure scenarios; and addition of a general population determination. Details of these changes are below.

In the final risk evaluation, EPA updated the POD for acute exposures from the draft risk evaluation based on updated analyses performed in response to peer review comments. This updated POD for acute exposures resulted in some changes to acute risk estimates, which impacted unreasonable risk determinations.

EPA has also removed several uses of NMP that are not conditions of use under TSCA. While use of NMP as an inert ingredient in wood preservatives was included in the problem formulation and draft risk evaluation, upon further analysis of the details of this process, EPA has determined that this use falls outside TSCA's definition of "chemical substance." Under TSCA Section 3(2)(B)(ii), the definition of "chemical substance" does not include any pesticide (as defined in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)) when manufactured, processed, or distributed in commerce for use as a pesticide. EPA received a public comment describing the use of NMP in wood preservatives. In this case, NMP is used as an approved inert ingredient under FIFRA. EPA has concluded that this use of NMP falls within the aforementioned definitional exclusion and NMP, for this use, is not a "chemical substance" under TSCA.

Similarly, two uses of NMP in pharmaceutical manufacturing were included in the problem formulation and draft risk evaluation, namely as one of the uses of NMP as a functional fluid in a closed system and as one of the uses of NMP as an intermediate and reactant. Upon further analysis of the details of these uses, EPA has determined that these uses fall-outside TSCA's definition of "chemical substance." Under TSCA Section 3(2)(B)(vi), the definition of "chemical substance" does not include any food, food additive, drug, cosmetic, or device (as such terms are defined in Section 201 of the Federal Food, Drug, and Cosmetic Act) when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic, or device. While EPA has identified industrial and commercial use of NMP as a functional fluid (closed systems) and processing of NMP as a reactant or intermediate as conditions of use of NMP when under the TSCA definition of chemical substance, EPA has removed mention of pharmaceutical applications in these conditions of use. EPA has concluded that both uses of NMP fall within the aforementioned definitional exclusion, and NMP, for these uses, is not a "chemical substance" under TSCA.

In the draft risk evaluation, EPA made a preliminary determination for the consumer use of NMP as adhesive and sealant, single component glues and adhesives, including lubricant additives and two-component glues and adhesives, including some resins. After further review of the consumer products, EPA has revised the subcategory in the final risk evaluation and renamed the condition of use to be consumer use of NMP in adhesives and sealants in glues and adhesives, including lubricant adhesives and sealants.

EPA uses representative Occupational Exposure Scenarios and Consumer Exposure Scenarios to generate risk estimates. Sometimes the same Exposure Scenario is used for several conditions of use, and some unreasonable risk determinations are based on multiple exposure scenarios. In the draft risk evaluation, EPA made single preliminary determinations for several industrial and commercial uses of NMP when many of these uses were represented by the same Occupational Exposure Scenarios. Based on peer review, public comments, and data received, EPA has now made final unreasonable risk determinations based on additional Occupational Exposure Scenarios that more accurately reflect specific conditions of use of industrial and commercial use of NMP in paints and coatings, adhesives and sealants, electrical equipment appliance and component manufacturing, semiconductor manufacturing, and lithium ion battery manufacturing. As a result, two preliminary determinations in the draft risk evaluation were separated into several unreasonable risk determination in this final risk evaluation. Specifically, the preliminary unreasonable risk determination for the industrial and commercial use of NMP in paints and coatings, paint additives and coating additives, and adhesives and sealants not described by other codes was separated into five unreasonable risk determinations in the final risk evaluation. The preliminary unreasonable risk determination for the industrial and commercial use of NMP in solvents (for cleaning and degreasing) and for other uses in manufacturing lithium ion batteries was separated into several unreasonable risk determinations in the final risk evaluation.

In the final risk evaluation EPA added additional screening level analyses of general population oral and dermal exposures to NMP in surface water. Exposure to the general population via surface water can occur through recreational activities (*e.g.*, swimming).

Table 5-2. Crosswalk of Updates in Presentation of Unreasonable Risk Determinations between Draft and Final Risk Evaluations

Unreasonable Risk Determinations in Final Risk Evaluation	Unreasonable Risk Determinations in Draft Risk Evaluation
• Industrial and commercial use in paints and coatings in lacquers, stains, varnishes, primers and floor finishes, and powder coatings in surface preparation	• Industrial and commercial use in paint and coatings (lacquers, stains, varnishes, primers and floor finishes, and powder coatings, surface preparation), in paint additives and coating additives not described by other codes in several manufacturing sectors, and in adhesives and sealants, several types
• Industrial and commercial use in paint additives and coating additives not described by other codes in computer and electronic product manufacturing in electronic parts manufacturing.	
• Industrial and commercial use in paint additives and coating additives not described by other codes in computer and electronic parts manufacturing for use in semiconductor manufacturing.	
• Industrial and commercial use in paint additives and coating additives not described by other codes in multiple manufacturing sectors	
• Industrial and commercial use in adhesives and sealants including binding agents, single component glues and adhesives, including lubricant adhesives, and two-component glues and adhesives including some resins	
• Industrial and commercial use as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing	• Industrial and commercial use as a solvent (for cleaning or degreasing) use in electrical equipment, appliance and component manufacturing and for other uses in manufacturing lithium ion batteries
• Industrial and commercial use as a solvent for cleaning and degreasing in electrical equipment, appliance and component manufacturing for use in semiconductor manufacturing	
• Industrial and commercial use in other uses in lithium ion battery manufacturing	
• Consumer use in adhesives and sealants in glues and adhesives, including lubricant adhesives and sealants	• Consumer use as adhesive and sealant, single component glues and adhesives, including lubricant adhesives and two-component glues and adhesives, including some resins

5.4 Unreasonable Risk Determination Conclusion

5.4.1 No Unreasonable Risk Determinations

TSCA Section 6(b)(4) requires EPA to conduct risk evaluations to determine whether chemical substances present unreasonable risk under their conditions of use. In conducting risk evaluations, "EPA will determine whether the chemical substance presents an unreasonable risk of injury to health or the environment under each condition of use within the scope of the risk evaluation…" 40 CFR 702.47. Pursuant to TSCA Section 6(i)(1), a determination of "no unreasonable risk" shall be issued by order and considered to be final agency action. Under EPA's implementing regulations, "[a] determination made by EPA that the chemical substance, under one or more of the conditions of use within the scope of the risk evaluations, does not present an unreasonable risk of injury to health or the environment will be issued by order and considered to be a final Agency action, effective on the date of issuance of the order." 40 CFR 702.49(d).

EPA has determined that the following conditions of use of NMP do not present an unreasonable risk of injury to health or the environment:

- Distribution in commerce (Section 5.2.1.11, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Industrial and commercial use in ink, toner, and colorant products in printer ink and inks in writing equipment (Section 5.2.1.19, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Industrial and commercial use in other uses in soldering materials (Section 5.2.1.22, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Industrial and commercial use in other uses in fertilizer and other agricultural chemical manufacturing, processing aids and solvents (Section 5.2.1.28, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Consumer use in paint and coating removers (Section 5.2.1.29, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Consumer use in adhesive removers (Section 5.2.1.30, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Consumer use in paints and coatings in lacquer, stains, varnishes, primers and floor finishes (Section 5.2.1.31, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Consumer use in paint additives and coating additives not described by other codes in paints and arts and crafts paints (Section 5.2.1.32, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Consumer use in other uses in automotive care products (Section 5.2.1.34, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Consumer use in other uses in cleaning and furniture care products, including wood cleaners, gasket removers (Section 5.2.1.35, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)
- Consumer use in other uses in lubricant and lubricant additives, including hydrophilic coatings (Section 5.2.1.36, Section 5.2.1.38, Section 5.2.2, Section 4, and Section 3)

This subsection of the final risk evaluation therefore constitutes the order required under TSCA Section 6(i)(1), and the "no unreasonable risk" determinations in this subsection are considered to be final agency action effective on the date of issuance of this order. All assumptions that went into reaching the determinations of no unreasonable risk for these conditions of use, including any considerations excluded for these conditions of use, are incorporated into this order.

The support for each determination of "no unreasonable risk" is set forth in Section 5.2 of the final risk evaluation, "Detailed Unreasonable Risk Determinations by Condition of Use." This subsection also constitutes the statement of basis and purpose required by TSCA Section 26(f).

5.4.2 Unreasonable Risk Determinations

EPA has determined that the following conditions of use of NMP present an unreasonable risk of injury to health:

- Domestic manufacture
- Import
- Processing: as a reactant or intermediate in plastic material and resin manufacturing and other non-incorporative processing
- Processing: incorporation into a formulation, mixture or reaction product in multiple industrial sectors
- Processing: incorporation into articles in lubricants and lubricant additives in machinery manufacturing
- Processing: incorporation into articles in paint additives and coating additives not described by other codes in transportation equipment manufacturing
- Processing: incorporation into articles as a solvent (which becomes part of product formulation or mixture), including in textiles, apparel and leather manufacturing
- Processing: incorporation into articles in other sectors, including in plastic product manufacturing
- Processing: repackaging in wholesale and retail trade
- Processing: recycling
- Industrial and commercial use in paints, coatings, and, adhesive removers
- Industrial and commercial use in paints and coatings in lacquers, stains, varnishes, primers and floor finishes, and powder coatings, surface preparation
- Industrial and commercial use in paint additives and coating additives not described by other codes in computer and electronic product manufacturing in electronic parts manufacturing
- Industrial and commercial use in paint additives and coating additives not described by other codes in computer and electronic product manufacturing for use in semiconductor manufacturing
- Industrial and commercial use in in paint additives and coating additives not described by other codes in several manufacturing sectors
- Industrial and commercial use as a solvent (for cleaning or degreasing) use in electrical equipment, appliance and component manufacturing
- Industrial and commercial use as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing for use in semiconductor manufacturing
- Industrial and commercial use in processing aids, specific to petroleum production in petrochemical manufacturing, in other uses in oil and gas drilling, extraction and support activities, and in functional fluids (closed systems)
- Industrial and commercial use in adhesives and sealants including binding agents, single component glues and adhesives, including lubricant adhesives, and two-component glues and adhesives including some resins
- Industrial and commercial use in other uses in anti-freeze and de-icing products, automotive care products, and lubricants and greases
- Industrial and commercial use in other uses in metal products not covered elsewhere, and lubricant and lubricant additives including hydrophilic coatings
- Industrial and commercial use in other uses in laboratory chemicals

- Industrial and commercial uses in other uses in lithium ion battery manufacturing
- Industrial and commercial use in other uses in cleaning and furniture care products, including wood cleaners and gasket removers
- Consumer use in adhesives and sealants in glues and adhesives, including lubricant adhesives and sealants
- Disposal

EPA will initiate TSCA Section 6(a) risk management actions on these conditions of use as required under TSCA Section 6(c)(1). Pursuant to TSCA Section 6(i)(2), the "unreasonable risk" determinations for these conditions of use are not considered final agency actions.

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APPENDICES

Appendix A REGULATORY HISTORY

A.1 Federal Laws and Regulations

Table_Apx A-1. Federal Laws and Regulations

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
EPA Statutes/Regulations		
Toxic Substances Control Act (TSCA) – Section 6(a)	If EPA evaluates the risk of a chemical substance, in accordance with TSCA Section 6(b)(A), and concludes that the manufacture (including import), processing, distribution in commerce, disposal of such chemical substance, or any combination of these activities, presents an unreasonable risk of injury to human health or the environment, then EPA shall, by rule, take one or more of the actions described in TSCA Section 6(a)(1)-(7) to ensure the chemical substance no longer presents an unreasonable risk.	Proposed rule (82 FR 7464) regulating NMP uses in paint and coating removal
Toxic Substances Control Act (TSCA) – Section 6(b)	Directs EPA to promulgate regulations to establish processes for prioritizing chemical substances and conducting risk evaluations on priority chemical substances. In the meantime, EPA was required to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments.	NMP is on the initial list of 10 chemical substances to be evaluated for unreasonable risk of injury to health or the environment (81 FR 91927, December 19, 2016)
Toxic Substances Control Act (TSCA) – Section8(a)	The TSCA Section 8(a) Chemical Data Reporting (CDR) Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the US.	NMP manufacturing, importing, processing and use information is reported under the CDR rule (76 FR 50816, August 16, 2011).
Toxic Substances Control Act (TSCA) – Section8(b)	EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical substance manufactured,	NMP was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	processed, or imported in the United States.	review process (60 FR 16309, March 29, 1995).
Toxic Substances Control Act (TSCA) – Section 8(e)	Manufacturers (including importers), processors and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment.	Seven notifications of substantial risk (Section 8(e)) received (2007 – 2010) (US EPA, ChemView. Accessed April 13, 2017).
Toxic Substances Control Act (TSCA) – Section 4	Provides EPA with authority to issue rules and orders requiring manufacturers (including importers) and processors to test chemical substances and mixtures.	Six submissions from a test rule (Section 4) received in the mid-1990s. (US EPA, ChemView. Accessed April 13, 2017).
Emergency Planning and Community Right-To-Know Act (EPCRA) – Section 313	Requires annual reporting from facilities in specific industry sectors that employ 10 or more full time equivalent employees and that manufacture, process, or otherwise use a TRI-listed chemical in quantities above threshold levels. A facility that meets reporting requirements must submit a reporting form for each chemical for which it triggered reporting, providing data across a variety of categories, including activities and uses of the chemical, releases and other waste management (*e.g.*, quantities recycled, treated, combusted) and pollution prevention activities (under Section 6607 of the Pollution Prevention Act). This data includes on-site and off-site data as well as multimedia data (*i.e.*, air, land and water).	NMP is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 1, 1995.
Federal Food, Drug and Cosmetic Act (FFDCA) – Section 408	FFDCA governs the allowable residues of pesticides in food. Section 408 of the FFDCA provides EPA with the authority to set tolerances (rules that establish maximum allowable residue limits), or exemptions from the requirement of a tolerance, for all residues of a pesticide (including both active and inert ingredients) that are in or on food. Prior to issuing a tolerance or exemption from tolerance, EPA must determine that the tolerance or exemption is "safe."	NMP is currently approved for use as a solvent and co-solvent inert ingredient in pesticide formulations for both food and non-food uses and is exempt from the requirements of a tolerance limit (40 CFR Part 180.920).

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	Sections 408(b) and (c) of the FFDCA define "safe" to mean the Agency has a reasonable certainty that no harm will result from aggregate exposures to the pesticide residue, including all dietary exposure and all other exposure (*e.g.*, non-occupational exposures) for which there is reliable information. Pesticide tolerances or exemptions from tolerance that do not meet the FFDCA safety standard are subject to revocation. In the absence of a tolerance or an exemption from tolerance, a food containing a pesticide residue is considered adulterated and may not be distributed in interstate commerce.	
Clean Air Act (CAA) – Section 111 (b)	Requires EPA to establish new source performance standards (NSPS) for any category of new or modified stationary sources that EPA determines causes, or contributes significantly to, air pollution which may reasonably be anticipated to endanger public health or welfare. The standards are based on the degree of emission limitation achievable through the application of the best system of emission reduction which (considering the cost of achieving reductions and non-air quality health and environmental impacts and energy requirements) EPA determines has been adequately demonstrated.	NMP is subject to CAA Section 111 Standards of Performance for New Stationary Sources of Air Pollutants for volatile organic compound (VOC) emissions from synthetic organic chemical manufacturing industry distillation operations (40 CFR Part 60, subpart NNN) and reactor processes (40 CFR Part 60, Subpart RRR).
Clean Air Act (CAA) – Section 183(e)	Section 183(e) requires EPA to list the categories of consumer and commercial products that account for at least 80 percent of all VOC emissions in areas that violate the National Ambient Air Quality Standards for ozone and to issue standards for these categories that require "best available controls." In lieu of regulations, EPA may issue control techniques guidelines if the guidelines are determined to be substantially as effective as regulations.	NMP is listed under the National Volatile Organic Compound Emission Standards for Aerosol Coatings (40 CFR part 59, subpart E).
Clean Air Act (CAA) – Section 612	Under Section 612 of the CAA, EPA's Significant New Alternatives Policy	Under EPA's SNAP program, EPA listed NMP as an acceptable

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	(SNAP) program reviews substitutes for ozone depleting substances within a comparative risk framework. EPA publishes lists of acceptable and unacceptable alternatives. A determination that an alternative is unacceptable, or acceptable only with conditions, is made through rulemaking.	substitute for "straight organic solvent cleaning (with terpenes, C620 petroleum hydrocarbons, oxygenated organic solvents such as ketones, esters, alcohols, etc.)" for metals, electronics and precision cleaning and "Oxygenated organic solvents (esters, ethers, alcohols, ketones)" for aerosol solvents (59 FR, March 18, 1994).
Safe Drinking Water Act (SDWA) – Section 1412 (b)	Every 5 years, EPA must publish a list of contaminants (1) that are currently unregulated, (2) that are known or anticipated to occur in public water systems, and (3) which might require regulations under SDWA. EPA must also determine whether to regulate at least five contaminants from the list every 5 years.	NMP was identified on both the Third (2009) and Fourth (2016) Contaminant Candidate Lists (74 FR 51850, October 8, 2009) (81 FR 81099 November 17, 2016).
Other Federal Statutes/Regulations		
Occupational Safety and Health Act (OSHA)	Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress, or unsanitary conditions. Under the Act, OSHA can issue occupational safety and health standards including such provisions as Permissible Exposure Limits (PELs), exposure monitoring, engineering and administrative control measures and respiratory protection.	OSHA has not established a PEL for NMP.
Federal Food, Drug and Cosmetic Act (FFDCA)	Provides the U.S Food and Drug Administration (FDA) with authority to oversee the safety of food, drugs and cosmetics.	Food and Drug Administration identifies NMP as an "Indirect Additive Used in Food Contact Substances" specifically as: 1) an adjuvant substance in the preparation of slimicides (21 CFR 176.300), 2) an adjuvant substance in the production of polysulfone resin

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
		authorized for use as articles intended for use in contact with food (21 CFR 177.1655) and 3) a residual solvent in polyetherone sulfone resins authorized as articles for repeated use in contact with food (21 CFR 177.2440). FDA also identifies NMP as a Class 2 solvent, namely a solvent that "should be limited in pharmaceutical products because of their inherent toxicity." FDA established a Permissible Daily Exposure (PDE) for NMP of 5.3 mg/day with a concentration limit of 530 ppm. FDA's Center for Veterinary Medicine developed a method in 2011 for detection of the residues of NMP in edible tissues of cattle (21 CFR 500.1410)
Federal Hazardous Material Transportation Act	Section 5103 of the Act directs the Secretary of Transportation to: Designate material (including an explosive, radioactive material, infectious substance, flammable or combustible liquid, solid or gas, toxic, oxidizing or corrosive material and compressed gas) as hazardous when the Secretary determines that transporting the material in commerce may pose an unreasonable risk to health and safety or property. Issue regulations for the safe transportation, including security of hazardous material in intrastate, interstate and foreign commerce.	The Department of Transportation (DOT) has designated NMP as a hazardous material, and there are special requirements for marking, labeling and transporting it (49 CFR Part 171, 49 CFR 172, 40 CFR § 173.202 and 40 CFR § 173.242.

A.2 State Laws and Regulations

Table_Apx A-2. State Laws and Regulations

State Actions	Description of Action
State Air Regulations	New Hampshire (Env-A 1400: Regulated Toxic Air Pollutants) lists NMP as a regulated toxic air pollutant.

State Actions	Description of Action
	Vermont (Vermont Air Pollution Control Regulations, 5261) lists NMP as a hazardous air contaminant.
Chemicals of Concern to Children	Several states have adopted reporting laws for chemicals in children's products that include NMP including Oregon (OAR 333-016-2000), Vermont (18 V.S.A. Sections 1771 to 1779) and Washington state (WAC 173-334-130). Minnesota has listed NMP as a chemical of concern to children (Minnesota Statutes 116.9401 to 116.9407).
State Permissible Exposure Limits	California PEL is 1 ppm as an 8hr TWA, along with a skin notation (Cal Code Regs, title 8, Section 5155).
State Right-to-Know Acts	Massachusetts (454 CMR 21.00), New Jersey (42 N.J.R. 1709(a)) and Pennsylvania (Chapter 323. Hazardous Substance List).
Other	In California, NMP is listed on Proposition 65 (Cal. Code Regs. Title 27, Section 27001) due to reproductive toxicity. California OEHHA lists a Maximum Allowable Dose Level (MADL) for inhalation exposure = 3,200 µg/day MADL for dermal exposure = 17,000 µg/day. The California Department of Toxic Substances Control (DTSC) Safer Consumer Products Program lists NMP as a Candidate Chemical for development toxicity and reproductive toxicity. In addition, DTSC is moving to address paint strippers containing NMP and specifically cautioned against replacing methylene chloride with NMP. In August 2018 the California DTSC Safer Consumer Products program proposed to list Paint and Varnish Strippers and Graffiti Removers Containing NMP as a priority product citing (1) potential for human and other organism exposure to NMP in paint and varnish strippers and graffiti removers; and (2) the exposure has the potential to contribute to or cause significant or widespread adverse impacts. DTSC published a Product-Chemical Profile for Paint and Varnish Strippers and Graffiti Removers Containing NMP to support the listing. California Department of Public Health's Hazard Evaluation System and Information Service (HESIS) issued a Health Hazard Advisory on NMP in 2006 and updated the Advisory in June 2014. The Advisory is aimed at workers and employers at sites where NMP is used.

A.3 International Laws and Regulations

Table_Apx A-3. Regulatory Actions by Other Governments and Tribes

Country/Organization	Requirements and Restrictions
European Union	In 2011, NMP was listed on the Candidate list as a Substance of Very High Concern (SVHC) under regulation (EC) No 1907/2006 – REACH. In March 2017, NMP was included in the public consultation of chemicals recommended for inclusion in Annex XIV of the ECHA under Annex (Authorisation list) of regulation (EC) No 1907/2006 – REACH. In 2013, the Netherlands submitted a proposal under REACH to restrict manufacturing and all industrial and professional uses of NMP where

Country/Organization	Requirements and Restrictions
	workers' exposure exceeds a level specified in the restriction ECHA database. Accessed April 18, 2017). On April 18, 2018, the European Union added NMP to REACH Annex XVII, the restricted substances list. The action specifies three conditions of restriction. The conditions are: 1) NMP shall not be placed on the market as a substance on its own or in mixtures in concentrations greater than 0.3% after May 9, 2020, unless manufacturers, importers and downstream users have included chemical safety reports and SDSs with Derived No-Effect Levels (DNELs) relating to workers' exposures of 14,4 mg/m^3 for exposure by inhalation and 4,8 mg/kg/day for dermal exposure; 2) NMP shall not be manufactured, or used, as a substance on its own or in mixtures in a concentration equal to or greater than 0.3% after May 9, 2020 unless manufacturers and downstream users take the appropriate risk management measures and provide the appropriate operational conditions to ensure that exposure of workers is below the DNELs specified above: and 3) the restrictions above shall apply from May 9, 2024 to placing on the market for use, or use, as a solvent or reactant in the process of coating wires.
Australia	NMP was assessed under Human Health Tier III of the Inventory Multi-tiered Assessment and Prioritisation (IMAP) (National Industrial Chemicals Notification and Assessment Scheme, NICNAS, 2017, Human Health Tier III assessment for 2-Pyrrolidinone, 1methyl-. Accessed April,18 2017).
Japan	NMP is regulated in Japan under the following legislation: • Act on the Evaluation of Chemical Substances and Regulation of their Manufacture, etc. (Chemical Substances Control Law) • Industrial Safety and Health Act (National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP). Accessed April 18, 2017).
European Union and Australia, Austria, Belgium, Canada (Ontario), Denmark, Finland, France, Germany, Ireland, Italy, Latvia, New Zealand, Poland, Spain, Sweden, Switzerland, The Netherlands, Turkey and the United Kingdom.	Occupational exposure limits (OELs) for NMP (GESTIS International limit values for chemical agents (OELs) database. Accessed April 18, 2017).

Appendix B LIST OF SUPPLEMENTAL DOCUMENTS

1. Associated Systematic Review Data Quality Evaluation and Data Extraction Documents – Provides additional detail and information on individual study or data evaluations and data extractions including criteria and scoring results.

    a. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020h)
    b. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Data Quality Evaluation of Physical and Chemical Properties Studies. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020a)
    c. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020j)
    d. *Final Risk Evaluation for n-Methylpyrrolidone (NMP) Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data - Common Sources. Docket EPA-HQ-OPPT-2019-0236.* (U.S. EPA, 2020k)
    e. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Data Quality Evaluation of Consumer and General Population Exposure Studies. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020g)
    f. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Studies. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020i)
    g. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies - Animal and In Vitro Studies. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020l)
    h. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies - Epidemiological Studies. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020m)
    i. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Updates to the Data Quality Criteria for Epidemiological Studies.* (U.S. EPA, 2020o)
    j. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Systematic Review Supplemental File: Data Extraction Tables for Epidemiological Studies. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020u)

2. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Supplemental Information on Occupational Exposure Assessment. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020f) – Provides additional details and information on the occupational exposure assessment including PBPK modeling inputs and air concentration model equations, inputs, and outputs.

3. *Final Risk Evaluation for n-Methylpyrrolidone (NMP), Supplemental Information on Consumer Exposure Assessment. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020b) – Provides additional details and information on the consumer exposure assessment, including Consumer Exposure Model (CEM) approach, inputs and sensitivity analysis.

4. *Final Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1-Methyl-) (NMP), Benchmark Dose Modeling Supplemental File. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020e) – Provides additional details and results of the benchmark dose modeling of the human health hazard endpoints.

5. *Final Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information File on Occupational Risk Calculations. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020s)

6. *Final Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information on Consumer Exposure Assessment, Consumer Exposure Model and Multi-Chamber Concentration and Exposure Model Input Parameters. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020c)

7. *Final Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information File on Consumer Exposure Assessment, Consumer Exposure Model and Multi-Chamber Concentration and Exposure Model Outputs. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020d)

8. *Final Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information File on Consumer Exposure Assessment PBPK Model Inputs and Outputs, and Consumer Risk Calculations. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020p)

9. *Final Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Information File on PBPK Model Code. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020v)

Appendix C MASS BALANCE

EPA attempted to develop a mass balance to account for the amount of NMP entering and leaving all facilities in the United States. EPA attempted to quantify the amount of NMP associated with each of its life cycle stages from introduction into commerce in the U.S. (from both domestic manufacture and import), processing, use, release, and disposal using 2016 CDR, 2015 TRI, literature, and public comments. Due to limitations in the reasonably available data (*e.g.*, reporting thresholds, CBI, data from different years), the mass balance may not account for all of the NMP in commerce in the U.S. or could potentially allocate portions of the production volume incorrectly. The following subsections described EPA's approach to developing the mass balance and the result of the mass balance.

C.1 Approach for Developing the Mass Balance

EPA used the reported aggregated production volume of 160,818,058 lbs from the 2016 CDR data as the amount of NMP manufactured and imported to the U.S. (U.S. EPA, 2016a). Starting with this volume, EPA attempted to estimate the portion of the volume used domestically versus or exported. The export volume was estimated to be 14,601,983 lbs in 2015; however, this does not account for export volumes claimed as CBI in the 2016 CDR (U.S. EPA, 2016a). The domestic use volume was assumed to be anything not reported as exported in the 2016 CDR plus any volume reported as transferred for off-site recycling in the 2015 TRI. EPA only considered the off-site recycling volume as EPA assumes any volume reported for on-site recycling is reused at the site with consumption, disposal, and treatment of the recycled volume accounted for in the facility's other reported TRI values and thus already accounted for in the mass balance. EPA assumed the volume reported for off-site recycling is reintroduced into commerce similar to virgin (*i.e.*, unused directly from manufacturer or importer) NMP. This resulted in a total of 158,320,923 lbs, or 98% of the total PV, being used domestically.

Use volumes were determined based on 2016 CDR (U.S. EPA, 2016a), EPA's 2015 TSCA Work Plan Chemical Risk Assessment n-Methylpyrrolidone: Paint Stripper Use (U.S. EPA, 2015c), public comments (EaglePicher Technologies, 2020a; Fujifilm Holdings America Corporation, 2020; Celanese Engineered, 2017; Saft American, 2017; Thomas, 2017), and 2015 TRI releases for sites that use NMP as a reactant (calculated with assumed reaction extent) (U.S. EPA, 2016b). Based on these sources, an estimated 25% of the domestic use volume (38,587,620 lbs) is used as a reactant, 9% (14,248,883 lbs) is used for paint stripping, 1.5% (2,425,000 lbs), is used for chemical processing excluding formulation, 1.2% (1,847,567 lbs) is used in the electronics industry, 0.46% (728,000 lbs) is used in paints and coatings, 0.33% (521,000 lbs) is used as a solvent for cleaning and degreasing, 0.11% (181,000 lbs) is used in ink, toner, and colorant products, 0.002% (3,080 lbs) is used as a processing aid specific to petroleum production, and 0.001% (1,760 lbs) is used in adhesives and sealants. Because some of these estimates are from 2016 CDR (and does not account for CBI volumes) or from individual companies and trade associations (as opposed to the entire industry), they may not represent the entire volume of NMP for these uses. Therefore, the remaining 63% of the domestic use volume (99,507,013 lbs) is used in miscellaneous uses, including those already mentioned.

During manufacture, processing, and use, a portion of volume of NMP at a given site may be released to the environment or end up in waste streams that are ultimately sent for on- or off-site treatment, disposal, energy recovery, or recycling. EPA used data from the 2015 TRI to quantify volumes associated with each end-of-life activities (U.S. EPA, 2016b). 2015 TRI data was grouped into the following categories of end-of-life activities: wastewater discharges, water discharges, land disposal, air emissions, off-site recycling, energy recovery, and waste treatment.

The volume estimated for wastewater discharges includes the total volume reported by facilities as transferred to off-site wastewater treatment (non-POTW) and off-site POTW treatment. It does not account for subsequent removal from wastewater streams into air or sludge that may occur at such treatment sites. The volume estimated for water discharges includes volumes reported by facilities for on-site surface water discharges. The amount calculated for land disposal includes the releases from all on-site and off-site underground injection, surface impoundment, land application, landfills, and any other land disposal reported in the 2015 TRI (U.S. EPA, 2016b). The volume estimated for air emissions includes the total reported fugitive air emissions and stack air emissions from 2015 TRI reporters (U.S. EPA, 2016b).

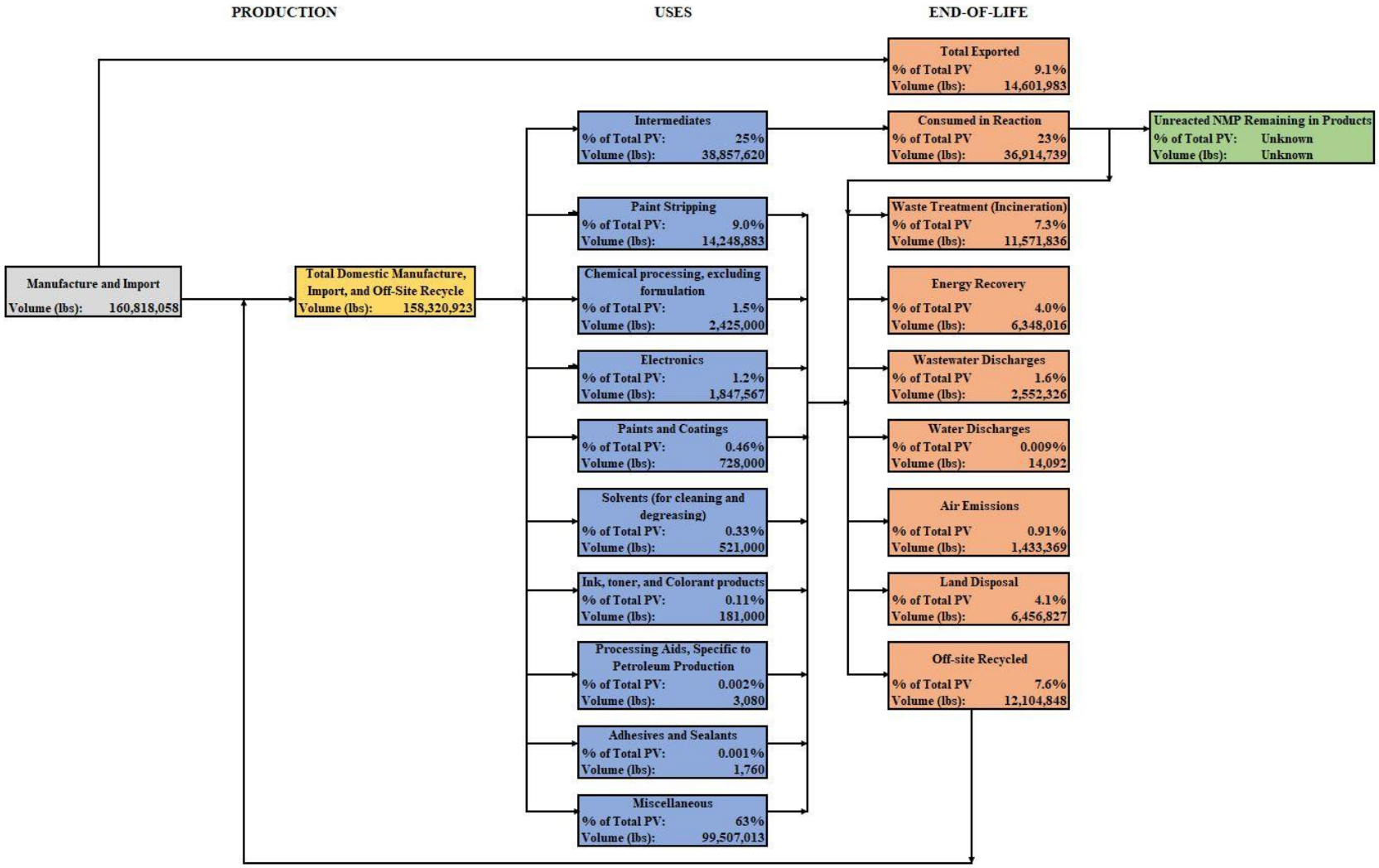
For recycling, TRI includes volumes for both on- and off-site recycling. As stated above, EPA assumed that any volume reported for on-site recycle is reused at the site with consumption, disposal, and treatment of the recycled volume accounted for in the facility's other reported TRI values and not further considered for the mass balance. EPA assumed the volume reported for off-site recycling is reintroduced into commerce similar to virgin (*i.e.*, unused directly from manufacturer or importer) NMP.

Any unused, spent, or waste NMP not accounted for above is expected to be sent for further waste treatment. These methods can be reported to TRI specifically as energy recovery or generally as waste treatment. However, volumes reported as sent for off-site energy recovery or treatment can be double counted if the site receiving the waste NMP is also required to report to TRI for NMP. To attempt to account for these transfers, EPA mapped reported off-site transfers for treatment or energy recovery using RCRA IDs and subtracted out any volume reported as transferred to another NMP reporter. The treatment and energy recovery volumes also assume 100% destruction/removal efficiencies which is likely unrealistic. Therefore, some portion of these values may also be counted in releases.

