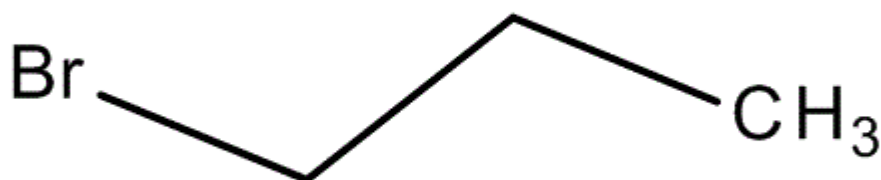




**Risk Evaluation for
1-Bromopropane
(*n*-Propyl Bromide)**

CASRN: 106-94-5



August 2020

Trial Exhibit

100

Food & Water v. EPA
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Authors

Stan Barone (Deputy Division Director), Nhan Nguyen (Management Lead), Katherine Anitole (Staff Lead), Ariel Hou (Staff Lead), Kevin Vuilleumier (Staff Lead), Chris Brinkerhoff, Ana Corado, Susan Euling, Zaida Figueroa, Garrett Jewett, David Lynch, Greg Macek, Paul Matthai, Bethany Masten, Albert Monroe, Alie Muneer, Sharon Oxendine, Andrea Pfahles-Hutchens, Shannon Rebersak, Mitchell Sumner, Amy Shuman, Eva Wong, Yintak Woo (formerly with EPA)

Contributors

Johanna Congleton (EPA/ORD), Catherine Gibbons (EPA/ORD), Jeff Gift (EPA/ORD), Roman Mezencey (EPA/ORD), Ravi Subramaniam (EPA/ORD), Lily Wang (EPA/ORD), Scott Masten (NIH), Diane Spencer (NIH), Shannon Berg (CDC/NIOSH), Robert Daniels (CDC/NIOSH), Senthilkumar Perumal Kuppusamy (CDC/NIOSH), Thomas Lentz (CDC/NIOSH), Richard Niemeier (CDC/NIOSH), Christine Whittaker (CDC/NIOSH)

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Docket

Supporting information can be found in public docket [EPA-HQ-OPPT-2019-0235](#).

Disclaimer

Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

ABBREVIATIONS

AC	Acute concentration
ACGIH	American Conference of Governmental Industrial Hygienists
ACH	Air changes per hour
ADAF	Age-dependent adjustment factor
ADC	Average daily concentration
ADR	Acute dose rate
ADR _{pot}	Potential acute dose rate
AEGL	Acute exposure guideline level
AER	Air exchange rate
APF	Assigned protection factor
Apx	Appendix
AT	Averaging time
Atm	Atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BL	Baseline
BMCL	Benchmark concentration, lower confidence limit(s)
BMD	Benchmark dose
BMDL	Benchmark dose, lower confidence limit(s)
BMR	Benchmark response level
BLS	Bureau of Labor Statistics
BOD	Biochemical oxygen demand
BOP	3-Bromo-1-hydroxypropanone
BW	Body weight
C	Contaminant concentration
C _{air}	Air concentration

°C	Degree Celsius
CAA	Clean Air Act
C _{FF}	Average far field concentration
C _{FFTWA}	Time weighted average far field concentration
C _{NF}	Average near field concentration
C _{NFTWA}	Time weighted average near field concentration
C _{p pot}	Modeled peak concentration
CASRN	Chemical Abstracts Service Registry Number
CBI	Confidential business information
CCD	Chemical Control Division
CCRIS	Chemical Carcinogenesis Research Information System
CDR	Chemical Data Reporting
CEM	Consumer exposure module
CESSD	Chemistry, Economics, and Sustainable Strategies Division
CI	Confidence interval
cm	Centimeter(s)
cm ³	Cubic meter(s)
CNS	Central nervous system
CO ₂	Carbon dioxide
COC	Concentration of Concern
CSAC	Chemical Safety Advisory Committee
CYP	Cytochrome P450
DE _v	Duration of an event
DIY	Do-it-yourself
DNA	Deoxyribonucleic acid
EC	Engineering controls
ECA	Enforceable consent agreement
ED	Exposure duration

EF	Exposure frequency
E-FAST2	Exposure and Fate Assessment Screening Tool Version 2
EFH	Exposure Factors Handbook
EMIC	Environmental Mutagens Information Center
EPA	Environmental Protection Agency
ERG	Eastern Research Group, Inc.
EU	European Union
EvapTime	Evaporation time
FF	Far field
FQ	Frequency of product use
FSA	Free surface area
ft	Foot/feet
ft ²	Square foot/feet
ft ³	Cubic foot/feet
g	Gram(s)
g/cm ³	Grams per cubic centimeters
g/L	Grams per liter
G	Average generation rate
GM	Geometric mean
GSD	Geometric standard deviation
GD	Gestational day
GENE-TOX	Genetic Toxicology Data Bank
GSH	Glutathione (reduced)
H _{NF}	Near field height
HAPs	Hazardous air pollutants
HCV	Human cancer value
HEC	Human equivalent concentration
HED	Human equivalent dose

HHE	Health Hazard Evaluation
hr	Hour(s)
HSDB	Hazardous Substances Data Bank
HSIA	Halogenated Solvents Industry Alliance
IA	Indoor air
IARC	International Agency for Research on Cancer
IMIS	Integrated Management Information System
InhR	Inhalation rate
IRIS	Integrated Risk Information System
IUR	Inhalation unit risk
k	Emission rate
K _{ow}	Octanol: water partition coefficient
kg	Kilogram(s)
K _{oc}	Soil organic carbon-water partitioning coefficient
L	Liter(s)
lb	Pound(s)
L _{NF}	Near field length
LADC	Lifetime average daily concentration
LADD	Lifetime average daily dose
LEV	Local exhaust ventilation
LT	Lifetime
LOAEL	Lowest-observed-adverse-effect level
MA	Model-averaging
m	Meter(s)
m ²	Square meter(s)
m ³	Cubic meter(s)
MCCEM	Multi-Chamber Concentration and Exposure Model
µg/m ³	Microgram(s) per cubic meter

mg	Milligram(s)
mg/kg-bw	Milligram(s) per kilogram body weight
mg/L	Milligram(s) per liter
mg/m ³	Milligram(s) per cubic meter
mg/mL	Milligram(s) per milliliter
min	Minute(s)
MITI	Ministry of International Trade and Industry
Mlbs	Million of pounds
mm Hg	Millimeters of mercury
MMOA	Mutagenic Mode of Action
MOA	Mode of Action
MOE	Margin of exposure
MOE _{acute}	Margin of exposure for acute exposures
MOE _{chronic}	Margin of exposure for chronic exposures
MOU	Memorandum of understanding
MW	Molecular weight
NAICS	North American Industry Classification System
NAPL	Nonaqueous phase liquid
NAS	National Academies of Science
NCI	National Cancer Institute
NCTR	National Center for Toxicological Research
NLogistic	Nested Logistic
NEI	National Emissions Inventory
NESHAP	National Emissions Standards for Hazardous Air Pollutants
NF	Near field
NF/FF	Near field/far field
NHANES	National Health and Nutrition Examination Survey
NICNAS	National Industrial Chemicals Notification and Assessment Scheme

NIH	National Institutes of Health
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standards and Technology
nm	Nanometer(s)
NOAEL	No-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHSC	National Occupational Health and Safety Commission
NJDEP	New Jersey Department of Environmental Protection
NPS	Nonpoint source
NTP	National Toxicology Program
OAR	Office of Air and Radiation
OCSP	Office of Chemical Safety and Pollution Prevention
OECD	Organization for Economic Co-operation and Development
ONU	Occupational non-user
OPPT	Office of Pollution Prevention and Toxics
OR	Odds ratio
OSHA	Occupational Safety and Health Administration
OSWER	Office of Solid Waste and Emergency Response
OW	Office of Water
oz	Ounce(s)
PA	Personal air
PBZ	Personal breathing zone
PEL	Permissible exposure limit
PESS	Potentially exposed or susceptible subpopulations
PERC	Perchloroethylene
PID	Photoionization detector
PND	Postnatal day
POD	Point of departure

POTW	Publicly Owned Treatment Works
ppb	Parts per billion
ppm	Parts per million
PS	Point Source
PVC	Polyvinyl chloride
Q _{FF}	Far field ventilation rate
Q _{NF}	Near field ventilation rate
QA	Quality assurance
QC	Quality control
RCRA	Resource Conservation and Recovery Act
REACH	Registration Evaluation Authorization and Restriction of Chemicals
RfC	Reference concentration
RfD	Reference dose
RR	Rate ratio
RTECS	Registry of Toxic Effects of Chemical Substances
s	Second(s)
SAB	Science Advisory Board
SARA	Superfund Amendments and Reauthorization Act
SCG	Scientific Consulting Group, Inc.
SD	Standard deviation
SDS	Safety data sheet(s)
SDWA	Safe Drinking Water Act
SNAP	Significant New Alternative Policy for ozone depleting substances
SVHC	Substance of Very High Concern
t	Time
TCA	Trichloroacetic acid
TCE	Trichloroethylene
TOXLINE	Toxicology Literature Online

TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	Time-weighted average
UF	Uncertainty factor
UF _S	Subchronic to chronic uncertainty factor
UF _A	Interspecies uncertainty factor
UF _H	Intraspecies uncertainty factor
UF _L	LOAEL to NOAEL uncertainty factor
UF _D	Database uncertainty factor
US EPA	United States Environmental Protection Agency
V _{FF}	Far field volume
v_{NF}	Indoor wind speed
V _{NF}	Near field volume
VOC	Volatile organic compound
VP	Vapor pressure
WWTP	Waste water treatment plant
WNF	Near field width
WY	Working years
Yr (s)	Year(s)

EXECUTIVE SUMMARY

This risk evaluation for 1-bromopropane (or 1-BP) 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 § 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 § (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 § 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 § 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. To meet these TSCA § 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 through 10).

1-BP has a wide-range of uses, including as a solvent for cleaning and degreasing (including vapor degreasing, cold cleaning, and aerosol degreasing). A variety of consumer and commercial products use 1-BP as adhesives and sealants, in furniture care products, in dry cleaning, spot cleaning and other liquid, spray, and aerosol cleaners, and in automotive care products. 1-BP is subject to federal and state regulations and reporting requirements. 1-BP has been a reportable Toxics Release Inventory (TRI) chemical under Section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) since 2016. It is listed under the Clean Air Act (CAA), under the National Volatile Organic Compound Emission Standards for Aerosol Coatings ([40 CFR](#)

[Part 59 Subpart E](#)), and is under Section 612 of the CAA, under the Significant New Alternatives Policy (SNAP) program.

EPA evaluated the following categories of conditions of use: manufacturing; processing; distribution in commerce; industrial, commercial and consumer uses; and disposal.¹ Total production volume (domestic manufacture plus import) of 1-BP has increased from 2012 to 2015 ([U.S. EPA, 2016a](#)). 1-BP's volume has increased because it has been an alternative to ozone-depleting substances and chlorinated solvents. Import volumes for 1-BP reported to the 2016 CDR are between 10 million and 25 million pounds per year ([U.S. EPA, 2016a](#)).

Approach

EPA used reasonably available information (defined in 40 CFR 702.33 as “information that EPA possesses, or can reasonably 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 published since the publication of previous analyses. 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 Scope Document ([U.S. EPA, 2017d](#)) and Problem Formulation ([U.S. EPA, 2018c](#)), EPA identified the conditions of use and presented three conceptual models and an analysis plan for this 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 (identified in Section 1.4.1 of this final risk evaluation).² EPA carried out a quantitative and qualitative assessment of the following:

- Risks to terrestrial and sediment-dwelling aquatic species from exposure to water and soil by considering physical-chemical and fate properties of 1-BP. Risks to aquatic species in the water column from releases to surface water by comparing estimated environmental exposures to available environmental hazard data.

¹ Although EPA has identified both industrial and commercial uses here for purposes of distinguishing scenarios in this analysis, the Agency interprets the authority to cover “any manner or method of commercial use” under TSCA Section 6(a)(5) to reach both.

² EPA did not identify any “legacy uses” or “associated disposals” of 1-BP, as those terms are described in EPA’s Risk Evaluation Rule, 82 FR 33726 (July 20, 2017). Therefore, no such uses or disposals were added to the scope of the risk evaluation for 1-BP following the issuance of the opinion in *Safer Chemicals, Healthy Families v. EPA*, 943 F.3d 397 (9th Cir. 2019).

- Risk to workers from inhalation and dermal exposures and to occupational non-users (ONUs)³ from inhalation exposures, by comparing the estimated acute and chronic exposures to human health hazards.
- Risks to consumers from inhalation and dermal exposures and to bystanders from inhalation exposures, by comparing the estimated acute exposures to human health hazards.
- Risk to bystanders from inhalation exposures from insulation (off-gassing), as described in Section 2.3.2.4, by comparing the estimated chronic exposures to (non-cancer and cancer) health hazards.
- Risks to general population from exposure to water, sediment, and soil by considering physical-chemical properties, environmental fate properties, and environmental release estimates.

In the Problem Formulation, EPA conducted a preliminary analysis of risks to terrestrial and aquatic species based on the potential exposure pathways through air, water, and soil identified in the conceptual model for environmental releases and wastes (Figure 1-5). This preliminary environmental risk assessment qualitatively considered the physical-chemical and environmental fate properties (high volatility, high water solubility and low Log K_{ow}) to determine that risks were not likely for terrestrial and sediment-dwelling aquatic species due to the low potential for exposure. These approaches were initially presented in the Problem Formulation and are brought forward to this document to make a final risk determination because the initial evaluation was sufficient to make a risk determination. EPA preliminarily characterized potential risks to water column dwelling aquatic species quantitatively by conducting a screening-level assessment that calculated risk quotients (RQ) by comparing estimated environmental concentrations to environmental hazard data for aquatic species to identify potential risks to aquatic organisms. TRI data were used to estimate exposures to water-column-dwelling aquatic organisms from releases to surface water. In the Problem Formulation as well as the draft Risk Evaluation, hazard thresholds, known as Concentrations of Concern (COCs) were calculated for aquatic species using reasonably available environmental hazard data, which included a single acute fish toxicity study identified in the Ecological Hazard Literature Search Results for 1-BP, as well as summaries of environmental hazard data identified for 1-BP in the ECHA Database. As explained in Sections 3.1 and 4.1, the preliminary risk assessment for water column-dwelling aquatic species was updated in this final risk evaluation due to uncertainties about the data presented in summary format in the ECHA database.

EPA attempted to obtain the full study reports for the environmental hazard data summaries described in ECHA, which were used the draft risk evaluation. After conducting outreach efforts, EPA was unable to identify a US-based data owner of the full study reports and review these studies for data quality. Because EPA could not obtain these full study reports, the discussion of the data in the ECHA study summaries was removed from the final risk assessment. In contrast,

³ ONUs are workers who do not directly handle 1-BP but perform work in an area where 1-BP is present.