The end-of-life stage also accounts for NMP that is consumed in a reaction from reactant uses. To estimate the amount that is consumed in reaction, EPA identified in the sites in TRI that report NMP uses as a reactant and subtracted out the volume reported as released, disposed of, or otherwise managed as waste at each site from the intermediate use volume and assumed the remainder was consumed. EPA acknowledges that some portion of the intermediate use volume may remain as unintended impurities in products from the reaction; however, this volume cannot be quantified.

C.2 Results and Uncertainties in the Mass Balance

Figure_Apx C-1 shows the result of the mass balance. The overall percentage of NMP accounted for at the end-of-life is 83% of the 2016 CDR production volume. The 17% of the volume that is unaccounted for is most likely due to limitations in reporting requirements (*e.g.*, reporting thresholds) for TRI resulting in certain sites not being required to report. Other sources of uncertainty include comparison of data from different years, calculated volume of NMP used as a reactant based on 2015 TRI data and assumed reaction extent, CBI on exported volumes, double counting of treatment and energy recovery volumes, and unknown volumes of unreacted NMP remaining in products.

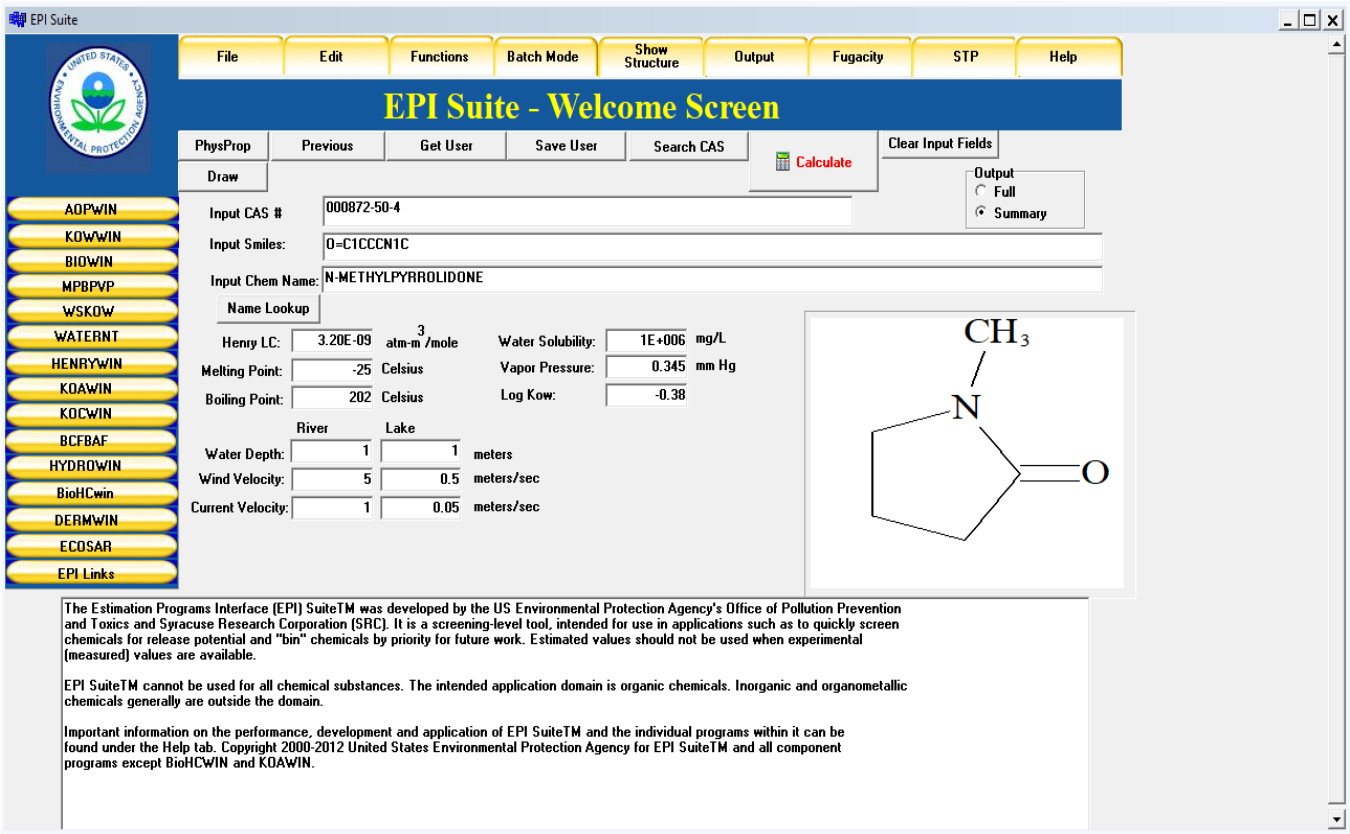


Figure_Apx C-1. NMP Mass Balance

Appendix D FATE AND TRANSPORT

EPI Suite™ Model Inputs

To set up EPI Suite™ for estimating fate properties of NMP, NMP was identified using the "Name Lookup" function. The physical and chemical properties were input based on the values in Table 1-1. EPI Suite™ was run using default settings (*i.e.*, no other parameters were changed or input).



Figure_Apx D-1. EPI Suite™ Model Inputs for Estimating NMP Fate and Transport Properties

Table_Apx D-1. Biodegradation Study Summary for NMP

Study Type (year)	Initial Concentration	Inoculum Source	(An)aerobic Status	Duration	Result	Comments	Affiliated Reference	Data Quality Evaluation results of Full Study Report
Water								
Other; Degradation kinetics of NMP in liquid culture under various parameters	≥500 to ≤2000 mg/L	activated sludge, industrial, adapted	aerobic	28h	Biodegradation parameter: half-life: 50%/5.05h	The reviewer agreed with this study's overall quality level.	Cai et al. (2014)	High
Other; Semi-continuous activated sludge test following ASTM (1975) procedure for biodegradation of synthetic detergents	100 ppm	activated sludge, domestic (adaptation not specified)	aerobic	7d	Biodegradation parameter: percent removal: 95%/7d after 5-day incremental acclimation period (primary biodegradation; complete mineralization not observed)	The reviewer agreed with this study's overall quality level.	Chow and Ng (1983)	High
Other; Static die-away test similar to the method recommended by the British Standard Technical Committee of Synthetic Detergents	100 ppm	activated sludge, domestic (adaptation not specified)	aerobic	14d	Biodegradation parameter: COD: 45%/14d; Biodegradation parameter: percent removal: 95%/14d	The reviewer agreed with this study's overall quality level.	Chow and Ng (1983)	High
Coupled-units test (adaptation of the OECD Confirmatory Test; OECD, 1976)	≥12 mg C/L	Communal sewage treatment plant effluent (adaptation not specified)	Aerobic	4-12 weeks	Biodegradation parameter: DOC: 99%	The reviewer agreed with this study's overall quality level.	Gerike and Fischer (1979)	High
OECD-screening, OECD 301E	3-20 mg C/L	Surface water	Aerobic	19 days	Biodegradation parameter: DOC: 99%/1 day	The reviewer agreed with this study's overall quality level.	Gerike and Fischer (1979)	High

EPA OPPTS 835.3200 (Zahn-Wellens / EMPA Test OECD 302B)	400 mg C/L	Industrial sewage treatment plant	Aerobic	14 days	Biodegradation parameter: DOC: 98%	The reviewer agreed with this study's overall quality level.	Gerike and Fischer (1979)	High
EPA OPPTS 835.3110 (Ready Biodegradability); STURM OECD 301B (CO_2 Evolution)	10 mg C/L	Surface water	Aerobic	28 days	Biodegradation parameter: DOC: 97%	The reviewer agreed with this study's overall quality level.	Gerike and Fischer (1979)	High
EPA OPPTS 835.3100 (Aerobic Aquatic Biodegradation; MITI OECD 301C)	50 mg C/L	Sewage treatment plant	Aerobic	4 days	Biodegradation parameter: DOC: 95%	The reviewer agreed with this study's overall quality level.	Gerike and Fischer (1979)	High
EPA OPPTS 835.3100 (Aerobic Aquatic Biodegradation; Closed bottle OECD 301D)	1 mg C/L	Surface water	Aerobic	30 days	Biodegradation parameter: BODT30: 88%	The reviewer agreed with this study's overall quality level.	Gerike and Fischer (1979)	High
Other; Method based on Chow & Ng (1983) The biodegradation of n-methyl-2-pyrrolidone in water by sewage bacteria. Water Research 17, 117–118.	50 g/L	Activated sludge from municipal wastewater treatment plant in Zlin, Czech Republic and from an industrial WTP in Slovenska Lupca, Slovak Republic	Aerobic	10 days	Biodegradation parameter: test material: 100%/4days	The reviewer agreed with this study's overall quality level.	Křížek et al. (2015)	High
Other; semi-continuous system	92-200 mg/L	Activated sludge (adaptation not specified) from the Fukashiba Joint Waste Water Treatment Plant	aerobic	24h	Biodegradation parameter: TOC: 92% Biodegradation parameter: percent DOC: 94%	The reviewer agreed with this study's overall quality level. Also reviewed in HERO ID 4140473.	Matsui et al. (1975)	High

					Biodegradation parameter: percent removal: >98%			
OECD Guideline 301 C (Ready Biodegradability: Modified MITI Test (I)); Reported as Japanese MITI test	Not reported in secondary source	activated sludge, domestic (adaptation not specified)	aerobic	28d	Biodegradation parameter: BOD: 73%/28d	The reviewer agreed with this study's overall quality level.	Toxicology and Regulatory Affairs (2003)	Medium
Other; Biodegradation of NMP in municipal sewage under static and flow-through conditions and influence of NMP concentrations on non-adapted sludge	≥50 to ≤20000 g/L	activated sludge, adapted	aerobic	≤206h	Biodegradation parameter: theoretical oxygen uptake: 52-93%/≤206h	The reviewer downgraded this study's overall quality rating. They noted: Analytical methods were unclear which limits interpretation of the study results.	Gomolka and Gomolka (1981)	Medium
Soil								
Other; Non-guideline laboratory test	1.7 mg/kg	three types of soils (clay, loam, and sand)	Not specified	3 months	Biodegradation parameter: elimination half-life: 4.0 to 11.5d (soil); 4.0, 8.7, and 11.5d (clay, loam and sand) Biodegradation parameter: percent removal: ≥90%/21d	The reviewer agreed with this study's overall quality level.	Shaver (1984)	Medium

Table_Apx D-2. Photolysis Study Summary for n-Methyl-2-pyrrolidone

Study Type (year)	Wavelength Range	Duration	Result	Comments	Affiliated Reference	Data Quality Evaluation results of Full Study Report
Air						
Other; Rate constants for atmospheric reactions of 1-methyl-2-pyrrolidinone with OH radicals, NO_3 radicals, and O_3 measured and products of the OH radical and NO_3 radical reactions investigated	>300 nm	8-25 min	Photodegradation parameter: indirect photolysis: rate constant: for reaction with OH radicals: (2.15 ± 0.36)E-11 cm^3 $molecule^{-1}$ s^{-1}; Reaction with NO_3 radicals: (1.26 ± 0.40)E-13 cm^3 $molecule^{-1}$ s^{-1}	The reviewer agreed with this study's overall quality level.	Aschmann and Atkinson (1999)	High
Water						
Photocatalytic decomposition in aqueous solution using light sources of UVA, UVC, and UVLED	254 nm to 385 nm	120 min	Photodegradation parameter: indirect photolysis w/ and w/o catalyst: rate constant: 0.0125 min^{-1} to 0.0454 min^{-1}	Study performed in the presence of catalyst or at wavelengths not relevant to environmental conditions.	Aliabadi et al. (2012)	Unacceptable

Appendix E RELEASES TO THE ENVIRONMENT

Systematic Review for Environmental Exposures

During problem formulation, it was determined that the aquatic exposure pathway would not be further analyzed for NMP. The PECO was updated accordingly and all of the "on-topic" studies that entered the process were screened out at Level 3, prior to data evaluation. However, "on-topic" exposure literature for NMP did follow the systematic review process. 132 references were identified as "on-topic" and subjected to an initial title/abstract screen (Level 1) and proceeded to full-text screening (Level 2 and 3). 29 references proceeded to a "Gateway" screen (Level 3), intended to consider alignment with the current PECO. Only 22 references that entered Level 3 moved forward to data evaluation (Level 4).

First-tier Aquatic Exposure Assessment for NMP

EPA used data from EPA's TRI to estimate NMP concentrations released to ambient water by discharging facilities. This "first-tier" exposure assessment was used to derive conservative estimates of NMP surface water concentrations near facilities that reported the highest NMP water releases. EPA identified the top 12 industries reporting the highest NMP water releases and used the reported information to estimate surface water concentrations based on the 2015 TRI data and EPA's Exposure and Fate Assessment Screening Tool, Version 2014. The environmental release data used for this first-tier aquatic exposure assessment and reported in the NMP Problem Formulation can be found in Table 1-4 (U.S. EPA, 2018c). For this final risk evaluation, EPA also used updated, 2018 TRI release data.

Surface Water Concentrations

Surface water concentrations were estimated for multiple scenarios using E-FAST 2014, which can be used to estimate site-specific surface water concentrations based on estimated loadings of NMP into receiving water bodies. For TRI, the facilities' reported release quantities can be based on estimates from monitoring data or measurements (*i.e.*, continuous, random, or periodic), mass balance calculations, published or site-specific emission factors, or other approaches such as engineering calculations or best engineering judgment. E-FAST 2014 incorporates stream dilution at the point of release using stream flow distribution data contained within the model. Site-specific stream flow data are applied using a National Pollutant Discharge Elimination System (NPDES) code. If a specific discharger's NPDES code could not be identified within the E-FAST database, a surrogate site or generic Standard Industrial Classification (SIC) code was applied.

EPA considered multiple scenarios to estimate NMP concentrations in surface water resulting from industrial discharges. EPA used the first-tier, PDM within EPA's Exposure and Fate Assessment Screening Tool (E-FAST), and 2015 and more recent 2018 TRI facility release data, facilities reporting the largest releases of NMP were modeled based on the assumption of 12 or 250 days of release. The 12-day release scenario represents an acute exposure scenario wherein periodic maintenance and cleaning activities could result in monthly releases. The 250-day release scenario represents a chronic exposure scenario in which standard operations may result in continuous, or more protracted discharges of NMP. Six facilities reported direct discharges of NMP to surface waters and seven facilities reported transfer of NMP to a municipal treatment facility also known as a POTW facility for treatment and discharge into surface waters.

EPA did not identify water monitoring data for NMP during its review of the national surface water monitoring database. The 2015 and 2018 TRI data on direct and indirect environmental releases were used to estimate NMP concentrations in surface water. Direct releases represent environmental releases of NMP that are discharged directly from a facility into a receiving water body (after treatment),

whereas indirect releases are releases from the POTW where the facility has transferred NMP. The POTW releases are discharges to surface water that occur following treatment. EPA used an estimated removal rate of 92% in estimating NMP remaining in treated wastewater from indirect POTW discharges. Because TRI reported facility direct releases are the amounts at discharge, EPA estimates of surface water concentrations did not account for any additional treatment by an onsite system. The predicted surface water concentrations presented in below in Table_Apx E-1 are associated with a low flow – 7Q10, which is an annual minimum seven-day average stream flow over a ten-year recurrence interval. No post-release degradation or removal mechanisms (*e.g.*, hydrolysis, aerobic degradation, photolysis, volatilization) are applied in the calculation of the modeled surface water concentrations.

For the facility transferring NMP waste to the POTW in Pensacola, Florida, the POTW diverts 85% of its treated wastewater for reuse in other industrial facilities as process water. Only 15% of the treated wastewater is discharged into the receiving water of Perdido Bay. EPA therefore, estimated the NMP stream/receiving water concentration based on 15% of total NMP-containing treated wastewater discharged.

To capture "high-end" surface water concentrations, EPA compiled the release data for nine facilities that reported the largest NMP direct water releases. This represented 100 % of the total volume of NMP reported as a direct discharge to surface water during the 2015 and 2018 TRI reporting periods. Since there were many more facilities reporting indirect releases of NMP to surface water, seven of the facilities reporting the largest indirect water releases (representing ~ 11% of the total number of facilities reporting indirect discharges) were compiled. The volume of NMP released from these facilities encompassed more than 87% of the total volume of NMP reported as an indirect discharge to surface water.

The "high-end" surface water concentrations (*i.e.*, those obtained assuming a low stream flow for the receiving water body) from all PDM runs ranged from 4.2 µg/L to 228 µg/L, for the acute (*i.e.*, fewer than 20 days of environmental releases per year) and 1.6E-04 µg/L to 1,022 µg/L chronic exposure scenario (*i.e.*, more than 20 days of environmental releases per year assumed), respectively. The maximum acute scenario concentration was 228 µg/L and the maximum chronic scenario concentration was 1,022 µg/L. Comparing these concentrations with the respective aquatic ecological COCs of 100,000 µg/L for acute and 1,770 µg/L for chronic results in no exceedances for the acute scenario and no exceedances for the chronic scenario > 20 days (see Table 4-2). EPA does not anticipate a concern to aquatic organisms from NMP discharges to surface waters.

Table_Apx E-1. Releases of NMP to Surface Waters

Top Facility Discharges (2015/2018)		Onsite NMP Wastewater Releases[a] (lbs/yr)		NMP Transfers to Offsite POTW[b] (lbs/yr)	
Facility	**State**	**2015**	**2018**	**2015**	**2018**
Fortron Industries	NC	8,987	250	0	0
Spruance Plant	VA	4,602	4,672	0	0
GlobalFoundries	VT	451	736	0	0
BASF Corp.	AL	N/A	550		0
American Refining Group	PA	26.83	13	0	0
Essex Group, Fort Wayne	IN	22.1	44	0	
GlobalFoundries	NY	N/A	14		0
BASF Corp.	MI	2	11	269	304
Essex Group, Franklin	IN	N/A	2		0
Koch Membrane	MA			533,525	957,817
Pall Corp.,	FL			154,798	171,762
Air Products	MO			150,011	151,780
GVS; GE Healthcare: Westborough POTW	MA			154,651	141,758
Intel, Aloha; Intel, Ronler Acres: Rock Creek STP, Hillsboro[b]	OR			680,000	348,000
Veolia ES Technical Solutions, LLC	NJ				395,169
Intel Corp	AZ				163,000
Caterpillar, Inc	IL				144,672
Cree, Inc	NC				142,605
Pall Filtration	CA				125,631

[a] GVS and GE Healthcare facilities both discharge to the same Massachusetts (MA0100412) POTW. These releases (89,958 lbs/yr and 51,800 lbs/yr, respectively in 2018 and 100,606 lbs/yr and 54,045 lbs/yr, respectively in 2015) were combined to reflect POTW inflows.

[b] Intel-Aloha and Intel Ronler Campus both discharge to the Hillsboro POTW (Rock Creek STP, NPDES: OR0029777) so their releases (98,000lb/yr and 250,000, respectively in 2018 and 170,000 and 510,000, respectively in 2015) were combined to reflect the POTW inflows.

Table_Apx E-2. Estimated NMP Surface Water Concentrations

Top Facility Discharges (2015/2018)		PDM; Stream NMP Concentrations (2015)			PDM; Stream NMP Concentrations (2018)		
Facility	**State**	**Acute 12 day (µg/L)**	**Chronic 250 day (µg/L)**	**# Days COC Exceeded (1,770 µg/L)**	**Acute 12 day (µg/L)**	**Chronic 250 or 300 day (µg/L)**	**# Days COC Exceeded (1,770 µg/L)**
Direct Discharger Facilities							
Fortron Industries,	NC	224.00	10.75	0	6.2	2.5E-01	0

Top Facility Discharges (2015/2018)		PDM; Stream NMP Concentrations (2015)			PDM; Stream NMP Concentrations (2018)		
Facility	**State**	**Acute 12 day (µg/L)**	**Chronic 250 day (µg/L)**	**# Days COC Exceeded (1,770 µg/L)**	**Acute 12 day (µg/L)**	**Chronic 250 or 300 day (µg/L)**	**# Days COC Exceeded (1,770 µg/L)**
Spruance Plant,	VA	119.70	5.75	0	121	4.9	0
GlobalFoundries	VT	44.49	2.14	0	73	3.4	0
BASF, McIntosh	AL				7.6	2.9E-01	0
American Refining Group	PA	8.49	4.0E-01	0	4.2	1.7E-01	0
Essex Group, Fort Wayne	IN	5.56	2.7E-01	0	228	9.2	0
GlobalFoundries	NY				49	2.3	0
BASF Corp	MI	1.1E-03	4.9E-04	0	6.2E-03	5.4E-04	0
Essex Group Franklin	IN				30	1.4	0
Indirect Discharger Facilities							
Koch Membrane	MA		60	0		90	0
Pall Corp.[a]	FL		878	0		812	0
Air Products	MO		636	0		427	0
GVS; GE Healthcare[b]	MA		1,327	0		1,012	0
Intel, Aloha; Intel, Ronler Acres: Rock Creek[c]	OR		1,995	2		1,022	0
Veolia ES Technical Solutions, LLC[d]	NJ					28	0
Intel Corp.[e]	AZ					0	0
Caterpillar, Inc	IL					8.6E-01	0
Cree, Inc[d]	NC					22	0
Pall Filtration	CA					36	0

[a] Surface water concentration represents 15% of Pall Corporation wastewater sent to POTW for treatment and release. Remaining 85% of Pall Corporation discharges are sent to other industries for beneficial use.

[b] The total predicted NMP surface water concentration resulting from Westborough POTW releases is listed. The contribution from GVS is 643 ug/L and GE Healthcare is 369ug/L in 2018 and 863 ug/L and 464 ug/L, respectively, in 2015.

[c] The total predicted NMP surface water concentration resulting from Hillsboro POTW releases is listed. The contribution from Intel, Aloha is 288 ug/L and Intel, Ronler Acres is 734 ug/L in 2018 and 499 ug/L and 1,496 ug/L, respectively in 2015.

[d] The Veolia and Cree facilities transfer wastewater to a wastewater treatment facility that treats and removes 92% NMP and then is assumed to discharge remaining wastewater to the local POTW for treatment and discharge to surface waters

[e] The Intel, Chandler, Arizona facility discharges to several water reclamation facilities. These facilities do not discharge to surface waters, instead treated wastewaters are used for groundwater recharge and/or beneficial use per Arizona state permit requirements.

Appendix F OCCUPATIONAL EXPOSURES

Section F.1 contains information gathered by EPA in support of understanding glove use for pure NMP and for using NMP-containing formulations. For more information, including the results of an NMP glove permeability study, refer to the Crook and Simpson (2007) citation noted below as Health Safety Laboratory (2007).

F.1 Information on Gloves for Pure NMP and for Formulations containing NMP

Section F.1.1 contains information gathered by EPA in support of understanding glove use for pure NMP and for paint and coatings removal using NMP formulations. Section F.1.2 contains information on gloves and respirators from SDSs for NMP and NMP-containing Products.

F.1.1 Specifications for Gloves for Pure NMP and in Paint and Coating Removal Formulations containing NMP

Section F.1.1 contains information gathered by EPA in support of understanding glove use for pure NMP and for paint and coatings removal using NMP formulations (EPA-HQ-OPPT-2016-0231-0200). This information may be generally useful for a broader range of uses of NMP and is presented for illustrative purposes.

Summary on Suitable Gloves for Pure NMP and in Formulations

For scenarios where gloves can provide protection to achieve benchmark MOEs, gloves should be tested to determine whether they are protective against the specific formulation of the product that contains NMP. Several studies found in the literature indicate that the best types of glove material to protect against dermal exposure to pure NMP are Silver Shield, Butyl Rubber and Ansell Barrier laminate film. The next best types of glove among those studied to use for NMP exposure would be Neoprene and Natural Rubber/Latex. Among the studies, Silver Shield provided the best protection against NMP, whether it was in pure form or part of a tested formulation. Detailed information on these and other glove types which were evaluated for their permeation characteristics against NMP are provided below. The cited studies' results may be a good starting point for determining glove types to consider for glove testing.

Gloves for Pure NMP

There are many factors that determine proper chemical-resistant glove selection. In addition to the specific chemical(s) utilized, the most important factors include duration, frequency, and adversity of chemical exposure. The degree of dexterity required for the task and associated physical stress to the glove are also significant considerations. The manner in which employees are able to doff the various glove types to best prevent skin contamination is also important but sometimes overlooked.
Generally, dermal exposures to the solvents in paint and coating removal formulations may be assumed to be frequent or lengthy and may result in significant exposure. These assumptions affect the proper choice of glove type and errs on the side of caution, which is advised for any PPE decision since PPE is the last line of defense against exposure in an industrial hygienist's hierarchy of controls.

Table_Apx F-1 below summarizes commonly used industrial hygiene literature (*e.g.*, glove selection guides, manufacturer publications, etc.) and capture the highest rated glove types from each reference. Consideration of all factors (breakthrough time, qualitative indicator (QI), and other issues raised in the comments field) allow an overall determination of effectiveness.

Table_Apx F-1. Glove Types Evaluated for Pure NMP

Reference	Glove Type	Breakthrough Time	Qualitative Indicator	Comments
1	Ansell Barrier (Laminate Film) Glove	>480 mins	Very well suited	Degradation rate: Good-Excellent. Permeation rate: Excellent
	Natural Rubber	75 mins	Very well suited	Degradation rate: Excellent. Permeation rate: Very Good
	Butyl	>480 mins	Very well suited	Degradation rate: Excellent
2	Neoprene over Natural Rubber (Best Chem Master)	>480 mins	Safest, best selection	Highest rating attainable
	Butyl	>480 mins	Safest, best selection	Highest rating attainable
	Neoprene (Chloroflex)	>480 mins	Safest, best selection	Highest rating attainable
4	Butyl	8 hrs	Good for total immersion	Degradation rate: Excellent
	Natural Rubber	1.26 hrs	Good for accidental splash protection and intermittent contact	Degradation rate: Fair
	Nitrile	1.45 hrs	Good for accidental splash protection and intermittent contact	Degradation rate: Fair
8	Neoprene	226 mins	Used for high chemical exposure	Specific glove evaluated is Chem Ply N-440
	Natural Latex / Neoprene / Nitrile	50 mins	Used for repeated chemical contact	Specific glove evaluated is Trionic O-240
10	Silver Shield (North)	Not Provided	Recommended	Silver Shield and Butyl rubber gloves are the only two glove types recommended by this source
	Butyl	Not Provided	Recommended	

Based on the information from Table_Apx F-1, the three best types of glove material to protect against pure NMP dermal exposure are Silver Shield, Butyl Rubber and Ansell Barrier laminate film. The next best types of glove to use for pure NMP exposure would be Neoprene and Natural Rubber/Latex. As mentioned previously, Silver Shield gloves do not provide acceptable dexterity for most workers, so they are commonly worn as a base glove with a tighter-fitting glove (*e.g.,* latex) over the top. Alternatively, Butyl Rubber or Ansell Barrier laminate film gloves could be worn and would provide significant protection.

Key Points and Examples for Paint and Coating Removal Formulations

The U.S. EPA's Safety, Health and Environmental Management Division's (SHEMD) Guideline 44 (Personal Protective Equipment) states that when working with mixtures and formulated products, the chemical component with the shortest break-through time must be considered when determining the appropriate glove type for protection against chemical hazards unless specific test data are available (SHEMD, 2004). Additionally, an industrial hygienist will consider the formulation's chemical

properties, including the highest hazard component of the formulation, and whether individual components produce synergistic degradation effects. Typically, specific test data for formulations are not available and best judgment, based on these considerations provides the basis for glove type selection. However, in this case there are a few publications that specifically address glove types for use with methylene chloride and NMP as part of paint and coating removal formulations.

In early 2002, an article entitled "A Comparative Analysis of Glove Permeation Resistance to Paint Stripping Formulations" (Stull et al., 2002) specifically examined which glove types provide the best protection to users of commercial paint and coating removal products. Twenty different glove types were evaluated for degradation and resistance to permeation under continuous and/or intermittent contact with seven different paint and coating removal formulations in a multiple-phase experiment. Paint and coating removal formulations included some that were methylene chloride-based and others that were NMP-based. The study found that gloves made of Plastic Laminate (*e.g.,* Silver Shield) resisted permeation by the majority of paint and coating removal while Butyl Rubber provided the next best level of permeation resistance against the majority of formulations. However, Butyl Rubber gloves did show rapid permeation for methylene chloride-based formulations and would not be recommended for methylene chloride. It should be noted that PVA gloves, shown to be effective against pure methylene chloride, were not evaluated. Interestingly, more glove types resisted permeation of NMP-based formulations than conventional solvent-based products such as methylene chloride. The results showed that relatively small-molecule, volatile, chemical-based solvents cause somewhat more degradation and considerably more permeation of glove types as compared with NMP-based formulations against the same gloves. Key conclusions include the following: "However, paint stripper formulations represent varying multichemical mixtures and, ultimately, commercial paint strippers must be individually evaluated for permeation resistance against selected gloves" (Stull et al., 2002), and, "because of several potential synergistic effects well established in the literature and in this study for mixture permeation, it is highly recommended that glove selection decisions be based on testing of the commercial paint stripper against the specific glove in question" (Stull et al., 2002).

Another study from in 2007 entitled "Protective Glove Selection for Workers using NMP-Containing Products: Graffiti Removal" essentially came to the same conclusion; of the gloves studied Silver Shield gloves provide the best protection against NMP-based paint and coating removal formulations (Health Safety Laboratory, 2007). The study states that "Butyl gloves, used with caution would be a second choice" (Health Safety Laboratory, 2007). The increased dexterity and robustness of Butyl gloves were noted as an advantage of Butyl over Silver Shield. Key recommendations include that gloves should be "tested against all relevant chemical formulations as a matter of routine in order to inform glove selection" (Health Safety Laboratory, 2007) and "assumptions of glove choice based on the use of model compounds or similar formulations should be made with extreme caution (Health Safety Laboratory, 2007)." Additionally, Crook recommended that "The BS EN 374-3 continuous contact test and its successors should remain the benchmark for chemically protective glove type decisions" (Health Safety Laboratory, 2007).

In summary, these studies indicate that glove permeation continuous contact testing of each formulation is necessary to provide proper protection. These studies' results may be a good starting point for determining glove types to consider for permeation testing. The studies found that among gloves tested Silver Shield provide the best protection against both methylene chloride and NMP, whether they are in pure form or as part of a tested formulation. The best alternative for protection against methylene chloride would be PVA gloves, while the best alternative for NMP protection would be Butyl Rubber gloves. A more task-specific decision on appropriate glove type selection could be

made through employee interviews and observation of tasks using methylene chloride- or NMP-containing products.

F.1.2 Information on Gloves and Respirators from SDSs for NMP and NMP-containing Products

EPA reviewed SDSs for neat NMP and products containing NMP for information on glove and respiratory protection. Specifically, EPA reviewed SDSs for each occupational exposure scenario assessed in Section 2.4.1.2. EPA compiled the recommended glove materials and respiratory protection for each occupational exposure scenario from the reviewed SDSs (total of 21 SDSs were reviewed) in Table_Apx F-2. For neat NMP and NMP-containing products, the SDSs recommend a variety of glove materials, including butyl rubber (8 SDSs), nitrile rubber (9 SDSs), neoprene (8 SDSs), natural rubber (4 SDSs), polyvinyl chloride (PVC) (4 SDSs), latex (2 SDSs), and Teflon (1 SDS). Note that many of the reviewed SDSs included multiple glove material recommendations. Almost half of the reviewed SDSs indicated that respiratory protection was not needed under normal conditions with adequate ventilation, unless exposure limits are exceeded or workers experience irritation or other symptoms (10 of 21 SDSs). Three SDSs recommend the use of respirators with organic vapor cartridges. Four SDSs recommend the use of particulate filters in instances where mist or dusts may form while using the NMP-containing product. Four SDSs recommend the use of a self-contained breathing apparatus (SCBA) for emergency situations, such as spills, that can create intensive or prolonged exposure. Note that many of the reviewed SDSs included respiratory protection recommendations, based on the exposure scenario (*i.e.*, normal use, emergency, potential for mist or dust).

Table_Apx F-2. Recommended Glove Materials and Respiratory Protection for NMP and NMP-Containing Products from SDSs

Applicable Occupational Exposure Scenario	Material, NMP wt.%	Recommended Glove Material	Recommended Respiratory Protection	Source
Manufacturing; Repackaging; Chemical Processing, Excluding Formulation; Incorporation into a Formulation, Mixture or Reaction Product; Laboratory Use	Neat, 99-100%	Butyl rubber	No specific respirator recommended. SDS indicates to use an approved respirator if exposure limits are exceeded.	Tedia High Purity Solvents (2011)
Manufacturing; Repackaging; Chemical Processing, Excluding Formulation; Incorporation into a Formulation, Mixture or Reaction Product; Laboratory Use	Neat, 99%	Nitrile rubber, neoprene, butyl rubber	Industrial uses: Organic gases and vapors filter Type A Brown conforming to EN14387. Laboratory Use: Half mask, Valve filtering; or, Half mask, plus filter	Thermo Fisher Scientific (2019)
Application of Paints, Coatings, Adhesives and Sealants	Mixture, >85%	Butyl rubber or Teflon gloves	If vapors or mists are generated, wear a NIOSH/MSHA approved organic vapor/mist respirator or an air supplied respirator as appropriate. Use only self-contained breathing apparatus for emergencies.	AZEK (2015)
Application of Paints, Coatings, Adhesives and Sealants	Mixture, <1%	Polymer laminate; nitrile gloves may be worn over polymer laminate gloves to improve dexterity	Half facepiece or full facepiece air-purifying respirator suitable for organic vapors and particulates.	3M (2018)
Application of Paints, Coatings, Adhesives and Sealants	Mixture, <1%	Nitrile gloves	No specific respirator recommended. SDS indicates to use an approved respirator if	TLS (2013)

Applicable Occupational Exposure Scenario	Material, NMP wt.%	Recommended Glove Material	Recommended Respiratory Protection	Source
			exposure limits are exceeded.	
Printing and Writing	Mixture, >15%	Neoprene, butyl, or nitrile rubber	No specific respirator recommended. SDS indicates to use an approved respirator if exposure limits are exceeded.	Voxel Inc (2015)
Printing and Writing	Mixture, 0-5%	Neoprene, butyl, or nitrile rubber gloves with cuffs	No specific respirator recommended. SDS indicates to use an approved respirator if exposure limits are exceeded.	Novacentrix (2016)
Metal Finishing [a]	Mixture, 1-5%	Rubber gloves	No specific respirator recommended. SDS indicates to use an approved respirator if exposure limits are exceeded.	U.S. Chemical (2012)
Metal Finishing [a]; Automotive Car Servicing (aerosol use) [b]	Mixture, unspecified NMP concentration	Nitrile or polyvinyl chloride (PVC) gloves	No specific respirator recommended. SDS indicates to use an approved respirator if exposure limits are exceeded.	Simoniz USA (2012)
Removal of Paints, Coatings, Adhesives, and Sealants	Mixture, 20-30%	Butyl Rubber	Half facepiece or full facepiece air-purifying respirator suitable for organic vapors.	3M (2014)
Removal of Paints, Coatings, Adhesives, and Sealants	Mixture, 41%	Use gloves chemically resistant to this material (Neoprene, Nitrile, PVC)	No specific respirator recommended. SDS indicates to use an approved respirator if	TLS (2016)

Applicable Occupational Exposure Scenario	Material, NMP wt.%	Recommended Glove Material	Recommended Respiratory Protection	Source
			exposure limits are exceeded.	
Cleaning	Mixture, 90-95%	PVC-lined, latex, or Nitrile gloves	Normal use: Use NIOSH approved respiratory protection. Emergency: Self-contained breathing apparatus, air-line respirator, full-face respirator	Crest (2011)
Cleaning	Mixture, 1-5%	Natural Latex or Rubber	Normal use: not required. Emergency: A2P2 - Combo filter: gas filter type A with medium capacity and a class P2 particle filter.	Prestige (2010)
Automotive Car Servicing (aerosol use) [b]	Mixture, 30-40%	Neoprene	No specific respirator recommended. SDS indicates to use an approved respirator if exposure limits are exceeded.	Slide (2018)
Electronics Manufacturing	Mixture, unspecified NMP concentration	Butyl rubber	In case of low exposure, use cartridge respirator. In case of intensive or longer exposure, use self-contained breathing apparatus.	MicroChem (2012)
Electronics Manufacturing	Mixture, 0-1%	Neoprene or natural rubber gloves if handling an open or leaking battery	Not necessary under normal conditions.	Lenmar Battery (2014)
Soldering	Mixture, 1-3%	Nitrile rubber or natural rubber	When ventilation is not sufficient to remove	Kester (2017)

Applicable Occupational Exposure Scenario	Material, NMP wt.%	Recommended Glove Material	Recommended Respiratory Protection	Source
			fumes from the breathing zone, a safety approved respirator or self-contained breathing apparatus should be worn.	
Fertilizer Application	Mixture, <1%	Neoprene gloves	Wear air supplied respiratory protection if exposure concentrations are unknown. In case of inadequate ventilation or risk of inhalation of dust, use suitable respiratory equipment with particle filter.	Koch Agronomic (2011)
Fertilizer Application	Mixture, <10%	Chemical resistant gloves	Wear air supplied respiratory protection if exposure concentrations are unknown. In case of inadequate ventilation or risk of inhalation of mist, use suitable respiratory equipment with particle filter.	Koch Agronomic (2018)
Wood Preservatives	Mixture, <1%	Chemical-resistant gloves (such as barrier laminate, butyl rubber, nitrile rubber, neoprene rubber, polyvinyl chloride, vitro)	No specific respirator recommended. SDS indicates to use an approved respirator if exposure limits are exceeded.	Osmose Utilities (2015)

Applicable Occupational Exposure Scenario	Material, NMP wt.%	Recommended Glove Material	Recommended Respiratory Protection	Source
Recycling and Disposal [c]	Reclaimed neat NMP, 99-100%	Chemical resistant gloves	Use NIOSH-certified, air-purifying respirators with organic vapor cartridges when concentration of vapor or mist exceeds applicable exposure limits. Protection provided by air-purifying respirators is limited.	Safety-Kleen (2015)

[a] These products are recommended for use on metal parts, but EPA does not know the extent to which these products may be used within the six operations listed under metal finishing at 40 CFR 433.10.
[b] These SDSs are for aerosol cleaning products. EPA does not know the extent to which these products are used in the automotive service industry.
[c] Safety-Kleen is a waste management company; however, this SDS does not explicitly state that the NMP has been reclaimed.

Appendix G CONSUMER EXPOSURES

G.1 Overview of the E-FAST/CEM Model

The Exposure and Fate Assessment Screening Tool Version 2 (E-FAST2) Consumer Exposure Module (CEM) was selected for the consumer exposure modeling as the most appropriate model to use due to the lack of reasonably available emissions and monitoring data for NMP uses other than paint removers under consideration. Moreover, EPA did not have the input parameter data from specific NMP product chamber studies required to run more complex indoor air models for the consumer products under the scope of this assessment. CEM uses high-end input parameters/assumptions to generate conservative, upper-bound inhalation exposure estimates for aerosol spray products. The advantages of CEM are the following:

1. CEM model has been peer-reviewed.
2. CEM accommodates the inputs reasonably available for the products containing NMP in the indoor air model.
3. CEM uses the same calculation engine to compute indoor air concentrations from a source as the Multi-Chamber Concentration and Exposure Model (MCCEM) but does not require measured emission values (*e.g.*, chamber studies).

Modeling Air Concentrations

The model used a two-zone representation of a house to calculate the potential acute dose rate (mg/kg-bw/day) of NMP for users and non-users. Zone 1 represents the area where the consumer is using the product, whereas Zone 2 represents the remainder of the house. Zone 2 can be used for modeling passive exposure to non-users in the home (bystanders), such as children.

The general steps of the calculation engine within the CEM model included:

1. Introduction of the chemical (*i.e.*, NMP) into the room of use (Zone 1),
2. Transfer of the chemical to the rest of the house (Zone 2) due to exchange of air between the different rooms,
3. Exchange of the house air with outdoor air and,
4. Summation of the exposure doses as the modeled occupant moves about the house

The chemical of concern (*i.e.*, NMP) enters the room air through two pathways: (1) overspray of the product and (2) evaporation from a thin film. Six percent (6%) of the product was assumed to become instantly aerosolized (*i.e.*, product overspray) and was available for inhalation.
The CEM model uses data from the evaporation of a chemical film to calculate the rate of the mass evaporating from the application surface covered during product use (Chinn, 1981). The model assumes air exchanges from the room of use (Zone 1) and the rest of the house (Zone 2) according to interzonal flow. The model also allows air exchange from the house (Zone 1 & 2) with the outdoor air.

EPA used the default activity pattern in CEM based on the occupant being present in the home for most of the day. As the occupants moved around the house in the model, the NMP air concentration would vary. The exposure to the calculated air concentrations were summed using CEM to estimate a potential 24-hr dose.

The user's exposure to NMP depends on their activity pattern (*i.e.*, how much time using the product, as well as the time in the room of use or in the rest of the house) as to the concentration of NMP in the air

within each of these areas. Based on the varying air concentrations estimated by the CEM model over a 24-hour period, EPA then used the PBPK model to estimate internal dose of NMP from inhalation.

Chronic exposure assessments were not performed for any of the consumer COUs because the frequency of product used is unlikely to present a concern for chronic exposure.

Modeling Dermal Exposure

Since consumers do not always wear gloves when using consumer products, EPA modeled dermal exposures for all NMP-containing products. Though CEM can estimate dermal exposures using a chemical permeability coefficient, EPA used the PBPK model to estimate the internal dose of NMP as it is absorbed through the skin both from direct contact of the liquid product and through absorption of vapor through skin. The PBPK model thus, estimated the total internal dose of NMP through combined routes of exposure: inhalation, dermal and vapor through skin and was used to estimate exposures in the Paint Remover Risk Assessment.

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Supplemental Consumer Exposure and Risk Estimation Technical Report for NMP in Paint and Coating Removal [RIN 2070-AK07]

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1. Introduction

EPA performed this technical analysis of consumer exposure scenarios for the use of n-methylpyrrolidone (NMP) in paint and coating removal. Consistent with its final TSCA Work Plan Chemical Risk Assessment for NMP (EPA, 2015), this analysis adds additional exposure scenarios associated with the use of NMP in consumer paint and coating removal.

2. Executive Summary

In 2015, EPA completed a risk assessment for NMP in paint and coating removal (EPA, 2015)[10]. The NMP risk assessment found risks of concern for occupational use and certain consumer uses of NMP in paint and coating removal. EPA conducted exposure modeling and risk analyses to investigate additional exposure parameters to those included in the NMP risk assessment.

The NMP risk assessment evaluated risks based on emissions data from a brush-applied product. This supplemental analysis used the same modeling methods to evaluate exposures and estimate risks from larger projects. This additional exposure modeling describes the same product type (paint and coating removal product) as in the NMP risk assessment, but with extended application times, increased product use and altered user behavior.

The expanded consumer exposure modeling used the Multi-Chamber Concentration and Exposure Model (MCCEM) (EPA 2010), the same model used in the NMP risk assessment. MCCEM was used to estimate 24-hr indoor air concentrations of NMP (*i.e.*, acute exposure) for the additional consumer exposure modeling scenarios described here. These air concentrations were calculated for both users[11] and bystanders[12] of paint and coating removal products containing NMP in a residential setting. Generally, the modeling reported in this document adopted many of the input parameters and assumptions described in the NMP risk assessment, with the exception of those variations necessary to evaluate additional consumer exposure scenarios.

The risk calculations used physiologically based pharmacokinetic (PBPK) modeling to incorporate both the airborne exposure, calculated in this document, and the dermal exposures resulting from product use. This is the same methodology as was applied in the NMP risk assessment. The results of the risk calculations are discussed in the Section 6 of this document. As expected, the larger projects modeled in this analysis resulted in larger indoor air concentrations and longer dermal exposures and based on those higher exposures, concerns for developmental effects were found for some of the additional exposure scenarios evaluated.

3. Background of Consumer Exposure Analysis for Paint and Coating Removal Products Presented in EPA's NMP Risk Assessment

[10] EPA (U.S. Environmental Protection Agency). 2015. *TSCA Work Plan Chemical Risk Assessment, n-Methylpyrrolidone: Paint Stripper Use, CASRN: 872-50-4.* Office of Pollution Prevention and Toxics, Washington, DC. https://www.epa.gov/sites/production/files/2015-11/documents/nmp_ra_3_23_15_final.pdf.

[11] Users are directly involved of the application of the painter remover to a painted surface.

[12] Non-users are other inhabitants of the home that spend most of their day inside but do not enter the room where the paint remover is used.

The assessment of consumer use of paint and coating removal products in the NMP risk assessment used information from products containing NMP and surveys of users to estimate concentrations of NMP in indoor air due to product use (EPA, 2015). The parameters and their origins are explained in the NMP risk assessment, specifically in Section 2.2 and Appendix E (EPA, 2015).

In the NMP risk assessment and in this supplemental analysis, EPA used MCCEM to estimate NMP inhalation exposures for the consumer use scenarios (EPA 2010). This modeling approach was selected because emission data were reasonably available from chamber studies for a product containing NMP. The model used a multi-zone representation of a house to calculate the NMP exposure levels for consumers (users) and bystanders (non-users). In this model, the room in which the product was used was represented by one or two zones, and the rest of the house (ROH) volume represents another zone. The user was assumed to spend time in the room of use on the day of use, whereas the non-user was modeled as spending the day in the rest of the house or outside (EPA, 2015).

The modeling approach integrated assumptions and input parameters about the chemical emission rate over time, the volume of the house and the room of use, the air exchange rate and interzonal airflow rate. The model also considered the exposed individual's location during and after product use (EPA 2010).

MCCEM was used to calculate minute by minute air concentrations based on the behavior patterns assumed in the model. A description of the original modeled inputs and their sources as well as a description of how MCCEM was implemented for paint removers is also in the NMP risk assessment (EPA, 2015).

4. Additional Exposure Analysis for Consumer Paint and Coating Removal

Modeling using the same methodology was conducted for additional consumer exposure scenarios to aid in understanding how exposures and risk might change by varying certain user behaviors or product application techniques. The same consumer exposure model, MCCEM, used for the NMP risk assessment was also used for the additional modeling described in this document.

The parameters that were varied in the new modeling runs are (1) the size of the paint and coating removal project, (2) the type of project undertaken (furniture, flooring and bathtub) and (3) time lapsed prior to when the paint scrapings were removed from the house. Tables 2-5 of the NMP risk assessment contain a list of other parameters used in the consumer exposure modeling.

The consumer exposure scenarios in the NMP risk assessment were based on the mass of paint and coating removal product that was used by the 50^{th} and 80^{th} percentile consumers from a survey of consumers that reported the use of a paint and coating removal product. This mass of paint and coating removal product was used to determine the amount of painted surface area from which paint could be removed, which was converted into a representative project. In the NMP risk assessment, this was described as, for example a set of shelves, coffee table, bathtub, or a chest of drawers. For this supplemental analysis, consideration was expanded to include the potential for larger consumer projects involving paint and coating removal, such as a dining set (table and chairs) and an entire room floor. An additional model run for the bathtub scenario was included to evaluate exposures if the product was used twice to completely remove paint from the surface of the tub.

Finally, the scenarios modeled in the NMP risk assessment described a consumer that removed the scrapings to an outdoor garbage bin after the second scraping event. A model scenario, or run, was added in this supplemental analysis to evaluate the impact of removing the scrapings more promptly. Removing the scrapings from the room of use could reduce the mass of NMP volatilizing in the room and consequently could reduce exposures for both the user and bystanders.

The minute by minute outputs of these MCCEM runs were entered into a PBPK model developed for the NMP risk assessment.

Table_Apx G-1 and Table_Apx G-2 summarize the variants in modeling parameters for the additional exposure model runs.

Table_Apx G-1. NMP Consumer Brush- and Roller-Applied Paint Removal Scenario Descriptions and Parameters

Case ID	NMP Released				Removal Method	Room of Use		Rest of House		User Location During Wait and Break Period	Non-User Location
	Wt. Fract.	Area Treated, ft^2	App Rate, sf/min	Release Fraction		Volume, m^3	ACH, hr^{-1}	Volume m^3	ACH, hr^{-1}		
A1	0.5	10 Coffee table	2	0.8695	5-min. brush application, 30-min. wait, and 10-min. scrape per application; process repeated after completion of first scrape. Scrapings removed from house after last scrape.	54	Open windows 1.26	438	0.45	ROH	ROH (entire time)
A2							Closed Windows 0.45				
B1		25 Chest of drawers	2		12.5-min. brush application, 30-min. wait, and 25-min. scrape per application; process repeated after completion of first scrape. Scrapings removed from house after last scrape.		Open windows 1.26				
B2							Closed Windows 0.45				
C1		100 Dining table and 8 chairs	2 (Table) 1 (Chairs)		82-min. brush application, 18-min. wait, and 125-min. scrape per application; process repeated after 30-min. break. Scrapings removed from house after 2nd scrape.		Open windows 1.26				
C2							Closed Windows 0.45				
C3					Same as Scenario C1 except scrapings removed after each scrape.		Open windows 1.26				
D1		240 Floors	4		1-hour roller-application, 1-hour wait, 1.5-hour scrape; process repeated after 1-hour break. Scrapings removed from house after each scrape.		Open windows 1.26				
D2							Closed Windows 0.45				
E1		36 bathtub	2		18-min. brush application, 30-min. wait, and 36-min. scrape per application; process repeated with no break. Scrapings removed from house after 2nd scrape.	Source Cloud 1 m^3 Bathroom 9 m^3	0.18	483	0.18		
E2					Same as Scenario E1 except entire process is repeated after 1-hour break.						

Table_Apx G-2. NMP Consumer Spray-Applied Paint Removal Scenario Descriptions and Parameters

Case ID	NMP Released				Removal Method **	Room of Use		Rest of House		User Location During Wait and Break Period	Non-User Location
	Wt. Fract.	Area Treated, ft^2	App Rate, sf/min	Release Fraction		Volume, m^3	ACH, hr^{-1}	Volume, m^3	ACH, hr^{-1}		
F 1	0.5	100 Dining table and 8 chairs Table (36 sf) Chairs (64 sf)	4 (Table) 2 (Chairs)	0.8695	41-min. spray application, 30-min. wait, and 125-min. scrape per application; process repeated after 1-hour break. Scrapings removed from house after 2nd scrape.	54	Open windows 1.26	438	0.45	ROH	ROH (entire time)
F 2							Closed Windows 0.45				
F 3					Same as Scenario F1 except scrapings removed after each scrape.		Open windows 1.26				
G 1		240 Floors	4 *		1-hour spray application, 1-hour wait, 1.5-hour scrape; process repeated after 1-hour break. Scrapings removed from house after last scrape.		Open windows 1.26				
G 2							Closed Windows 0.45				
H 1		36 bathtub	4		9-min. spray application, 30-min. wait, and 36-min. scrape per application; process repeated with no break. Scrapings removed from house after 2nd scrape.	Source Cloud 1 m^3	0.18	483	0.18		
H 2					Same as Scenario H1 except entire process is repeated after 1-hour break.	Bathroom 9 m^3					

* The application rate for spray-on floors was kept the same as for roll-on floors (Professional Judgment).
** All spray-applied cases use the "high" volatility model, which assumes the first exponential mass increases by 10-fold.
Wt. Fract. = Weight Fraction, ROH=Rest of House

5. Exposure Modeling Results

As in the NMP risk assessment, the indoor air concentrations generated by MCCEM were combined with dermal exposures in a PBPK model. The outputs of that model are the basis for the risk findings for the consumer use of NMP for paint and coating removal in the following scenarios. Calculations are in a reference spreadsheet in a separate appendix titled Appendix B - Spreadsheet: Details of NMP Exposure Model Results.

For the purpose of comparing these higher-end consumer exposures to occupational exposures calculated in the NMP Risk Assessment, EPA also calculated indoor air concentrations using an 8-hour time weighted average (TWA) exposure (see Table D-1 in Appendix D). The PBPK model used the minute-by-minute values generated by MCCEM, not these 8-hour values.

6. Risk Estimation

Risks for acute exposures were estimated for the minute-by-minute exposure concentrations generated by MCCEM and dermal exposures with the PBPK model. The same methodology as was used for the NMP risk assessment with additional risk estimates assuming dermal exposure to NMP during the time of application and scraping. The risks for developmental effects were evaluated with a margin of exposure (MOE) approach using the health hazard value derived in the NMP risk assessment. The hazard value is the peak blood concentration of 216 mg/L and the benchmark MOE (the total of the uncertainty factors) is 30. The evaluation hazard values, their origins, and application to risk estimation are explained in the NMP risk assessment, specifically in Sections 3 and 4 (EPA, 2015). The risk estimates for the exposure concentrations in this supplemental analysis are shown in Table_Apx G-3.

Risks for acute exposures for developmental effects were found for users during larger projects in the additional scenarios evaluated. Risks were only found for non-users in the ROH in the largest project (G2).

Table_Apx G-3. Risk Estimates for Additional Scenarios for Users Assuming Dermal Exposure During Application and Scrapping

Scenario	Glove Use	MOE for POD C_{max} 216 mg/L benchmark MOE = 30	
		C_{max} (mg/L)	MOE
A1. Coffee Table, Brush Application in Workshop, Windows Open	Gloves	0.27	796
	No Gloves	1.99	108
A2. Coffee Table, Brush Application in Workshop, Windows Closed	Gloves	0.30	718
	No Gloves	2.02	107
B1. Chest, Brush Application in Workshop, Windows Open	Gloves	0.65	332
	No Gloves	3.76	58
	Gloves	0.77	282

Scenario	Glove Use	MOE for POD C_{max} 216 mg/L benchmark MOE = 30	
		C_{max} (mg/L)	MOE
B2. Chest, Brush Application in Workshop, Windows Closed	No Gloves	3.88	55.7
C1. Dining table and chairs, Brush Application in Workshop, Windows Open	Gloves	3.37	64.1
	No Gloves	13.31	**16.2**
C2. Dining table and chairs, Brush Application in Workshop, Windows Closed	Gloves	4.40	49.0
	No Gloves	14.50	**14.9**
C3. Dining table and chairs, Brush Application in Workshop, Windows Open, Scrapings removed after each scrap	Gloves	2.60	83.2
	No Gloves	12.44	**17.4**
D1. Floors, Roller Application in Workshop, Windows Open	Gloves	4.40	49.1
	No Gloves	11.76	**18.4**
D2. Floors, Roller Application in Workshop, Windows Closed	Gloves	5.58	38.7
	No Gloves	13.36	**16.2**
E1. Bathtub, Brush Application in Bathroom, C_{sat} = 1,013 mg/m^3, 2 Applications	Gloves	4.17	52
	No Gloves	7.81	**28**
E2. Bathtub, Brush Application in Bathroom, C_{sat} = 1,013 mg/m^3, 4 Applications	Gloves	6.39	34
	No Gloves	10.02	**22**
F1. Dining table and chairs, Spray Application in Workshop, Windows Open	Gloves	9.39	**23**
	No Gloves	14.72	**15**
F2. Dining table and chairs, Spray Application in Workshop, Windows Closed	Gloves	12.02	**18.0**
	No Gloves	18.42	**11.7**
F3. Dining table and chairs, Spray Application in Workshop, Windows Open	Gloves	9.27	**23.3**
	No Gloves	14.21	**15.2**
G1. Floors, Spray Application in Workshop, Windows Open	Gloves	23.03	**9.4**
	No Gloves	26.19	**8.2**
G2. Floors, Spray Application in Workshop, Windows Closed	Gloves	30.11	**7.2**
	No Gloves	33.61	**6.4**
	Gloves	22.72	**9.5**

Scenario	Glove Use	MOE for POD C_{max} 216 mg/L benchmark MOE = 30	
		C_{max} (mg/L)	MOE
H1. Bathtub, Spray Application in Bathroom, C_{sat} = 1,013 mg/m^3, 2 Applications	No Gloves	25.32	**8.5**
H2. Bathtub, Spray Application in Bathroom, C_{sat} = 1,013 mg/m^3, 4 Applications	Gloves	33.64	**6.4**
	No Gloves	38.62	**5.6**

7. Uncertainties and Data Limitations

The modeling of additional scenarios described here has all the same uncertainties listed in the final NMP risk assessment document.

Furthermore, it may be unlikely that a spray-applied paint and coating removal product would be used on projects as large as those modeled in this document. Spray-applied paint and coating removal products may be more useful for surfaces that are curved or irregular and are difficult to cover with a brush or roller. However, this does not prevent the potential use of spray-applied products in the manner modeled.

8. Conclusions

As expected, the larger projects resulted in larger indoor air concentrations of NMP. New 8-hour TWA air concentrations were calculated based on the user's pattern of moving in the home. These updated user behavior adjusted TWA air concentrations are many times larger than those presented in the NMP risk assessment.

The modeling results showed a small decline in exposure when scrapings from the room of use were removed more promptly (*i.e.*, removed after each scrape and within 4 hours rather than at the completion of the project up to 8 hours). However, this variable is not a primary factor in the calculated values from MCCEM.

As expected, the larger projects resulted in higher NMP peak blood concentrations. Risks were identified for developmental effects for the larger projects.

9. References

EPA (US Environmental Protection Agency). 2010. *Multi-Chamber Concentration and Exposure Model (MCCEM) Version 1.2*. https://www.epa.gov/tsca-screening-tools/forms/mccem-multi-chamber-concentration-and-exposure-model-download-and-install (accessed on April 29, 2016).

EPA (U.S. Environmental Protection Agency). 2015. *TSCA Work Plan Chemical Risk Assessment, n-Methylpyrrolidone: Paint Stripper Use, CASRN: 872-50-4.* Office of Pollution Prevention and Toxics, Washington, DC. https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/tsca-work-plan-chemical-risk-assessment-n-0

10. Appendix A

Types of Paint Removal Modeling Scenarios:

A. Coffee table (surface area = 10 ft^2; App. rate = 2 sf/min; Total duration = 90 minutes)
1. Brush-On, Workshop, User in rest of house (ROH) during wait time, ROH=0.45 Air changes per hour (ACH), Workshop = 1.26 ACH, Interzonal air flow (IZ) = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS OPEN)
2. Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS CLOSED)

B. Chest of drawers (surface area = 25 ft^2; App. rate = 2 sf/min; Total duration = 135 min)
1. Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH, IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS OPEN)
2. Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS CLOSED)

C. Dining table and chairs (surface area = 100 ft^2 (36 ft^2 for table and 64 $ft^2$for chairs, 8 @ 8 ft^2); App. rate = 2 sf/min table (18 min), 1 sf/min chairs (64 min); 18 minute wait, Scrape rate 0.8 sf/min (125 min), 30 minute break; Total duration = 8 hours)
1. Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH, IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS OPEN)
2. Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS CLOSED)
3. Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH, IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS OPEN)

D. Floor paint removal (surface area = 240 ft^2; App. rate = 4 sf/min; 1 hour wait, Scrape rate = 2.67 (1.5 hour), 1 hour break; Total duration = 8 hours)
1. Roll-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH, IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS OPEN)
2. Roll-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS CLOSED)

E. Bathtub paint removal (surface area = 36 ft^2; App. rate = 2 sf/min; Total duration = 2.8 hours (2 apps); 6.6 hours (4 apps))
1. Brush-On, Bathroom + Source Cloud, User in ROH during wait time, ROH=0.18 ACH, Bathroom = 0.18 ACH, IZ (source cloud/bathroom, bathroom/ROH) = 80 / 35 m^3/hr., 0.5 Weight Fraction (C_{sat} = 1013 mg/m^3), Scrapings removed after 2nd scrape (NO WINDOWS, 2 applications)
2. Brush-On, Bathroom + Source Cloud, User in ROH during wait time, ROH=0.18 ACH, Bathroom =0.18 ACH, IZ (source cloud/bathroom, bathroom/ROH) = 80 / 35 m^3/hr., 0.5 Weight Fraction (C_{sat} = 1013 mg/m^3), Scrapings removed after 2nd and 4th scrapes (NO WINDOWS, 4 applications)

F. Dining table and chairs (surface area = 100 ft^2 (36 ft^2 for table and 64 $ft^2$for chairs, 8 @ 8 ft^2); App. rate = 4 sf/min table (9 min), 2 sf/min chairs (32 min); 30 minute wait, Scrape rate 0.8 sf/min (125 min), 1 hour break; Total duration = 7 hours)
1. Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH, IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS OPEN)
2. Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS CLOSED)

3. Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH, IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS OPEN)

G. Floor paint removal (surface area = 240 ft^2; App. rate = 4 sf/min; 1 hour wait, Scrape rate = 2.67 sf/min (1.5 hour), 1 hour break; Total duration = 8 hours)

1. Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH, IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS OPEN)
2. Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS CLOSED)

H. Bathtub paint removal (surface area = 36 ft^2; App. rate = 4 sf/min; Total duration = 2.5 hours (2 apps); 6 hours (4 apps))

1. Spray-On, Bathroom + Source Cloud, User in ROH during wait time, ROH=0.18 ACH, Bathroom = 0.18 ACH, IZ (source cloud/bathroom, bathroom/ROH) = 80 / 35 m^3/hr., 0.5 Weight Fraction (Csat = 1013 mg/m^3), Scrapings removed after 2nd scrape (NO WINDOWS, 2 applications)
2. Spray -On, Bathroom + Source Cloud, User in ROH during wait time, ROH=0.18 ACH, Bathroom =0.18 ACH, IZ (source cloud/bathroom, bathroom/ROH) = 80 / 35 m^3/hr., 0.5 Weight Fraction (Csat = 1013 mg/m^3), Scrapings removed after 2nd and 4th scrapes (NO WINDOWS, 4 applications)

Unchanged modeling parameters for all scenarios

- House volume = 492 m^3
- Paint stripper consumer weight fraction = 0.5 (upper end)
- Non-user location = ROH (entire time)

Table_Apx G-4. Time Schedule for Brush- and Roller-Applied Paint and Coating Removal with Repeat Application

Scenario	Elapsed Time From Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
A. Brush application to coffee table in workshop, central tendency scenario *(App rate = 2 sf/min)*	0-5 (Workshop)	5-35 (ROH)	35-45 (Workshop)	0	45-50 (Workshop)	50-80 (ROH)	80-90 (Workshop)
B. Brush application to chest in workshop, upper-end scenario for user & non-user *(App rate = 2 sf/min)*	0-12.5 (Workshop)	12.5-42.5 (ROH)	42.5-67.5 (Workshop)	0	67.5-80 (Workshop)	80-110 (ROH)	110-135 (Workshop)
C. Brush application to dining table and chairs in workshop, central tendency scenario *(App rate = 2 sf/min for table; 1 sf/min for chairs)*	0-82 (Workshop)	82-100 (ROH)	100-225 (Workshop)	225-255 (ROH)	255-337 (Workshop)	337-355 (ROH)	355-480 (Workshop)
D. Roller application to floor *(App rate = 4 sf/min)*	0-60 (Workshop)	60-120 (ROH)	120-210 (Workshop)	210-270 (ROH)	270-330 (Workshop)	330-390 (ROH)	390-480 (Workshop)
E. Brush application to bathtub *(App rate = 2 sf/min)* E1 = 2 applications	0-18 (Src Cloud)	18-48 (ROH)	48-84 (Src Cloud)	0	84-102 (Src Cloud)	102-132 (ROH)	132-168 (Src Cloud)
E2 = 4 apps (repeat 1st 2 apps after 1 hour break, total time = 396 min.)	228-246 (Src Cloud)	246-276 (ROH)	276-312 (Src Cloud)		312-330 (Src Cloud)	330-360 (ROH)	360-396 (Src Cloud)

Table_Apx G-5. Time Schedule for Spray-Applied Paint and Coating Removal with Repeat Application

Scenario	Elapsed Time From Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
F. Spray application to dining table and chairs in workshop, central tendency scenario *(App rate = 4 sf/min for table; 2 sf/min for chairs)*	0-41 (Workshop)	41-71 (ROH)	71-196 (Workshop)	196-256 (ROH)	256-297 (Workshop)	297-327 (ROH)	327-452 (Workshop)
G. Spray application to floors *(App rate = 4 sf/min)*	0-60 (Workshop)	60-120 (ROH)	120-210 (Workshop)	210-270 (ROH)	270-330 (Workshop)	330-390 (ROH)	390-480 (Workshop)
H. Spray application to bathtub *(App rate = 4 sf/min)* H1 = 2 applications	0-9 (Src Cloud)	9-39 (ROH)	39-75 (Src Cloud)	0	75-84 (Src Cloud)	84-114 (ROH)	114-150 (Src Cloud)
H2 = 4 apps (repeat 1st 2 apps after 1 hour break, total time = 360 min.)	210-219 (Src Cloud)	219-249 (ROH)	249-285 (Src Cloud)		285-294 (Src Cloud)	294-324 (ROH)	324-360 (Src Cloud)

Src Cloud = Source Cloud

NMP Summaries

Formula:	C5H9NO
CASRN:	872-50-4
Molecular Weight:	99.13 g/mol
Density:	1.028 g/cm^2 (liquid)
Appearance:	clear liquid
Melting Point:	-24 °C = -11 °F = 249 K
Boiling Point:	203 °C = 397 °F = 476 K
Conversion units: 1 ppm =	4.054397 mg/m^3
Saturation Concentration:	~1,013 mg/m^3 (equivalent to a vapor pressure of 0.190 Torr at 25 °C, used in Scenario 5, based on (OECD, 2007a). See Section D.3)
Saturation Concentration:	~640 mg/m^3 (representing the upper end of the saturation concentration values associated with "normal humidity conditions." See Section D.3)

NMP Scenario A1. Coffee Table, Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH (= 68 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS OPEN)

MCCEM Input Summary

Application Method:
Brush-on`

Volumes:
Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	68 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Coffee table = 10 sq. ft. surface area
Applied product mass = 108 g/sq. ft. = 1,080 g
Applied NMP = 1,080 g × 0.5 (wt. fraction) = 540 g
Total NMP mass released (theoretical, both exponentials) = 1,080 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) = 469.53 g
Mass released per app = 234.77 g

For each of the 2 applications:
k_1 = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
E_{01} = Mass * k_1 = 0.008*234.77*32.83 = 61.7 g/hr. (**NOTE:** only k and Mass are needed as inputs)
k_2 = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
E_{02} = Mass * k_2 = 0.992*234.77*0.00237 = 0.55 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)					
	Apply 1	***Wait 1***	***Scrape 1***	***Apply 2***	***Wait 2***	***Scrape 2***
A1) Coffee Table, Brush-On, Workshop, User ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS OPEN	0-5 (Wkshp)	5-35 (ROH)	35-45 (Wkshp)	45-50 (Wkshp)	50-80 (ROH)	80-90 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (22 hours, 30 minutes)

Model Run Time:
0-24 hours
User takes out scrapings after 90 minutes; emissions truncated.

NMP Scenario A2. Coffee Table, Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS CLOSED)

MCCEM Input Summary

Application Method:
Brush-on

Volumes:
Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	24.3 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Coffee table = 10 sq. ft. surface area
Applied product mass = 108 g/sq. ft. = 1,080 g
Applied NMP = 1,080 g × 0.5 (wt. fraction) = 540 g
Total NMP mass released (theoretical, both exponentials) = 1,080 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) = 469.53 g
Mass released per app = 234.77 g

For each of the 2 applications:
k_1 = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
E_{01} = Mass * k_1 = 0.008*234.77*32.83 = 61.7 g/hr. (**NOTE:** only k and Mass are needed as inputs)
k_2 = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
E_{02} = Mass * k_2 = 0.862*234.77*0.00237 = 0.55 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)					
	Apply 1	***Wait 1***	***Scrape 1***	***Apply 2***	***Wait 2***	***Scrape 2***
A2) Coffee Table, Brush-On, Workshop, User ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS CLOSED	0-5 (Wkshp)	5-35 (ROH)	35-45 (Wkshp)	45-50 (Wkshp)	50-80 (ROH)	80-90 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (22 hours, 30 minutes)

Model Run Time:
0-24 hours
User takes out scrapings after 90 minutes; emissions truncated.

NMP Scenario B1. Chest, Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH (= 68 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS OPEN)

MCCEM Input Summary

Application Method:
Brush-on

Volumes:
Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	68 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Chest = 25 sq. ft. surface area
Applied product mass = 2,700 g
Applied NMP = 2,700 g × 0.5 (wt. fraction) = 1,350 g
Total NMP mass released (both exponentials) = 2,700 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) =1173.8 g
Mass released per app = 586.9 g

For each of the 2 applications:
k_1 = 32.83/hr
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
E_{01} = Mass * k_1 = 0.008*586.9*32.83 = 154.1 g/hr. (**NOTE:** only k and Mass are needed as inputs)
k_2 = 0.00237/hr
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
E_{02} = Mass * k_2 = 0.992*586.9*0.00237 = 1.38 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)					
	Apply 1	***Wait 1***	***Scrape 1***	***Apply 2***	***Wait 2***	***Scrape 2***
B1) Chest, Brush-On, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS OPEN	0-12.5 (Wkshp)	12.5-42.5 (ROH)	42.5-67.5 (Wkshp)	67.5-80 (Wkshp)	80-110 (ROH)	110-135 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (21 hours, 45 minutes)

Model Run Time:
0-24 hours

User takes out scrapings after 135 minutes; emissions truncated.