EPA reviewed a single acute fish toxicity study in the environmental hazard data using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a), where it was rated high quality. To reduce uncertainties about relying on a single acute fish study to characterize environmental hazard to all aquatic species across acute and chronic exposure, EPA incorporated ECOSAR (v2.0) (EPA, 2017) modeling⁴ results into the discussion of environmental hazard and risk, a commonly utilized practice for the environmental hazard assessment of new chemical substances. These predicted hazard endpoints were in agreement with the single fish study in that they both indicated the 1-BP presents a moderate hazard. The result of the analysis conducted using the acute fish study and ECOSAR modeling (v.2.0) (EPA, 2017) did not identify risks to aquatic species under the conditions of use within the scope of the risk evaluation.

EPA evaluated exposures to 1-BP in occupational and consumer settings for the conditions of use included in the scope of the risk evaluation, listed in Section 1.4. In occupational settings, EPA evaluated acute and chronic inhalation exposures to workers and ONUs, and acute and chronic dermal exposures to workers. EPA used inhalation monitoring data from literature sources, where reasonably available and that met data evaluation criteria, as well as modeling approaches, where reasonably available, to estimate potential inhalation exposures. Dermal doses for workers were modeled in these scenarios since dermal monitoring data were not reasonably available. In consumer settings, EPA evaluated acute inhalation exposures to both consumers and bystanders, and acute dermal exposures to consumers. EPA also evaluated chronic inhalation exposure to bystanders resulting from off-gassing of 1-BP from rigid board insulation installed within a residence. Inhalation exposures and dermal doses in these scenarios were modeled since inhalation and dermal monitoring data were not reasonably available. These analyses are described in Section 2.3 of this risk evaluation.

EPA evaluated reasonably available information for human health hazards and identified hazard endpoints for non-cancer effects and cancer effects following acute and chronic exposures. EPA used the *Framework for Human Health Risk Assessment to Inform Decision Making* (U.S. EPA, 2014c) to evaluate, extract, and integrate 1-BP's human health hazard and dose-response information. EPA reviewed key and supporting information from previous hazard assessments as well as reasonably available information on 1-BP's human health hazards. These data sources⁵ included published and non-published data sources, including key and supporting studies identified in and evaluated in the *2016 Draft Risk Assessment* (U.S. EPA, 2016c). EPA relied heavily on the *2016 Draft Risk Assessment* (U.S. EPA, 2016c) to inform hazard characterization. EPA also screened and evaluated new studies that were published between January 1, 2009 and March 1, 2017).

⁴ More information about the ECOSAR program can be found at: <https://www.epa.gov/tsc-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model>

⁵ 1-BP does not have an existing EPA IRIS Assessment.

EPA developed a hazard and dose-response analysis using endpoints observed in inhalation hazard studies, evaluated the weight of the scientific evidence considering the EPA and National Research Council (NRC) risk assessment guidance, and selected the points of departure (POD) for non-cancer endpoints following acute and chronic exposures, and inhalation unit risk and cancer slope factors for cancer risk estimates. Potential health effects of 1-BP exposure described in the literature include: liver toxicity, kidney toxicity, reproductive toxicity, developmental toxicity, neurotoxicity, and cancer. EPA identified non-cancer PODs for acute inhalation and dermal exposures based on developmental effects (*i.e.*, decreased live litter size, and increases in post-implantation loss), the most sensitive HECs/dermal HEDs derived for an acute exposure duration ([WIL Research, 2001](#)). The non-cancer PODs for chronic inhalation exposures are based on liver toxicity, kidney toxicity, reproductive toxicity, developmental toxicity and neurotoxicity. EPA used the HEC/dermal HED specific to each health effect domain: liver (increased hepatocellular vacuolization; ([WIL Research, 2001](#))), kidney (increased pelvic mineralization; ([WIL Research, 2001](#))), reproductive system (decreased seminal vesicle weight; ([Ichihara et al., 2000b](#))), developmental effects (F1 decreased live litter size, F0 post-implantation loss – NLogistic model; ([WIL Research, 2001](#))), nervous system (decreased traction time; ([Honma et al., 2003](#))). EPA searched for but did not identify toxicity studies by the dermal route that were adequate for dose-response assessment. Therefore, dermal candidate values were derived by route-to-route extrapolation from the inhalation PODs mentioned above. No physiologically based pharmacokinetic/ pharmacodynamic (PBPK/PD) models that would facilitate route-to-route extrapolation have been identified. By the criteria presented in EPA's *Guidelines for Carcinogen Risk Assessment* ([U.S. EPA, 2005a](#)), 1-BP may be considered "*Likely to be Carcinogenic in Humans*" based on the positive findings for carcinogenicity in more than one test species, together with positive findings for the direct reactivity of 1-BP with DNA and suggestive but inconclusive evidence for genetic toxicity. In a two-year cancer bioassay with 1-BP exposures via the inhalation route ([NTP, 2011a](#)), increases in the incidence of skin tumors (keratoacanthoma/squamous cell carcinomas) in male F344 rats, rare large intestine adenomas in female F344 rats, and alveolar/bronchiolar adenomas or carcinomas (combined) in female B6C3F1 mice were observed. EPA calculated cancer risk estimates using a linear model and cancer slope factors based on these endpoints.

Risk Characterization

Environmental Risk: EPA qualitatively considered physical-chemical and environmental fate properties of 1-BP and determined that exposures of 1-BP to terrestrial species and sediment-dwelling aquatic species are expected to be low and risks are not expected. EPA calculated a risk quotient (RQ) by comparing the estimated concentration of 1-BP in surface water resulting from aquatic releases to the hazard thresholds for aquatic species in order to characterize the risks to water column-dwelling aquatic organisms. EPA did not identify any exceedances, as all RQ values for acute and chronic exposure leading to risks are <1. An RQ that does not exceed 1 indicates that the exposure concentrations of 1-BP are less than the concentrations that would cause an effect to organisms in the aquatic pathways and risk concerns for these organisms were not identified. The

results of the risk characterization are in Section 4.1, including a table that summarizes the RQs for risks associated with acute and chronic exposures.

Human Health Risks: For workers and ONUs, EPA estimated potential non-cancer risks resulting from acute or chronic inhalation exposure using a Margin of Exposure (MOE) approach. EPA also estimated potential cancer risk from chronic inhalation exposures to 1-BP using inhalation unit risk slope factors values multiplied by the chronic exposure for each COU. Similarly for dermal exposure to workers, EPA used the MOE approach and dermal cancer slope factors to estimate non-cancer and cancer risks, respectively.

For workers, risks for non-cancer effects following acute and chronic inhalation exposures were indicated under high-end exposure levels for most conditions of use if personal protective equipment (PPE) was not used. Cancer risks were also identified following both inhalation and dermal exposure for most conditions of use if PPE was not used. With the use of respiratory protection, worker exposures were reduced, but some conditions of use continued to present non-cancer and cancer risks following inhalation exposure under high-end exposure levels even with PPE (APF = 50). With the use of protective gloves (PF = 5), dermal risks were mitigated for all conditions of use. EPA's risk estimates for workers are presented in Section 4.2.3 and Section 4.2.5.

For ONUs, risks for non-cancer and cancer effects following acute and chronic exposures were also indicated for central tendency and high-end inhalation exposure levels for most conditions of use. Because ONUs do not directly handle 1-BP in the workplace, they are not assumed to use respiratory protection. ONUs are not assumed to be dermally exposed to 1-BP and dermal risks to ONUs were not evaluated. EPA's risk estimates for ONUs are presented in Section 4.2.3.

EPA estimated non-cancer risks resulting from acute inhalation exposures for the consumer users and bystanders. EPA estimated non-cancer risks resulting from acute dermal exposures for the consumer users. EPA estimated non-cancer risks resulting from chronic inhalation exposures and cancer risks for bystanders from insulation (off-gassing) of 1-BP following installation of THERMAX™ rigid board insulation within a residence as described in Section 2.3.2.4. These exposures were modeled with a range of user intensities, described in detail in Section 2.3.2.1. EPA assumed that consumer users or bystanders would not use PPE and that all exposures, except those associated with insulation condition of use, would be acute, rather than chronic in nature.

Risks for developmental effects following acute inhalation exposures were indicated for most consumer conditions of use for both the consumer users and bystanders under low, medium and high intensity use conditions. Risks for developmental effects following acute dermal exposures were indicated for four of eight conditions of use evaluated for dermal exposure for the consumer users. The insulation (off-gassing) condition of use did not indicate risks for bystanders. EPA's estimates for consumer user and bystander risks for each consumer condition of use evaluated are presented in Section 4.2.3 and Section 4.2.4.

For the general population, EPA considered reasonably available physical-chemical properties, environmental release, and environmental fate information to characterize risk from water,

sediment, and soil. As described further in Section 4.5.2.3, EPA does not expect general population exposure from contaminated drinking water or groundwater, and therefore did not identify risk for these pathways.

Uncertainties: Key assumptions and uncertainties in the environmental risk estimation are related to the quality of the environmental hazard data for 1-BP. Only one environmental hazard study was identified by EPA and evaluated for data quality. Five studies were available only as European Chemical Agency (ECHA) summaries in the chemical registration database for 1-BP, but EPA was not able to obtain the full study reports, so these studies were not utilized in the assessment. In addition, data on the environmental hazards of 1-BP following chronic exposure were not identified, so estimates of chronic hazard to environmental receptors were based on extrapolations from acute toxicity data.

For the human health risk estimation, key assumptions and uncertainties are related to data on exposure monitoring, exposure model input parameters, and their representativeness for that COU. One key model assumption is that workers and occupational non-users remain in their respective work zones, which may result in an overestimate of exposure for workers, and an underestimate for ONUs. An additional source of uncertainty is the inhalation to dermal route-to-route extrapolations, which is a source of uncertainty in the risk assessment for dermal cancer and non-cancer risk estimates. For assessing cancer risks, EPA chose to model the lung tumor results from a cancer bioassay in mice (selected as the POD considered protective for the other tumor types); however, there is uncertainty regarding the modeling of these tumor types for humans. Assumptions and key sources of uncertainty are detailed in Section 4.3.

EPA's assessments, risk estimations, and risk determinations account for uncertainties throughout the risk evaluation. 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 1-BP 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. The consideration of uncertainties support the Agency's risk determinations, each of which is supported by substantial evidence, as set forth in detail in later sections of this final risk evaluation.

Potentially Exposed or Susceptible Subpopulations (PESS): TSCA § 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 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 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. For consideration of the potentially exposed groups, EPA considered 1-BP exposures to be higher among workers using 1-BP and ONUs in the vicinity of 1-BP use than the exposures experienced by the general population, and among consumers and bystanders associated with the use of consumer products. While it is anticipated that there may be differential 1-BP metabolism based on lifestyle, currently there are no data available, therefore the impact of this cannot be quantified. Similarly, while it is known that there may be genetic differences that influence CYP2E1 metabolic capacity, there may also be other metabolizing enzymes that are functional and impact vulnerability. There is insufficient data to quantify these differences for risk assessment purposes. See additional discussions in Section 4.4.1. EPA’s unreasonable risk determinations are based on high-end exposure estimates for workers and high intensity use scenarios for consumers and bystanders in order to capture individuals who are PESS.

Heterogeneity among humans is an uncertainty associated with extrapolating the derived PODs to a diverse human population. One component of human variability is toxicokinetic, such as variations in CYP2E1 and glutathione transferase activity in humans ([Arakawa et al., 2012](#); [Trafalis et al., 2010](#)) which are involved in 1-BP metabolism in humans and discussed in Section 3.2.3. EPA did not have chemical-specific information on susceptible subpopulations, or the distribution of susceptibility in the general population that could be used to adjust the default intraspecies UF_H . As such, EPA used an intraspecies UF_H of 10 for the risk assessment based on default factors for toxicokinetic and toxicodynamic variability.

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 § 702.33).” Exposures to 1-BP were evaluated by inhalation and dermal routes separately. Inhalation and dermal exposures are assumed to occur simultaneously for workers and consumers. EPA chose not to employ simple additivity of exposure pathways at this time within a condition of use due to the lack of a physiologically based pharmacokinetic (PBPK) model for 1-BP. See additional discussions in Section 4.4.2.

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 § 702.33).” In this risk evaluation, EPA considered sentinel exposure as the high-end exposure given the details of the conditions of use and the evaluated exposure scenarios. In cases where sentinel exposures result in MOEs greater than the benchmark or cancer risk lower than the benchmark, EPA did no further analysis because sentinel exposures represent

the worst-case scenario. EPA's decision for unreasonable risk are based on high-end exposure estimates to capture individuals with sentinel exposure.

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.

Unreasonable Risk of Injury to the Environment: The physical-chemical and environmental fate properties (high volatility, high water solubility and low Log K_{ow}) of 1-BP indicate low potential for exposure to terrestrial and sediment-dwelling aquatic species. In addition, for all conditions of use, EPA did not identify any exceedances of benchmarks to aquatic organisms from exposures to 1-BP in surface waters. EPA characterized the environmental risk based on one high quality study, supplemented with predicted toxicity values for acute and chronic exposure based on the Ecological Structure Activity Relationships (ECOSAR) Class modeling program. Based on the risk estimates, the environmental effects of 1-BP, the exposures, physical-chemical properties of 1-BP and consideration of uncertainties, EPA determined that there is no unreasonable risk of injury to the environment from all conditions of use of 1-BP.

Unreasonable Risks of Injury to Health: EPA's determination of unreasonable risk for specific conditions of use of 1-BP listed below are based on health risks to workers, ONUs, consumers, or bystanders from consumer use. For acute exposures, EPA evaluated unreasonable risk of developmental toxicity based on animal studies (*i.e.*, decreased live litter size and post-implantation loss) and used the most sensitive endpoint to make the unreasonable risk determination (*i.e.*, post-implantation loss). For chronic exposures, EPA also based the unreasonable risk determination also on developmental toxicity; however, EPA evaluated other non-cancer effects (*e.g.*, additional developmental toxicity, reproductive toxicity, liver toxicity, kidney toxicity, neurotoxicity). For chronic exposures, EPA also evaluated unreasonable risk of cancer from skin, intestinal and lung tumors. EPA considered the uncertainties associated with the reasonably available information to justify the linear cancer dose-response model when compared to other available models.

Unreasonable Risk of Injury to Health of the General Population: As part of the Problem Formulation for BP ([U.S. EPA, 2018c](#)), EPA found that 1-BP exposures to the general population may occur from the conditions of use due to releases to air, water or land. Based on the qualitative assessment described in the Problem Formulation for 1-BP, EPA determined that there is no unreasonable risk to general population from all conditions of use from drinking water, surface water, or sediment pathways via the oral and dermal routes. The exposures to general population via ambient air and disposal pathways falls under the jurisdiction of other environmental statutes administered by EPA, *i.e.*, CAA and RCRA. 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 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 deadline for completing risk evaluations. EPA has therefore tailored the scope of the risk evaluation for 1-BP using authorities in TSCA section 6(b) and 9(b)(1). EPA did not evaluate risk to the general population from ambient air and disposal pathways for any conditions of use, and the no unreasonable risk determinations do not account for exposures to the general population from ambient air and disposal pathways.