NMP Scenario B2. Chest, Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS CLOSED)

MCCEM Input Summary

Application Method:
Brush-on

Volumes:
Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	24.3 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Chest = 25 sq. ft. surface area
Applied product mass = 2,700 g
Applied NMP = 2,700 g × 0.5 (wt. fraction) = 1,350 g
Total NMP mass released (both exponentials) = 2,700 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) =1173.8 g
Mass released per app = 586.9 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.008*586.9*32.83 = 154.1 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.992*586.9*0.00237 = 1.38 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)					
	Apply 1	***Wait 1***	***Scrape 1***	***Apply 2***	***Wait 2***	***Scrape 2***
B2) Chest, Brush-On, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS CLOSED	0-12.5 (Wkshp)	12.5-42.5 (ROH)	42.5-67.5 (Wkshp)	67.5-80 (Wkshp)	80-110 (ROH)	110-135 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (21 hours, 45 minutes)

Model Run Time:
0-24 hours
User takes out scrapings after 135 minutes; emissions truncated.

NMP Scenario C1. Dining table and chairs, Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH (= 68 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS OPEN)

MCCEM Input Summary
Application Method: Brush-on

Volumes: Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	68 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Table = 36 sq. ft. surface area; Chairs = 64 sq. ft. surface area
Applied product mass = 10,800 g
Applied NMP = 10,800 g × 0.5 (wt. fraction) = 5,400 g
Total NMP mass released (both exponentials) = 10,800 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) =4695.3 g
Mass released per app = 2347.65 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.008*2347.65*32.83 = 616.6 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.992*2347.65*0.00237 = 5.52 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
C1) Dining table and chairs, Brush-On, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS OPEN	0-82 (Wkshp)	82-100 (ROH)	100-225 (Wkshp)	225-255 (ROH)	255-337 (Wkshp)	337-355 (ROH)	355-480 (Wkshp)

User in ROH at the end of Scraping 2

User in ROH for the remainder of the run (16 hours)

Model Run Time:
0-24 hours
User takes out scrapings after 480 minutes; emissions truncated.

NMP Scenario C2. Dining table and chairs, Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS CLOSED)

MCCEM Input Summary
Application Method:
Brush-on

Volumes:
Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	24.3 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Table = 36 sq. ft. surface area; Chairs = 64 sq. ft. surface area
Applied product mass = 10,800 g (Application rate = 108 g/sf)
Applied NMP = 10,800 g × 0.5 (wt. fraction) = 5,400 g
Total NMP mass released (both exponentials) = 10,800 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) =4695.3 g
Mass released per app = 2347.65 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.008*2347.65*32.83 = 616.6 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.992*2347.65*0.00237 = 5.52 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
C2) Dining table and chairs, Brush-On, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS CLOSED	0-82 (Wkshp)	82-100 (ROH)	100-225 (Wkshp)	225-255 (ROH)	255-337 (Wkshp)	337-355 (ROH)	355-480 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (16 hours)

Model Run Time:
0-24 hours
User takes out scrapings after 480 minutes; emissions truncated.

NMP Scenario C3. Dining table and chairs, Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH (= 68 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS OPEN)

MCCEM Input Summary
Application Method:
Brush-on

Volumes:
Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	68 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Table = 36 sq. ft. surface area; Chairs = 64 sq. ft. surface area
Applied product mass = 10,800 g (Application rate = 108 g/sf)
Applied NMP = 10,800 g × 0.5 (wt. fraction) = 5,400 g
Total NMP mass released (both exponentials) = 10,800 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) =4695.3 g
Mass released per app = 2347.65 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.008*2347.65*32.83 = 616.6 g/hr. (**NOTE:** only k and Mass are needed as inputs)

$\mathbf{k_2}$ = 0.00237/hr.

% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP

$\mathbf{E_{02}}$ = Mass * k_2 = 0.992*2347.65*0.00237 = 5.52 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
C3) Dining table and chairs, Brush-On, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS OPEN	0-82 (Wkshp)	82-100 (ROH)	100-225 (Wkshp)	225-255 (ROH)	255-337 (Wkshp)	337-355 (ROH)	355-480 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (16 hours)

Model Run Time:
0-24 hours
User takes out scrapings after 225 and 480 minutes; emissions truncated.

NMP Scenario D1. Floor, Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH (= 68 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS OPEN)

MCCEM Input Summary
Application Method:
Brush-on

Volumes:
Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	68 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Floor = 240 sq. ft. surface area
Applied product mass = 25,920 g (Application rate = 108 g/sf)
Applied NMP = 25,920 g × 0.5 (wt. fraction) = 12,960 g
Total NMP mass released (both exponentials) = 25,920 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) =11,268.7 g
Mass released per app = 5634.4 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.008*5634.4*32.83 = 1479.8 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.992*5634.4*0.00237 = 13.25 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
D1) Floor, Roll-on, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS OPEN	0-60 (Wkshp)	60-120 (ROH)	120-210 (Wkshp)	210-270 (ROH)	270-330 (Wkshp)	330-390 (ROH)	390-480 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (16 hours)

Model Run Time:
0-24 hours
User takes out scrapings after 210 and 480 minutes; emissions truncated.

NMP Scenario D2. Floor, Brush-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS CLOSED)

MCCEM Input Summary
Application Method:
Brush-on

Volumes:
Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	24.3 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Floor = 240 sq. ft. surface area
Applied product mass = 25,920 g (Application rate = 108 g/sf)
Applied NMP = 25,920 g × 0.5 (wt. fraction) = 12,960 g

Total NMP mass released (both exponentials) = 25,920 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) =11,268.7 g
Mass released per app = 5634.4 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.008*5634.4*32.83 = 1479.8 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.992*5634.4*0.00237 = 13.25 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
D2) Floor, Roll-on, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS CLOSED	0-60 (Wkshp)	60-120 (ROH)	120-210 (Wkshp)	210-270 (ROH)	270-330 (Wkshp)	330-390 (ROH)	390-480 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (16 hours)

Model Run Time:
0-24 hours
User takes out scrapings after 210 and 480 minutes; emissions truncated

NMP Scenario E1. Bathroom, Brush-On, Bathroom + Source Cloud, User in ROH during wait time, ROH=0.18 ACH, Bathroom = 0.18 ACH, IZ (source cloud/bathroom, bathroom/ROH) = 80, 35 m^3/hr., 0.5 Weight Fraction (Csat = 1013 mg/m^3), Scrapings removed after 2nd scrape (WINDOWS CLOSED, 2 applications)

MCCEM Input Summary
MCCEM saturation concentration constraint invoked at 1013 mg/m^3
Application Method: Brush-on

Volumes:
Bathroom Volume = 9 m^3 (8 m^3 after subtracting source cloud zone)
Source Cloud Volume = 1 m^3
ROH volume = 492 – 9 = 483 m^3

Airflows:

Bathroom-outdoors	1.6 m^3/h
Source cloud - bathroom	80 m^3/h

Source cloud - outdoors	0
ROH-outdoors	86.9 m^3/h (0.18 ACH)
Bathroom-ROH	35 m^3/h

NMP Mass Released:
Bathtub = 36 sq. ft. surface area
Applied product mass = 3,888 g (Application rate = 108 g/sf)
Applied NMP = 3,888 g × 0.5 (wt. fraction) = 1,944 g
Total NMP mass released (both exponentials) = 3,888 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) = 1690.3 g
Mass released per app = 845.15 g

For each of the 2 applications:
k_1 = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
E_{01} = Mass * k_1 = 0.008*845.15.4*32.83 = 222.0 g/hr. (**NOTE:** only k and Mass are needed as inputs)
k_2 = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
E_{02} = Mass * k_2 = 0.992*845.15*0.00237 = 1.99 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	**Elapsed Time from Time Zero, Minutes (Product User Location)**					
	Apply 1	***Wait 1***	***Scrape 1***	***Apply 2***	***Wait 2***	***Scrape 2***
E1) Bathtub, Brush-On, Bathroom + Source Cloud, User in ROH during wait time, 0.18 ACH, 0.5 Wt. Fract.	0-18 (SrcCloud)	18-48 (ROH)	48-84 (SrcCloud)	84-102 (SrcCloud)	102-132 (ROH)	132-168 (SrcCloud)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (21 hours, 12 minutes)

Model Run Time:
0-24 hours
User takes out scrapings after 168 minutes; emissions truncated.

NMP Scenario E2. Bathroom, Brush-On, Bathroom + Source Cloud, User in ROH during wait time, ROH=0.18 ACH, Bathroom = 0.18 ACH, IZ (source cloud/bathroom, bathroom/ROH) = 80, 35 m^3/hr., 0.5 Weight Fraction (Csat = 1013 mg/m^3), Scrapings removed after 2nd and 4th scrapes (WINDOWS CLOSED, 4 applications)

MCCEM Input Summary
MCCEM saturation concentration constraint invoked at 1013 mg/m^3
Application Method: Brush-on

Volumes:

Bathroom Volume = 9 m^3 (8 m^3 after subtracting source cloud zone)
Source Cloud Volume = 1 m^3
ROH volume = 492 – 9 = 483 m^3

Airflows:

Bathroom-outdoors	1.6 m^3/h
Source cloud - bathroom	80 m^3/h
Source cloud - outdoors	0
ROH-outdoors	86.9 m^3/h (0.18 ACH)
Bathroom-ROH	35 m^3/h

NMP Mass Released:
Bathtub = 36 sq. ft. surface area
Applied product mass = 3,888 g (Application rate = 108 g/sf)
Applied NMP = 3,888 g × 0.5 (wt. fraction) = 1,944 g
Total NMP mass released (both exponentials) = 3,888 g × 0.5 (wt. fraction) × 0.8695 (release fraction, theoretical) = 1690.3 g
Mass released per app = 845.15 g

For each of the 2 applications:
k_1 = 32.83/hr.
% Mass for Exponential 1 = 0.7% of Total mass applied = 0.007/0.8695 = 0.8% of released NMP
E_{01} = Mass * k_1 = 0.008*845.15.4*32.83 = 222.0 g/hr. (**NOTE:** only k and Mass are needed as inputs)
k_2 = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
E_{02} = Mass * k_2 = 0.992*845.15*0.00237 = 1.99 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	**Elapsed Time from Time Zero, Minutes (Product User Location)**					
	Apply 1 & 3	***Wait 1 & 3***	***Scrape 1 & 3***	***Apply 2 &4***	***Wait 2 &4***	***Scrape 2 &4***
	E2) Bathtub, Brush-On, Bathroom + Source Cloud, User in ROH during wait time, 0.18 ACH, 0.5 Weight Fraction					
1st and 2nd Application	0-18 (SrcCloud)	18-48 (ROH)	48-84 (SrcCloud)	84-102 (SrcCloud)	102-132 (ROH)	132-168 (SrcCloud)
3rd and 4th Application	228-246 (SrcCloud)	246-276 (ROH)	276-312 (SrcCloud)	312-330 (SrcCloud)	330-360 (ROH)	360-396 (SrcCloud)

User in ROH at the end of Scraping 2 and 4
User in ROH for the remainder of the run (17 hours, 24 minutes)

Model Run Time:
0-24 hours
User takes out scrapings after 168 and 396 minutes; emissions truncated.

NMP Scenario F1. Dining table and chairs, Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH (= 68 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS OPEN)

MCCEM Input Summary
Application Method: Spray-on
Volumes: Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	68 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Table = 36 sq. ft. surface area; Chairs = 64 sq. ft. surface area
Applied product mass = 8,100 g (Application rate = 81 g/sf)
Overspray = 0.05*8,100 g = 405 g
Total Product Mass = 8,100 + 405 = 8,505 g
Total NMP Mass = 8,505 g × 0.5 (wt. fraction) = 4,252.5 g
Total NMP mass released (both exponentials) = 4,252.5 x 0.8695 (release fraction, theoretical) = 3697.5 g
Mass released per app = 1848.8 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 7.0% of Total mass applied = 0.07/0.8695 = 8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.08*1848.8*32.83 = 4855.7 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 79.95% of applied NMP = 0.7995/0.8695 = 91.9% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.919*1848.8*0.00237 = 4.03 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
F1) Dining table and chairs, Spray-On, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS OPEN	0-41 (Wkshp)	41-71 (ROH)	71-196 (Wkshp)	196-256 (ROH)	256-297 (Wkshp)	297-327 ROH)	327-452 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (16 hours, 28 minutes)

Model Run Time:
0-24 hours
User takes out scrapings after 452 minutes; emissions truncated.

NMP Scenario F2. Dining table and chairs, Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after 2nd scrape (WINDOWS CLOSED)

MCCEM Input Summary
Application Method: Spray-on
Volumes: Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	24.3 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Table = 36 sq. ft. surface area; Chairs = 64 sq. ft. surface area
Applied product mass = 8,100 g (Application rate = 81 g/sf)
Overspray = 0.05*8,100 g = 405 g
Total Product Mass = 8,100 + 405 = 8,505 g
Total NMP Mass = 8,505 g × 0.5 (wt. fraction) = 4,252.5 g
Total NMP mass released (both exponentials) = 4,252.5 x 0.8695 (release fraction, theoretical) = 3697.5 g
Mass released per app = 1848.8 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 7.0% of Total mass applied = 0.07/0.8695 = 8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.08*1848.8*32.83 = 4855.7 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 79.95% of applied NMP = 0.7995/0.8695 = 91.9% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.919*1848.8*0.00237 = 4.03 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
F2) Dining table and chairs, Spray-On, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS CLOSED	0-41 (Wkshp)	41-71 (ROH)	71-196 (Wkshp)	196-256 (ROH)	256-297 (Wkshp)	297-327 ROH)	327-452 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (16 hours, 28 minutes)

Model Run Time:
0-24 hours
User takes out scrapings after 452 minutes; emissions truncated.

NMP Scenario F3. Dining table and chairs, Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH (= 68 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS OPEN)

MCCEM Input Summary
Application Method: Spray-on
Volumes: Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	68 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Table = 36 sq. ft. surface area; Chairs = 64 sq. ft. surface area
Applied product mass = 8,100 g (Application rate = 81 g/sf)
Overspray = 0.05*8,100 g = 405 g
Total Product Mass = 8,100 + 405 = 8,505 g
Total NMP Mass = 8,505 g × 0.5 (wt. fraction) = 4,252.5 g
Total NMP mass released (both exponentials) = 4,252.5 x 0.8695 (release fraction, theoretical) = 3697.5 g
Mass released per app = 1848.8 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 7.0% of Total mass applied = 0.07/0.8695 = 8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.08*1848.8*32.83 = 4855.7 g/hr. (**NOTE:** only k and Mass are needed as inputs)

$\mathbf{k_2}$ = 0.00237/hr.

% Mass for Exponential 2 = 79.95% of applied NMP = 0.7995/0.8695 = 91.9% of released NMP

$\mathbf{E_{02}}$ = Mass * k_2 = 0.919*1848.8*0.00237 = 4.03 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
F3) Dining table and chairs, Spray-On, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS OPEN	0-41 (Wkshp)	41-71 (ROH)	71-196 (Wkshp)	196-256 (ROH)	256-297 (Wkshp)	297-327 ROH)	327-452 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (16 hours, 28 minutes)

Model Run Time:
0-24 hours
User takes out scrapings after 196 and 452 minutes; emissions truncated.

NMP Scenario G1. Floor, Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 1.26 ACH (= 68 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS OPEN)

MCCEM Input Summary
Application Method: Spray-on
Volumes: Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	68 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Floor = 240 sq. ft. surface area
Applied product mass = 19,440 g (Application rate = 81 g/sf)
Overspray = 0.05*19,440 g = 972 g
Total Product Mass = 19,440 + 972 = 20,412 g
Total NMP Mass = 20,412 g × 0.5 (wt. fraction) = 10,206 g
Total NMP mass released (both exponentials) = 10,206 x 0.8695 (release fraction, theoretical) = 8,874.1 g
Mass released per app = 4437.1 g

For each of the 2 applications:

$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 7.0% of Total mass applied = 0.07/0.8695 = 8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.08*4437.1*32.83 = 11,653.6 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 79.95% of applied NMP = 0.7995/0.8695 = 91.9% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.919*4437.1*0.00237 = 9.66 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
G1) Floor, Spray-on, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS OPEN	0-60 (Wkshp)	60-120 (ROH)	120-210 (Wkshp)	210-270 (ROH)	270-330 (Wkshp)	330-390 (ROH)	390-480 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (16 hours)

Model Run Time:
0-24 hours
User takes out scrapings after 210 and 480 minutes; emissions truncated.

NMP Scenario G2. Floor, Spray-On, Workshop, User in ROH during wait time, ROH=0.45 ACH, Workshop = 0.45 ACH (= 24.3 m^3/hr.), IZ = 107 m^3/hr., 0.5 Weight Fraction, Scrapings removed after each scrape (WINDOWS CLOSED)

MCCEM Input Summary
Application Method: Spray-on
Volumes: Workshop volume = 54 m^3
ROH volume = 492 – 54 = 438 m^3

Airflows:

Workshop-outdoors	24.3 m^3/h
ROH-outdoors	197.1 m^3/h (0.45 ACH)
Workshop-ROH	107 m^3/h

NMP Mass Released:
Floor = 240 sq. ft. surface area
Applied product mass = 19,440 g (Application rate = 81 g/sf)
Overspray = 0.05*19,440 g = 972 g
Total Product Mass = 19,440 + 972 = 20,412 g
Total NMP Mass = 20,412 g × 0.5 (wt. fraction) = 10,206 g
Total NMP mass released (both exponentials) = 10,206g x 0.8695 (release fraction, theoretical) =8,874.1 g

Mass released per app = 4437.1 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 7.0% of Total mass applied = 0.07/0.8695 = 8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.08*4437.1*32.83 = 11,653.6 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 79.95% of applied NMP = 0.7995/0.8695 = 91.9% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.919*4437.1*0.00237 = 9.66 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)						
	Apply 1	***Wait 1***	***Scrape 1***	***Break***	***Apply 2***	***Wait 2***	***Scrape 2***
G2) Floor, Spray-on, Workshop, User in ROH during wait time, 0.45 ACH, 0.5 Weight Fraction, WINDOWS CLOSED	0-60 (Wkshp)	60-120 (ROH)	120-210 (Wkshp)	210-270 (ROH)	270-330 (Wkshp)	330-390 (ROH)	390-480 (Wkshp)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (16 hours)

Model Run Time:
0-24 hours
User takes out scrapings after 210 and 480 minutes; emissions truncated

NMP Scenario H1. Bathroom, Spray-On, Bathroom + Source Cloud, User in ROH during wait time, ROH=0.18 ACH, Bathroom = 0.18 ACH, IZ (source cloud/bathroom, bathroom/ROH) = 80, 35 m^3/hr., 0.5 Weight Fraction (Csat = 1013 mg/m^3), Scrapings removed after 2nd scrape (WINDOWS CLOSED, 2 applications)

MCCEM Input Summary
MCCEM saturation concentration constraint invoked at 1013 mg/m^3
Application Method: Spray-on
Volumes: Bathroom Volume = 9 m^3 (8 m^3 after subtracting source cloud zone)
Source Cloud Volume = 1 m^3
ROH volume = 492 – 9 = 483 m^3

Airflows:

Bathroom-outdoors	1.6 m^3/h
Source cloud - bathroom	80 m^3/h
Source cloud - outdoors	0
ROH-outdoors	86.9 m^3/h (0.18 ACH)
Bathroom-ROH	35 m^3/h

NMP Mass Released:
Bathtub = 36 sq. ft. surface area
Applied product mass = 2,916 g (Application rate = 81 g/sf)
Overspray = 0.05*2,916 g = 145.8 g
Total Product Mass = 2,916 + 145.8 = 3,061.8 g
Total NMP Mass = 3,061.8 g × 0.5 (wt. fraction) = 1,530.9 g
Total NMP mass released (both exponentials) = 1530.9 x 0.8695 (release fraction, theoretical) =1331.1 g
Mass released per app = 665.6 g

For each of the 2 applications:
$\mathbf{k_1}$ = 32.83/hr.
% Mass for Exponential 1 = 7.0% of Total mass applied = 0.07/0.8695 = 8% of released NMP
$\mathbf{E_{01}}$ = Mass * k_1 = 0.08*665.6*32.83 = 1748.1 g/hr. (**NOTE:** only k and Mass are needed as inputs)
$\mathbf{k_2}$ = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
$\mathbf{E_{02}}$ = Mass * k_2 = 0.919*665.6*0.00237 = 1.45 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode	Elapsed Time from Time Zero, Minutes (Product User Location)					
	Apply 1	***Wait 1***	***Scrape 1***	***Apply 2***	***Wait 2***	***Scrape 2***
H1) Bathtub, Spray-On, Bathroom + Source Cloud, User in ROH during wait time, 0.18 ACH, 0.5 Wt. Fract.	0-9 (Src Cloud)	9-39 (ROH)	39-75 (Src Cloud)	75-84 (Src Cloud)	84-114 (ROH)	114-150 (Src Cloud)

User in ROH at the end of Scraping 2
User in ROH for the remainder of the run (21 hours, 30 minutes)

Model Run Time:
0-24 hours
User takes out scrapings after 150 minutes; emissions truncated.

NMP Scenario H2. Bathroom, Spray-On, Bathroom + Source Cloud, User in ROH during wait time, ROH=0.18 ACH, Bathroom = 0.18 ACH, IZ (source cloud/bathroom, bathroom/ROH) = 80, 35 m^3/hr., 0.5 Weight Fraction (Csat = 1013 mg/m^3), Scrapings removed after 2nd and 4th scrapes (WINDOWS CLOSED, 4 applications)

MCCEM Input Summary
MCCEM saturation concentration constraint invoked at 1013 mg/m^3
Application Method: Spray-on
Volumes: Bathroom Volume = 9 m^3 (8 m^3 after subtracting source cloud zone)
Source Cloud Volume = 1 m^3
ROH volume = 492 – 9 = 483 m^3

Airflows:

Bathroom-outdoors	1.6 m^3/h

Source cloud - bathroom	80 m^3/h
Source cloud - outdoors	0
ROH-outdoors	86.9 m^3/h (0.18 ACH)
Bathroom-ROH	35 m^3/h

NMP Mass Released:
Bathtub = 36 sq. ft. surface area
Applied product mass = 2,916 g (Application rate = 81 g/sf)
Overspray = 0.05*2,916 g = 145.8 g
Total Product Mass = 2,916 + 145.8 = 3,061.8 g
Total NMP Mass = 3,061.8 g × 0.5 (wt. fraction) = 1,530.9 g
Total NMP mass released (both exponentials) = 1530.9 x 0.8695 (release fraction, theoretical) =1331.1 g
Mass released per app = 665.6 g

For each of the 2 applications:
k_1 = 32.83/hr.
% Mass for Exponential 1 = 7.0% of Total mass applied = 0.07/0.8695 = 8% of released NMP
E_{01} = Mass * k_1 = 0.08*665.6*32.83 = 1748.1 g/hr. (**NOTE:** only k and Mass are needed as inputs)
k_2 = 0.00237/hr.
% Mass for Exponential 2 = 86.2% of applied NMP = 0.862/0.8695 = 99.2% of released NMP
E_{02} = Mass * k_2 = 0.919*665.6*0.00237 = 1.45 g/hr. (**NOTE:** only k and Mass are needed as inputs)

Application Times and Activity Patterns:

Episode Bathtub, Spray-On, Bathroom + Source Cloud, User in ROH during wait time, 0.18 ACH, 0.5 Wt. Fract	**Elapsed Time from Time Zero, Minutes (Product User Location)**					
	Apply 1 & 3	***Wait 1 & 3***	***Scrape 1 & 3***	***Apply 2 &4***	***Wait 2 &4***	***Scrape 2 &4***
	E2) Bathtub, Brush-On, Bathroom + Source Cloud, User in ROH during wait time, 0.18 ACH, 0.5 Weight Fraction					
1st and 2nd Application	0-9 (Wkshp)	9-39 (ROH)	39-75 (Wkshp)	75-84 (Wkshp)	84-114 (ROH)	114-150 (Wkshp)
3rd and 4th Application	210-219 (Wkshp)	219-249 (ROH)	249-285 (Wkshp)	285-294 (Wkshp)	294-324 (ROH)	324-360 (Wkshp)

User in ROH at the end of Scraping 2 and 4
User in ROH for the remainder of the run (18 hours)

Model Run Time:
0-24 hours
User takes out scrapings after 150 and 360 minutes; emissions truncated.

Appendix B - Spreadsheet: Details of NMP Exposure Model Results
See the separate spreadsheet loaded into this docket (EPA-HQ-OPPT-2016-0231) for the zone-specific and exposure concentrations predicted by MCCEM.

Appendix C - Spreadsheet: NMP Risk Estimation
See the separate spreadsheet loaded into this docket (EPA-HQ-OPPT-2016-0231) for risk calculations.

Appendix D

Table D-1. Eight-hour TWA exposures for additional scenarios

Scenario	Individual	8-Hour TWA exposure	
		mg/m^3	ppm
A1. Coffee Table, Brush Application in Workshop, Windows Open	User	2.2	0.5
	Non-User	1.5	0.4
A2. Coffee Table, Brush Application in Workshop, Windows Closed	User	3.1	0.8
	Non-User	2.2	0.5
B1. Chest, Brush Application in Workshop, Windows Open	User	7.7	1.9
	Non-User	4.3	1.1
B2. Chest, Brush Application in Workshop, Windows Closed	User	10.7	2.6
	Non-User	6.1	1.5
C1. Dining table and chairs, Brush Application in Workshop, Windows Open	User	70.2	17.3
	Non-User	24.7	6.1
C2. Dining table and chairs, Brush Application in Workshop, Windows Closed	User	97.7	24.1
	Non-User	35.0	8.6
C3. Dining table and chairs, Brush Application in Workshop, Windows Open, Scrapings removed after each scrap	User	54.5	13.4
	Non-User	19.1	4.7
D1. Floors, Roller Application in Workshop, Windows Open	User	110.9	27.4
	Non-User	45.0	11.1
D2. Floors, Roller Application in Workshop, Windows Closed	User	150.6	37.1
	Non-User	63.7	15.7
E1. Bathtub, Brush Application in Bathroom, C_{sat} = 1,013 mg/m^3, 2 Applications	User	78.8	19.4
	Non-User	20.4	5.0
E2. Bathtub, Brush Application in Bathroom, C_{sat} = 1,013 mg/m^3, 4 Applications	User	148.9	36.7
	Non-User	35.7	8.8
F1. Dining table and chairs, Spray Application in Workshop, Windows Open	User	227.1	56.0
	Non-User	94.8	23.4
F2. Dining table and chairs, Spray Application in Workshop, Windows Closed	User	319.3	78.8
	Non-User	133.8	33.0

Scenario	Individual	8-Hour TWA exposure	
		mg/m^3	ppm
F3. Dining table and chairs, Spray Application in Workshop, Windows Open	User	218.4	53.9
	Non-User	92.1	22.7
G1. Floors, Spray Application in Workshop, Windows Open	User	540.1	133.2
	Non-User	214.2	52.8
G2. Floors, Spray Application in Workshop, Windows Closed	User	724.6	178.7
	Non-User	303.1	74.8
H1. Bathtub, Spray Application in Bathroom, C_{sat} = 1,013 mg/m^3, 2 Applications	User	339.4	83.7
	Non-User	109.2	26.9
H2. Bathtub, Spray Application in Bathroom, C_{sat} = 1,013 mg/m^3, 4 Applications	User	640.9	158.1
	Non-User	192.8	47.6
C_{sat} = Saturation Concentration			

Appendix H ENVIRONMENTAL HAZARDS

EPA has reviewed acceptable ecotoxicity studies for NMP according to the data quality evaluation criteria found in *The Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). The results of these ecotoxicity study evaluations can be found in the *Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Studies. Docket EPA-HQ-OPPT-2019-0236* (U.S. EPA, 2020i). The data quality evaluation indicated these studies are of high confidence and are used to characterize the environmental hazards of NMP. These studies support that hazard of NMP to aquatic organisms is low and that no further evaluation is required.

The acceptable aquatic studies that were evaluated for NMP are summarized in Table_Apx H-1. The hazard of these studies has been reported (U.S. EPA, 2006b; OECD, 2007; Danish Ministry of the Environment, 2015; U.S. EPA, 2015c and Environment Canada, 2017) as stated in the NMP Problem Formulation (U.S. EPA, 2018c).

Table_Apx H-1. On-topic aquatic toxicity studies that were evaluated for NMP

Test Species	Fresh/ Salt Water	Duration	Endpoint	Concentration(s)	Test Analysis	Effect(s)	References	Data Quality Evaluation
Fish								
Fathead minnow (*Pimephales promelas*)	Fresh	96-h	LC_{50} = 1072 mg/L	389, 648, 1080, 1800, 3000, 5000 mg/L	Static, Nominal	Mortality	GAF (1979)	High
Rainbow trout (*Salmo Gairdneri*)	Fresh	96-h	LC_{50} = 3048 mg/L	778, 1296, 2160, 3600, 6000, 10,000 mg/L	Static, Nominal	Mortality	GAF (1979)	High
Rainbow trout (*Oncorhynchus mykiss*)	Fresh	96-h	LC_{50} > 500 mg /L	0, 500 mg/L	Static, Nominal	Mortality	BASF (1983)	High
Orfe (*Leuciscus idus*)	Fresh	96-h	LC_{50} = 4030 mg/L	100, 215, 464, 1000, 2150, 4640, 10,000 mg/L	Static, Nominal	Mortality	BASF (1986)	High
Aquatic Invertebrates								
Water flea (*Daphnia magna*)	Fresh	48-h	LC_{50} = 4897 mg/L	389, 648, 1080, 1800, 3000, 5000, 8333 mg/L	Static, Nominal	Mortality	GAF (1979)	High
Water flea (*Daphnia magna*)	Fresh	21-day	NOEC=12.5 mg/L LOEC= 25 mg/L	0.39, 0.78, 1.56, 3.13, 6.25, 12.5, 25, 50, 100 mg/L	Static, Nominal	Reproduction	BASF (2001) [a]	High
Grass shrimp (*Palaemonetes vulgaris*)	Salt	96-h	LC_{50}= 1107 mg/L	360, 600, 1000, 1667, 2775 mg/L	Static, Nominal	Mortality	GAF (1979)	High
Scud (*Gammarus sp*)	Fresh	96-h	LC_{50}= 4655 mg/L	389, 648, 1080, 1800, 3000, 5000, 8333 mg/L	Static, Nominal	Mortality	GAF (1979)	High
Mud crabs (*Neopanope texana sayi*)	Salt	96-h	LC_{50}= 1585 mg/L	360, 600, 1000, 1667, 2775 mg/L	Static, Nominal	Mortality	GAF (1979)	High

Test Species	Fresh/ Salt Water	Duration	Endpoint	Concentration(s)	Test Analysis	Effect(s)	References	Data Quality Evaluation
Algae								
Algae (*Scenedemus subspicatus*)	Fresh	72-h	E_bC_{50}=600 ErC_{50}=673 mg/L	7.8, 15.6, 31.3, 62.5, 125, 250, 500 mg/L	Static, Nominal	Biomass Growth rate	BASF (1989)	High
Algae (*Scenedemus subspicatus*)	Fresh	72-h	LOEC=250 NOEC=125	7.8, 15.6, 31.3, 62.5, 125, 250, 500 mg/L	Static, Nominal	Growth	BASF (1989)	High

[a] Reservation of Rights: BASF has agreed to share this toxicity study report ("Study Report") with US EPA, at its written request, for EPA 's use in implementing a statutory requirement of the Toxic Substances Control Act ("TSCA "). Every other use, exploitation, reproduction, distribution, publication or submission to any other party requires BASF's written permission, except as otherwise provided by law. The submission of this Study Report to a public docket maintained by the United States Environmental Protection Agency is not a waiver of BASF's ownership rights. No consent is granted for any other third-party use of this Study Report for any purpose, in any jurisdiction. Specifically, and by example, no consent is granted allowing the use of this Study Report by a private entity in requesting any regulatory status, registration or other approval or benefit, whether international, national, state or local, including but not limited to the Registration, Evaluation, Authorisation and Restriction of Chemicals ("REACH") regulation administered by European Chemicals Agency ("ECHA"), an agency of the European Union.