Unreasonable Risk of Injury to Health of Workers: EPA evaluated non-cancer effects from acute and chronic inhalation and dermal occupational exposures and cancer from chronic inhalation and dermal occupation exposures 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 developmental effects resulting from acute and chronic inhalation exposure, and cancer from chronic inhalation exposure. EPA determined an unreasonable risk of injury to workers of cancer from chronic dermal exposure from one condition of use: the industrial and commercial use of 1-BP in dry cleaning solvents, spot cleaners and stain removers.

EPA generally assumes compliance with OSHA requirements for protection of workers, including the implementation of the hierarchy of controls. In support of this assumption, EPA used reasonably available information indicating that some employers, particularly in the industrial setting, are providing appropriate engineering, administrative controls, or PPE to their employees consistent with OSHA requirements. While OSHA has not issued a specific PEL for 1-BP, EPA assumes some use of PPE due to the hazard alert⁶ for occupational exposure to 1-BP jointly issued by OSHA and NIOSH and the Threshold Limit Value™ (TLV™) adopted by the American Conference of Governmental Industrial Hygienists (ACGIH™). EPA does not have reasonably available information to support this assumption for each condition of use; however, 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

⁶ <https://www.cdc.gov/niosh/docs/2013-150/pdfs/2013-150.pdf?id=10.26616/NIOSH PUB2013150>

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 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 accounts for reasonably available information and professional judgement related to worker protection practices, and addresses uncertainties regarding availability and use of PPE.

For each condition of use of 1-BP, EPA assumes the use of a respirator with an APF of 10 to 50. Similarly, EPA assumes the use of gloves with PF of 5. However, EPA assumes that for some conditions of use, the use of respirators is not a standard industry practice, based on best professional judgement given the burden associated with the use of respirators, including the expense of the equipment and the necessity of fit-testing and training for proper use. Similarly, EPA does not assume that as a standard industry practice that workers in dry cleaning facilities use gloves.

The unreasonable risk determinations reflect the severity of the effects associated with the occupational exposures to 1-BP and incorporate EPA assumptions of PPE use (respirators with APF from 10 to 50 and gloves with PF of 5). A full description of EPA's unreasonable risk determination for each condition of use, including the PPE assumptions, is in Section 5.2.

Unreasonable Risk of Injury to Health of Occupational Non-Users (ONUs): ONUs are workers who do not directly handle 1-BP but perform work in an area where 1-BP is present. EPA evaluated non-cancer effects to ONUs from acute and chronic inhalation occupational exposures and cancer from chronic inhalation 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 1-BP 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 of 1-BP use. Non-cancer effects and cancer from dermal occupational exposures to ONUs were not evaluated because ONUs are not dermally exposed to 1-BP. For inhalation exposures, EPA, where possible, estimated ONUs' exposures and described the risks separately from workers directly exposed. When the difference between ONUs' exposures and workers' exposures cannot be quantified, EPA assumed that ONUs' inhalation exposures are lower than inhalation exposures for workers directly handling the chemical substance. 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 and dermal exposures to determine if there was unreasonable risk of injury to consumers' health. 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 exposures to determine if there was unreasonable risk of injury to bystanders' health. For one consumer condition of use (use of 1-BP in insulation), EPA also evaluated non-cancer effects and cancer from chronic inhalation

exposures. EPA did not evaluate non-cancer effects from dermal exposures to bystanders because bystanders are not dermally exposed to 1-BP. 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. 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 1-BP 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 presented 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
<ul style="list-style-type: none">• Manufacturing (domestic manufacturing)• Manufacturing (import)• Processing: as a reactant• Processing: incorporation into articles• Processing: repackaging• Processing: recycling• Distribution in commerce• Commercial and consumer uses of building/construction materials (insulation)• Disposal

EPA has determined that the following conditions of use of 1-BP present an unreasonable risk of injury. 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.

Processing that Present an Unreasonable Risk
<ul style="list-style-type: none">• Incorporation into a formulation, mixture or reaction product

Industrial and Commercial Uses that Present an Unreasonable Risk
<ul style="list-style-type: none">• Industrial and commercial use as solvent for cleaning and degreasing in vapor degreaser (batch vapor degreaser – open-top, inline vapor degreaser)

Industrial and Commercial Uses that Present an Unreasonable Risk

- Industrial and commercial use as solvent for cleaning and degreasing in vapor degreaser (batch vapor degreaser – closed-loop)
- Industrial and commercial use as solvent for cleaning and degreasing in cold cleaners
- Industrial and commercial use as solvent in aerosol spray degreaser/cleaner
- Industrial and commercial use in adhesives and sealants
- Industrial and commercial use in dry cleaning solvents, spot cleaners and stain removers
- Industrial and commercial use in liquid cleaners (*e.g.*, coin and scissor cleaner) and liquid spray/aerosol cleaners
- Other industrial and commercial uses: arts, crafts, hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner, refrigerant flush); anti-adhesive agents (mold cleaning and release product); electronic and electronic products and metal products; functional fluids (close/open-systems) – refrigerant/cutting oils; asphalt extraction; laboratory chemicals; and temperature indicator – coatings

Consumer Uses that Present an Unreasonable Risk

- Consumer use as solvent in aerosol spray degreasers/cleaners
- Consumer use in spot cleaners and stain removers
- Consumer use in liquid cleaners (*e.g.*, coin and scissor cleaners)
- Consumer use in liquid spray/aerosol cleaners
- Consumer use in arts, crafts, hobby materials (adhesive accelerant)
- Consumer use in automotive care products (refrigerant flush)
- Consumer use in anti-adhesive agents (mold cleaning and release product)

1 INTRODUCTION

This document is the final risk evaluation for 1-bromopropane (1-BP) under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. 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, on June 22, 2016.

The Agency published the *Scope of the Risk Evaluation for 1-BP* ([U.S. EPA, 2017d](#)) in June 2017, and the Problem Formulation in June 2018 ([U.S. EPA, 2018c](#)), which represented the analytical phase of risk evaluation in which “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 ([U.S. EPA, 2018c](#)) for 1-BP and has considered the comments specific to 1-BP, as well as more general comments regarding EPA's chemical risk evaluation approach for developing the risk evaluations for the first 10 chemicals EPA is evaluating. The Problem Formulation identified conditions of use within the scope of the risk evaluation and presented three conceptual models and an analysis plan. Based on EPA's analysis of the conditions of use, physical-chemical and fate properties, environmental releases, and exposure pathways, the preliminary conclusions of the Problem Formulation were that further analysis of exposure pathways, to workers and consumers was necessary in this risk evaluation; and that further analysis for environmental release pathways leading to surface water, sediment, or land-applied biosolid exposures to ecological receptors was not necessary in this risk evaluation. EPA subsequently published a draft risk evaluation for 1-BP in August 2019 and has taken public and peer review comments. 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.

As per EPA's final Risk Evaluation Rule, [Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act](#) (82 FR 33726), the 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 section 6(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 702.45). As explained in the Risk Evaluation Rule (82 FR 33726 (July 20, 2017)), the purpose of peer review is for the independent review of the science underlying the risk assessment. Peer review will therefore address 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.

As EPA explained in the Risk Evaluation Rule (82 [FR](#) 33726 (July 20, 2017)), 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 will be most effective in this role if they received 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 preceded peer review on the draft risk evaluation. EPA responded to public and peer review comments received on the [Draft Risk Evaluation](#) and explained changes made to the draft risk evaluation for 1-BP 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 as it developed use dossiers, Scope Documents, and Problem Formulations. At each step, EPA has 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 ([U.S. EPA, 2018c](#)) of 1-BP.

In this final risk evaluation, Section 1 presents the basic physical-chemical properties of 1-BP, as well as a background on uses, regulatory history, conditions of use and conceptual models, with particular emphasis on any changes since the publication of the [Draft Risk Evaluation](#). Section 1 also includes a discussion of the systematic review process utilized in this risk evaluation. Section 2 provides the analysis and discussion of the exposures, both human and environmental, that can be expected based on the conditions of use for 1-BP. Section 3 discusses environmental and human health hazards of 1-BP. Risk characterization is presented in Section 4, which integrates and assesses the best available science and “reasonably available information”⁷ 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 any uncertainties and how they impact the risk evaluation. In Section 4.5.2.3, the agency presents the risk determination of whether risks posed by the chemical substance under the conditions of use are “unreasonable” as required under TSCA (15 U.S.C. 2605(b)(4)).

1.1 Physical and Chemical Properties

1-BP is a colorless liquid with a sweet odor. It is a brominated hydrocarbon that is slightly soluble in water. 1-BP is a volatile organic compound (VOC) that exhibits high volatility, a low boiling

⁷ “Reasonably available information means information that EPA possesses or can reasonably generate, obtain, and synthesize for use in risk evaluations, considering the deadlines specified in TSCA section 6(b)(4)(G) for completing such evaluation. Information that meets the terms of the preceding sentence is reasonably available information whether or not the information is confidential business information, that is protected from public disclosure under TSCA Section 14.”

point, low flammability and no explosivity. Figure 1-1 presents the chemical structure and Table 1-1 summarizes the physical-chemical properties of 1-BP.

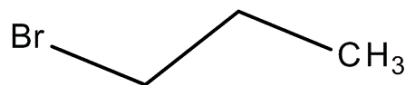


Figure 1-1. Chemical Structure of 1-Bromopropane

Table 1-1. Physical-Chemical Properties of 1-BP

Property	Value ^a	Reference
Molecular formula	C ₃ H ₇ Br	O'Neil (2013)
Molecular weight	122.99	O'Neil (2013)
Physical form	Colorless liquid; sweet hydrocarbon odor	O'Neil (2013)
Melting point	-110°C	O'Neil (2013)
Boiling point	71°C at 760 mmHg	O'Neil (2013)
Density	1.353 g/cm ³ at 20°C	O'Neil (2013)
Vapor pressure	110.8 mmHg (14.77 kPa) at 20°C	Boublík et al. (1984)
Vapor density	4.25 (relative to air)	Patty et al. (1963)
Water solubility	2.450 g/L at 20°C	Yalkowsky et al. (2010)
Octanol/water partition coefficient (Log K _{ow})	2.10	Hansch (1995)
Henry's Law constant	7.3x10 ⁻³ atm·m ³ /mole (calculated)	U.S. EPA (2012c)
Flash point	22°C	O'Neil (2013)
Autoflammability	490°C	NFPA (2010)
Viscosity	0.489 mPa·s at 25°C	Haynes and Lide (2010)
Refractive index	1.4341	O'Neil (2013)
Dielectric constant	8.09 at 20°C	Haynes and Lide (2010)
^a Measured unless otherwise noted.		

1.2 Uses and Production Volume

The information on the conditions of use is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (*e.g.*, published literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories of use may be grouped under multiple CDR categories.

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](#)).

CDR, information from commenters, and types of available products show that the primary use of 1-BP is degreasing. The exact use volumes associated with degreasing is CBI⁸ in the 2016 CDR ([U.S. EPA, 2016a](#)). EPA evaluated activities resulting in exposures associated with distribution in commerce (*e.g.*, loading, unloading) throughout the various lifecycle stages and conditions of use (*e.g.*, manufacturing, processing, industrial use, consumer use, disposal) rather than as a single distribution scenario. EPA expects that some commercial products containing 1-BP are also available for purchase by consumers, such that many products are used in both commercial and consumer applications/scenarios.

The 2016 CDR reporting data on the production volume for 1-BP are provided in Table 1-2 and come from EPA’s CDR database ([U.S. EPA, 2016a](#)). This information has not changed from that provided in the Scope Document ([EPA-HQ-OPPT-2016-0741-0049](#)).

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

Reporting Year	2012	2013	2014	2015
Total Aggregate Production Volume (lbs)	18,800,000	24,000,000	18,500,000	25,900,000

^a The CDR data for the 2016 reporting period is available via ChemView (<https://chemview.epa.gov/chemview>) ([U.S. EPA, 2016a](#)). Because of the CBI substantiation process required by amended TSCA, the CDR data available in the Scope Document ([EPA-HQ-OPPT-2016-0741-0049](#)) is more specific than currently in ChemView.

According to data collected in EPA’s 2016 Chemical Data Reporting (CDR) Rule, 25.9 million pounds of 1-BP were manufactured in or imported into the United States in 2015 ([U.S. EPA,](#)

⁸ EPA does have access to and does review all CBI information in this process. EPA has also reviewed all CBI claims referred to in this risk evaluation, and these claims have been substantiated and approved by EPA.

[2016a](#)). Data publicly reported indicate that there are two domestic manufacturers and eight importers of 1-BP in the United States.

Total production volume (domestic manufacture plus import) of 1-BP has increased from 2012 to 2015, as can be seen in Table 1-2 ([U.S. EPA, 2016a](#)). 1-BP's volume has increased because it has been an alternative to ozone-depleting substances and chlorinated solvents. Import volumes for 1-BP reported to the 2016 CDR are between 10 million and 25 million pounds per year ([U.S. EPA, 2016a](#)).

1.3 Regulatory and Assessment History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to 1-BP. EPA compiled a regulatory summary from federal, state, international and other government sources, as cited in Appendix A.

Federal Laws and Regulations

1-BP is subject to federal statutes or regulations, in addition to TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

State Laws and Regulations

1-BP is subject to state statutes or regulations implemented by state agencies or departments. 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

1-BP 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.

Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-3). Depending on the source, these assessments may include information on conditions of use, hazards, exposures, and potentially exposed or susceptible subpopulations. EPA found no additional assessments beyond those listed in the Scope Document ([Scope Document; EPA-HQ-OPPT-2016-0741-0049](#)) and the Problem Formulation document ([U.S. EPA, 2018c](#)).

In addition to using this information, EPA conducted a full review of the relevant data and information collected in the initial comprehensive search (see *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, [EPA-HQ-OPPT-2016-0741-0048](#)) using the literature search and screening strategies documented in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)). Thus, EPA considered data and information that has been made available since these assessments were conducted.