Appendix I HUMAN HEALTH HAZARDS

I.1 Hazard and Data Evaluation Summaries

I.1.1 Hazard and Data Evaluation Summary for Acute and Short-term Oral Exposure Studies

Table_Apx I-1. Hazard and Data Evaluation Summary for Acute and Short-term Oral Exposure Studies

Target Organ/ System	Study Type	Species, Strain, Sex (Number /group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect	Reference	Data Quality Evaluation
Body Weight	Short-term (1-30 days)	Rat, Other, Male (5)	0, 149, 429, 1234, 2019 mg/kg-bw/day (0, 2000, 6000, 18,000, and 30,000 ppm)	4 weeks	NOAEL = 429 mg/kg - bw/day	NOAEL = 429 mg/kg - bw/day	Decreased body weight and altered testes and liver weights were observed at 1234 mg/kg-bw/day and above. Degeneration/atrophy of testicular seminiferous tubules were observed 1/5 males at 1234 mg/kg-bw/day and in 5/5 at 2019 mg/kg-bw/day. Increased incidence of centrilobular hepatocellular hypertrophy and decreased serum glucose were observed at 1234 mg/kg-bw/day and above.	Malek et al. (1997)	High
Body Weight	Short-term (1-30 days)	Rat, Other Female (5)	0, 161, 493, 1548, 2268 mg/kg-bw/day (0, 2000, 6000, 18,000, and 30,000 ppm)	4 weeks	NOAEL = 1548 mg/kg - bw/day	NOAEL = 1548 mg/kg - bw/day	Decreased body weight and body weight gain were observed at 2268 mg/kg-bw/day. Increased serum total protein, albumin, and cholesterol levels and increased incidence of centrilobular hepatocellular hypertrophy, hypocellular bone marrow, and thymic atrophy were also observed at 2268 mg/kg-bw/day.	Malek et al. (1997)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number /group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect	Reference	Data Quality Evaluation
Body Weight	Short-term (1-30 days)	Mouse, B6C3F1, Female (5)	0, 180, 920, 2970, 4060 mg/kg-bw/day (0, 500, 2500. 7500, 10,000 ppm)	4 weeks	Not Reported	NOAEL = 4060 mg/kg - bw/day	No exposure-related effects	NMP Producers Group (1994)	High
Body Weight	Short-term (1-30 days)	Mouse B6C3F1, Male (5)	0, 130, 720, 2130, 2670 mg/kg-bw/day (0, 500, 2500. 7500, 10,000 ppm)	4 weeks	Not Reported	NOAEL = 2670 mg/kg - bw/day	No exposure-related effects	NMP Producers Group (1994)	High
Clinical Chemistry/ Biochemical	Short-term (1-30 days)	Rat Sprague-Dawley, Male (5)	0, 250, 500, 1000 mg/kg-bw/day	5 days/ week for 5 weeks	Not Reported	NOAEL = 250 mg/kg - bw/day	Decreased serum creatinine	Gopinathan et al. (2013)	Medium
Endocrine	Short-term (1-30 days)	Rat, Other, Female (5)	0, 161, 493, 1548, 2268 mg/kg-bw/day (0, 2000, 6000, 18000, and 30000 ppm)	4 weeks	NOAEL = 1548 mg/kg - bw/day	NOAEL = 1548 mg/kg - bw/day	Decreased body weight and body weight gain were observed at 2268 mg/kg-bw/day. Increased serum total protein, albumin, and cholesterol levels and increased incidence of centrilobular hepatocellular hypertrophy, hypocellular bone marrow, and thymic atrophy were also observed at 2268 mg/kg-bw/day.	Malek et al. (1997)	High
Hemato-logical and Immune	Short-term (1-30 days)	Rat, Sprague-Dawley, Male (5)	0, 250, 500, 1000 mg/kg-bw/day	5 days/ week for 5 weeks	Not Reported	NOAEL = 1000 mg/kg - bw/day	No mortalities occurred and no changes were reported for hematology parameters or liver or spleen weights.	Gopinathan et al. (2013)	Medium
Hepatic	Short-term (1-30 days)	Rat, Sprague-Dawley, Male (5)	0, 250, 500, 1000 mg/kg-bw/day	5 days/ week for 5 weeks	Not Reported	NOAEL = 1000 mg/kg - bw/day	No mortalities occurred and no changes were reported for hematology parameters or liver or spleen weights.	Gopinathan et al. (2013)	Medium

Target Organ/ System	Study Type	Species, Strain, Sex (Number /group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect	Reference	Data Quality Evaluation
Hepatic	Short-term (1-30 days)	Rat, Other Female (5)	0, 161, 493, 1548, 2268 mg/kg-bw/day (0, 2000, 6000, 18,000, and 30,000 ppm)	4 weeks	NOAEL = 1548 mg/kg - bw/day	NOAEL = 1548 mg/kg - bw/day	Decreased body weight and body weight gain were observed at 2268 mg/kg-bw/day. Increased serum total protein, albumin, and cholesterol levels and increased incidence of centrilobular hepatocellular hypertrophy, hypocellular bone marrow, and thymic atrophy were also observed at 2268 mg/kg-bw/day.	Malek et al. (1997)	High
Hepatic	Short-term (1-30 days)	Mouse, B6C3F1, Female (5)	0, 180, 920, 2970, 4060 mg/kg-bw/day (0, 500, 2500. 7500, 10,000 ppm)	4 weeks	Not Reported	NOAEL = 4060 mg/kg - bw/day	No exposure-related effects	NMP Producers Group (1994)	High
Hepatic	Short-term (1-30 days)	Mouse, B6C3F1, Male (5)	0, 130, 720, 2130, 2670 mg/kg-bw/day (0, 500, 2500. 7500, 10,000 ppm)	4 weeks	Not Reported	NOAEL = 2670 mg/kg - bw/day	No exposure-related effects	NMP Producers Group (1994)	High
Mortality	Short-term (1-30 days)	Rat, Sprague-Dawley, Male (5)	0, 250, 500, 1000 mg/kg-bw/day	5 days/ week for 5 weeks	Not Reported	NOAEL = 1000 mg/kg - bw/day	No mortalities occurred and no changes were reported for hematology parameters or liver or spleen weights.	Gopinathan et al. (2013)	Medium
Mortality	Short-term (1-30 days)	Mouse, B6C3F1, Male (5)	0, 130, 720, 2130, 2670 mg/kg-bw/day (0, 500, 2500, 7500, 10000 ppm)	4 weeks	NOAEL = 0.048	NOAEL = 1125 mg/kg - bw/day	Mortality in a male mouse that also showed renal effects. Death was considered related to treatment.	Malek et al. (1997)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number /group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect	Reference	Data Quality Evaluation
Mortality	Short-term (1-30 days)	Mouse, B6C3F1, Female (5)	0, 180, 920, 2970, 4060 mg/kg-bw/day (0, 500, 2500. 7500, 10,000 ppm)	4 weeks	Not Reported	NOAEL = 4060 mg/kg - bw/day	No exposure-related effects	NMP Producers Group (1994)	High
Mortality	Short-term (1-30 days)	Mouse, B6C3F1, Male (5)	0, 130, 720, 2130, 2670 mg/kg-bw/day (0, 500, 2500. 7500, 10,000 ppm)	4 weeks	Not Reported	NOAEL = 2670 mg/kg - bw/day	No exposure-related effects	NMP Producers Group (1994)	High
Not Reported	Short-term (1-30 days)	Rat, Sprague-Dawley, Male (5)	0, 250, 500, 1000 mg/kg-bw/day	5 days/ week for 5 weeks	Not Reported	NOAEL = 250 mg/kg - bw/day	Decreased serum creatinine	Gopinathan et al. (2013)	Medium
Not Reported	Short-term (1-30 days)	Rat, Sprague-Dawley, Male (5)	0, 250, 500, 1000 mg/kg-bw/day	5 days/ week for 5 weeks	Not Reported	NOAEL = 250 mg/kg - bw/day	Decreased serum creatinine	Gopinathan et al. (2013)	Medium
Renal	Short-term (1-30 days)	Rat, Sprague-Dawley, Male (5)	0, 250, 500, 1000 mg/kg-bw/day	5 days/ week for 5 weeks	Not Reported	Not Reported	Mottled kidneys were reported bilaterally with a combined incidence in all dose groups (250, 500, and 1000 mg/kg-bw/day) of 8/15. This was not observed in controls. No changes were reported for urine chemistry parameters or kidney weights. Incidences of mottled kidneys for each dose group were not reported, so I did not assign a NOAEL or LOAEL for renal effects.	Gopinathan et al. (2013)	Medium

Target Organ/ System	Study Type	Species, Strain, Sex (Number /group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect	Reference	Data Quality Evaluation
Renal	Short-term (1-30 days)	Mouse, B6C3F1, Female (5)	0, 180, 920, 2970, 4060 mg/kg-bw/day (0, 500, 2500. 7500, 10,000 ppm)	4 weeks	NOAEL = 920 mg/kg - bw/day	NOAEL = 920 mg/kg - bw/day	Dark yellow urine in all animals at Dose 3, 4, and 5. Cloudy swelling of the distal renal tubule in 3/5 females at Dose 5	NMP Producers Group (1994)	High
Renal	Short-term (1-30 days)	Mouse, B6C3F1, Male (5)	0, 130, 720, 2130, 2670 mg/kg-bw/day (0, 500, 2500. 7500, 10,000 ppm)	4 weeks	NOAEL = 720 mg/kg - bw/day	NOAEL = 720 mg/kg - bw/day	Dark yellow urine in all animals at Dose 3, 4, and 5. Cloudy swelling of the distal renal tubule in 2/5 males at Dose 4. and 4/5 males at Dose 5	NMP Producers Group (1994)	High

I.1.2 Hazard and Data Evaluation Summary for Reproductive and Developmental Oral Exposure Studies

Table_Apx I-2. Hazard and Data Evaluation Summary for Reproductive and Developmental Oral Exposure Studies

Target Organ/ System	Study Type	Species, Strain, Sex (Number / group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Body Weight	Two-generation reproduction study	Rat, Sprague-Dawley (30/sex/ group)	0, 50, 160, 500 mg/kg/day	10 weeks prior to mating, throughout mating, gestation, lactation, and rest periods between pregnancies over two generations	NOAEL= 160 mg/kg-bw/day	NOAEL= 160 mg/kg-bw/day	Reduced maternal body weight gain from gestational day 0-20 during both litters of the parental generation in the high dose group	Exxon (1991)	High
Body Weight	Developmental	Rat, Sprague-Dawley (25/ group)	0, 40, 125, 400 mg/kg/day	Daily exposure on gestational days (GD) 6-15	NOAEL= 125 mg/kg-bw/day	NOAEL= 125 mg/kg-bw/day	Reduced maternal body weight gain at 400 mg/kg-bw/day	Exxon (1992)	High
Body Weight	Two-generation reproduction study	Rat, Sprague-Dawley (30/sex/ group)	0, 50, 160, 350/500 mg/kg/day	10 weeks prior to mating, throughout mating, gestation, lactation, and rest periods between pregnancies over two generations	NOEL= 350 mg/kg-bw/day	NOAEL = 350 mg/kg-bw/day	Reduced maternal body weight gain from gestational day 0-20 during the first litter of the parental generation in the high dose group (500 mg/kg-bw/day)	NMP Producers Group, (1999a)	High
Body Weight	Two-generation reproduction study	Rat, Wistar (25/sex/ group)	0, 50, 160, 350/500 mg/kg/day	10 weeks prior to mating, throughout mating, gestation, lactation, and rest periods between pregnancies over two generations	NOAEL= 160 mg/kg-bw/day	NOAEL = 160 mg/kg-bw/day	Reduced maternal body weight gain from gestational day 0-20 during both litters of the parental generation in the high dose group	NMP Producers Group (1999c)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number / group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Body Weight	Reproductive	Rat, Male (22-24)	0, 100, 300, 1000 mg/kg-bw/day	5 days/ week for 10 weeks prior to mating and 1 week during mating	Not Reported	NOAEL = 300 mg/kg - bw/day	Significant body weight decrement of at least 10% in paternal rats exposed prior to mating in the high dose group	Sitarek et al. (2008)	High
Offspring Survival, Growth, and Develop-ment	Two-generation reproduction study	Rat, Sprague-Dawley (30/sex/ group)	0, 50, 160, 500 mg/kg/day	10 weeks prior to mating, throughout mating, gestation, lactation, and rest periods between pregnancies over two generations	NOAEL= 160 mg/kg-bw/day	NOAEL= 160 mg/kg-bw/day	Significant decrease in offspring survival indices and growth rates and increase in the number of stillborn pups in both generations in the high dose group	Exxon (1991)	High
Offspring Survival, Growth, and Develop-ment	Developmental	Rat, Sprague-Dawley (25/ group)	0, 40, 125, 400 mg/kg/day	Daily exposure on gestational days (GD) 6-15	NOAEL= 125 mg/kg-bw/day	NOAEL= 125 mg/kg-bw/day	Reduced fetal body weights, reduced ossification sites in proximal phalanges of the hindpaw, at 400 mg/kg-bw/day	Exxon (1992)	High
Offspring Survival, Growth, and Develop-ment	Two-generation reproduction study	Rat, Sprague-Dawley (30/sex/ group)	0, 50, 160, 350/500 mg/kg/day	10 weeks prior to mating, throughout mating, gestation, lactation, and rest periods between pregnancies over two generations	NOEL= 160 mg/kg-bw/day	NOAEL = 50 mg/kg-bw/day	Significant decrease in pup survival through PND4 and decrease in pup body weights in both generations in the high dose group; significant decrease in pup body weights at PND 7-21 in the second litter of the second generation in the 160 mg/kg/day dose group; significant increase in stillborn pups in the first litter of the first generation in the high dose group	NMP Producers Group (1999a)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number / group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Offspring Survival, Growth, and Develop-ment	Two-generation reproduction study	Rat, Wistar (25/sex/ group)	0, 50, 160, 350/500 mg/kg/day	10 weeks prior to mating, throughout mating, gestation, lactation, and rest periods between pregnancies over two generations	NOAEL= 160 mg/kg-bw/day	NOAEL= 160 mg/kg-bw/day	Significant increase in the number of stillborn pups in the first generation high dose group and decrease in pup survival through PND4 in both generations in the high dose group	NMP Producers Group (1999c)	High
Offspring Survival, Growth, and Develop-ment	Developmental	Rat, Sprague-Dawley (15-16)	0, 125, 250, 500, 750 mg/kg-bw/day	Daily exposure on gestational days (GD) 6-20	NOAEL= 125 mg/kg-bw/day	NOAEL= 125 mg/kg-bw/day	Significant increase in resorptions/ post-implantation losses, increased skeletal malformations, and decreased fetal body weights	Saillenfait et al. (2002)	High
Offspring Survival, Growth, and Develop-ment	Reproductive	Rat, Other, Male (22-24)	0, 100, 300, 1000 mg/kg-bw/day	5 days/ week for 10 weeks prior to mating and 1 week during mating	Not Reported	NOAEL = 100 mg/kg - bw/day	Significant decrease in offspring viability through PND4 following paternal exposure prior to mating	Sitarek et al. (2008)	High
Offspring Survival, Growth, and Develop-ment	Reproductive	Rat, Wistar, Female (22-28)	0, 150, 450, 1000 mg/kg-bw/day	5 days/ week for two weeks before mating, during gestation and lactation	LOAEL = 150 mg/kg-bw/day	LOAEL = 150 mg/kg-bw/day	Significant decrease in pup survival within three weeks of birth at all doses; number of live pups was reduced at 1000mg/kg-bw/day	Sitarek et al. (2012)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number / group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Repro-ductive	Subchronic (30-90 days)	Dog, Beagle, Both (6/sex)	0, 24, 75, 246 mg/kg-bw/day in males; 0, 24, 76, 246 mg/kg-bw/day in females (actual concentrations)	13 weeks	Not Reported	NOAEL = 246 mg/kg - bw/day	No effects on reproductive organs, hematological/ immune, body weight, relative organ (liver, kidney, spleen, heart, thyroid, adrenal glands, brain, and pituitary) weights.	Becci et al. (1983)	High
Repro-ductive	Two-generation reproduction study	Rat, Sprague-Dawley (30/sex/ group)	0, 50, 160, 500 mg/kg/day	10 weeks prior to mating, throughout mating, gestation, lactation, and rest periods between pregnancies over two generations	NOAEL = 160 mg/kg - bw/day	LOAEL = 50 mg/kg - bw/day	Significant reductions in male fertility, female fecundity at all doses tested in both litters of the second generation; increased numbers of second generation females with microscopic changes in the uterus and ovaries, including decreased numbers of corpora lutea and decreased implantation sites in the high dose group; increased incidence of smaller than normal testes in second generation parental males in the high dose group	Exxon (1991)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number / group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Repro-ductive	Short-term (1-30 days)	Mouse, B6C3F1, Male (5)	0, 130, 720, 2130, 2670 mg/kg-bw/day (0, 500, 2500. 7500, 10,000 ppm)	4 weeks	Not Reported	NOAEL = 2670 mg/kg - bw/day	No exposure-related effects	NMP Producers Group/ BASF (1994)	High
Repro-ductive	Short-term (1-30 days)	Rat, Other, Male (5)	0, 149, 429, 1234, 2019 mg/kg-bw/day (0, 2000, 6000, 18,000, 30,000 ppm)	4 weeks	NOAEL = 429 mg/kg - bw/day	NOAEL = 429 mg/kg - bw/day	Decreased body weight and altered testes and liver weights were observed at 1234 mg/kg-bw/day and above. Degeneration/atrophy of testicular seminiferous tubules were observed 1/5 males at 1234 mg/kg-bw/day and in 5/5 at 2019 mg/kg-bw/day. Increased incidence of centrilobular hepatocellular hypertrophy and decreased serum glucose were observed at 1234 mg/kg-bw/day and above.	Malek et al. (1997)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number / group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Repro-ductive	Two-generation reproduction study	Rat, Sprague-Dawley (30/sex/ group)	0, 50, 160, 350/500 mg/kg/day	10 weeks prior to mating, throughout mating, gestation, lactation, and rest periods between pregnancies over two generations	NOEL= 350 mg/kg-bw/day	NOAEL = 350 mg/kg-bw/day	No significant reduction reported in male or female fertility; no significant difference from controls reported on estrous cycles, sperm parameters, reproductive organ weights or histopathological findings in ovaries or testes	NMP Producers Group (1999a)	High
Repro-ductive	Two-generation reproduction study	Rat, Wistar (25/sex/ group)	0, 50, 160, 350/500 mg/kg/day	10 weeks prior to mating, throughout mating, gestation, lactation, and rest periods between pregnancies over two generations	NOAEL for fertility = 350 mg/kg-bw/day	NOAEL for fertility = 350 mg/kg-bw/day; NOEAL for testes weights = 50 mg/kg-bw/day	No significant reduction reported in male or female fertility; no significant difference from controls reported on estrous cycles, sperm parameters, or histopathological findings in ovaries or testes; Significant change in testes weights relative to body weight in mid and high dose groups in both generations.	NMP Producers Group (1999c)	High
Repro-ductive	Subchronic (30-90 days)	Rat, Other, Male (10)	0, 1, 169, 433, 1057 mg/kg-bw/day (0, 3000, 7500, 18,000 ppm)	90 days	Not Reported	NOAEL = 1057 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number / group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Repro-ductive	Subchronic (30-90 days)	Mouse, Both (20/sex)	0, 277, 619, 1931 mg/kg-bw/day (0, 1000, 2500, 7500 ppm)	90 days	Not Reported	NOAEL = 1931 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High
Repro-ductive	Chronic (>90 days)	Rat, Other, Male (62)	0, 66.4, 207, 678 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	Not Reported	NOAEL = 207 mg/kg - bw/day	Biliateral degeneration/atrophy of seminiferous tubules in the tests, bilateral oligospermia/germ cell debris in the epididymites, centrilobular fatty change in the liver	Malley et al. (2001)	High
Repro-ductive	Chronic (>90 days)	Rat, Other, Female (62)	0, 87.8, 283, 939 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	Not Reported	NOAEL = 939 mg/kg - bw/day	No exposure-related adverse effects	Malley et al. (2001)	High
Repro-ductive	Chronic (>90 days)	Mouse, B6C3F1, Male (50)	0, 89, 173, 1089 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	Not Reported	NOAEL = 1089 mg/kg - bw/day	No adverse effects	Malley et al. (2001)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number / group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Repro-ductive	Chronic (>90 days)	Mouse, B6C3F1, Female (50)	0, 115, 221, 1399 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	Not Reported	NOAEL = 1399 mg/kg - bw/day	No adverse effects	Malley et al. (2001)	High
Repro-ductive	Reproductive	Rat, Other, Male (22-24)	0, 100, 300, 1000 mg/kg-bw/day	5 days/ week for 10 weeks prior to mating and 1 week during mating	Not Reported	NOAEL = 300 mg/kg - bw/day	Significant increase in male infertility, damage to seminiferous epithelium and significant reduction in thyroid weight at 1000 mg/kg-bw/day	Sitarek et al. (2008)	High
Repro-ductive	Reproductive	Rat, Wistar, Female (22-28)	0, 150, 450, 1000 mg/kg-bw/day	5 days/ week for two weeks before mating, during gestation and lactation	NOAEL = 150 mg/kg-bw/day	NOAEL = 150 mg/kg-bw/day	Significant decrease in female fertility index	Sitarek et al. (2012)	High

I.1.3 Hazard and Data Evaluation Summary for Reproductive and Developmental Inhalation Exposure Studies

Table_Apx I-3. Hazard and Data Evaluation Summary for Reproductive and Developmental Inhalation Exposure Studies

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Body Weight	Developmental	Rat, Sprague-Dawley, Female (25-26)	0, 122, 243, 487 mg/m^3	6 hours/ day; 7 days/ week for 15 weeks	NOAEL= 122 mg/m^3	NOAEL = 122 mg/m^3	LOAEL for decreased maternal weight gain at 243 mg/m^3. Maternal food intake also decreased at 487 mg/m^3.	Saillenfait et al. (2003)	High
Neuro-logical/ Behavior	Reproductive	Rat, Other, Both (10M and 20F)	0, 42, 206, 472 mg/m^3	6 hours/ day 7 days/ week for 143 weeks	Not Reported	NOAEL = 42 mg/m^3	F0 dams exhibited decreased response to auditory stimuli at the highest dose.	Solomon et al. (1995)	High
Offspring Survival, Growth, and Develop-ment	Developmental	Rat, Other, Female (25)	0, 100, 360 mg/m^3	6 hours/ day 7 days/ week for 10 weeks	Not Reported	NOAEL = 360 mg/m^3	No effects on uterine or litter parameters, fetal weight or length, or incidence of gross, soft tissue, or skeletal anomalies	Lee et al. (1987)	High
Offspring Survival, Growth, and Develop-ment	Reproductive	Rat, Other, Both (10M and 20F)	0, 42, 206, 472 mg/m^3	6 hours/ day; 7 days/ week for 143 weeks	Not Reported	NOAEL = 42 mg/m^3	Decreased F1 offspring weights per litter from PND 1 to PND 21, and decreased fetal body weight in developmental phase of study, at highest dose	Solomon et al. (1995)	High
Offspring Survival, Growth, and Develop-ment	Developmental	Rat, Sprague-Dawley, Female (25-26)	0, 122, 243, 487 mg/m^3	6 hours/ day; 7 days/ week for 15 weeks	NOAEL= 243 mg/m^3	NOAEL= 243 mg/m^3	Reduced fetal weight at 487 mg/m^3 exposure	Saillenfait et al. (2003)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Repro-ductive	Chronic (>90 days)	Rat, Crj: CD(SD), Both (120)	0, 41, 405 mg/m^3	6 hours/ day 5 days/ week	Not Reported	NOAEL = 41 mg/m^3	Mammary gland hyperplasia	DuPont (1982)	Medium
Repro-ductive	Chronic (>90 days)	Rat, Crj: CD(SD), Both (120)	0, 41, 405 mg/m^3	6 hours/ day 5 days/ week	Not Reported	NOAEL = 405 mg/m^3	No adverse effects reported based on histopathology of epididymites and prostate	DuPont (1982)	Medium
Repro-ductive	Reproductive	Rat, Other, Both (10M and 20F)	0, 42, 206, 472 mg/m^3	6 hours/ day 7 days/ week for 143 weeks	NOAEL = 472 mg/m^3	NOAEL = 472 mg/m^3	No significant difference in reproductive performance or adult body weight. Study notes condensation on inside of high dose chambers, which precluded achieving target concentration of 527 mg/m^3.	Solomon et al. (1995)	High

I.1.4 Hazard and Data Evaluation Summary for Reproductive and Developmental Dermal Exposure Studies

Table_Apx I-4. Hazard and Data Evaluation Summary for Reproductive and Developmental Dermal Exposure Studies

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Growth and develop ment	Developmental	Sprague-Dawley, Female (25)	0, 75, 237 and 750 mg/kg-bw/day	Days 6-15 of gestation	Not reported	NOAEL= 237 mg/kg-bw/day	Decreased number of live fetuses per dam and increased percentage of resorption sites and skeletal abnormalities as well as maternal toxicity indicated by reduced body weight gain at the highest dose	Becci et al. (1982)	Medium

I.1.5 Hazard and Data Evaluation Summary for Sub-chronic and Chronic Non-cancer Inhalation Exposure Studies

Table_Apx I-5. Hazard and Data Evaluation Summary for Sub-chronic and Chronic Non-cancer Inhalation Exposure Studies

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Body Weight	Chronic (>90 days)	Rat, Crj: CD(SD), Both (120)	0, 41, 405 mg/m^3	6 hours/ day 5 days/week	Not Reported	NOAEL = 405 mg/m^3	Body weight was significantly decreased in 405 mg/m^3 males (but only 6% lower than controls). Effects on mortality, hematology and clinical chemistry parameters, the kidney, and cancer incidence were not temporally- and/or concentration-related, and/or were not toxicologically relevant (*e.g.*, decreased cancer incidence).	DuPont (1982)	Medium
Clinical Chem-istry/ Biochem-ical	Chronic (>90 days)	Rat, Crj: CD(SD), Both (120)	0, 41, 405 mg/m^3	6 hours/ day 5 days/week	Not Reported	NOAEL = 405 mg/m^3	Body weight was significantly decreased in 405 mg/m^3 males (but only 6% lower than controls). Effects on mortality, hematology and clinical chemistry parameters, the kidney, and cancer incidence were not temporally- and/or concentration-related, and/or were not toxicologically relevant (*e.g.*, decreased cancer incidence).	DuPont (1982)	Medium
Hemato-logical and Immune	Chronic (>90 days)	Rat, Crj: CD(SD), Both (120)	0, 41, 405 mg/m^3	6 hours/ day 5 days/week	Not Reported	NOAEL = 405 mg/m^3	Body weight was significantly decreased in 405 mg/m^3 males (but only 6% lower than controls). Effects on mortality, hematology and clinical chemistry parameters, the kidney, and cancer incidence were not temporally- and/or concentration-related, and/or were not toxicologically relevant (*e.g.*, decreased cancer incidence).	DuPont (1982)	Medium

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concen-trations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Mortality	Chronic (>90 days)	Rat, Crj: CD(SD), Both (120)	0, 41, 405 mg/m^3	6 hours/ day 5 days/week	Not Reported	NOAEL = 405 mg/m^3	Body weight was significantly decreased in 405 mg/m^3 males (but only 6% lower than controls). Effects on mortality, hematology and clinical chemistry parameters, the kidney, and cancer incidence were not temporally- and/or concentration-related, and/or were not toxicologically relevant (*e.g.*, decreased cancer incidence).	DuPont (1982)	Medium
Not Reported	Chronic (>90 days)	Rat, Crj: CD(SD), Both (120)	0, 41, 405 mg/m^3	6 hours/ day 5 days/week	Not Reported	NOAEL = 405 mg/m^3	Body weight was significantly decreased in 405 mg/m^3 males (but only 6% lower than controls). Effects on mortality, hematology and clinical chemistry parameters, the kidney, and cancer incidence were not temporally- and/or concentration-related, and/or were not toxicologically relevant (*e.g.*, decreased cancer incidence).	DuPont (1982)	Medium

I.1.6 Hazard and Data Evaluation Summary for Sub-chronic and Chronic Non-cancer Oral Exposure Studies

Table_Apx I-6. Hazard and Data Evaluation Summary for Sub-chronic and Chronic Non-cancer Oral Exposure Studies

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Body Weight	Sub-chronic (30-90 days)	Mouse, Both (20/sex)	0, 277, 619, 1931 mg/kg-bw/day (0, 1000, 2500, 7500 ppm)	90 days	Not Reported	NOAEL = 1931 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High
Body Weight	Sub-chronic (30-90 days)	Rat, Other, Male (20-26)	0, 169, 433, 1057 mg/kg-bw/day (0, 3000, 7500, 18,000 ppm)	90 days	NOAEL = 0.048	NOAEL = 1057 mg/kg - bw/day	Body weight effects not considered adverse (associated with decreased food consumption, indicating palatability issue)	Malley et al. (1999)	High
Body Weight	Sub-chronic (30-90 days)	Rat, Other, Female (20-26)	0, 217, 565, 1344 mg/kg-bw/day (0, 3000, 7500, 18,000 ppm)	90 days	NOAEL = 0.048	NOAEL = 1344 mg/kg - bw/day	Body weight effects within 10% of control	Malley et al. (1999)	High
Body Weight	Chronic (>90 days)	Rat, Other, Male (62)	0, 66.4, 207, 678 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	NOAEL = 207 mg/kg - bw/day	NOAEL = 207 mg/kg - bw/day	Study authors report a study NOAEL of 207 mg/kg/day in male rats based on 25% decrease in terminal body weight and increased incidence of severe chronic progressive nephropathy.	Malley et al. (2001)	High
Body Weight	Chronic (>90 days)	Rat, Other, Female (62)	0, 87.8, 283, 939 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	NOAEL = 283 mg/kg - bw/day	NOAEL = 283 mg/kg - bw/day	Study authors report a study NOAEL of 283 mg/kg/day in female rats based on 35% decrease in terminal body weight.	Malley et al. (2001)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Body Weight	Chronic (>90 days)	Mouse, B6C3F1, Male (50)	0, 89, 173, 1089 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	Not Reported	NOAEL = 1089 mg/kg - bw/day	No adverse effects	Malley et al. (2001)	High
Body Weight	Chronic (>90 days)	Mouse, B6C3F1, Female (50)	0, 115, 221, 1399 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	Not Reported	NOAEL = 1399 mg/kg - bw/day	No adverse effects	Malley et al. (2001)	High
Hematological and Immune	Sub-chronic (30-90 days)	Dog, Beagle Both (6/sex)	0, 24, 75, 246 mg/kg-bw/day in males; 0, 24, 76, 246 mg/kg-bw/day in females	13 weeks	Not Reported	NOAEL = 246 mg/kg - bw/day	No effects on reproductive organs, hematological/immune , body weight, relative organ (liver, kidney, spleen, heart, thyroid, adrenal glands, brain, and pituitary) weights.	Becci et al. (1983)	High
Hepatic	Sub-chronic (30-90 days)	Rat, Other, Male (10)	0, 169, 433, 1057 mg/kg-bw/day (0, 3000, 7500, 18,000 ppm)	90 days	Not Reported	NOAEL = 1057 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High
Hepatic	Sub-chronic (30-90 days)	Rat, Other, Female (20-26)	0, 217, 565, 1344 mg/kg-bw/day (0, 3000, 7500, 18,000 ppm)	90 days	Not Reported	NOAEL = 1344 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High
Hepatic	Sub-chronic (30-90 days)	Mouse, Both (20/sex)	0, 277, 619, 1931 mg/kg-bw/day (0, 1000, 2500, 7500 ppm)	90 days	Not Reported	NOAEL = 1931 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Hepatic	Chronic (>90 days)	Rat, Other, Male (62)	0, 66.4, 207, 678 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	Not Reported	NOAEL = 207 mg/kg - bw/day	Biliateral degeneration/atrophy of seminiferous tubules in the tests, bilateral oligospermia/germ cell debris in the epididymites, centrilobular fatty change in the liver	Malley et al. (2001)	High
Hepatic	Chronic (>90 days)	Rat, Other, Female (62)	0, 87.8, 283, 939 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	Not Reported	NOAEL = 939 mg/kg - bw/day	No exposure-related adverse effects	Malley et al. (2001)	High
Hepatic	Chronic (>90 days)	Mouse, B6C3F1, Female (50)	0, 115, 221, 1399 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	NOAEL = 221 mg/kg - bw/day	NOAEL = 221 mg/kg - bw/day	Study authors reported a study NOAEL of 221 mg/kg/day for female mice based on increased liver weight, increased incidence of hepatocellular basophilic foci, eosinophilic foci, and cellular alterations in liver, and increased hepatocellular adenoma and carcinoma.	Malley et al. (2001)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Hepatic	Chronic (>90 days)	Mouse, B6C3F1, Male (50)	0, 89, 173, 1089 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	NOAEL = 89 mg/kg - bw/day	NOAEL = 89 mg/kg - bw/day	Study authors report a study NOAEL of 89 mg/kg/day in male mice based on increased liver weight in the mid- and high-dose groups. At the high dose, additional effects included increased incidence of hepatocellular hypertrophy, clear cell foci, eosinophilic foci, and cellular alterations in the liver.	Malley et al. (2001)	High
Mortality	Sub-chronic (30-90 days)	Rat, Other, Male (10)	0, 169, 433, 1057 mg/kg-bw/day (0, 3000, 7500, 18,000 ppm)	90 days	Not Reported	NOAEL = 1057 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High
Mortality	Sub-chronic (30-90 days)	Rat, Other, Female (20-26)	0, 217, 565, 1344 mg/kg-bw/day (0, 3000, 7500, 18,000 ppm)	90 days	Not Reported	NOAEL = 1344 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High
Mortality	Sub-chronic (30-90 days)	Mouse, Both (20/sex)	0, 277, 619, 1931 mg/kg-bw/day (0, 1000, 2500, 7500 ppm)	90 days	Not Reported	NOAEL = 1931 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High
Mortality	Chronic (>90 days)	Rat, Other, Male (62)	0, 66.4, 207, 678 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	NOAEL = 0.048	NOAEL = 66.4 mg/kg - bw/day	Decreased survival at 207 mg/kg/day (21%) compared with control (32%)	Malley et al. (2001)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Mortality	Chronic (>90 days)	Rat, Other, Female (62)	0, 87.8, 283, 939 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	Not Reported	NOAEL = 939 mg/kg - bw/day	No exposure-related adverse effects	Malley et al. (2001)	High
Mortality	Chronic (>90 days)	Mouse, B6C3F1, Male (50)	0, 89, 173, 1089 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	Not Reported	NOAEL = 1089 mg/kg - bw/day	No adverse effects	Malley et al. (2001)	High
Mortality	Chronic (>90 days)	Mouse, B6C3F1, Female (50)	0, 115, 221, 1399 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	Not Reported	NOAEL = 1399 mg/kg - bw/day	No adverse effects	Malley et al. (2001)	High
Renal	Sub-chronic (30-90 days)	Rat, Other, Male (10)	0, 169, 433, 1057 mg/kg-bw/day (0, 3000, 7500, 18,000 ppm)	90 days	Not Reported	NOAEL = 1057 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High
Renal	Sub-chronic (30-90 days)	Rat, Other, Female (20-26)	0, 217, 565, 1344 mg/kg-bw/day (0, 3000, 7500, 18,000 ppm)	90 days	Not Reported	NOAEL = 1344 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High
Renal	Sub-chronic (30-90 days)	Mouse, Both (20/sex)	0, 277, 619, 1931 mg/kg-bw/day (0, 1000, 2500, 7500 ppm)	90 days	Not Reported	NOAEL = 1931 mg/kg - bw/day	No adverse effects.	Malley et al. (1999)	High

Target Organ/ System	Study Type	Species, Strain, Sex (Number/ group)	Doses/ Concentrations	Duration	Author Reported NOAEL/ LOAEL	EPA Identified NOAEL/ LOAEL	Effect Measured	Reference	Data Quality Evaluation
Renal	Chronic (>90 days)	Rat, Other, Male (62)	0, 66.4, 207, 678 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	NOAEL = 207 mg/kg - bw/day	NOAEL = 207 mg/kg - bw/day	Study authors report a study NOAEL of 207 mg/kg/day in male rats based on 25% decrease in terminal body weight and increased incidence of severe chronic progressive nephropathy.	Malley et al. (2001)	High
Renal	Chronic (>90 days)	Rat, Other Female (62)	0, 87.8, 283, 939 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	Not Reported	NOAEL = 939 mg/kg - bw/day	No exposure-related adverse effects	Malley et al. (2001)	High
Renal	Chronic (>90 days)	Mouse, B6C3F1 - Male (50)	0, 89, 173, 1089 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	Not Reported	NOAEL = 1089 mg/kg - bw/day	No adverse effects	Malley et al. (2001)	High
Renal	Chronic (>90 days)	Mouse, B6C3F1 - Female (50)	0, 115, 221, 1399 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	Not Reported	NOAEL = 1399 mg/kg - bw/day	No adverse effects	Malley et al. (2001)	High