Table 1-3. Assessment History of 1-BP

Authoring Organization	Assessment
EPA Assessments	
Office of Chemical Safety and Pollution Prevention (OCSPP)/Office of Pollution Prevention and Toxics (OPPT)	TSCA work plan chemical risk assessment: Peer review draft 1-bromopropane: (n-Propyl bromide) spray adhesives, dry cleaning, and degreasing uses CASRN: 106-94-5 [2016 Draft Risk Assessment (U.S. EPA, 2016c)]
Office of Air Quality Planning and Standards (OAQPS)	Draft notice to grant the petition to add 1-BP to the list of HAPs (https://www.regulations.gov/document?D=EPA-HQ-OAR-2014-0471-0062)
Other U.S.-Based Organizations	
National Institute for Occupational Safety and Health (NIOSH)	Criteria for a Recommended Standard: Occupational Exposure to 1-Bromopropane (2016)
Agency for Toxic Substances and Disease Registry (ATSDR)	Toxicological Profile for 1-Bromopropane (2017)

1.4 Scope of the Evaluation

1.4.1 Conditions of Use Included in the Risk Evaluation

TSCA § 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.” Conditions of use have not changed since the issuance of the 1-BP Problem Formulation ([U.S. EPA, 2018c](#)) on June 11, 2018; thus, the conditions of use described in the 1-BP Problem Formulation, and reproduced below in Table 1-4, remain the same. No additional information was received by EPA following the publication of the problem formulation that would require updating the conditions of use (Table 2-2) or the life cycle diagram as presented in the June 2018 Problem Formulation ([U.S. EPA, 2018c](#)).

The life cycle diagram in Figure 1-2 depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial, consumer), distribution and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period ([U.S. EPA, 2016a](#)). EPA will evaluate activities resulting in exposures associated with distribution in commerce (*e.g.*, loading, unloading) throughout the various lifecycle stages and conditions of use (*e.g.*, manufacturing, processing, industrial use, consumer use, disposal) rather than as a separate distribution scenario.

EPA has not exercised its authority in TSCA section 6(b)(4)(D) to exclude any 1-BP conditions of use from the scope of the 1-BP risk evaluation.

Table 1-4. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	References
Manufacture	Domestic manufacture	Domestic manufacture	U.S. EPA (2016a)
	Import	Import	U.S. EPA (2016a)
Processing	Processing as a reactant	Intermediate in all other basic inorganic chemical manufacturing, all other basic organic chemical manufacturing, and pesticide, fertilizer and other agricultural chemical manufacturing	U.S. EPA (2016a)
	Processing - incorporating into formulation, mixture or reaction product	Solvents for cleaning or degreasing in manufacturing of: <ul style="list-style-type: none"> - all other chemical product and preparation - computer and electronic product - electrical equipment, appliance and component - soap, cleaning compound and toilet preparation - services 	U.S. EPA (2016a)
	Processing - incorporating into articles	Solvents (which become part of product formulation or mixture) in construction	U.S. EPA (2016a) ; Public Comment, EPA-HQ-OPPT-2016-0741-0017
Processing	Repackaging	Solvent for cleaning or degreasing in all other basic organic chemical manufacturing	U.S. EPA (2016a)
	Recycling	Recycling	U.S. EPA (2016a) ; Use Document, EPA-HQ-OPPT-2016-0741-0003
Distribution in commerce	Distribution	Distribution	U.S. EPA (2016a) ; Use Document, EPA-HQ-OPPT-2016-0741-0003

Table 1-4. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	References
Industrial/ commercial use	Solvent (for cleaning or degreasing)	Batch vapor degreaser (<i>e.g.</i> , open-top, closed-loop)	U.S. EPA (2016c) ; Public Comment, EPA-HQ-OPPT-2016-0741-0014 ; Public Comment, EPA-HQ-OPPT-2016-0741-0015 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		In-line vapor degreaser (<i>e.g.</i> , conveyORIZED, web cleaner)	Kanegsberg and Kanegsberg (2011) ; Public Comment, EPA-HQ-OPPT-2016-0741-0014 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		Cold cleaner	U.S. EPA (2016c) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		Aerosol spray degreaser/cleaner	U.S. EPA (2016c) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016 ; Public Comment, EPA-HQ-OPPT-2016-0741-0018 ; Public Comment, EPA-HQ-OPPT-2016-0741-0020
	Adhesives and sealants	Adhesive chemicals - spray adhesive for foam cushion manufacturing and other uses	U.S. EPA (2016c) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
Industrial/ commercial/use	Cleaning and furniture care products	Dry cleaning solvent	U.S. EPA (2016c) ; Public Comment, EPA-HQ-OPPT-2016-0741-0005 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		Spot cleaner, stain remover	U.S. EPA (2016c) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016 ; Public Comment, EPA-HQ-OPPT-2016-0741-0022
		Liquid cleaner (<i>e.g.</i> , coin and scissor cleaner)	Use Document, EPA-HQ-OPPT-2016-0741-0003
		Liquid spray/aerosol cleaner	Use Document, EPA-HQ-OPPT-2016-0741-0003

Table 1-4. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	References
Industrial/ commercial/use (continued)	Other uses	Arts, crafts and hobby materials - adhesive accelerant	U.S. EPA (2016c)
		Automotive care products - engine degreaser, brake cleaner	Use Document, EPA-HQ-OPPT-2016-0741-0003
		Anti-adhesive agents - mold cleaning and release product	U.S. EPA (2016c) ; Public Comment, EPA-HQ-OPPT-2016-0741-0014 ; Public Comment, EPA-HQ-OPPT-2016-0741-0015 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016 ; Public Comment, EPA-HQ-OPPT-2016-0741-0018
		Building/construction materials not covered elsewhere - insulation	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0027
		Electronic and electronic products and metal products	U.S. EPA (2016a) ; Public Comment, EPA-HQ-OPPT-2016-0741-0016 ; Public Comment, EPA-HQ-OPPT-2016-0741-0024
		Functional fluids (closed systems) - refrigerant	Use Document, EPA-HQ-OPPT-2016-0741-0003
		Functional fluids (open system) - cutting oils	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0014
		Other - asphalt extraction	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
		Other - laboratory chemicals ^c	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-2016-0741-0059
		Temperature indicator – coatings	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0014 ; Public Comment, EPA-HQ-OPPT-2016-0741-0016
Consumer uses	Solvent (for cleaning or degreasing)	Aerosol spray degreaser/cleaner	U.S. EPA (2016c) ;

Table 1-4. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	References
	Cleaning and furniture care products	Spot cleaner, stain remover	U.S. EPA (2016c) ; Public Comment, EPA-HQ-OPPT-2016-0741-0022
		Liquid cleaner (<i>e.g.</i> , coin and scissor cleaner)	Use Document, EPA-HQ-OPPT-2016-0741-0003
		Liquid spray/aerosol cleaner	Use Document, EPA-HQ-OPPT-2016-0741-0003
Consumer uses (continued)	Other uses	Arts, crafts and hobby materials - adhesive accelerant	U.S. EPA (2016c)
		Automotive care products – refrigerant flush	U.S. EPA (2016c)
		Anti-adhesive agents - mold cleaning and release product	U.S. EPA (2016c)
		Building/construction materials not covered elsewhere - insulation	Use Document, EPA-HQ-OPPT-2016-0741-0003 ; Public Comment, EPA-HQ-OPPT-2016-0741-0027
Disposal (Manufacturing, Processing, Use)	Disposal	Municipal waste incinerator	2016 TRI Data (updated October 2017) U.S. EPA (2017f)
		Off-site waste transfer	

^aThese categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent conditions of use of 1-BP in industrial and/or commercial settings.

^bThese subcategories reflect more specific uses of 1-BP.

^c “Other – laboratory chemicals” was changed from “Temperature indicator – laboratory chemicals” since the problem formulation because other uses of 1-BP as a laboratory chemical were identified.

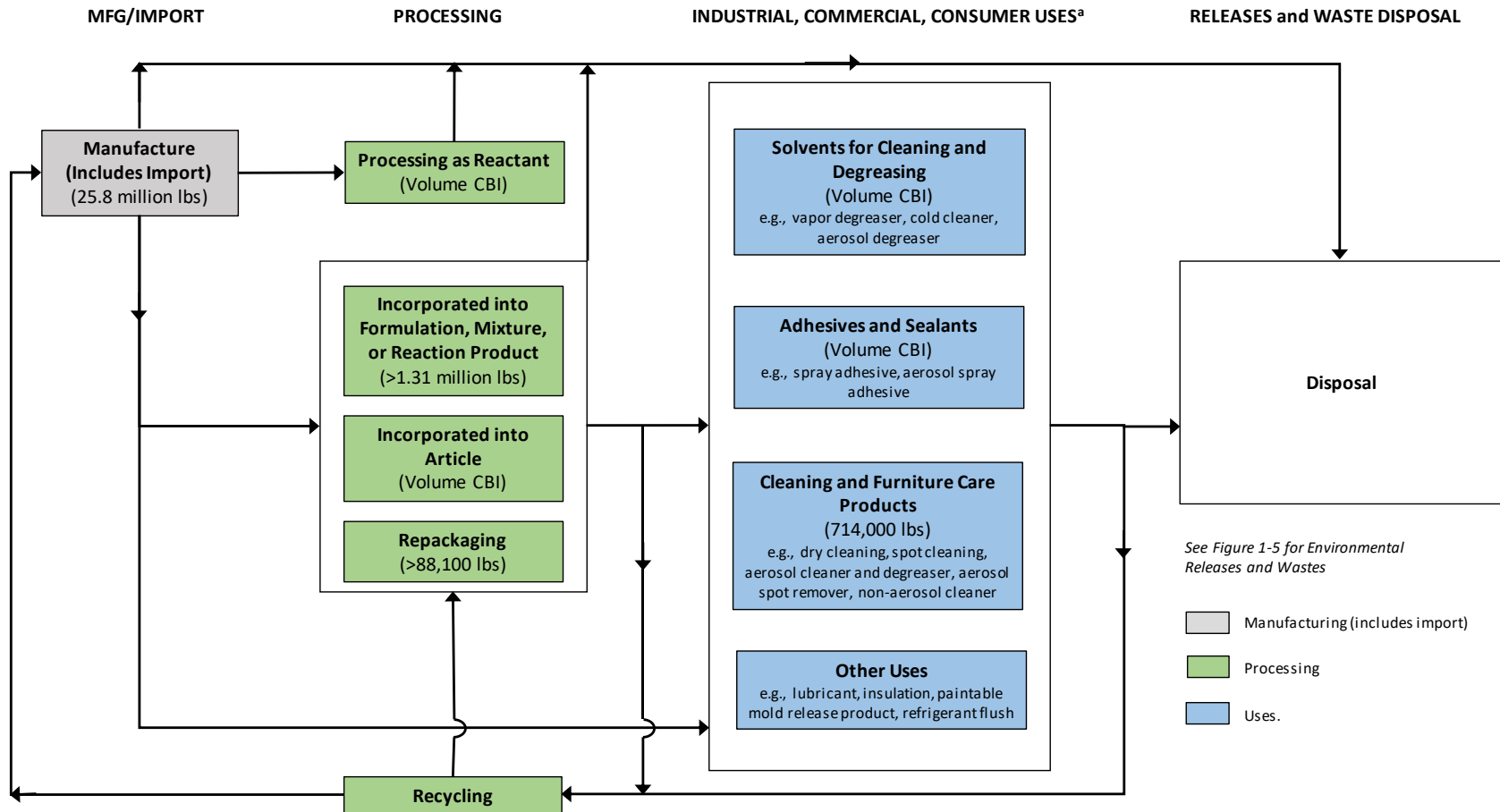


Figure 1-2. 1-BP Life Cycle Diagram

^a See Table 1-4 for additional uses not mentioned specifically in this diagram.

1.4.2 Exposure Pathways and Risks Addressed by other EPA Administered 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.”
- TSCA section 18(d)(1): “Nothing in this chapter, nor any amendment made by the Frank R. Lautenberg Chemical Safety for the 21st Century Act, nor any rule, standard of performance, risk evaluation, or scientific assessment implemented pursuant to this chapter, shall affect the right of a State or a political subdivision of a State to adopt or enforce any rule, standard of performance, risk evaluation, scientific assessment, or any other protection for public health or the environment that— (i) is adopted or authorized under the authority of any other Federal law or adopted to satisfy or obtain authorization or approval under any other Federal law...”

TSCA authorities supporting tailored risk evaluations and intra-agency referrals

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. As EPA explained in the “Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act” (“Risk Evaluation Rule”), “EPA may, on a case-by-case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination.” 82 FR 33726, 33729 (July 20, 2017).

In the Problem Formulation documents for many of the first 10 chemicals undergoing risk evaluation, EPA applied the same 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.” The approach discussed in the Risk Evaluation Rule and applied in the Problem Formulation documents is informed by the legislative history of the amended TSCA, which supports the Agency’s exercise of discretion to focus the risk evaluation on areas that raise the greatest potential for risk. 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 the 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 Safe Drinking Water Act 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 a more 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 the 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 sections 2(c) & 18(d)(1)

Finally, TSCA sections 2(c) and 18(d) support 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’s 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 and State programs, and meet the statutory deadline for completing risk evaluations.

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

As referenced in the 1-BP Problem Formulation ([U.S. EPA, 2018c](#)), EPA, through its Office of Air and Radiation (OAR), issued a draft notice of the Agency’s rationale for granting the petition to add 1-BP to the list of HAPs contained in section 112(b)(1) of the Clean Air Act (CAA), 42 U.S.C. 7412. [82 FR 2354](#) (Jan. 9, 2017). Since publication of the 1-BP Problem Formulation and the release of the draft 1-BP Risk Evaluation, EPA, through its OAR, issued a final notice to grant the petition to add 1-BP to the list of HAPs contained in section 112(b)(1) of the CAA, 42 U.S.C. 7412. [85 FR 36851](#) (June 18, 2020). This will trigger a regulatory process for reducing air emissions of 1-BP under the CAA, as outlined in the final notice – See [85 FR at 36854](#). The docket number for the draft and final OAR notices granting the petition is Docket ID No. [EPA-HQ-OAR-2014-0471](#).

As a result of the preliminary findings presented by petitioners showing increased cancer risks to the general population as a result of exposure to 1-BP via ambient air, which is relied upon, in part, by the OAR in its draft⁹ and final¹⁰ notices to grant the petitions to list 1-BP as a hazardous air pollutant (HAP), along with other information submitted to the docket¹¹, EPA has identified risk for purposes of TSCA section 9(b). This finding is not intended to constitute a finding under the CAA section 112. EPA has elected to utilize its TSCA authorities under Section 9(b)(1) to

⁹ [82 Fed. Reg. 2,354](#) (January 9, 2017).

¹⁰ [85 Fed. Reg. 36,851](#) (June 18, 2020).

¹¹ Docket ID: EPA-HQ-OAR-2014-0471 available at: <https://www.regulations.gov/docket?D=EPA-HQ-OAR-2014-0471>

coordinate with the OAR and refer action regarding risk from ambient air emissions of 1-BP to the CAA. EPA has determined that risk from emissions to the ambient air of 1-BP could be eliminated or reduced to a sufficient extent by actions taken under the CAA. The CAA contains a list of HAPs and provides EPA with the authority to add to that list upon a showing by a petitioner that “emissions, ambient concentrations, bioaccumulation, or deposition” of a substance that is an “air pollutant” are “known to cause or may reasonably be anticipated to cause adverse effects to human health or adverse environmental effects” as specified in the under CAA section 112(b)(3). For stationary source categories emitting HAP, the CAA requires EPA to issue technology-based standards that require maximum achievable control technology (MACT). Eight years after promulgation of a standard, the CAA requires a residual risk review to ensure promulgated standards adequately protect public health and the environment. If residual risk is identified, the CAA directs EPA to revise standards to address the residual risk and ensure the standards adequately protect public health and the environment. The CAA thereby provides EPA with comprehensive authority to regulate emissions to ambient air of any hazardous air pollutant. OAR will use the authorities in the CAA to protect against risk from emissions to the ambient air of 1-BP and potential impacts to the public health and the environment. As a result, EPA did not evaluate hazards or exposures to the general population or terrestrial species from emissions to the ambient air of 1-BP.

EPA did not include the following disposal pathways in this risk evaluation due to risks being addressed by RCRA and SDWA:

- Releases from hazardous waste incinerators,
- On-site releases to land going to underground injection systems,
- On-site releases to RCRA Subtitle C hazardous waste landfills,
- On-site releases to land from RCRA Subtitle D municipal solid waste landfills,
- Exposures to the general population (including susceptible populations) or terrestrial species from such releases, and
- On-site release to land from industrial non-hazardous and construction/demolition waste landfills.

1-BP is regulated as a hazardous waste, waste code D001 (ignitable liquids, 40 CFR 261.21). The general RCRA standard in section 3004(a) for the technical (regulatory) criteria that govern the management (treatment, storage, and disposal) of hazardous waste (*i.e.*, Subtitle C) are those "necessary to protect human health and the environment," RCRA 3004(a). The regulatory criteria for identifying “characteristic” hazardous wastes and for “listing” a waste as hazardous also relate solely to the potential risks to human health or the environment. 40 C.F.R. §§ 261.11, 261.21-261.24. RCRA statutory criteria for identifying hazardous wastes require EPA to “tak[e] into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics.” Subtitle C controls cover not only hazardous wastes that are landfilled, but also hazardous wastes that are incinerated (subject to control under RCRA Subtitle C) or injected into UIC Class I

hazardous waste wells (subject to joint control under Subtitle C and the Safe Drinking Water Act (SDWA)). While permitted and managed by the individual states, municipal solid waste landfills are required by federal regulations to implement some of the same requirements as Subtitle C landfills. Industrial non-hazardous and construction/demolition waste landfills are primarily regulated under state regulatory programs. States must also implement limited federal regulatory requirements for siting, groundwater monitoring, and corrective action, and a prohibition on open dumping and disposal of bulk liquids. States may also establish additional requirements such as for liners, post-closure and financial assurance, but are not required to do so.

1.4.3 Conceptual Models

The conceptual models for this final risk evaluation are shown in Figure 1-3, Figure 1-4, and Figure 1-5. EPA considered the potential for hazards to human health and the environment resulting from exposure pathways outlined in the preliminary conceptual models of the 1-BP Scope Document ([U.S. EPA, 2017d](#)). These conceptual models indicate where potential exposures to 1-BP may result from industrial and commercial activities, consumer activities and uses, and environmental releases and wastes. The problem formulation documents refined the initial conceptual models and analysis plans that were provided in the Scope Documents ([U.S. EPA, 2018c](#)).

The pathways that are included in the final risk evaluation but received no additional analysis beyond the results of a screening level analysis or consideration of chemical-specific properties that were presented in the Problem Formulation ([U.S. EPA, 2018c](#)) are: water (drinking water; wastewater releases to surface water and resulting exposures to aquatic species); and exposure to terrestrial and aquatic species via land application of biosolids to soil and through volatilization and runoff. The analysis of these pathways is included in this final risk evaluation so that EPA can carry the findings forward to a risk determination.

EPA did not conduct further evaluation of potential risks resulting from exposure via drinking water pathways beyond what was presented in the Problem Formulation ([U.S. EPA, 2018c](#)). As described in the problem formulation, there is no data of 1-BP found in U.S. drinking water. TRI reporting from 2016 indicates zero pounds released to POTWs and five pounds released directly to water. TRI reporting from 2017 and 2018 indicate only one pound released to water per year. In addition, 1-BP is slightly soluble in water and volatilizes rapidly from water. As such, it is not expected to be present in drinking water supplied from public water systems.

Releases to wastewater or surface water are included in the scope of the risk evaluation, but have not been further analyzed since the Problem Formulation ([U.S. EPA, 2018c](#)). As discussed in the problem formulation, 1-BP is volatile and has a relatively high Henry's law constant. 1-BP is somewhat biodegradable and is not expected to sorb to solids in wastewater. Additionally, EPA's STP WTP model predicts 73% removal of 1-BP by volatilization in activated sludge treatment and 1% partitioning to biosolids. 1-BP discharged in wastewater treatment plant effluent to the aquatic environment would be subject to volatilization and biodegradation thereby reducing aquatic exposure. Although 1-BP is not a priority pollutant, 2016 TRI reporting indicates zero pounds released to POTWs and five pounds released directly to water, suggesting existing restrictions for

discharge to POTWs limits discharge of 1-BP to POTWs and ultimately to surface water. Based on the characteristics of environmental fate and industrial release information, exposure to the general population via surface water, drinking water and sediment is expected to be low. A screening-level comparison of estimated environmental exposure concentrations with environmental hazard thresholds was conducted in the problem formulation and indicated that risks were unlikely to result to aquatic species (both water-column and sediment dwelling) as a result of releases to surface water. This screening-level analysis has been carried over to the final risk evaluation from the Problem Formulation and is presented in Section 4.1. Consistent with the analysis plan of the Problem Formulation, no further analysis was conducted on these pathways.

Similarly, EPA included releases to terrestrial species (including soil-dwelling species) via land application of biosolids to soils within the scope of the risk evaluation, but no further analysis was conducted in this risk evaluation beyond what was presented in the Problem Formulation ([U.S. EPA, 2018c](#)). As mentioned above, exposure to terrestrial species via releases to air was not included in the scope of the assessment. Based on the log K_{OC} of 1.6, 1-BP is not expected to adsorb strongly to sediment or soil. If present in biosolids, 1-BP is expected to associate with the aqueous component and volatilize to air as the biosolids are applied to soil and allowed to dry. The high vapor pressure and other fate properties of 1-BP indicates soil is likely not a viable pathway of exposure for terrestrial, sediment or ecological species as 1-BP is expected to volatilize rapidly from soil. This is explained further in Section 3.1.3.

As explained in Section 1.4.2 of this final risk evaluation, EPA has utilized its TSCA authorities to coordinate with the Office of Air and Radiation regarding risk from ambient air emissions of 1-BP. EPA has determined that risk from ambient air emissions of 1-BP could be eliminated or reduced to a sufficient extent by actions taken under the CAA. As a result, EPA did not evaluate hazards or exposures to the general population or terrestrial species from ambient air emissions of 1-BP in this risk evaluation.

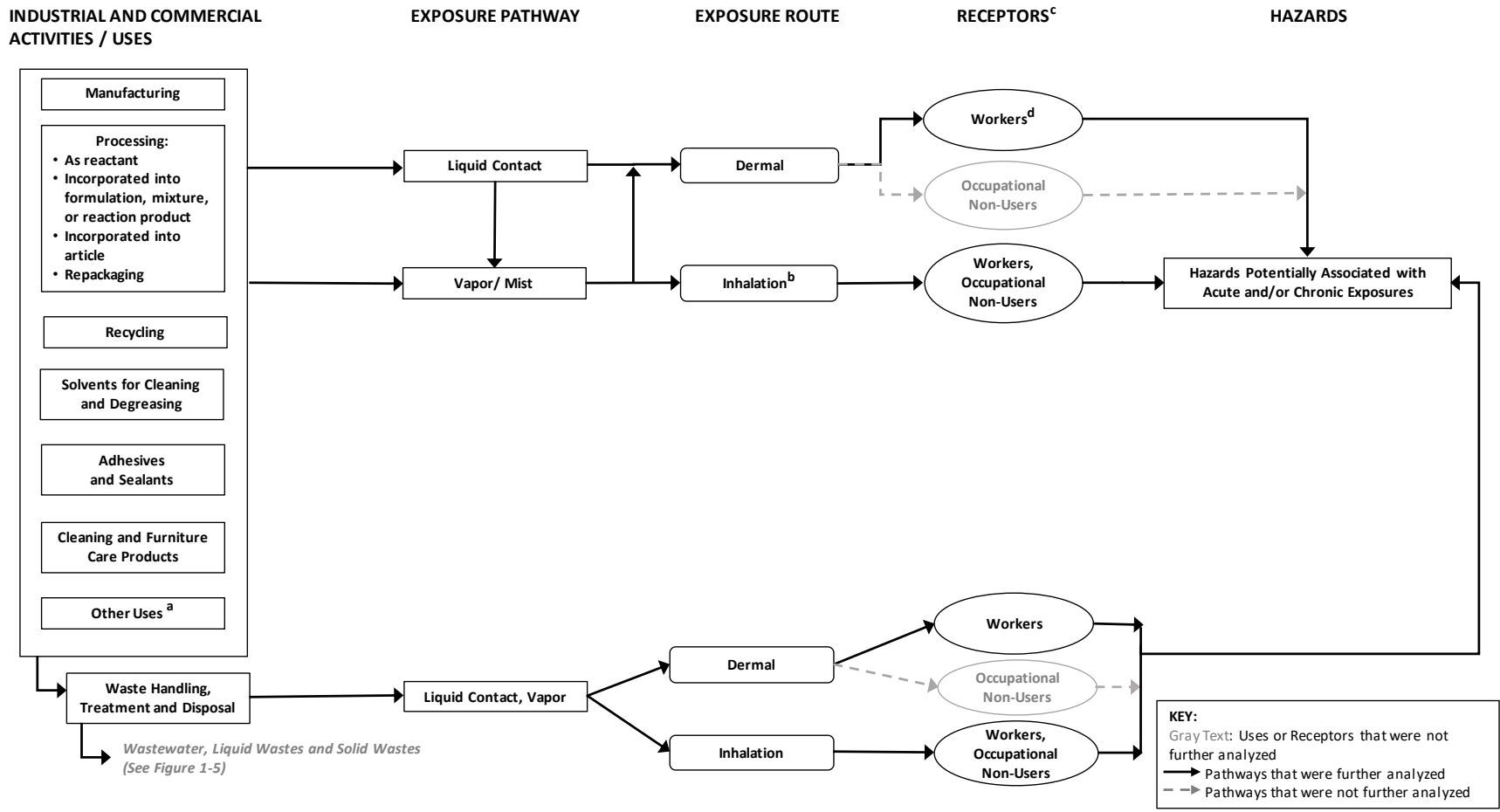


Figure 1-3. 1-BP Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of 1-BP that EPA analyzed in this risk evaluation.

^aSome products are used in both commercial and consumer applications. Additional uses of 1-BP are included in Table 1-4.

^b Exposure may occur through mists that deposit in the upper respiratory tract, however based on physical-chemical properties, mists of 1-BP will likely be rapidly absorbed in the respiratory tract or evaporate and were considered in the inhalation exposure assessment.

^cReceptors include potentially exposed or susceptible subpopulations.

^dEPA also considered the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

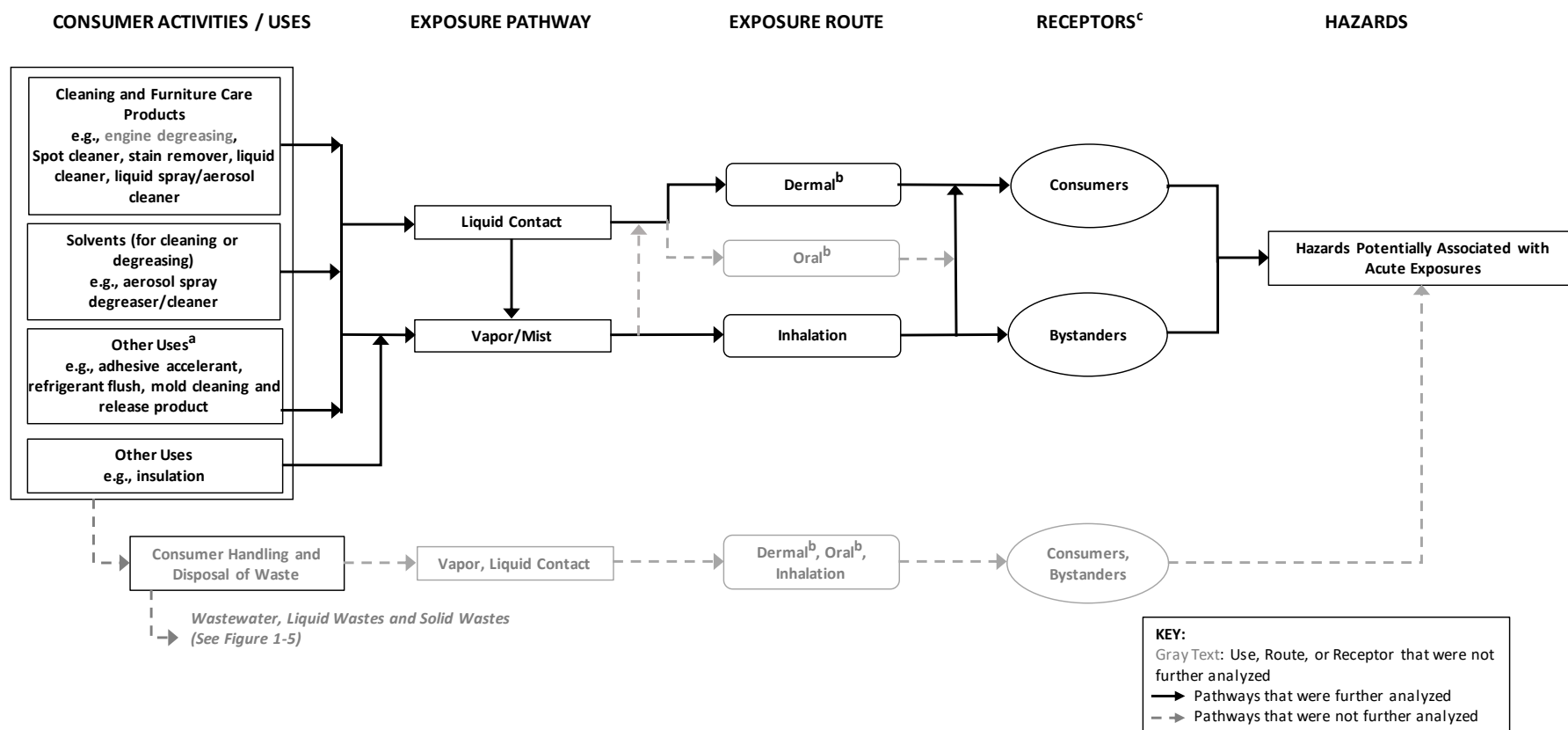


Figure 1-4. 1-BP Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of 1-BP that EPA analyzed in this risk evaluation.