I.1.7 Hazard and Data Evaluation Summary for Cancer Studies

Table_Apx I-7. Summary of Tumor Incidence Data from Animal Cancer Bioassays

Species/ Strain/ Sex (Number/group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
Rat/Crj: CD(SD)/ Both (120)	Inhalation, whole body	0, 41, 405 mg/m^3	6 hours/day 5 days/week for 2 years	Data not presented	Increased pituitary adenocarcinomas at 41 but not 405 mg/m^3 and at 18 but not 24 months	DuPont (1982) [a]	Medium (1.8)
Rat/Other/ Female (62)	Oral, dietary	0, 87.8, 283, 939 mg/kg-bw/day (0, 1600, 5000, 15,000 ppm)	2 years	0, 2, 3, 3	At least one mammary neoplasm	Malley et al. (2001) [b]	High (1.2)
Mouse/ B6C3F1/ Male (50)		0, 89, 173, 1089 mg/kg-bw/day (0, 600, 1200, 7200 ppm)	18 months	5, 2, 4, 12 [c]	Increased incidence of hepatocellular adenoma		
				4, 1, 3, 13 [c]	Increased incidence of hepatocellular carcinoma		
Mouse/B6C3F1/ Female (50)		0, 115, 221, 1399 mg/kg-bw/day (0, 600, 1200, 7200 ppm)		2, 2, 1, 7 [c]	Increased hepatocellular adenoma and carcinoma		
				0, 0, 0, 3 [c]	Increased hepatocellular carcinoma		

[a] This is the unpublished study of the published study identified as Lee et al. (1987)

[b] Unpublished study of the results in rats is available as NMP Producers Group (1997)

[c] $P < 0.05$ by Cochran-Armitage trend test

I.1.8 Hazard and Data Evaluation Summary for Genotoxicity and Mechanistic Studies

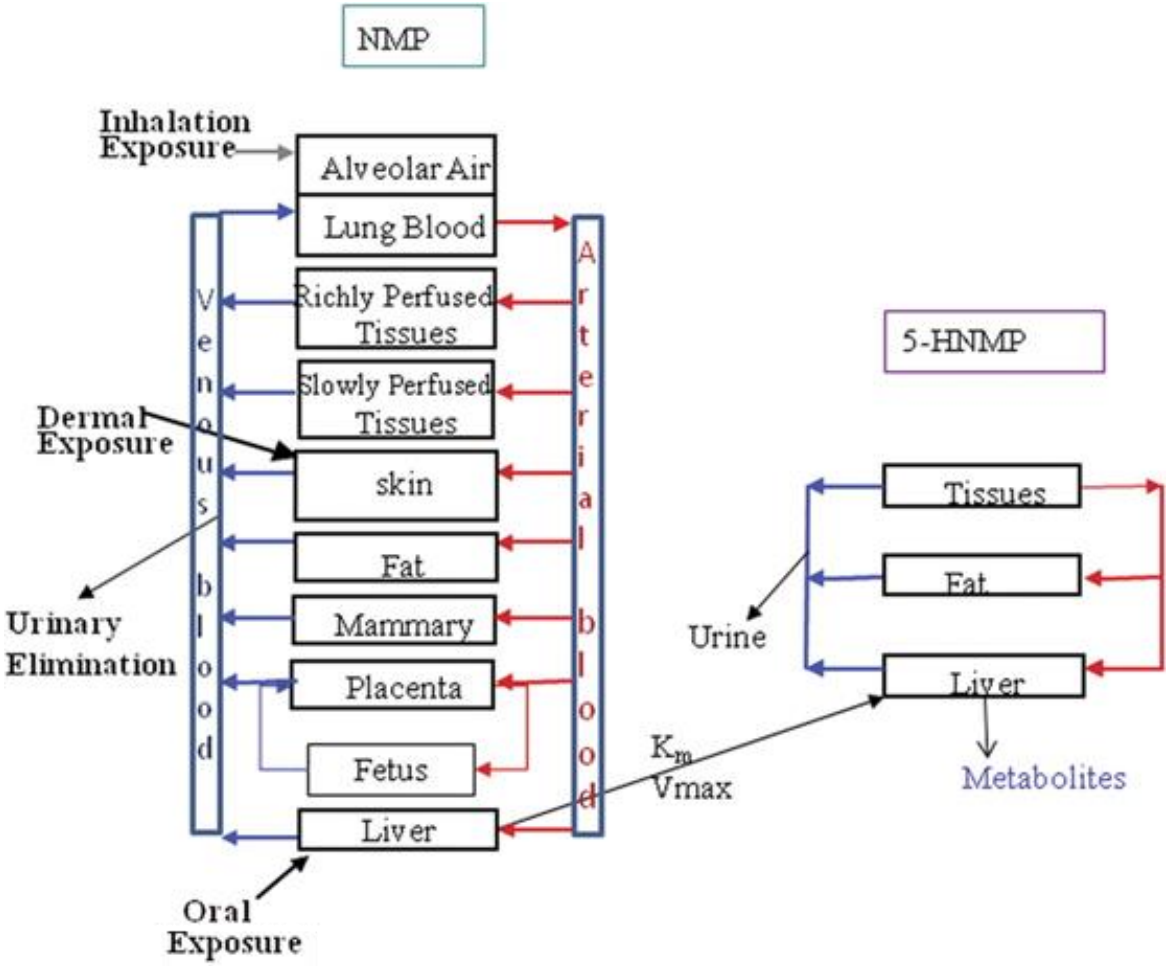
Table_Apx I-8. Summary of Genotoxicity and Mechanistic Data

Species	Exposure Route	Exposure Dose/Duration	Outcome	Comments	Reference	Data Quality Evaluation
Mice: NMRI	Oral gavage	Single dose of 0, 950, 1900, or 3800 mg/kg-bw	No increase in multinucleated erythrocytes	Authors report indications of systemic toxicity from NMP exposure. Authors conclude that results indicate a lack of clastogenic effect or spindle poison effect of NMP *in vivo*. Positive control responses demonstrate that the assay was able to detect such effects.	Engelhardt and Fleig (1993)	High
Chinese Hamster	Oral gavage	Single dose of 0, 1900, or 3800 mg/kg-bw	No increase in the number of mitoses containing structural or numerical chromosomal aberrations in bone marrow.	Authors report indications of systemic toxicity from NMP exposure. Authors conclude that results indicate a lack of clastogenic or aneugenic effect of NMP. Positive control responses demonstrate that the assay was able to detect structural and numerical chromosomal aberrations.		High
Salmonella (strains TA1535, TA1537, TA98, TA97, and TA100) and mammalian microsomes	*In vitro* Ames assay	0, 100, 333, 1000, 3333, or 10000 µg/plate (± S9 mix)	No mutagenic response reported for NMP with or without metabolic activation.	Salmonella mutagenicity was tested with and without mammalian microsomes. Arochlor-1254 induced S9 liver fractions were obtained from male Sprague-Dawley rats and male Syrian hamsters. Positive control responses demonstrate that the assay was able to detect mutagenic effects.	Mortelmans et al. (1986)	High
Salmonella (strains TA100, TA102, TA104, TA97, TA98, TA2638, UTH8413, UTH8414)	*In vitro* Ames assay (standard plate incorporation assay)	0, 0.01, 0.1, 1.0, 10, 100, or 1000 µM/plate (± S9 mix)	No mutagenic response reported for NMP with or without metabolic activation.	Test were performed using strains capable of detecting frameshifts, base-pair substitution, and excision repair. ; Arochlor-1254 induced S9 liver fractions were obtained from male Sprague-Dawley rats. In strains TA102 and TA104,, an increase in revertant numbers was reported but the increase was less than two-fold greater than background and did not demonstrate a linear dose-response.	Wells et al. (1988)	High

Species	Exposure Route	Exposure Dose/Duration	Outcome	Comments	Reference	Data Quality Evaluation
Salmonella (strains TA98, TA104)	*In vitro* Ames assay; (pre-incubation assay)	0.01 – 1000 µM/plate (± S9 mix)	No mutagenic response reported for NMP	Tests were performed following pre-incubation of NMP, S9 mix, and bacteria. Following pre-incubation, NMP was cytotoxic to Salmonella at the highest test concentrations		High
Not applicable	*In vitro* cell free binding assay	25 mM NMP	Percentage competition of NMP vs. control binding to each of the two BRDT binding domains was reported as 2.6% and 4.4% (where 0% indicates strongest binding interaction and 100% indicates absent binding)	BromoMax screening assay provides competitive binding data for a panel of bromodomain-containing proteins, including the testis-specific BRDT as well as BRD1, BRD2, BRD3, BRD4, BAZ2B, CREBBP, and TAF1. NMP binding to bromodomains contained in these proteins ranged from 0-8%.	Shortt (2014)	High
Not applicable	*In vitro* cell free binding assay	10 concentrations across 5 log units	IC50 for BRD2 = 3.3 mM IC50 for BRD4 = 3.4 mM	AlphaScreen binding assay was used to determine the effect of NMP on bromodomain binding ability for a panel of bromodomain-containing proteins. IC50s for BRD2 and BRD4 bromodomains were calculated from AlphaScreen results across a range of concentrations	Gjoksi (2015a); Gjoksi (2016)	High

Appendix J NMP PBPK MODELING

The PBPK models of Poet et al. (2010) (Figure_Apx J-1) describe the toxicokinetics of NMP in rats and humans. EPA has revised the models for use in this risk evaluation, and the models underwent scientific and technical evaluations consistent with those outlined in An umbrella Quality Assurance Project Plan (QAPP) for PBPK models (EPA, 2018e). These PBPK models were initially evaluated and revised by EPA in 2013 (U.S. EPA, 2013b). Further modifications and calibration were conducted by Dr. Torka Poet in 2014 (personal communication). In this update, additional data were considered to further calibrate and validate the model. Model calibration consists of using data to optimize parameters when those parameters are unknown or approximated, validation is used to show the fits of the model to other datasets. EPA then evaluated the version submitted by Dr. Poet in 2014 and made some additional corrections and modifications as described below.



Figure_Apx J-1. PBPK model structure.

PBPK model used to describe the disposition of NMP and its major metabolite 5-HNMP in rats and humans following oral, dermal, or inhalation exposures. Lines represent blood flow between compartments (QC, cardiac output [L/h]); Qi, blood flow to ‘‘i’’ tissue (L/h). The NMP parent model consists of seven parental tissue compartments, along with arterial and venous blood. (Figure from Poet et al. (2010)).

These PBPK models simulate the pharmacokinetics of NMP and its metabolite 5-HNMP in rats and humans, described briefly below. The models consist of nine main compartments: lung, richly perfused tissues, slowly perfused tissues, skin, fat, mammary, placenta, fetus and liver for NMP with a submodel for 5H-NMP. The model can simulate NMP exposures via the oral, inhalation and dermal routes. Dermal absorption occurs for contact with NMP liquid and vapor. Distribution of NMP to tissues is assumed to be flow-limited. The model includes mathematical descriptions of the growth of fetal and maternal tissues during gestation based on a previous PBPK model of pregnancy (Gentry et al., 2002). Due to extensive differences between rat and human gestation periods, separate rat and human models were developed. NMP metabolism was assumed to occur in the liver. NMP was assumed to be eliminated in exhaled air and urine. 5-HNMP was assumed to be eliminated by further metabolism and in urine. The physiological parameter values used in the model were obtained from the literature (Gentry et al., 2002; Brown et al., 1997b) and biochemical constants for absorption, metabolism and elimination were fit to the reasonably available toxicokinetic data (Payan et al., 2002; Akesson and Paulsson, 1997; NMP Producers Group, 1995a; Midgley et al., 1992; Wells and Digenis, 1988). Further description of the PBPK model are available in Poet et al. (2010), U.S. EPA (2013b), and the modifications described below. In this risk evaluation, EPA used a modified version of the PBPK models. Partition coefficients and parameters used in the EPA model are summarized in Table_Apx J-1 and Table_Apx J-2.

Table_Apx J-1. Tissue:Blood Partition Coefficients Used in the Rat and Human NMP PBPK Models

Tissue	Female Rat [a]	Human [a]
NMP		
Blood:air	450	450
Slowly-perfused:blood	0.74	0.46
Fat:blood	0.62	0.49
Liver:blood	1.02	0.82
Rapidly-perfused:blood	1.02	0.10
Skin:saline	0.42	0.42
Skin:blood	0.12	0.099
Skin:air	55	44.5
Lung:blood	0.1	0.10
Mammary:blood	1.0	0.49
Uterus:blood	0.34	0.08
Placenta:blood	0.309	0.1
Fetus:placenta	1.0	1.0
5-HNMP		
Liver:blood	3.0	NA [b]
Fat:blood	0.4	NA [b]
Placenta:blood	1.07	NA [b]
Fetus:placenta	1.0	

Tissue	Female Rat [a]	Human [a]
Rest-of-body:blood	0.73	NA [b]

[a] The PBPK models was developed specifically for female rats and humans, to simulate pregnancy. Hence, to the extent available, tissue partition data for females from (Poet et al., 2010) were used.
[b] The human PBPK model only has a single compartment for the amount of 5-HNMP in the body, hence does not have tissue:blood partition coefficients for this metabolite.

Table_Apx J-2. Summary of PBPK Model Parameters

Parameter	Rat [a]	Human [a]	Source
Body weight (kg)	Variable	Variable	Data set-specific
Tissue volumes (% body weight)			
Liver	3..66 [b]	3.1	Gentry et al. (2002); Brown et al. (1997a)
Lung	0.5 [b]	NA	Gentry et al. (2002); Brown et al. (1997a)
Blood (total)	6.7 [b]	0.79 [b]	Gentry et al. (2002); Brown et al. (1997a)
Rapidly perfused	7.1	4.2	Gentry et al. (2002); Brown et al. (1997a)
Slowly perfused	calculated	calculated	91%- (sum of other tissue %) Gentry et al. (2002); Brown et al. (1997a)
Fat	9.0	23	Gentry et al. (2002); Brown et al. (1997a)
Skin [d]	19.0	5.1	Brown et al. (1997a)
Flows (l/h/kg$^{0.75}$)			
Alveolar ventilation	15 [e]	16 [b,e]	Brown et al. (1997a)
Cardiac output	15 [e]	15 [e]	Brown et al. (1997a)
Percentage of cardiac output			
Liver	18.3	25.0	Gentry et al. (2002); Brown et al. (1997a)
Richly perfused	51.2	48.0	Gentry et al. (2002); Brown et al. (1997a)
Slowly perfused	calculated	calculated	100% - (sum of other flow %) Gentry et al. (2002); Brown et al. (1997a)
Fat	7.0	5.0	Gentry et al. (2002); Brown et al. (1997a)
Skin [d]	5.8 [b]	5.8 [b]	Gentry et al. (2002); Brown et al. (1997a)
Biochemical constants [f]			
NMP: $V_{max}C$ (mg/h/kg$^{0.75}$)	9 [c]	19.3 [c]	Optimized
NMP: K_m (mg/l)	225 [c]	150 [c]	Optimized
5-HNMP $V_{max}C$ (mg/h/kg$^{0.75}$)	0.009 [c]	NA	Optimized
5-HNMP: Km (mg/l)	4.9 [c]	NA	Optimized
5-HNMP 1st order: V_{k2} (L/h/kg$^{0.75}$)	NA	0.0359 [c]	Optimized
First order urinary elimination – not scaled			

Parameter	Rat [a]	Human [a]	Source
NMP: K_{UMNE} (L/h)	NA	0.103 [c]	Optimized
5-HNMP: K_{ME}	NA	2.75 [c]	Optimized
First order urinary elimination- scaled			
$K_L C$ NMP (L-kg$^{0.25}$/h) [g]	1.61 [c]	0.103 [c]	Optimized
$K_{LN} C$ 5-HNMP (L-kg$^{0.25}$/h) [g]	3.0E-4 [c]	NA	Optimized
Absorption			
Dermal liquid: $K_{PL,} P_{VL}$ (cm/h)	4.6E-3 [c]	4.78E-4 – 2.04E-3 [c,h]	Optimized
Dermal vapor: P_V (cm/h)	NA	16.4 [c]	Optimized
Stomach to liver (h^{-1})	1.5 [c]	1.36 [b]	Optimized
Stomach to intestines (h^{-1})	0.85 [c]	NA	Optimized
Intestines to liver (h^{-1})	0.006 [c]	NA	Optimized
Pregnancy-specific parameters			
Mammary tissue volume (% body weight)	1	0.62	Clewell et al. (2002); O'Flaherty et al. (1992)
Uterus tissue volume (% body weight)	0.2	0.14	O'Flaherty et al. (1992); ICRP (1975)
Mammary % of cardiac output	0.1 [b]	2.7	Clewell et al. (2002); O'Flaherty et al. (1992)
Uterus % of cardiac output	0.5	0.5 [b]	O'Flaherty et al. (1992); ICRP (1975)

Table modified from Poet et al. 2010.

[a] Values are for non-pregnant females (at start of gestation). Pregnancy-related changes are as described by Poet et al. (2010).

[b] Values in model code/scripts of Poet et al. (2010) that did not match values listed or were not reported in the publication. Since results of Poet et al. (2010) (figures, model output tables) were replicated using these values, they are considered the correct parameter values.

[c] Indicates parameters that have been revised since Poet et al 2010 based on recalibration described below

[d] Values are for total skin. The skin compartment simulated in the PBPK model was comprised solely of the area of the skin (and underlying volume) exposed to liquid. The remainder of the skin was included in the slowly perfused compartment

[e] Ventilation and cardiac rates are body-weight (BW) specific. Values shown here are the scaling constants. Given standard BW values of 0.25 kg for rats and 70 kg for humans, the resulting total flows (L/h) match those in Poet et al. (2010).

[f] V_{max} (mg/h) = $V_{max}C$ x BW$^{0.75}$

[g] K_L (L/h) = $K_L C$ / BW$^{0.25}$

[h] Increases with NMP weight fraction above 0.5.

J.1 Rat Model

Several corrections were made to the model code (.csl file) and supporting scripts (.m) files as received from Dr. Torka Poet (personal communication). The first few of these are general and described here.

Blood Flows
Since the placenta is a separate compartment for the 5-HNMP model, its blood-flow and volume were subtracted from the sums used for the 'rest of body' for 5-HNMP. Also, the term for blood flow from the placenta was added to the mixed-venous blood mass balance for 5-HNMP.

To assure flow mass balance, instead of calculating cardiac output (QC) as an initial amount plus the change from initial for each compartment, it was just calculated as the sum over all the compartments:

Equation J-1 Cardiac Output
! QC = QCINIT + (QFAT - QFATI) + (QMAM - QMAMI) + QPLA+ (QUTR - QUTRI)
QC = QFAT+QLIV+QSLW+QRAP+QSKN+QMAM+QPLA+QUTR ! PMS, 8-13-13

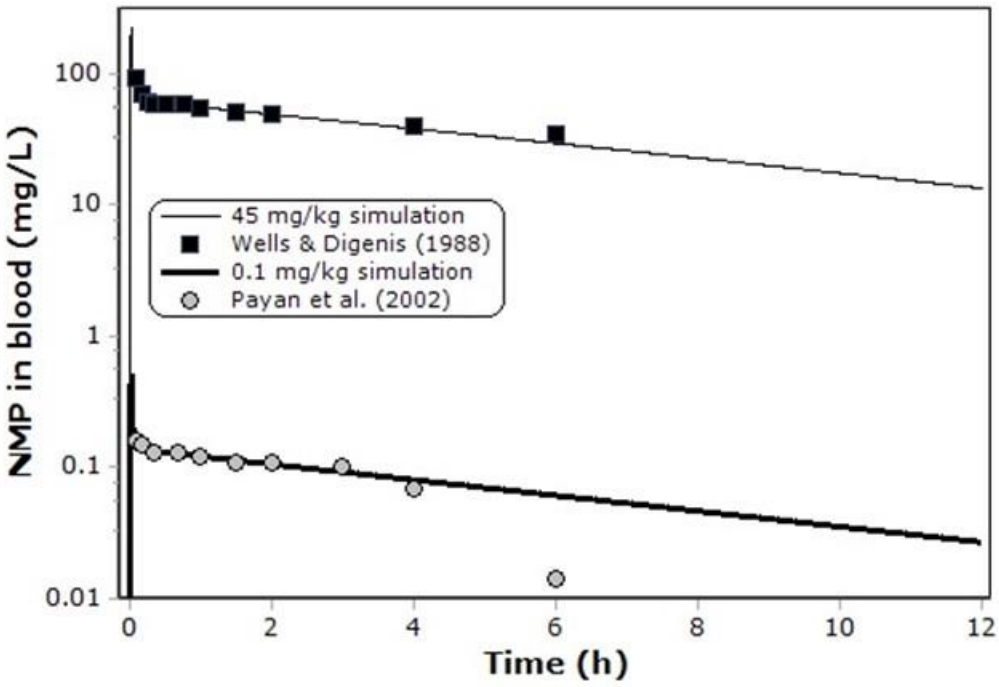
Parameter Consolidation
In the provided files, some physiological and chemical-specific parameter were set in separate scripts; *e.g.*, skin transport parameters in the dermal exposure scripts. This approach creates the potential for inconsistent parameters between different exposure simulations. Therefore, most parameters are now set in the ratparam.m script except those which are experimental control variables (*e.g.*, air concentration, duration of exposure) and pregnancy-specific parameters set in preg_rat_params.m. The final set of parameters used and any inconsistencies with previous values in ratparam.m that may have differed are noted in that script.

Recalibration (performed by T. Poet)
Additional data were used to calibrate and validate the intravenous, oral and dermal routes of exposure in rats. While plasma and urinary excretion data for major metabolite (5-HNMP) have also been reevaluated, primary attention has been paid to NMP, since the dose measure of interest are for the parent chemical. Model parameters for rats are set in the preg_rat_params.m and ratparam.m code scripts (preg_rat_params first calls ratparam), included in the acslX code package available with this assessment. Specific data and modeling choices for the rat are as follows.

Intravenous Data
All reasonably available intravenous data were obtained from studies that administered radiolabeled NMP. Most of the reasonably available studies only provided peak measured concentration and pharmacokinetic parameters. The study chosen to calibrate the model was that described by Payan et al. (2002), in which nulliparous rats were exposed to NMP doses ranging from 0.1 to 500 mg/kg. However, the authors only reported plasma NMP data for the lowest dose. This time-course data set was used to optimize metabolic rate parameters (VmaxC and Km) to describe the clearance of NMP from plasma. Unchanged NMP has only been found at very low levels in rat urine, so urinary elimination was set at a nominal value using a BW-scaled constant of KLNC= 0.0001 kg0.25/h. KLN = KLNC/(BW0.25) = 0.00014 h-1 for a 0.25-kg rat.

Payan et al. (2002) estimated the post-distribution metabolic rates of NMP from the disappearance of NMP from plasma in their studies. These estimated rates (Km=200 mg/L and VmaxC=1.5 mg/hr/kg0.75) were used as the seed values for the optimization carried out using the optimization routines supplied in acslX (v3.0.2.1; The AEgis Technologies Group, Inc, Huntsville, AL) in which the model was created. By starting with these values, it was hoped that the dose-range in that study would be represented and the optimized model would fit across doses. The final optimized parameters were Km= 225 mg/l and VmaxC=9 mg/hr/kg$^{0.75}$. Wells (1988) administered an intravenous dose of 45 mg/kg

to rats, which is 450x higher than the dose used for optimization and this was used to validate the metabolic rates over a large range (Figure_Apx J-2).

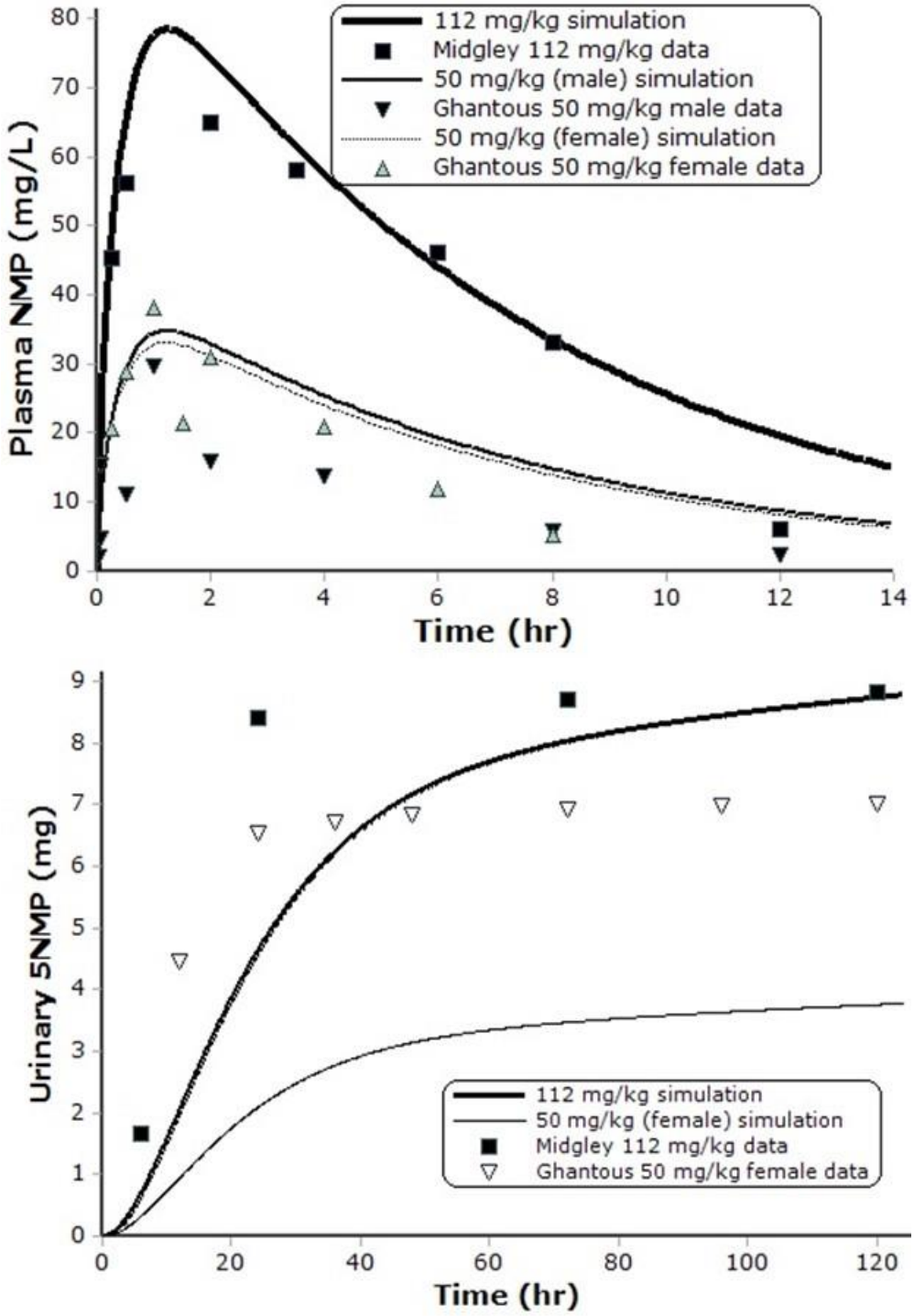


Figure_Apx J-2. Model Fits to IV Injection Data in Rats

Oral Data

All reasonably available oral exposure data were obtained from studies that administered radiolabeled NMP. The most valuable data sets are those that specifically measured NMP in blood (dose measure used in the assessment). NMP is highly metabolized and generally not found in urine as unchanged NMP. The study chosen to calibrate the oral absorption rate was described by Midgley et al. (1992). In this study, male and female rats received an oral gavage of 105 mg/kg (22.5 mg in rats weighing 192-239 g) NMP, co-exposed with 2-pyrrolidinone in a water vehicle. The authors concluded that 94.5% of the administered radiolabel was absorbed. However, when a constant (FRACOR) was fit to the data using the PBPK model the optimal value was found to be 93%.

The data indicate a rapid uptake and a slow elimination of NMP from plasma. Using the metabolic rate constants optimized to fit the intravenous dosing and the oral bioavailability measurements of Midgley et al. (1992), the model estimates of plasma NMP clearance resulted in a much higher AUC than the data indicated (Figure_Apx J-3). There is no suggestion of extra-hepatic (*i.e.*, intestinal) metabolism, so another mechanism to describe this absorption pattern was investigated. NMP is readily absorbed across membranes (see dermal absorption data discussion below) and for some chemicals absorption has been proposed to occur either in the stomach or quickly in the intestine, then more slowly during later phases of transport (Timchalk et al., 2002; Levitt et al., 1997; Staats et al., 1991). Therefore the original PBPK model was altered to include primary (stomach) and secondary (intestine) GI compartments to describe oral absorption following the description from Staats (1991). The resulting model predictions are vastly improved (Figure_Apx J-3). Using dual oral absorption results in ~75% of the absorbed dose (after multiplying by 93% bioavailability) being absorbed via the faster process and the remaining ~25% being more slowly absorbed. Also, an unusually high fraction of the radioactivity was found in the feed residue for the females in the NMP Producers Group (1995a) study, 4.5%, so the simulated dose for that group was decreased proportionately.



Figure_Apx J-3. Model Fits to Rat Oral PK Data

Dermal Model & Data

Corrections to the mass balance equations for the rat skin are as indicated in the commented code copied below. RASK is the rate of changes in the skin compartment. The equation for the amount in the compartment, ASK, includes the initial condition, ASK0, for the initial dermal application, but otherwise the correction to RASK makes it the standard format for PBPK models. As received the code

had multiplied CSK rather than CSKV (skin venous blood concentration) by the blood flow (QSKN) for the rate of efflux in blood and had not separately calculated CSKV.

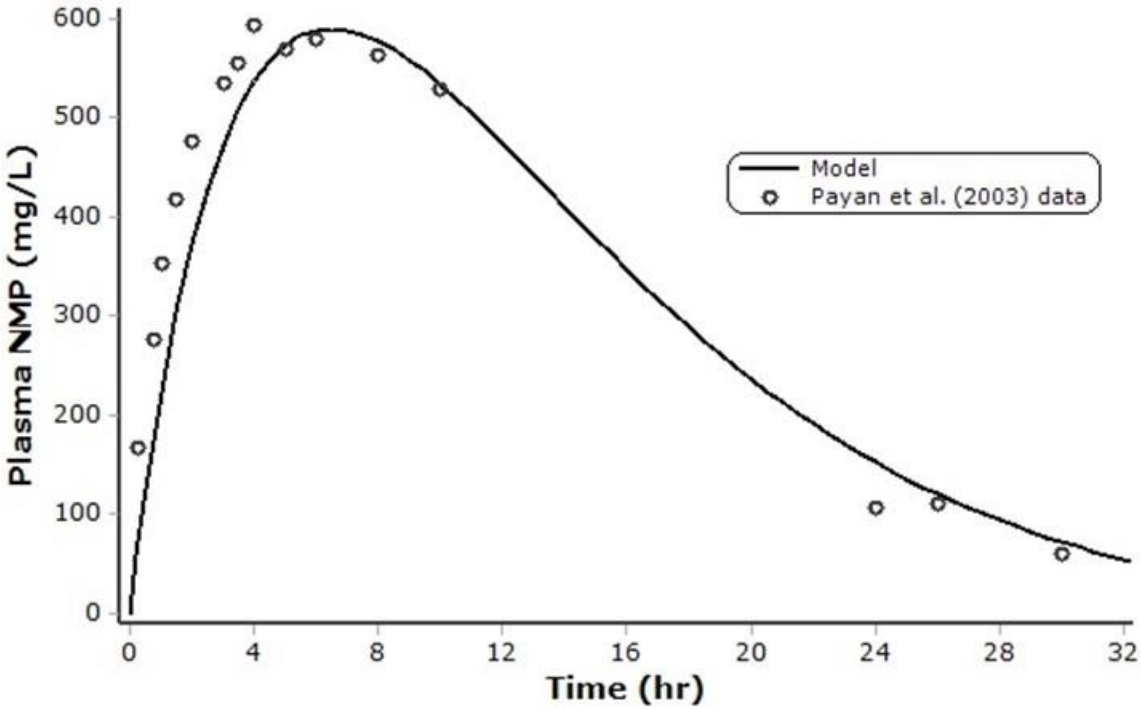
Equation J-2 Rat Skin Model Equations
RASK = QSKN*(CA - CSKV) + RADL ! NOW MINUS CSKV, NOT CSK; PMS 8-21-13
ASK = INTEG(RASK,ASKO) ! Initial value, ASKO, added for Becci et al. (1982)
! exposures; pms 8-14-13
CSK = ASK/VSK !'NMP IN SKIN, MG/L'
CSKV = CSK/PSKB ! NMP IN VENOUS BLOOD, PMS 8-22-13

The corresponding flow term for transfer from the skin to the mixed venous blood compartment was also corrected (*i.e.*, to use CVSK instead of CSK).

While these changes to the skin compartment equations initially degraded the fits to the dermal exposure considerably, it also appeared that the associated partition coefficients were not consistent with the measured values reported by Poet et al. (2010), Table 5. They were recalculated as follows:

Equation J-3 Rat Skin Partition Coefficients
Skin:liquid, PSKL = 0.42: % value as measured for skin:saline, vs. 450
Skin:blood, PSKB = 0.12: % (skin:saline)/(blood:saline)
Skin:air, PSKA = 55:
% (skin:saline)*(blood:air)/(blood:saline) = (skin:blood)*(blood:air)

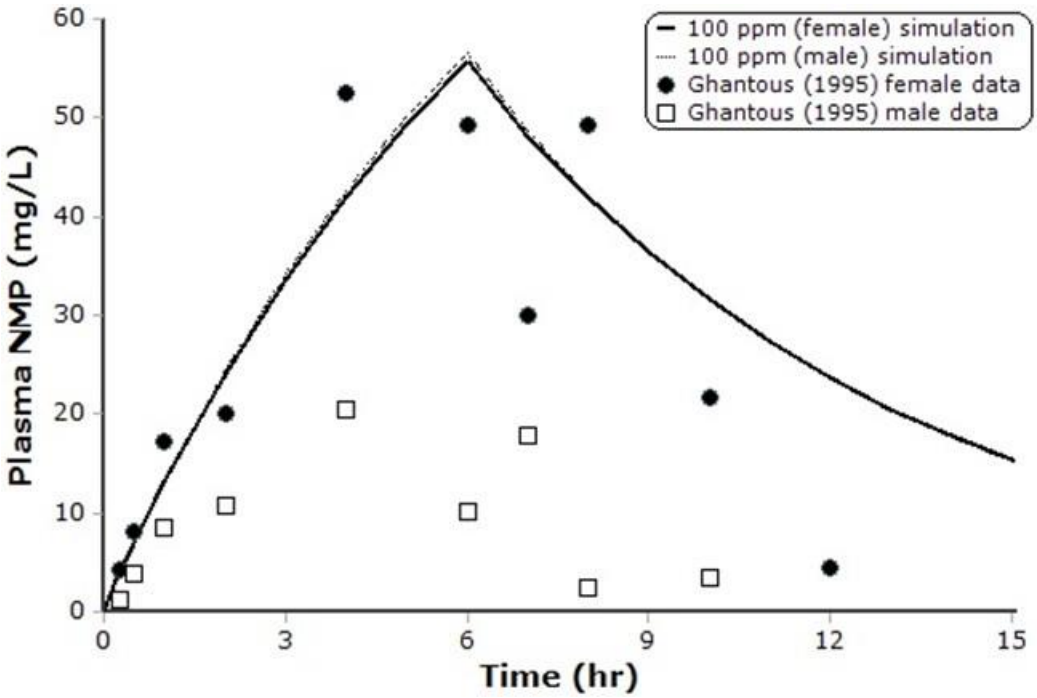
Developmental studies for NMP have been conducted by the dermal route (Becci et al., 1982). In the original PBPK model publication (Poet et al., 2010), the dermal route was assessed using a permeability coefficient (Kp) of 4.7×10^{-3} cm/hr that was approximated from *in vitro* studies (Payan et al., 2003). For the current assessment, the *in vivo* dermal exposure studies described by Payan (2003) were used to optimize Kp. In this study, rats were exposed to 200 µl of neat NMP. According to Payan et al., by 24 hrs after dosing, 80% of the NMP applied had penetrated the skin. The Kp value optimized to these data was estimated to be 4.6×10^{-3} cm/hr (Figure_Apx J-4), which is consistent with the range of Kp values estimated from the *in vitro* studies (from 2.0×10^{-3} to 7.7×10^{-3}cm/hr: Payan et al. (2002)).