^aSome products are used in both commercial and consumer applications. Additional uses of 1-BP are included in Table 1-4.

^b Dermal exposure may occur through skin contact with liquids; ingestion is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed.

^cReceptors include potentially exposed or susceptible subpopulations.

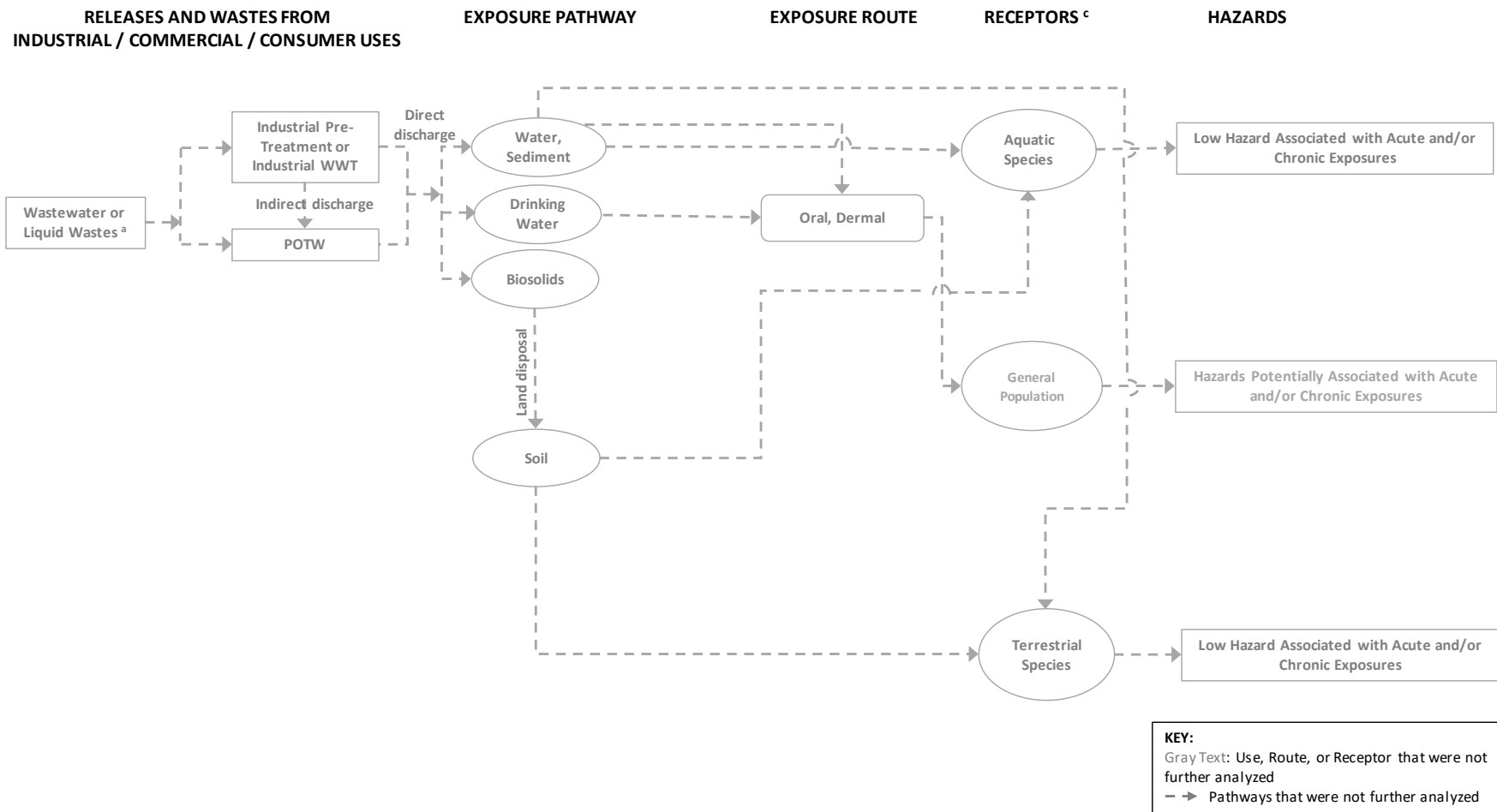


Figure 1-5. 1-BP Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The conceptual model presents the exposure pathways, exposure routes and hazards to environmental receptors from environmental releases and wastes of 1-BP that EPA analyzed in this risk evaluation.

^aIndustrial wastewater may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to publicly owned treatment works (POTW) (indirect discharge).

^bPresence of mist is not expected. Dermal and oral exposures are expected to be low.

^cReceptors 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 when making decision under Section 6 and to base decisions under Section 6 on the weight of 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 CFR 702.33).

To meet the TSCA science standards, EPA was guided by the 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 CFR 702.33).

EPA is implementing systematic review methods and approaches within the regulatory context of the amended TSCA. Although EPA will make an effort to adopt as many best practices as practicable from the systematic review community, EPA expects modifications to the process to ensure that the identification, screening, evaluation and integration of data and information can support timely regulatory decision making under the aggressive 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 different discipline-specific evidence supporting the risk evaluation (*e.g.*, environmental fate and transport; environmental release and occupational exposure; exposure to general population, consumers and environmental exposure; and environmental and human health hazard). 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 1-BP is described in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)), and the results of the title and abstract screening process were published in the *Strategy for Conducting Literature Searches for 1-BP (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, [EPA-HQ-OPPT-2016-0741-0047](#)).

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 considered 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”¹². Data sources that met the criteria were carried forward to the data evaluation stage. The inclusion and exclusion criteria for full text screening for 1-BP are available in Appendix F of the June 2018 Problem Formulation ([U.S. EPA, 2018c](#)).

Although EPA conducted a comprehensive search and screening process as described above, EPA made the decision to leverage the literature published in previous assessments¹³ when identifying relevant key and supporting data¹⁴ and information for developing the 1-BP risk evaluation. This is discussed in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)). In general, many of the key and supporting data sources were identified in the comprehensive *Strategy for Conducting Literature Searches for 1-BP (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, [EPA-HQ-OPPT-2016-0741-0047](#)). However, there were instances when EPA missed relevant references 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](#) document ([U.S. EPA, 2018a](#)). Other relevant key and supporting references were identified through targeted supplemental searches to support the analytical approaches and methods in the 1-BP risk evaluation (e.g., to locate specific information for exposure modeling) or to identify new data and information published after the date limits of the initial search.

EPA used previous chemical assessments to quickly identify relevant key and supporting information as a pragmatic approach to expedite the quality evaluation of the data sources, but many of those data sources were already captured in the comprehensive literature as explained above. EPA also considered newer information not taken into account by previous chemical assessments as described in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)). EPA then evaluated the confidence of the key and supporting data sources as well as newer information instead of evaluating the confidence of all the underlying evidence ever published on 1-BP fate and transport, environmental releases, environmental and human exposure and hazard potential. Such a comprehensive evaluation of all of the data and information published for 1-BP would be extremely labor intensive and could not be achieved under the TSCA statutory deadlines for most chemical substances especially those that have a data rich database. EPA also considered how

¹² 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.

¹³ Examples of existing assessments are EPA’s chemical assessments (e.g., previous work plan risk assessments, problem formulation documents), ATSDR’s Toxicological Profiles, EPA’s IRIS assessments and ECHA’s dossiers. This is described in more detail in the *Strategy for Conducting Literature Searches for 1-BP: Supplemental File for the TSCA Scope Document* ([U.S. EPA, 2017e](#))

¹⁴ Key and supporting data and information are those that support key analyses, arguments, and/or conclusions in the risk evaluation.

this evaluation of the key and supporting data and newer information would change the previous conclusions presented in the previous assessments.

Using this pragmatic approach, EPA evaluated the confidence of the key and supporting data sources as well as newer information instead of evaluating the confidence of all the underlying evidence published on 1-BP's fate and transport, environmental releases, environmental and human exposure and hazards. This allowed EPA to maximize 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 have an impact on the weight of the scientific evidence and ultimately the risk findings. The influential information (*i.e.*, key/supporting) came from a smaller pool of sources subject to the rigor of the TSCA systematic review process to ensure that the risk evaluation uses the best available science and the weight of the scientific evidence.

Figure 1-6 to Figure 1-9 depict the literature flow diagrams illustrating the results of this process for each scientific discipline-specific evidence supporting the risk evaluation. Each diagram provides the total number of references 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 criteria guiding the screening and data quality evaluation decisions.

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. 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 stages 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).

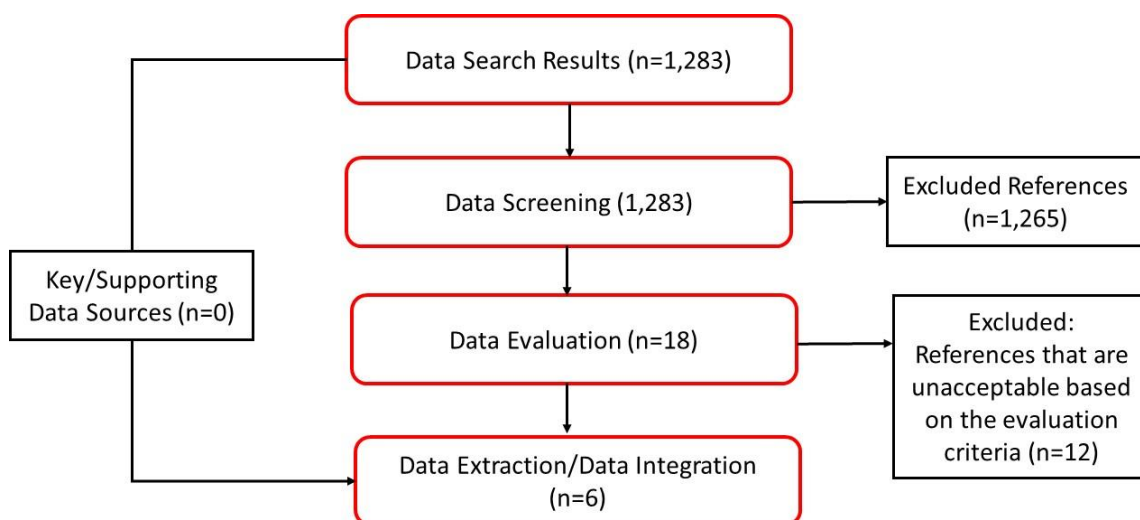


Figure 1-6. Literature Flow Diagram for Environmental Fate and Transport Data Sources

Note: Literature search results for the environmental fate and transport of 1-BP yielded 1,283 studies. Only the environmental fate and transport pathway for air was identified in the conceptual model. Other fate studies moving forward were used to inform general discussion of the environmental fate of 1-BP but were not used directly in the risk evaluation. 1,265 studies were determined to be off topic. The remaining 18 studies entered full text screening for the determination of relevance to the risk evaluation. All remaining studies were determined to be relevant and entered data evaluation. Twelve studies were deemed unacceptable based on the evaluation criteria for fate and transport studies and the remaining six studies were carried forward to data extraction.

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

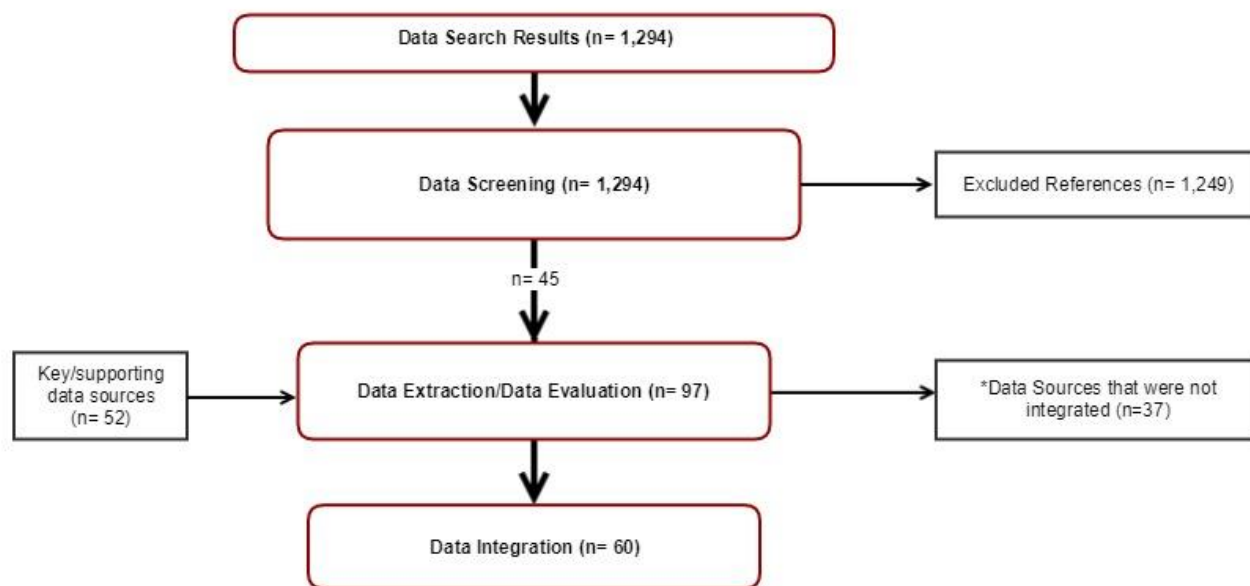


Figure 1-7. Literature Flow Diagram for Environmental Release and Occupational Exposure Data Sources

Note: Literature search results for environmental release and occupational exposure yielded 1,294 data sources. Of these data sources, 45 were determined to be relevant for the risk evaluation through the data screening process. In addition, EPA identified several data gaps and performed a supplemental, targeted search to fill these gaps (e.g., to locate information needed for exposure modeling). The supplemental search yielded 52 relevant data sources that bypassed the data screening step and were evaluated and extracted.

*The quality of data in these sources (n=37) 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. Sources that contain only environmental release data for the air pathway were evaluated but not integrated, because this pathway was determined to be out of scope during development of the risk evaluation. The data integration strategy for environmental release and occupational exposure data is discussed in Appendix K of the document titled "Final Risk Evaluation for 1-BP, Supplemental File: Information on Occupational Exposure Assessment (EPA, 2019f)."