Figure_Apx J-4. Model Fits to Dermal PK Data from Payan et al. (2003) in Rats

Inhalation

No parameters were optimized to simulate the inhalation exposures of female rats to 104 ppm NMP for 6 hr (NMP Producers Group, 1995a), 100% inhalation bioavailability was assumed. These data, like the oral exposure data from the same source, appear to be more variable than from other studies. The model fits to the data are shown in Figure_Apx J-5.



Figure_Apx J-5. Model Simulations vs. Inhalation PK Data from Ghantous (1995a) for NMP Inhalation in Rats

Exposure Control for Bioassay Simulations

Because both Becci et al. (1982) and Saillenfait et al. (2002) explicitly stated that the animal BWs were measured every 3rd day of gestation and the dermal/oral doses were adjusted accordingly on those days (as BW increases during pregnancy), corresponding conditional (if/then) statements were added to the 'GAVD' and 'REAPPLY' discrete blocks, to re-calculate the doses on those days.

The code for the dermal discrete blocks follows. ASK0 is the total absolute amount applied; DSK is the dose/kg BW. Because Becci et al. (1982) rubbed the material into the skin, it is assumed to be added directly into the skin compartment (ASK), rather than as a liquid on top. Hence the dose is given as an addition of ASK0 (mg/day applied) to ASK.

Equation J-4 Dermal Dosing Equations

```
DISCRETE SKWASH         ! PMS, 8-14-13
        ASK = 0.0 ! Assume skin washing in Becci et al. (1982) removes all NMP IN skin
        if (DAYS.LT.15.0) SCHEDULE REAPPLY.AT.(T+DOSEINTERVAL-TWASH)
END

DISCRETE REAPPLY        ! PMS, 8-14-13
        IF (ROUND(DAYS).EQ.9.0) ASKO=DSK*BW
        IF (ROUND(DAYS).EQ.12.0)        ASKO=DSK*BW
        IF (ROUND(DAYS).EQ.15.0)        ASKO=DSK*BW
        ASK = ASK + ASKO
        SCHEDULE SKWASH.AT.(T+TWASH)
END
```

Also, because Becci et al. (1982) washed the skin area exposed to dermal application at the end of a set time interval, a "SKWASH" discrete block was introduced at which time the amount in that patch of

skin was assumed to be momentarily reduced to zero. During periods of dermal application, transport from the liquid to the skin was turned on using the pulse function, DZONE. After removal of the liquid it was assumed that NMP in the skin patch could volatilize into the otherwise clean air, with the rate defined by the same permeability constants, but using the skin:air partition coefficient.

The rate of transfer to/from the skin area is then defined by:

Equation J-5 NMP Dermal Transport
RADL=(KPL*SA/1000.0)*((CSURF-(CSK/PSKL))*DZONE - (1.0-DZONE)*(CSK/PSKA))
! 2ND term, (1.0-DZONE)*(CSK/PSKA), allows for evaporative loss when DZONE=0

The primary part of this equation for transfer when liquid is in contact with the skin, (KPL*SA/1000.0)*(CSURF-(CSK/PSKL)), is identical to that used previously by McDougal (1986). Finally, a constant, CONCMGS, was introduced so that the air concentration could be set directly in mg/m^3. This is converted to the concentration in mg/L (CONCMG) in the code and added to the inhalation exposure, turned on and off using the switch, CIZONE, which is turned on and off using SCHEDULE/DISCRETE statements:

Equation J-6 NMP Vapor Exposure Control
CI = CCH*PULSE(0., DOSEINTERVAL,TCHNG) + CIZONE*CONCMG ! MG/L
! Added CIZONE*CONCMG, PMS, 8-13-13

J.2 Human Model

Human exposures to NMP will be primarily via the inhalation route; contribution from the dermal route (vapors or liquid) may also be significant if not primary for some scenarios. Ingestion of NMP is not expected to be a significant pathway in human populations. Both controlled and occupational human exposure data are reasonably available from the published literature. Controlled human biomonitoring studies were used to calibrate NMP and 5-HNMP metabolic rates and a workplace exposure assessment study was used to validate the model and exposure scenarios.

J.2.1 Corrections to Human Model Structure

NMP Metabolism and Urinary Elimination

Since the human PK data were consistent with a nearly linear model (first-order kinetics, including metabolism) estimation of a metabolic saturation constant, Km, using the traditional Michaelis-Menten equation for metabolism of NMP, was difficult. In particular as estimates of Km became larger, model fits became less sensitive to variation in its value. Therefore, equation was changed from the standard form, rate = Vmax*C/(Km + C), where C is the concentration of NMP in the liver, to the equivalent form, rate = VK1*C/(1 + AF1*C), where VK1 = Vmax/Km and AF1 = 1/Km. These two forms are mathematically identical given the relationship between parameters just shown. The affinity constant, AF1, can be easily bounded to be non-negative and possibly converge to zero, corresponding to an indeterminately large Km. Since VK represents hepatic metabolism, it was assumed to scale with BW the same as Vmax; *i.e.*, $VK1 = VK1C*BW^{0.75}$. The values of VmaxC and Km reported in Table I-2 are, correspondingly, VmaxC = VK1C/AF1 and Km = 1/AF1. The urinary elimination of NMP was assumed to be first order, rather than saturable, using a rate constant (KUMNE) that was not scaled by BW.

5-HNMP

Since 5-HNMP is not being considered as an internal metric for toxicity and its volume-of-distribution (VOD) appeared to be over-estimated using the original PBPK model structure and measured tissue

partition coefficients, its description was replaced with a classical one-compartment PK model. Further, as the metabolism of 5-HNMP also appeared to be linear and the data for estimating a Km value even weaker, a transformation of its metabolic rate equation like that for NMP described just above was assumed, but with the affinity assumed to be effectively zero, resulting in a first-order metabolic rate equation. As with NMP, the urinary elimination of 5-HNMP was also assumed to be first-order. The resulting model then becomes:

Equation J-7 5-HNMP Metabolism and Elimination
d A5H/dt = RAMET1*STOCH – RAMETM1 – RAUHP
(rate of change of amount of 5-HNMP)
CVEN1 = A5H/VOD5H (concentration of 5-HNMP in venous blood)
VOD5H = VOD5HC*BW (volume of distribution assumed to scale with BW)
RAMETM1 = ¬CVEN1 *VK2, where VK2 = VK2C*BW0.75
(rate of metabolism of 5-HNMP)
RAUHP = KME*CVEN1 (rate of urinary elimination of 5-HNMP)
RAMET1 = rate of NMP metabolism to 5-HNMP (mg NMP metabolized/h)
STOCH = ratio of 5-HNMP to NMP molecular weights.

Exposure and Timing Control

A table function, RESLVL, was added as a place-holder for reading in defined (consumer) inhalation exposure time-courses; specifically from EPA exposure assessment modeling.
A constant, GDstart, the day of gestation on which the simulation starts and a variable Gtime, the hrs into gestation, were added to facilitate separating exposure control from gestation timing.

A second set of DISCRETE/SCHEDULE blocks were added to allow for split exposure scenarios (morning/afternoon worker exposure; dual-episode consumer exposures). DZONE, set in the DISCRETE/SCHEDULE blocks, controls the time within a day when discontinuous exposure occurs. Czone is the product of DZONE and a pulse function used to control for days/week exposure in workplace scenarios:

Equation J-8 Vapor Exposure Scheduling
Czone = pulse(0.0,fullweek,hrsweek)*DZONE ! pms 8-20-13
! for a 5 day/wk exposure, use fullweek=7*24, hrsweek=5*24 (Dayswk=5)
! for a single day, fullweek=1e16, hrsweek=24 (Dayswk=1)

A binary constant, BRUSH, was added to set exposure scenarios when dermal contact with liquid occurs. For workplace scenarios, exposure to vapor and liquid are assumed to be simultaneous; *i.e.*, the worker leaves the location with NMP vapor and washes his/her hands when he/she has finished applying the material.

Skin Compartment
The original skin compartment which is coded to include uptake from liquid-dermal contact was renamed by adding "L" to the end, SK → SKL and a second skin compartment to account for concurrent vapor-skin uptake, SKV, was added. This was done because when the human model was calibrated for inhalation exposure, an exposed skin surface area of 6700 cm^2 was used. When this surface is reduced to ~ 0, predicted blood levels of NMP are reduced ~ 45%. Thus vapor uptake through the skin is a significant component of inhalation exposure and there is no reason to assume, a priori, that this uptake

(or desorption) does not occur through a similar area of exposed skin during workplace and consumer exposures, except for any area that would have liquid contact or otherwise be occluded (*e.g.*, by protective equipment). So, the SKV compartment allows for simultaneous absorption of vapor-through-skin that does not have liquid contact and from areas of skin with liquid contact. The surface area of SKV and SKL are SAV and SAL, respectively. SAL can set directly for different exposure scenarios.

To account for variations with individual BW, a parameter for the fraction of skin area exposed to vapor was introduced: SAVC, with SAV = SAVC*TSA, where TSA is the total body surface area. TSA is calculated for each individual based on BW and height. For EPA simulations, SAVC was set to 0.25, representing the head, neck, arms and hands, minus any area assumed to have liquid contact or covered with protective gloves or a facemask.

The rate for delivery from a liquid film to the 'SKL' skin compartment (also see further below) is then defined by:

Equation J-9 NMP Liquid Rate of Delivery to Skin

```
PVLU=PVLF(WF)
RADL = (PVLU*SAL/1000.0)*(CSURF-(CSKL/PSKL))*Czone*BRUSH
        ! Net rate of delivery to "L" skin from liquid, when liquid is there
```

PVLF is a linear interpolation TABLE function which supplies the permeability for liquid NMP (PVLU) as a function of the weight fraction (WF). In particular, PVLF is parameterized such that PVLU = 4.78×10^{-4} cm/h for WF ≤ 0.5, increasing linearly from that value to 2.05×10^{-3} cm/h for 0.5 ≤ WF ≤ 1.0. (Derivation of these values is described below, with human dermal absorption data.)

The equations for transfer of vapor (air concentration = CI) to the SKL compartment, which occurs during periods with no liquid/spray contact for the SKL compartment are similarly:

Equation J-10 NMP Vapor Rate of Delivery to Skin

```
RADVL = (PV*SAL/1000.0)*(CI - (CSKL/PSKA))*(1.0-Czone*BRUSH)
! Net rate of delivery to "L" skin from air, when liquid not present
```

Since the dermal exposures are to neat or highly concentrated preparations of NMP, it would not be appropriate to assume that the residual liquid volume on the skin remains constant as absorption occurs. Further assuming that water penetration of the skin is minimal, the amount of water in the liquid solution is assumed to remain constant. The initial volume on the skin is defined by a new constant VLIQ0 and the density of NMP at 40C (~ skin temperature) = DENSITY = 1.02×10^{6} mg/L. To avoid potential divide-by-zero errors, the nominal initial concentration (CONCL) is reduced by 1 mg/L (1 ppm) when computing the initial amount of NMP and water in the liquid:

Equation J-11 NMP Unabsorbed Fraction Remaining on Skin

```
DDN = (CONCL - 1.0)*VLIQ0*FAD
! Subtract 1 mg/L, ~ 1 ppm, from initial conc. to avoid VLIQ --> 0
AH20 = (DENSITY+1.0-CONCL)*VLIQ0 ! ... and add it to H20. pms 9-16-14
```

A mass-balance equation was then added to attract the remaining amount and volume on the skin surface, which is then used to calculate the concentration:

```
ASURF = INTEG(-RADL, DDN) ! Amount in liquid. DDN is the initial amount.
VLIQ = (AH20 + ASURF)/DENSITY
```

CSURF = ASURF/VLIQ

This volume balance is important for analysis and calibration of the dermal PK studies where small volumes (5 or 10 ml) were applied at the beginning of the exposure and not replenished. However, in workplace and consumer user exposures, it is assumed that fresh liquid is constantly replacing any NMP that is absorbed, keeping the surface concentration essentially constant. Therefore, the initial volume, VLQ0, is set to a large value (10^6 L) for those scenarios.

The skin partition coefficients were also recalculated as was done for the rat, with rat parameters for skin:saline and blood:air, but human blood:saline.

Tissue and Blood-Flow Mass Balances

The model had been previously coded with an alveolar blood compartment (ALV), but this was commented out in the DYNAMIC section. Therefore this volume fraction should not be subtracted when calculating the slowly-perfused volume. The fraction of blood-flow to slowly perfused tissue was updated to also account for the SKV compartment; on the other hand a separate skin compartment is not used for 5-HNMP, so the skin blood flow is NOT subtracted for the metabolite-slowly-perfused compartment (SLW5). These have all been corrected.

QSKCC (original fractional flow to the skin) had been subtracted twice, both in calculating QSLWC and then in the calculation of QSLW. The 2nd subtraction created a mass balance error and hence was removed. On the other hand, placental blood flow is now subtracted, so the total flow to slowly-perfused continues to total cardiac output minus all other tissue/group flows.

For tissues for which the volume changes with gestation day, the initial values were corrected to match the calculation in the DYNAMIC section, which apply at the first time-step. In the dynamic section, the calculation of QC was corrected to include the *increase* in placental flow (QPLA – QPLAI) rather than the total placental flow (QPLA), since QCINIT includes QPLAI. QSLW5 and VSLW5 (5-HNMP slow compartment flow and volume) are now calculated in the DYNAMIC section by subtraction. The calculation of QC was otherwise left in its original form, in contrast to the rat PBPK model.

Parameter Consolidation

Like the rat model, the human model physiological and biochemical parameters are now primarily set in a single script, human_params.m. Initial values for the metabolic and vapor-absorption (KPV) parameters were obtained by fitting Bader et al. (2006) inhalation data with the exception of the high-concentration data from one individual, but the data otherwise grouped without distinction between individuals (further details below). An alternate set of fitted parameters was obtained by fitting the data for each individual separately, focused on the low-concentration data and then calculating the average of each parameter across the individually-fitted values. This subset of parameters is selected by using human_avg_params.m. Since further analysis of the dermal absorption of liquid NMP showed that this uptake differed between neat (100%) NMP and diluted (50%) NMP, separate value of PVL were obtained for neat vs. diluted NMP (also see below). Hence only constants which define specific exposure scenarios (include skin areas exposed) and PVL are defined in the specific simulation scripts.

Inhalation Data

A study conducted by the Hannover Medical School, University of Dortmund, Germany (Bader and Van Thriel, 2006) was used to calibrate inhalation parameters of the model. In this study, 8 healthy, non-smoking, male volunteers were exposed to 10, 40 or 80 mg/m^3 NMP in an environmental chamber. Over

the course of several weeks, each volunteer was exposed sequentially to all 3 concentrations. The 8 volunteers were separated into 2 groups of 4 and each group was exposed in a shared chamber. The exposures were carried out in ascending concentrations, with a 1-week period between each session. Volunteers wore slacks and T shirts and thus had arms exposed to vapor. Blood was collected from each volunteer in the middle of the 6-hr exposure period, at the end of exposure (6 hr) and 1, 2, 3, 18 and 42 hrs after the end of exposure. Urine was also collected from each volunteer at times up to 42 hrs after the end of exposure. Because it is relatively rare to have blood and urine data for multiple exposure levels, multiple time points, in individuals, efforts were made to ensure the exposure scenarios for these data were modeled as accurately as possible.

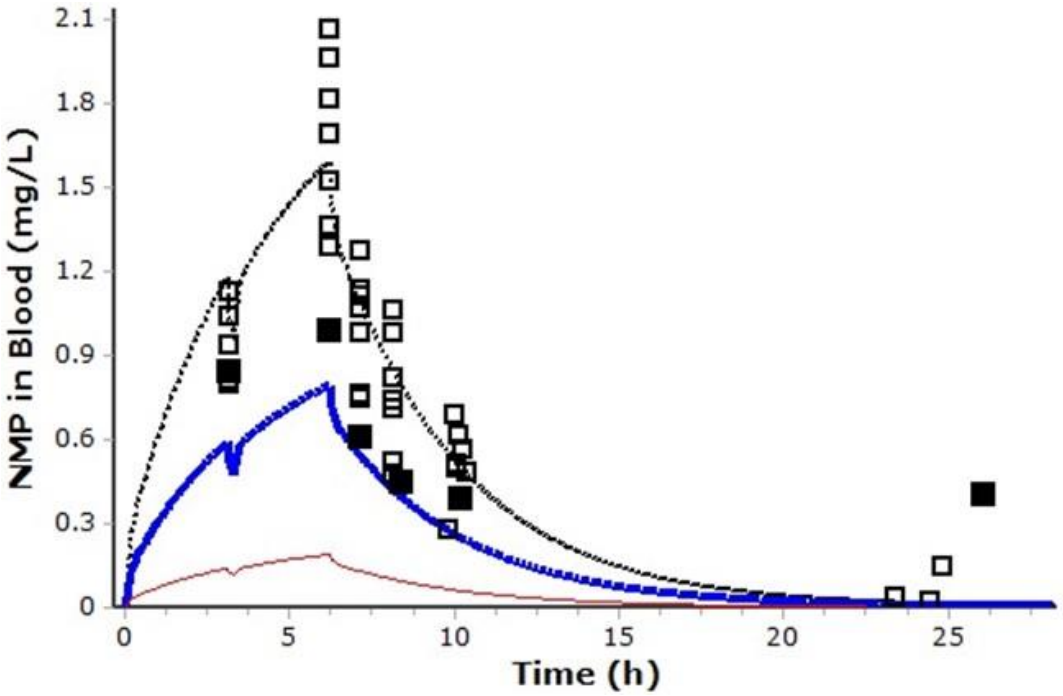
To collect the mid-exposure blood samples, volunteers left the chamber one at a time and moved to another room to have blood drawn and to give a urine sample. The data are consistent with a sharp drop in concentration for the mid-exposure blood sampling, when the peak NMP concentration measured at the end of the exposures are considered. In the report, the time taken to leave the chamber, walk to the new room, donate blood and urine was suggested to be about 10 minutes. However, exact times were not recorded. The notes indicate that the time between blood collection and urine collection was at least 5 minutes. In addition, the recorded times for collection of blood from first collected sample to last (*i.e.*, between the first and fourth volunteers to leave the chamber) was up to 55 minutes. If the times were equivalent for each subject and the volunteers only left the chamber as the previous volunteer returned, this would indicate an average of 12 minutes was needed for sample collection from each volunteer.

Based on a careful review of the data tables in Bader and van Thriel (2006) and personal communication with Dr. Michael Bader and Dr. Christoph van Thriel, it was determined that each subject entered and left the exposure chamber at different times as described just above and were likely not sampled at exactly the same time after the beginning and end of each exposure segment. While the total exposure time for each subject was monitored and kept to exactly 6 h on each exposure day, based on the timing of the blood and urine samples (taken outside the exposure chamber), it is clear that the study design was not exactly followed. In particular, while the morning and afternoon exposures were supposed to be 3 h each, the time between the mid-day and first afternoon blood samples was less than 3 h for some individuals in some exposures (and the mid-day sample was taken much later after noon for such samples). In these cases it seemed likely that the individual spent slightly more than 3 h in the chamber in the morning and slightly less in the afternoon, for that exposure. Based on the recorded data and communications, the exposure timing used for modeling and simulation was set to 3.1 h for the morning exposure, a mid-day break of 0.2 h (12 min) and 2.9 h for the afternoon exposure. Since individual subjects did not enter and exited the chamber at exactly the same time, the time of their entrance to the chamber for each exposure was estimated based on the recorded times of the blood and urine samples. The sample times used for modeling were then calculated relative to the estimated entry times.

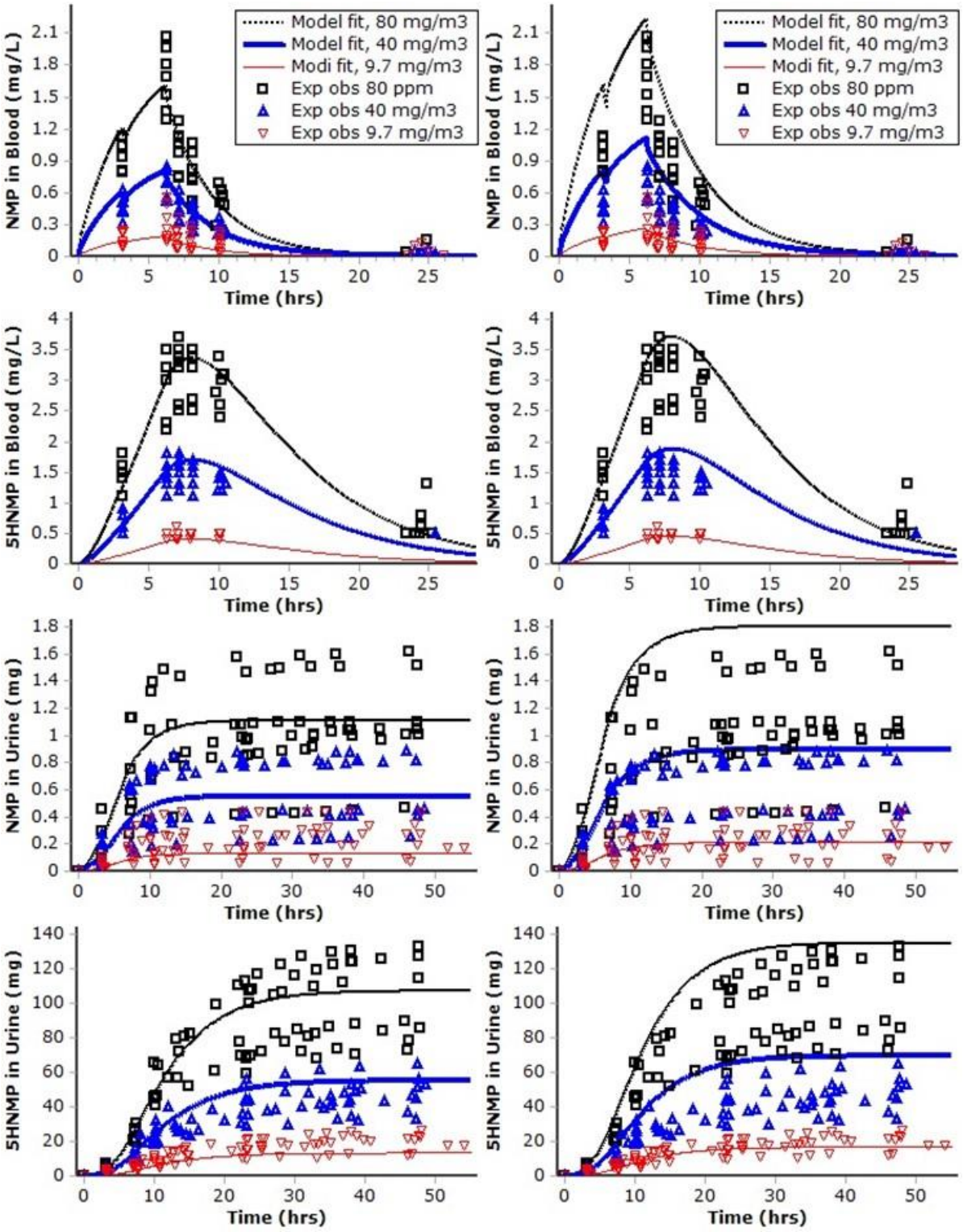
It was also clear that a number of the measurements, especially those of 5-HNMP for the low-concentration exposure, were recorded as the limit of detection (LOD), when the measured value fell below this limit. This was confirmed with Dr. Bader (personal communication). Therefore all measurements at/below the LOD were removed from the data set to avoid the bias they would otherwise introduce.
It also appeared that the high-concentration-exposure (80 mg/m^3) for one subject deviated substantially from the other subjects; see Figure_Apx J-6 below. Since the blood concentration at 6 h was well below those of the other subjects and that at 24 h well above (4 subjects had levels below the LOD), this individual's high concentration set was excluded from analysis of the grouped data. Blood

concentrations at the middle and low exposure for this individual were among the range of the other subjects, hence included in the group data.

With this one data set removed, the revised model was fit to the group data for exposures at 9.7 and 80 mg/m^3, by adjusting the following parameters: PV, VK1C, AF1, KUMNE, VK2C, VOD5HC and KME. Since the data for the 40 mg/m^3 exposure were consistent with the 80 mg/m^3, but the data for 9.7 mg/m^3 appeared not to be and it was considered especially important to describe low-concentration exposures, the 40 mg/m^3 data were excluded from this exercise. The resulting parameter values are as follows, with model fits to the group data shown in Figure_Apx J-7, left side. These fits are compared to ones obtained by fitting the data for each individual separately, where possible using only the low-concentration exposure data and then calculating the average across the individual fits for each parameter (right side of Figure_Apx J-7; details below).



Figure_Apx J-6. NMP Blood Concentration Data from Bader and van Thriel (2006)
Curves are simulations for 9.7, 40 and 80 mg/m^3 exposures. Squares are individual blood concentration data for the 80 mg/m^3 exposure. Solid squares are from the one individual with the highest BW and height (102 kg, 190 cm), compared to the other subjects (65-80 kg, 168-183 cm).



Figure_Apx J-7. Alternate Fits to Collective Data from Bader and van Thriel (2006)
Left panels show fits to the groped data for 9.7 and 80 mg/m^3 (data shown). Simulations in right panel used average of parameters fit to each individual separately, primarily for 9.7 mg/m^3 (see text for details).

Parameters fitted to group data for 9.7 and 80 mg/m^3 exposures	Average of parameters fit to data for each individual separately, primarily 9.7 mg/m^3
PV = 1.6 (cm/h)	PV = 16.4 (cm/h)
VK1C = 0.47 (L/(h*kg$^{0.75}$))	VK1C = 0.386 (L/(h*kg$^{0.75}$))
AF1 = 0.02 (L/mg)	AF1 = 0.02 (L/mg) [fixed at group-fit value]
VK2C = 0.035 (L/(h*kg$^{0.75}$))	VK2C = 0.0359 (L/(h*kg$^{0.75}$))
VOD5HC = 0.26 (L/kg)	VOD5HC = 0.243 (L/kg)
KME = 2.3 (L/h)	KME = 2.75 (L/h)
KUMNE = 0.092 (L/h)	KUMNE = 0.103 (L/h)

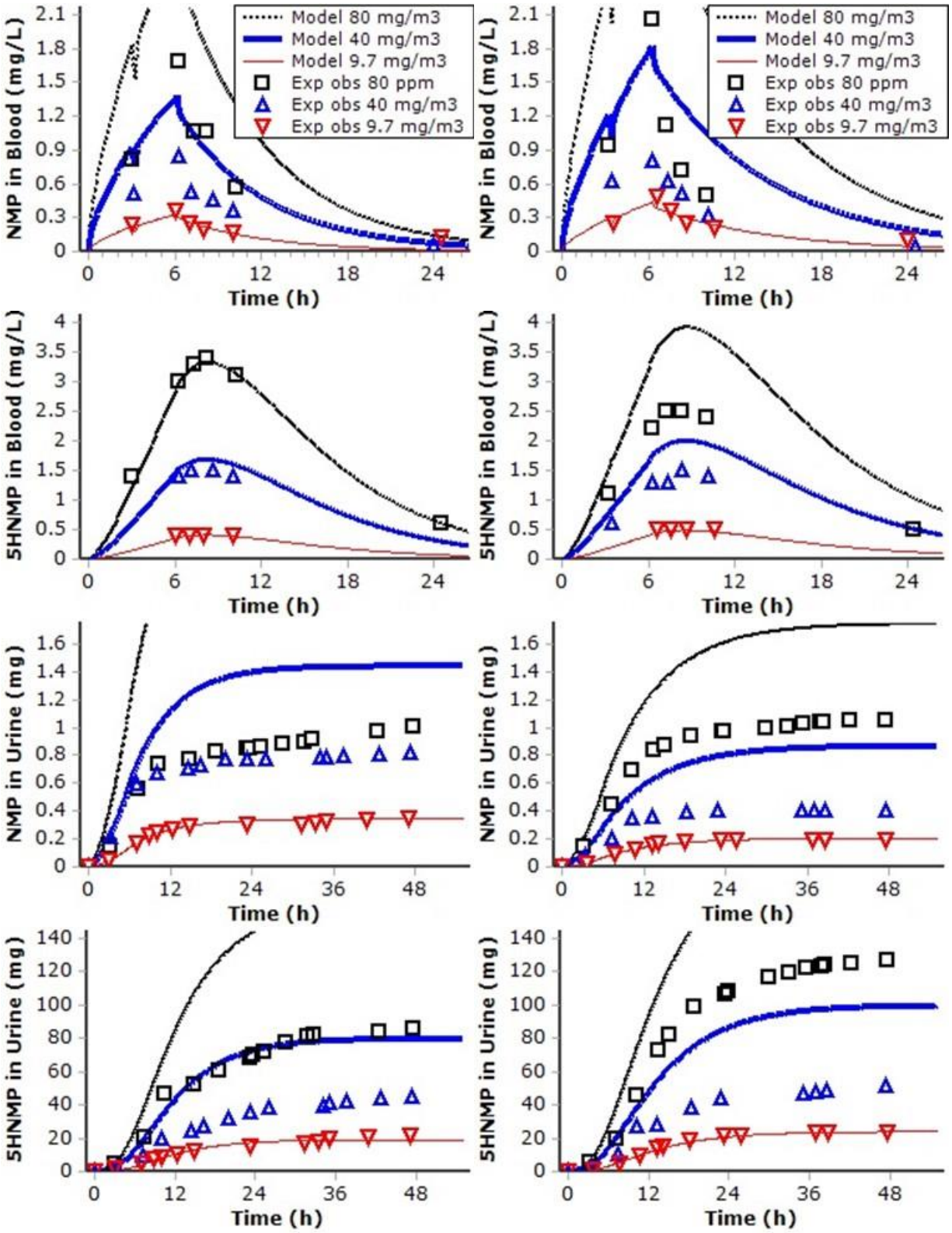
In their summary statistics, Bader and van Thriel (2006) reported group-averages of the peak NMP blood levels as being 0.293 mg/L for the 9.7 mg/m^3 and 1.585 mg/m^3. The ratio of these two (1.585/0.293 = 5.4), is considerably less than one would expect assuming linearity with exposure level (80/9.7 = 8.25) and is the opposite of what one would expect due to metabolic saturation of the conversion of NMP to 5-HNMP. This is not true for the ratio peak 5-HNMP levels in blood (8.08), however, which is comparable to the relative exposure level. If the nonlinearity in NMP blood levels were due to more efficient metabolism at the higher exposure level, then ratio of 5-HNMP blood levels would have been greater than expected.

Since the mechanism for the nonlinearity in blood NMP levels is unclear and it would be undesirable to under-estimate NMP blood levels and hence human risks at lower exposure levels, it was decided to estimate parameters using only the low-exposure data, if possible or with minimal use of the high-exposure data. (For two of the subjects the blood levels of 5-HNMP did not rise above the LOD for the low exposure, making it impossible to estimate VOD5HC for them. Hence the 80 mg/m^3 blood 5-HNMP data were also needed to estimate their parameters.) Given the observation that the high-exposure data for one subject was disparate from the other subjects, it also seemed possible that the apparent nonlinearity in the average PK data was due to the mixing of data from the 8 subjects in the study. Therefore, fits focused on the low-exposure data were conducted separately for each subject. Since limiting to the low-exposure data would provide almost no information on metabolic saturation and the affinity (AF1) obtained from the fits to the group data was quite low (0.02 L/mg), AF1 was held at that group-fit value for this exercise. The resulting parameter values are listed in Table_Apx J-3 and fits to the individual data shown in Figure_Apx J-8 through Figure_Apx J-11. In order to allow one to see the fit to the low concentration and otherwise compare the fits across individuals, the y-axis scale was held constant for each analyte across the individuals, though this meant that the simulation curves for the higher exposure data sometimes went off the top of the plot.