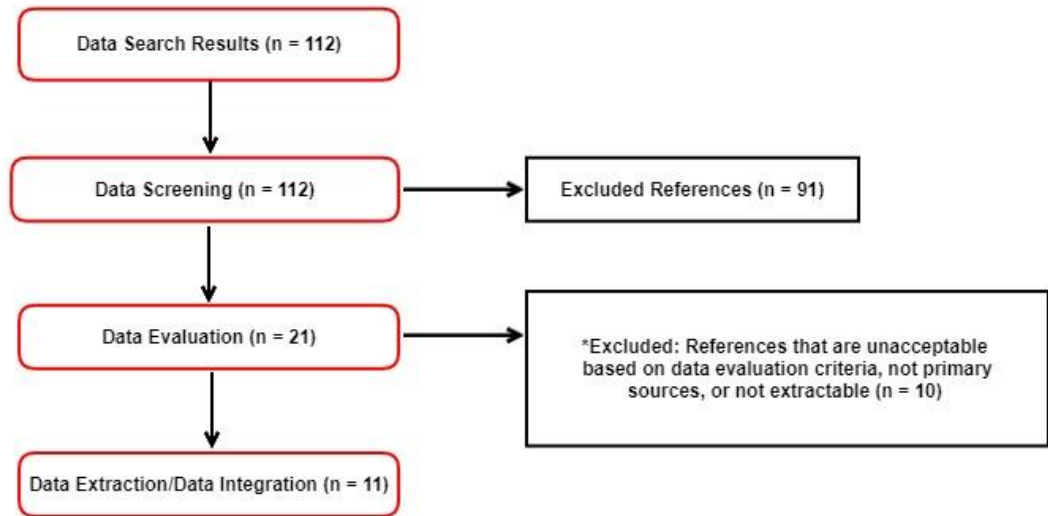


Figure 1-8. Literature Flow Diagram for Consumer and Environmental Exposure Data Sources

EPA conducted a literature search to determine relevant data sources for assessing exposures for 1-BP within the scope of the risk evaluation. This search identified 112 data sources. Of these, 91 were excluded during the screening of the title, abstract, and/or full text and 21 data sources were recommended for data evaluation. Following the evaluation process, 11 references were forwarded for further extraction and data integration.

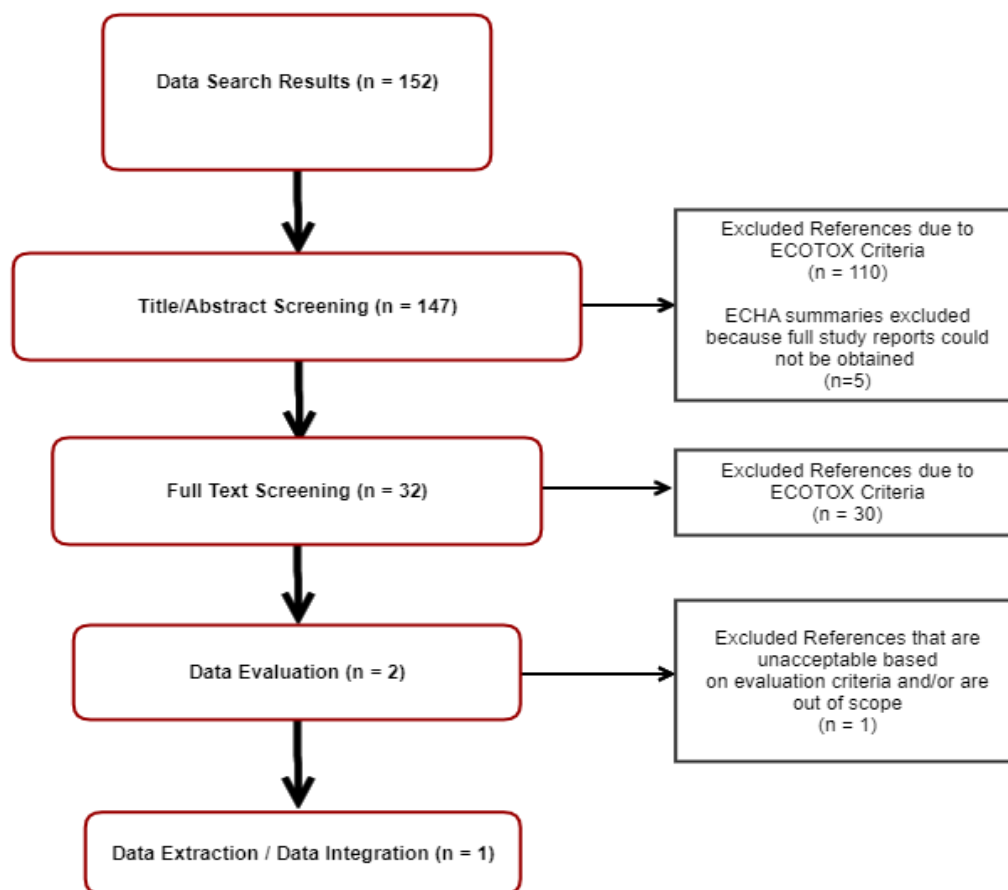


Figure 1-9. Literature Flow Diagram for Environmental Hazard Data Sources

Note: The environmental hazard data sources 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 references that were not relevant to the 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 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)).

The literature search process for environmental hazard data found 147 citations for 1-BP. At the title and abstract screening phase, 110 citations were excluded as off-topic using ECOTOX criteria. The remaining 32 citations underwent a more thorough full text screening using the same criteria to determine which citations should undergo data evaluation. Several studies were considered “out of scope” after the screening steps, and therefore excluded from data evaluation, due to the elimination of exposure pathways during the risk evaluation process. For data evaluation, EPA developed data quality evaluation criteria based on a combination of EPA’s ECOTOX criteria and the Criteria for Reporting and Evaluating Ecotoxicity Data (CRED). There were 2 citations that went to data evaluation. Only one study was used for data extraction/data integration.

5 environmental hazard studies were identified as summaries in the ECHA database for 1-BP. As the full study reports for these summaries could not be obtained by EPA, these were not evaluated during the data evaluation stage or utilized in the final risk evaluation. These citations were found independently from the ECOTOX process. During problem formulation, EPA made refinements to the conceptual models resulting in the elimination of the terrestrial exposure pathway from further analysis. Thus, environmental hazard data sources on terrestrial organisms were considered out of scope and excluded from data quality evaluation.

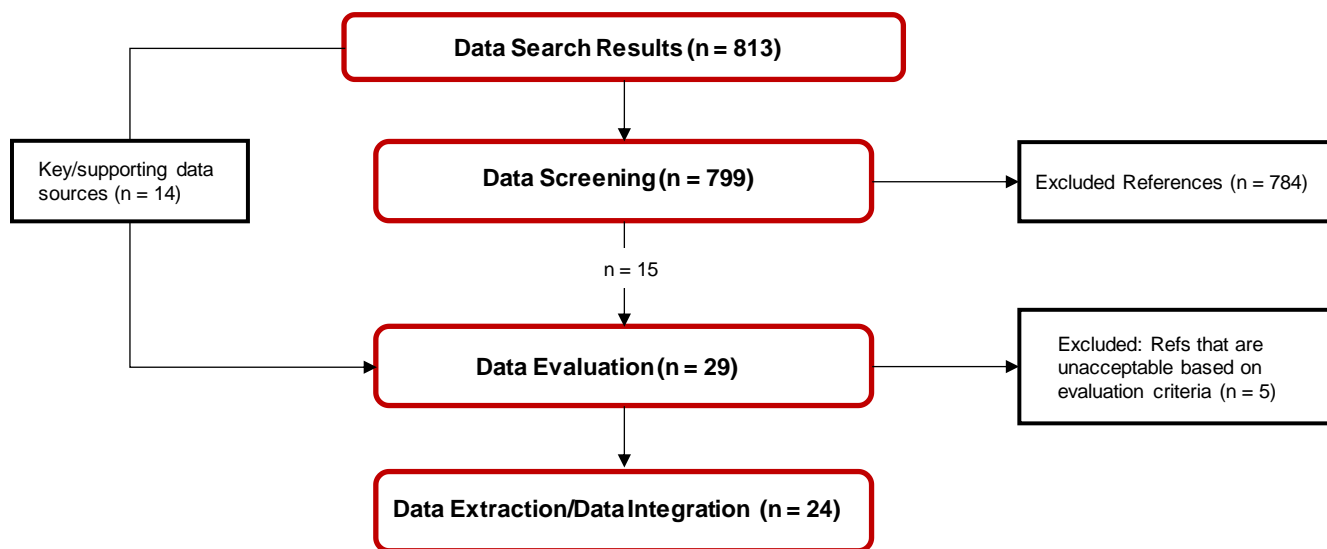


Figure 1-10. Literature Flow Diagram for Human Health Hazard Data Sources

Note: The literature search results for human health hazard of 1-BP yielded 813 studies. This included 14 key and supporting studies identified from previous EPA assessments. Of the 799 new studies screened for relevance, 784 were excluded as off topic. The remaining 15 new studies together with the 14 key and supporting studies entered data evaluation. Five studies were deemed unacceptable based on the evaluation criteria for human health hazard data sources and the remaining 24 studies were carried forward to data extraction/data integration. Additional details can be found in the *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)).

1.5.2 Data Evaluation

During the data evaluation stage, EPA assesses the quality of the data sources using the evaluation strategies and criteria described in Application of Systematic Review in TSCA Risk Evaluations ([U.S. EPA, 2018a](#)). For the data sources that passed full-text screening, EPA evaluated their quality and each data source received an overall confidence of high, medium, low or unacceptable.

The results of these data quality evaluations are provided in Sections 2.1 (Fate and Transport), 2.2 (Environmental Exposures), 2.3 (Human Exposures), 3.1 (Environmental Hazards) and 3.2 (Human Health Hazards). Additional information is provided in the appendices of the main document.

Supplemental files¹⁵ 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, relevancy, coherence and biological plausibility to make final conclusions regarding the weight of the scientific evidence. As stated in *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 available lines of evidence regarding 1-BP's chemical properties, environmental fate and transport properties, 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 influential information (*i.e.*, key and supporting data) that were found acceptable based on the data quality reviews as well as discussion of other scientific knowledge using the approach described in Section 1.5.1. The exposure section also describes whether aggregate or sentinel exposures to a chemical substance were considered under the conditions of use within the scope of the risk evaluation, and the basis for that consideration.

¹⁵ The supplemental files accompanying the risk evaluation are listed in Appendix B.

- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Updates to the Data Quality Criteria for Epidemiological Studies. ([EPA, 2019q](#)).
- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies. ([EPA, 2019l](#)).
- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation for Consumer Exposure ([EPA, 2019j](#)).
- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data. ([EPA, 2019m](#)).
- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data for Common Sources. ([EPA, 2019n](#)).
- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Studies. ([EPA, 2019k](#)).
- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies – Epidemiologic Studies. ([EPA, 2019p](#)).
- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies. EPA-HQ-OPPT-2019-0235 ([EPA, 2019o](#)).
- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction Tables for Environmental Fate and Transport Studies. ([EPA, 2019i](#)).
- Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction for Consumer Exposure ([EPA, 2019h](#)).

2 EXPOSURES

This section describes EPA's approach to assessing environmental and human exposures. First, the fate, transport, and releases of 1-BP into the environment are assessed; this information is integrated into an assessment of occupational, consumer, and environmental exposures for 1-BP. 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.

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

Following the inclusion of 1-BP on EPA's workplan list in 2012, EPA published a 2016 Draft Risk Assessment ([U.S. EPA, 2016c](#)) prior to passage of the Lautenberg Act amendments to TSCA. Since that time, EPA has published a Scope of the Risk Evaluation for 1-BP in 2017 ([Scope Document; EPA-HQ-OPPT-2016-0741-0049](#)), and Problem Formulation in 2018 ([U.S. EPA, 2018c](#)). EPA has incorporated the following refinements based on public comments and review of data since work began on 1-BP:

- Refined parameters for occupational exposure models;
- Expanded consumer uses evaluated for inhalation exposure; and
- Included evaluation for dermal exposure from industrial, commercial, and consumer use scenarios.

2.1 Fate and Transport

The environmental fate studies considered for this assessment are summarized in Table 2-1 and were supplemented by an updated literature search following Problem Formulation ([U.S. EPA, 2018c](#)).

2.1.1 Fate and Transport Approach and Methodology

EPA identified fate data for 1-BP through an extensive literature search, as described in EPA's *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)). Published and non-published data sources, including key and supporting studies identified in previous assessments, were evaluated during this process. EPA also relied heavily on the 2016 Draft Risk Assessment ([U.S. EPA, 2016c](#)) to inform the fate assessment for the final risk evaluation. EPA assessed the quality of a study based on the data quality criteria described in the Application of Systematic Review in TSCA Risk Evaluations ([U.S. EPA, 2018a](#)). Other fate estimates were based on modeling results from EPI Suite™ ([U.S. EPA, 2012b](#)), a predictive tool for physical-chemical and environmental fate properties. The data evaluation tables describing their review can be found in the supplemental document, Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies ([EPA, 2019l](#)).

The 1-BP environmental fate characteristics and physical-chemical properties used in fate assessment are presented in Table 2-1 and Table 1-1, respectively. EPA used EPI Suite™ estimations and reasonably available fate data to characterize the environmental fate and transport of 1-BP. As part of Problem Formulation ([U.S. EPA, 2018c](#)), EPA also analyzed the air, water, sediment, land application and biosolids pathways and determined no further analysis would be conducted on these pathways. The

results of the analyses are described in the Problem Formulation in June 2018 ([U.S. EPA, 2018c](#)) and presented again in Appendix C. Both this section and Appendix C may also cite other data sources as part of the reasonably available evidence on the fate and transport properties of 1-BP. EPA subjected these other data sources to the later phases of the systematic review process (*i.e.*, data evaluation and integration).

2.1.2 Summary of Fate and Transport

1-BP is a volatile liquid with high vapor pressure, high water solubility, and high mobility in soil. It is expected to exhibit low adsorption to soils and thus can migrate rapidly through soil to groundwater. 1-BP is slowly degraded by hydroxy radical oxidation when released to the atmosphere (half-life 9-12 days). Based on this estimated half-life in air, long range transport via the atmosphere is possible (see Appendix C). Volatilization and microbial degradation influence the fate of 1-BP when released to water, sediment, or soil. The vapor pressure of 1-BP is 110 mm Hg at 20°C, its water solubility is 2.45 g/L and its Henry's law constant is calculated as 7.3×10^{-3} atm-m³/mol. These physical-chemical properties input to the Volatilization from Water (WVol) model in EPISuite™ indicate that 1-BP will volatilize from a model river with a half-life on the order of an hour and from a model lake on the order four days. The Level III Fugacity model in EPA's EPISuite™ was used to estimate the steady state partitioning of 1-BP between air, water, soil and sediment. The model estimated that when 1-BP is continuously released to water, 80% of the mass would remain in water and 19% in air due in part to its water solubility. Biotic and abiotic degradation rates ranging from days to months have been reported ([U.S. EPA, 2012c](#); [Sakuratani et al., 2005](#); [Mabey and Mill, 1978](#)). Intermittent releases of 1-BP are not expected to result in long-term presence in the aquatic compartment due to volatilization and biodegradation.