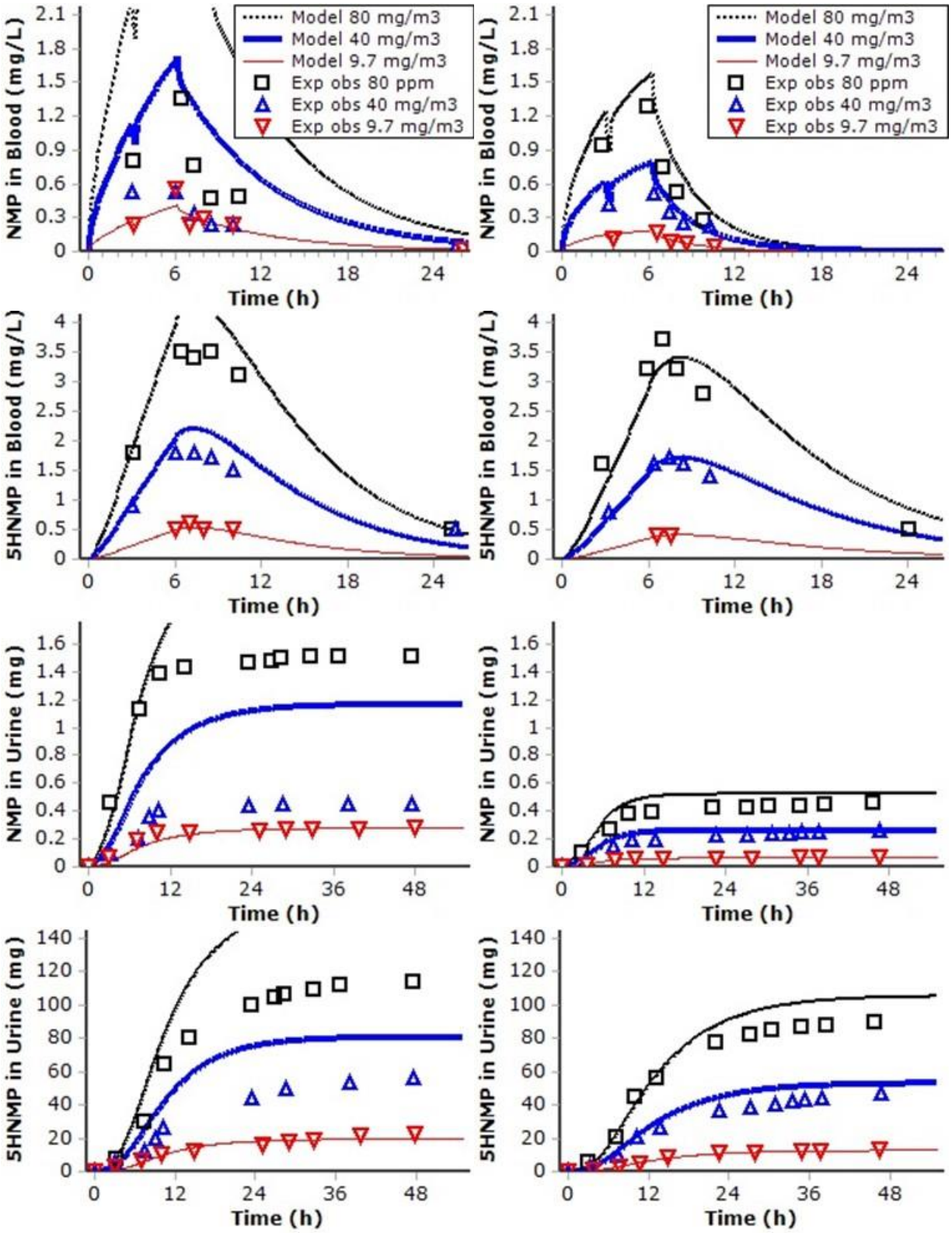
Table_Apx J-3. Estimated PBPK Parameters for Each Subject of the Bader and van Thriel (2006) Experiments

Subject	VK1C	KUMNE	PV	VK2C	KME	VOD5HC
1	0.25	0.11	19	0.017	3.2	0.2
4	0.17	0.042	34	0.004	3	0.14
10	0.22	0.069	35	0.027	2.8	0.12
12	0.63	0.046	12	0.044	1.9	0.39
14	0.57	0.2	10	0.08	2.5	0.4
16	0.45	0.06	0	0.08	1.9	0.2
17	0.38	0.2	20	0.02	4.3	0.26
25	0.42	0.1	1.5	0.015	2.4	0.23
average	**0.386**	**0.103**	**16.4**	**0.0359**	**2.75**	**0.243**

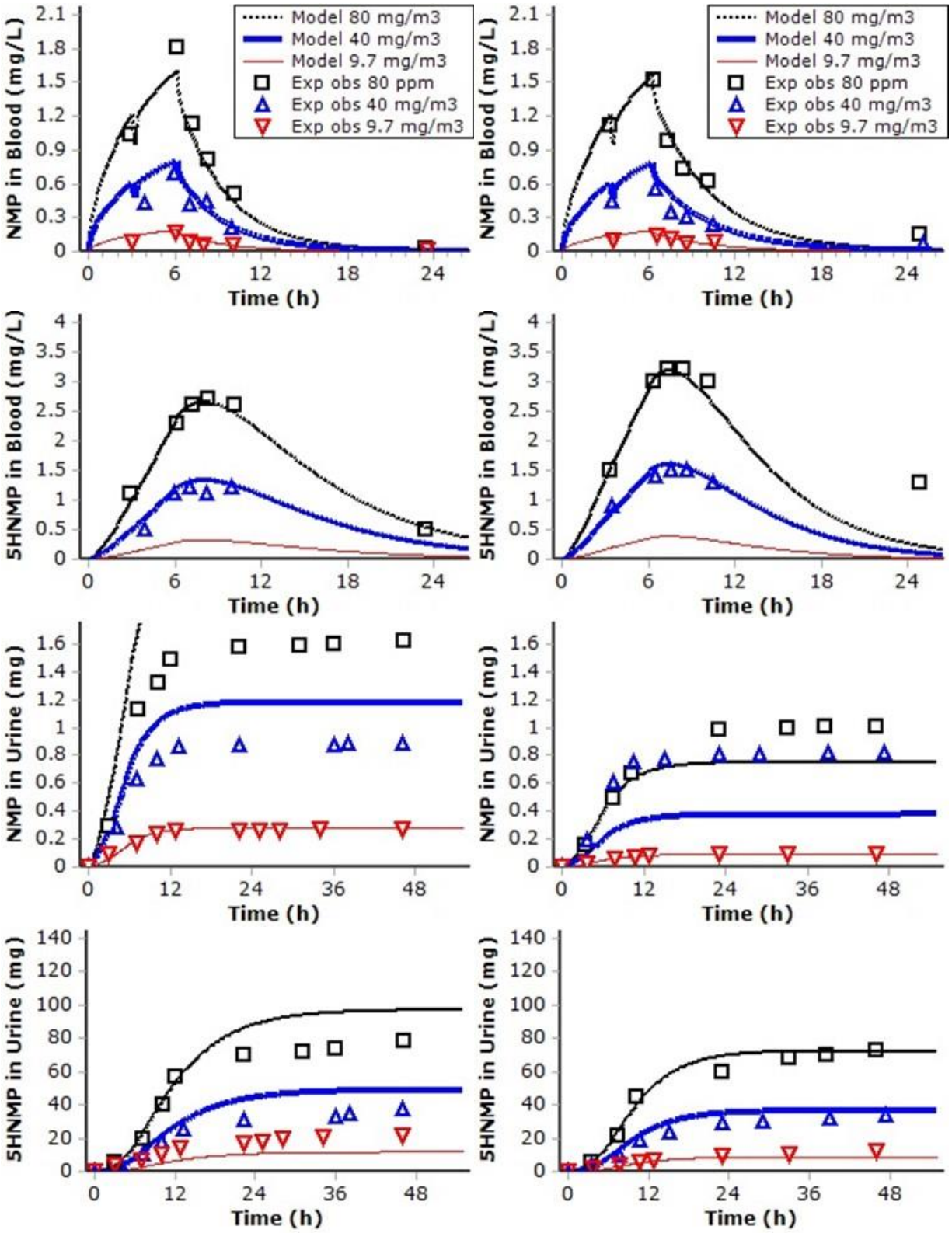
It is interesting to note that for half of the subjects (#12, #14, #16 and #25), the fits and data for NMP in blood show that the data are quite consistent with the essentially linear PBPK model, while for the other half the simulations with parameters fitted to the low-concentration data over-predict the high-concentration NMP data.



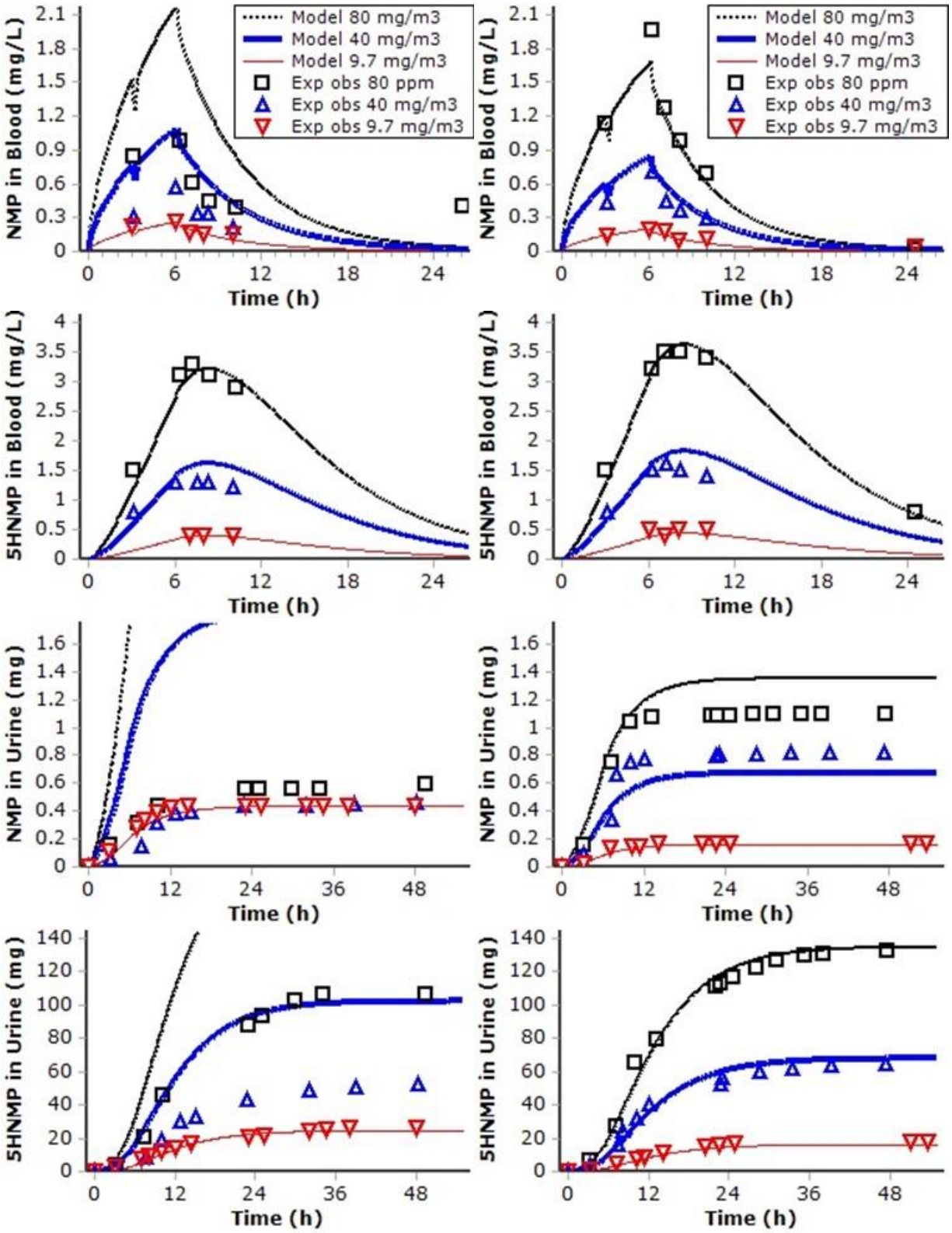
Figure_Apx J-8. Model Fits to Subjects 1 and 4 of Bader and van Thriel (2006)
Model fit separately to each subject. See text for details.



Figure_Apx J-9. Model Fits to Subjects 10 and 12 of Bader and van Thriel (2006)
Model fit separately to each subject. See text for details.



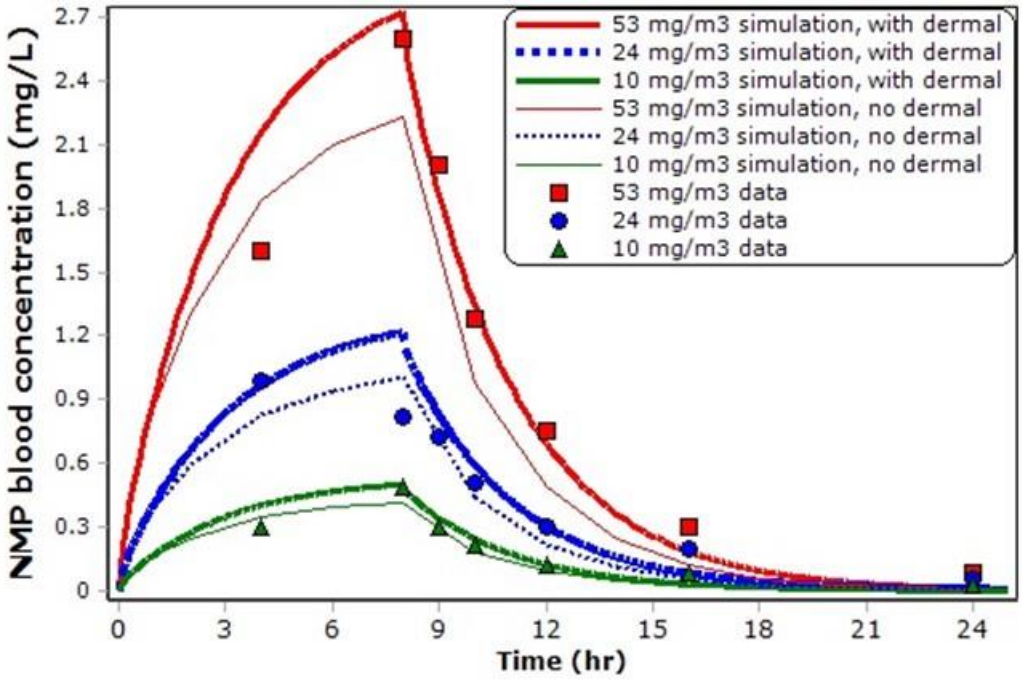
Figure_Apx J-10. Model Fits to Subjects 14 and 16 of Bader and van Thriel (2006)
Model fit separately to each subject. See text for details.



Figure_Apx J-11. Model Fits to Subjects 17 and 25 of Bader and van Thriel (2006)
Model fit separately to each subject. See text for details.

Dermal Data: Vapor and Liquid

Volunteers in the study described by Akesson and Paulsson (1997) wore shorts and t-shirts and thus also had dermal (vapor) exposures, as well as inhalation exposures, to NMP. The exposure concentrations for this study were similar to those of Bader et al (2005). With only inhalation exposures, the model under-predicted plasma NMP by about 25%, a vapor permeability coefficient, which accounts for both the skin permeability and the vapor/skin surface interaction, (PV) of 1.5 cm/hr was optimized to fit these data and is equivalent to the previously optimized value (Poet et al., 2010) (Figure_Apx J-12).



Figure_Apx J-12. Model Fits to Human Inhalation Data of Akesson and Paulsson (1997), With and Without Dermal Absorption of Vapors

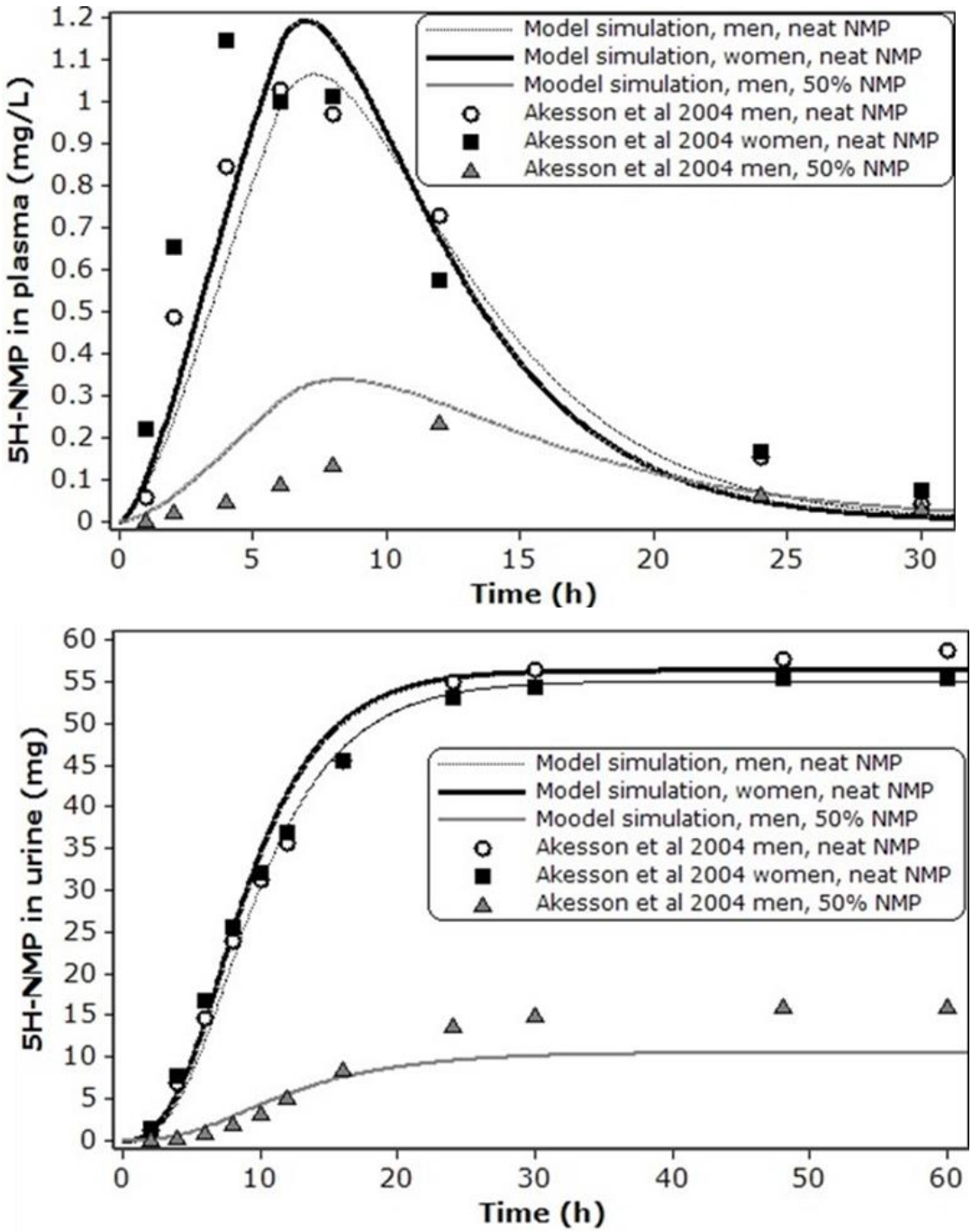
Model parameters were as obtained previously using the data of Bader and van Thriel (2006). Simulations are shown with dermal absorption of vapors included ("with dermal"; 25% of total surface area assumed exposed) or turned off ("no dermal").

Akesson et al. (2004) exposed 12 volunteers (6 male and 6 female) to 300 mg NMP either neat or diluted 50:50 in an aqueous solution. Blood and urine 5-HNMP concentrations were monitored for up to 9 days. The plasma 5-HNMP concentration was extracted from the figure using DigitizIt (Braunschweig, Germany). Urinary 5-HNMP concentrations were extrapolated to total amount eliminated using the assumption that the average urinary flow for an adult is 18 ml/kg-day (Heffernan et al., 2014). Aqueous dilution resulted in a slower time to reach peak plasma 5-HNMP and a reduction in peak plasma concentration. Because the urinary elimination constant (KME) for 5-HNMP was seen to vary among subjects when fitting the Bader and van Thriel (2006) data and we did not want a lack-of-fit to the urinary elimination data (which establish the mass balance, hence total amount absorbed) to adversely impact the fitting of the 5-HNMP blood levels, KME was also fit to each data set then. The optimized liquid permeability constant (PVL) for neat NMP was 2.05 x 10^{-3} cm/hr (with KME = 4.54L/hr). To fit the data from the diluted exposures, a lower PVL of 4.78x10^{-4} cm/h was needed (with KME = 2.10 L/hr) (Figure_Apx J-13). In the absence of absorption data for other concentrations, below and between 0.5 and 1.0, it was assumed that PVL is constant at the value estimated for 50% NMP when the NMP concentration is ≤ 50% and that it increases linearly from that value to the value estimated for

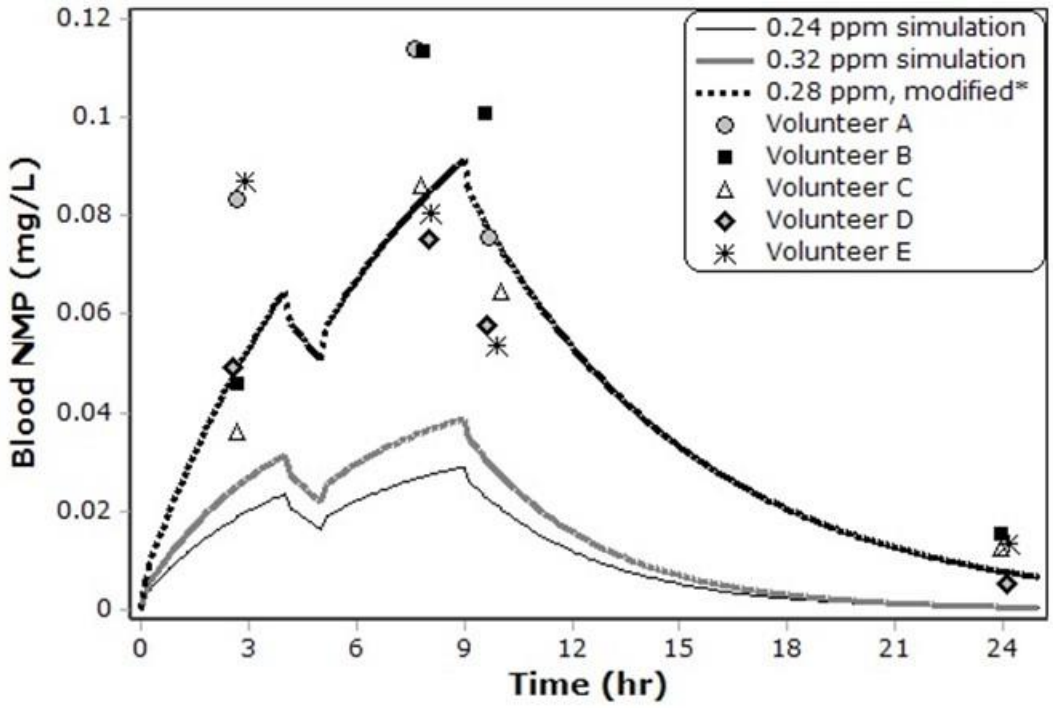
100% NMP for intermediate concentrations. The resulting PVL function was used in estimating human dermal absorption for neat and diluted NMP absorption, with KME kept at the value estimated with 50% NMP (2.1 L/hr). (Note that KME does not impact NMP blood levels and hence estimates of risk.)

Workplace Observer Study

In a biomonitoring study Xiaofei (2000) followed 4 workers and 5 observers in a lens manufacturing facility. The workers washed lenses with NMP, working 11-hr shifts with a 1-hr lunch break (total 12 hrs within the facility). Observers were stated to be in the facility from 8 am to 5 pm for a single day, but the tabulated exposure metrics indicated only 8 h of exposure, so it was assumed that they also took a 1-hr break (at noon). The mean exposures for the observers was 0.28 ppm, with a range from 0.24 to 0.32 ppm. The PBPK model underestimated plasma NMP concentrations for the workers (data not shown) and observer by ~3x when no dermal exposure is assumed (Figure_Apx J-14). However, droplets of NMP were noted on the lenses as the workers were moving those lenses to drying racks. Just assuming that these droplets were due to some aerosolized NMP and that the observers had a small surface area of skin exposed to such droplets, 0.2 cm^2, gave results that better fitted the blood data during the exposure, but the clearance after exposure appeared to be too rapid. Assuming that the average metabolic rate was ½ of that identified from the Bader and van Thriel (2006) data (*i.e.*, VK1C = 0.193 L/h-kg0.75) with an even smaller exposure to aerosol (0.1 cm^2 of exposed skin) resulted in simulations that matched the data well (Figure_Apx J-14). The lowest individual VK1C estimated for the Bader and van Thriel (2006) data was 0.17 L/h-kg0.75, so the value used here is not unreasonable. In summary, the un-adjusted model gave simulations that were within a factor of three of this data set and the discrepancy can be explained by a reasonable level of metabolic variability between the two study populations and a small amount of dermal contact.



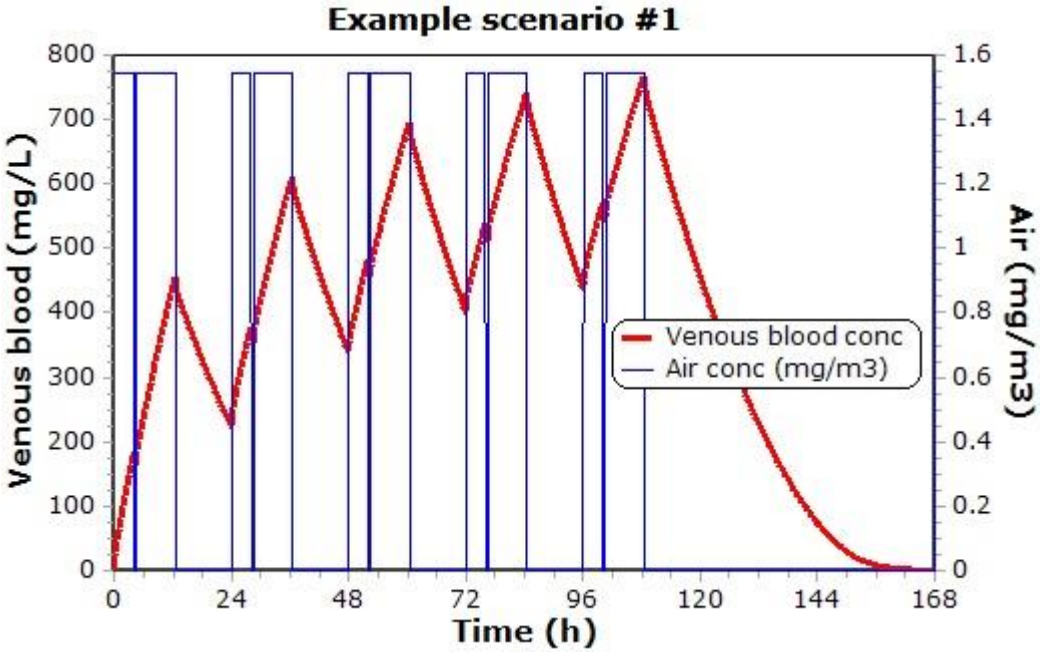
Figure_Apx J-13. Model Fits to Human Dermal Exposure Data of Akesson et al. (2004)
Upper panel shows simulation and data for metabolite 5H-NMP concentration in blood plasma and lower panel shows simulation and data for the cumulative total 5H-NMP excretion in urine.



Figure_Apx J-14. Workplace Observer Simulations Representing Subjects of Xioafei et al. (2000)
* Metabolic elimination was reduced to ½ that estimated from Bader and van Thriel (2006) data and 0.1 cm^2 of skin was assumed exposed to liquid aerosol.

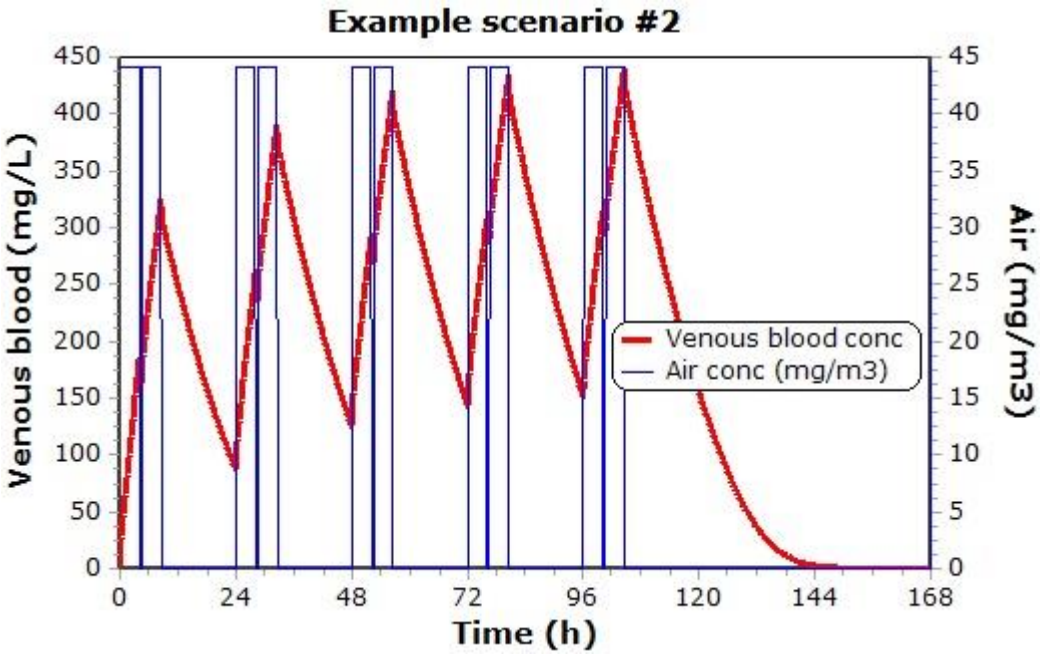
J.2.2 Changes in Blood Concentrations Predicted Over the Course of a Work Week

EPA evaluated the potential for NMP to accumulate in workers from week to week. To do this, EPA used the human PBPK model to predict blood concentrations over the course of a work week followed by a weekend with no exposure using several occupational exposure scenarios as examples to cover a range of exposure levels. Results are illustrated in the following figures. Even in the workers with the highest levels of exposure (Example scenario #1), the PBPK model predicts that blood concentrations of NMP may increase over the course of the work week but will be eliminated over the course of a weekend. Hence, no week-to-week accumulation is expected in humans under any anticipated workplace exposures.



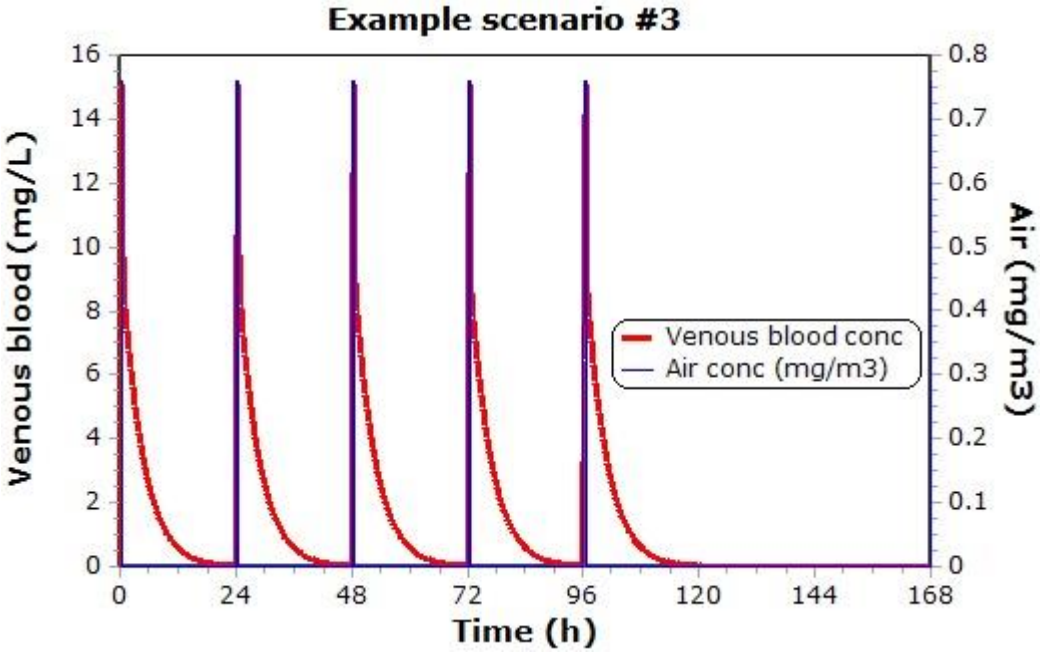
Figure_Apx J-15. Blood Concentrations Modeled for an Occupational Exposure Scenario with a High-end AUC prediction – 12 h shift.

Blood concentrations of NMP are shown over the course of a five-day work week followed by two days off. This plot shows model predictions for the 'lithium ion- drum handling' occupational exposure scenario based on a 12-hour shift (an OES representing a high-end AUC prediction).



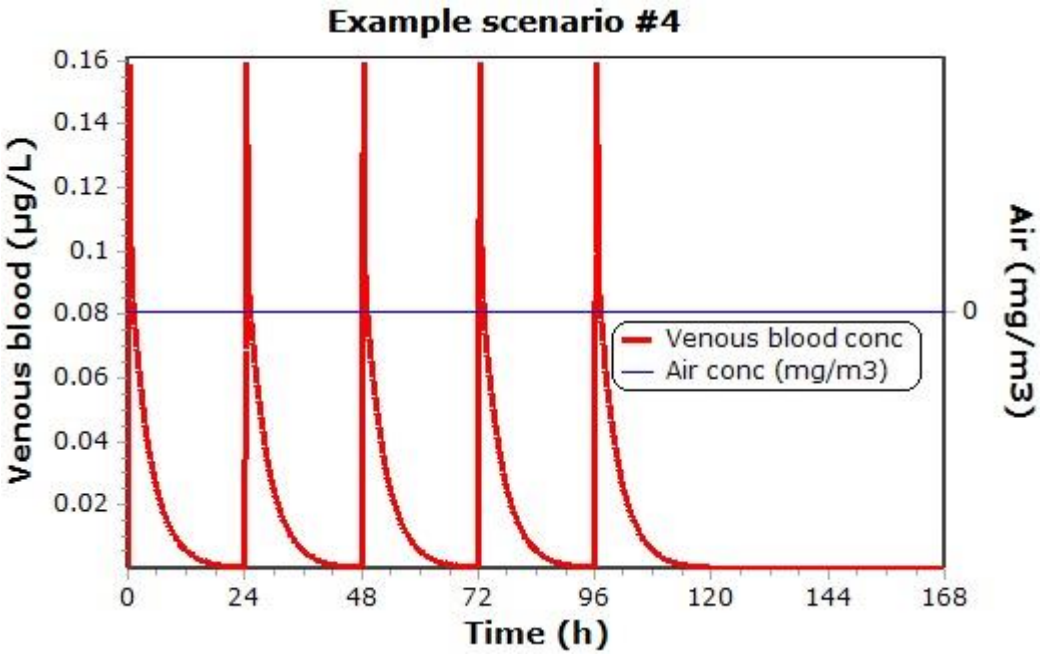
Figure_Apx J-16. Blood Concentrations Modeled for an Occupational Exposure Scenario with a High-end AUC prediction – 8 h shift.

This plot shows model predictions for the 'capacitor, resistor, coil, transformer and other inductor manufacturing' occupational exposure scenario based on an 8-hour shift (an OES representing a high-end AUC prediction).



Figure_Apx J-17. Blood Concentrations Modeled for an Occupational Exposure Scenario with a Mid-Range AUC.

Blood concentrations of NMP are shown over the course of a five-day work week followed by two days off. This plot shows model predictions for the 'recycling and disposal' occupational exposure scenario (an OES representing mid-range AUC prediction).



Figure_Apx J-18. Blood Concentrations Modeled for Occupational Exposure Scenario with Low-end AUC prediction.

Blood concentrations of NMP are shown over the course of a five-day work week followed by two days off. This plot shows model predictions for the 'printing and writing' occupational exposure scenario (an OES representing a low-end AUC prediction).