1-BP does not meet criteria to be classified as persistent or bioaccumulative ([Federal Register, 1999](#)). Biotic and abiotic degradation studies have not shown this substance to be persistent (overall environmental half-life of less than two months). No measured bioconcentration studies for 1-BP are available. An estimated bioaccumulation factor of 12 ([U.S. EPA, 2012b](#)) suggests that bioconcentration and bioaccumulation in aquatic organisms are low (*i.e.*, bioconcentration/bioaccumulation factors of less than 1000).

Table 2-1. Summary of Environmental Fate and Transport Properties

Property or Endpoint	Value ^a	References	Study Quality
Direct photodegradation	Not expected to undergo direct photolysis	HSDB (2017)	High
Indirect photodegradation	9-12 days (estimated for atmospheric degradation)	EPI Suite Version 4.10 (U.S. EPA, 2012b)	High
Hydrolysis half-life	26 days	U.S. EPA (2016c) (Mabey and Mill, 1978)	Low
Biodegradation	70% in 28 days (OECD 301C)	(Sakuratani et al., 2005)	Medium
Bioconcentration factor (BCF)	11 (estimated)	EPISuite Version 4.10 (U.S. EPA, 2012b)	High

Property or Endpoint	Value ^a	References	Study Quality
Bioaccumulation factor (BAF)	12 (estimated)	EPISuite Version 4.10 (U.S. EPA, 2012b)	High
Organic carbon:water partition coefficient (Log K _{oc})	1.6 (estimated)	EPISuite Version 4.10 (U.S. EPA, 2012b)	High
^a Measured unless otherwise noted			

2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport

The EPI Suite™ model (Version 4.1) ([U.S. EPA, 2012b](#)) was used to estimate several environmental fate properties for 1-BP in the absence of data (see Table 2-1). A full discussion of the performance of the individual property estimation methods used in EPISuite is available in the EPI Suite™ help files. No data on the bioconcentration or bioaccumulation potential of 1-BP was found and in the absence of measured values, bioconcentration and bioaccumulation factors were estimated. These properties were used to inform decisions on whether 1-BP has the potential to build up in aquatic and terrestrial species via exposure to water and diet and whether fish ingestion pathways of exposure should be included in the final risk evaluation. EPA compared measured BCF values for a series of halogenated ethanes and propanes and EPI Suite™ estimated BCF values. The largest observed error for BCF estimation was 0.56 log units and none of the chemicals had measured Log BCF values greater than 1.6. Thus, even if the estimate for 1-BP was subject to the maximum observed error, its log BCF would be expected to fall in the range of 0.5 to 1.5, indicating low bioconcentration potential (BCF <1000).

2.2 Environmental Exposures

2.2.1 Environmental Exposures Approach and Methodology

The manufacturing, processing, use and disposal of 1-BP can result in releases to the environment. Environmental exposures via air, water, sediment, biosolids and soil are all discussed in the environmental risk characterization section (Section 4.1). The predominance of these exposures is via the air pathway as reported releases to water was limited to 5 pounds in 2016 (See Appendix H). EPA did not conduct additional analysis of exposures to aquatic or terrestrial exposures beyond what was presented in the 2018 Problem Formulation ([U.S. EPA, 2018c](#)).

As described in the Problem Formulation ([U.S. EPA, 2018c](#)), an aquatic exposure assessment was conducted using 2016 TRI release information ([U.S. EPA, 2017f](#)) to model predicted surface water concentrations near discharging facilities. To examine whether near-facility surface water concentrations could approach aquatic concentrations of concern (COC) for 1-BP, EPA employed a conservative approach, using available modeling tools and data to estimate near-facility surface water concentrations resulting from reported releases of 1-BP to surface water. High-end surface water concentrations (*i.e.*, those obtained assuming low receiving water body stream flows) from all [E-FAST 2014](#) runs ranged from 0.19 µg/L to 77.9 µg/L. The E-FAST results were compared to the acute concentrations of concern of 13,460 µg/L (96-hour fish LC₅₀ ([Geiger et al., 1988](#))) and 3,640 µg/L (algae EC₅₀ based on ECOSAR modeling) and the chronic concentrations of concern of 673 µg/L (fish chronic value

estimated from Geiger (1988)) and 470 µg/L (daphnia ChV based on ECOSAR modeling) (see Table 4-1). This aquatic exposure analysis and additional details about the approach and results are presented in Appendix H. The analysis and determination of risk are presented in the risk characterization and risk determination sections, respectively.

2.3 Human Exposure Assessment

2.3.1 Occupational Exposures

EPA assessed occupational exposures following the analysis plan published in the June 2018 Problem Formulation (U.S. EPA, 2018c). Specific assessment methodology is described in further detail below for each type of assessment. Additional details of EPA’s occupational exposure assessment can be found in the *1-BP Supplemental File: Supplemental Information on Occupational Exposure Assessment* (EPA, 2019f). Table 2-2 presents a crosswalk of the industrial and commercial conditions of use (see Table 1-4) and the section of the risk evaluation in which occupational exposure for that use is assessed.

For the purpose of this assessment, EPA assumes workers and occupational non-users (ONU) are men and women of reproductive age (16 or older), including adolescents (16 to <21 years old). EPA guidance¹⁶ defines children as 0 to <21 years old and workers can be as young as 16 years old. Therefore, EPA defines adolescent workers as 16 to <21 years old. EPA also considers exposure to children who may be present at the workplace, such as small family-owned dry cleaners, an occupational exposure scenario recommended for assessment from the peer review of the 2016 Draft Risk Assessment of 1-BP (U.S. EPA, 2016c).

Table 2-2. Crosswalk of Subcategories of Use Listed in the Problem Formulation Document to Occupational Conditions of Use Assessed in the Final Risk Evaluation

Life Cycle Stage	Category ^a	Subcategory ^b	Assessed Condition of Use
Manufacture	Domestic manufacture	Domestic manufacture	Section 2.3.1.5 – Manufacture
	Import	Import	Section 2.3.1.6 – Import
Processing	Processing as a reactant	Intermediate in all other basic inorganic chemical manufacturing, all other basic organic chemical manufacturing, and pesticide, fertilizer and other agricultural chemical manufacturing	Section 2.3.1.7 – Processing as a Reactant

¹⁶ U.S. EPA. Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants (Final). EPA/630/P-03/003F. Available online at:

<https://www.epa.gov/risk/guidance-selecting-age-groups-monitoring-and-assessing-childhood-exposures-environmental>

Life Cycle Stage	Category ^a	Subcategory ^b	Assessed Condition of Use
Processing	Processing - incorporating into formulation, mixture or reaction product	Solvents for cleaning or degreasing in manufacturing of: <ul style="list-style-type: none"> - all other chemical product and preparation - computer and electronic product - electrical equipment, appliance and component - soap, cleaning compound and toilet preparation - services 	Section 2.3.1.8 – Processing – Incorporation into Formulation, Mixture, or Reaction Product
	Processing - incorporating into articles	Solvents (which become part of product formulation or mixture) in construction	Section 2.3.1.9 – Processing – Incorporation into Articles
	Repackaging	Solvent for cleaning or degreasing in all other basic organic chemical manufacturing	Section 2.3.1.10 – Repackaging
	Recycling	Recycling	Section 2.3.1.21 – Disposal, Recycling
Distribution in commerce	Distribution	Distribution	Not assessed as a separate operation; exposures/releases from distribution are considered within each condition of use.
Industrial/ commercial use	Solvent (for cleaning or degreasing)	Batch vapor degreaser (<i>e.g.</i> , open-top, closed-loop)	Section 2.3.1.11 – Batch Vapor Degreaser (Open-Top) Section 2.3.1.12 – Batch Vapor Degreaser (Closed-Loop)
		In-line vapor degreaser (<i>e.g.</i> , conveyORIZED, web cleaner)	Section 2.3.1.13 – In-line Vapor Degreaser
		Cold cleaner	Section 2.4.1.13 – Cold Cleaner
		Aerosol spray degreaser/cleaner	Section 2.3.1.15 – Aerosol Spray Degreaser/Cleaner
	Adhesives and sealants	Adhesive chemicals - spray adhesive for foam cushion manufacturing and other uses	Section 2.3.1.18 – Adhesive Chemicals (Spray Adhesives)
	Cleaning and furniture care products	Dry cleaning solvent	Section 2.3.1.16 – Dry Cleaning

Life Cycle Stage	Category ^a	Subcategory ^b	Assessed Condition of Use
		Spot cleaner, stain remover	Section 2.3.1.17 – Spot Cleaner, Stain Remover
		Liquid cleaner (<i>e.g.</i> , coin and scissor cleaner)	Section 2.3.1.20 – Other Uses
		Liquid spray/aerosol cleaner	Section 2.3.1.20 – Other Uses
Industrial/ commercial use	Other uses	Arts, crafts and hobby materials - adhesive accelerant	Section 2.3.1.20 – Other Uses
		Automotive care products - engine degreaser, brake cleaner	Section 2.3.1.15 – Aerosol Spray Degreaser/Cleaner
		Anti-adhesive agents - mold cleaning and release product	Section 2.3.1.20 – Other Uses
		Building/construction materials not covered elsewhere - insulation	Section 2.3.1.19 – THERMAX™ Installation
		Electronic and electronic products and metal products	Section 2.3.1.20 – Other Uses
		Functional fluids (closed systems) - refrigerant	
		Functional fluids (open system) - cutting oils	
		Other - asphalt extraction	
		Other - laboratory chemicals	
Temperature indicator – coatings			
Disposal (Manufacturing, Processing, Use)	Disposal	Municipal waste incinerator Off-site transfer	Section 2.3.1.21 – Disposal, Recycling
		Municipal waste incinerator	
		Off-site waste transfer	

^a These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent conditions of use of 1-BP in industrial and/or commercial settings.

^b These subcategories reflect more specific uses of 1-BP.

2.3.1.1 Number of Sites and Workers Approach and Methodology

Where available, EPA determined the number of sites and workers using data reported under the Chemical Data Reporting (CDR) Rule. The CDR Rule, issued under the TSCA, requires manufacturers and importers to report certain information on the chemicals they produce domestically or import into the United States. For the 2016 CDR cycle, manufacturers and importers of chemicals listed on the TSCA inventory were required to report if their production volume exceeded 25,000 pounds at a single site during any of the calendar years 2012, 2013, 2014 or 2015.

For conditions of use where CDR data are insufficient, EPA determined the number of sites that manufacture, process, and use 1-BP using reasonably available market data and data from Section 3 of the Toxics Release Inventory (TRI), “Activities and Uses of the Toxic Chemical at the Facility.” In addition, EPA determined the number of workers by analyzing Bureau of Labor Statistics (BLS) and U.S. Census data using the methodology described in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019f](#)).

Table 2-3 presents the confidence rating of data that EPA used to estimate number of sites and workers. Table 2-4 presents the estimated number of sites and workers in the occupational exposure scenarios assessed for 1-BP. Details of the estimates are available in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019f](#)).

Table 2-3. Data Evaluation of Sources Containing General Facility Estimates

Source Reference	Data Type	Confidence Rating	Condition of Use
(U.S. EPA, 2017a)	Number of Sites and Workers	High	Manufacture, Import, Processing as a Reactant, Processing – Incorporation into Formulation
(U.S. BLS, 2016)	Number of Workers	High	Processing – Incorporation into Articles, all conditions of use involving industrial and commercial uses of 1-BP, Disposal
(Bureau, 2015)	Number of Workers	High	
(IRTA, 2016)	Number of Sites	Medium	Batch Vapor Degreaser (Closed-Loop), In-line Vapor Degreaser
(U.S. EPA, 2013c)	Number of Sites	Medium	Aerosol Spray Degreaser/Cleaner
(Enviro Tech International, 2017)	Number of Sites	High	Dry Cleaning
(CDC, 2016)	Number of Sites	Medium	Batch Vapor Degreaser (Open-Top), Adhesive Chemicals (Spray Adhesive)
(U.S. EPA, 2017b, 2016b)	Number of Sites	Medium	Disposal

Table 2-4. Estimated Number of Sites and Workers in the Assessed Occupational Exposure Scenarios for 1-BP

Occupational Exposure Scenario	Number of Sites	Number of Workers	Number of ONUs
Manufacture	2	35 - 73	*
Import	8	31 - 103	*
Processing as a Reactant	3 - 27	30 - 72	*
Processing – Incorporation into Formulation, Mixture, or Reaction Product	33 - 99	220 - 1,046	*
Processing – Incorporation into Articles	1	15	4
Repackaging	<10	10 - <25	*

Batch Vapor Degreaser (Open-Top)	500 – 2,500	3,200 – 16,000 ^	1,500 – 7,300 ^
Batch Vapor Degreaser (Closed-Loop)	100	650 ^	290 ^
In-line Vapor Degreaser (ConveyORIZED)	800	5,200 ^	2,300 ^
Cold Cleaner	Not available +		
Aerosol Spray Degreaser / Cleaner	1,000 – 5,000	2,200 – 11,000 ^	240 – 1,200 ^
Dry Cleaning; Spot Cleaner, Stain Remover	8	24	8
Adhesive Chemicals (Spray Adhesives)	100 – 280	550 – 1,500 ^	950 – 2,700 ^
THERMAX™ Installation	Not available +		
Other Uses	Not available +		
Disposal, Recycling	>4	>49	>18

* - Data did not distinguish ONUs from workers.

^ - Values rounded to 2 significant digits.

+ - EPA does not have reasonably information to determine the number of sites, workers, and ONUs for this scenario.

2.3.1.2 Inhalation Exposures Approach and Methodology

To assess inhalation exposure, EPA reviewed reasonably available exposure monitoring data and mapped them to specific conditions of use. Monitoring data used in the occupational exposure assessment include data collected by government agencies such as OSHA and NIOSH, and data found in published literature. For each exposure scenario and worker job category (“worker” or “occupational non-user”), where available, EPA provided results representative of *central tendency* and *high-end* exposure levels. For datasets with six or more data points, central tendency and high-end exposures were estimated using the 50th and 95th percentile value from the observed dataset, respectively. For datasets with three to five data points, the central tendency and high-end exposures were estimated using the median and maximum values.¹⁷ For datasets with two data points, the midpoint and the maximum value were presented. Finally, datasets with only one data point were presented as-is. A dataset comprises the combined exposure monitoring data from all studies applicable to that condition of use.

EPA assumes workers are those who directly handle 1-BP at the facility. Occupational non-users are those who do not directly handle 1-BP but perform work in an area where the chemical is present.

For exposure assessment, where reasonably available, personal breathing zone (PBZ) monitoring data were used to determine the time-weighted average (TWA) exposure concentration. EPA evaluated monitoring data using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). The data are then integrated based upon the strength of the evidence in accordance with the Data Integration Strategy for occupational exposure assessment described in Appendix K of the *Supplemental Information on Occupational Exposure Assessment* (EPA,

¹⁷ If the median value is not available, EPA may use the mean (arithmetic or geometric), mode, or midpoint values of a distribution to represent the central tendency scenario.

[2019f](#)). All occupational inhalation exposure monitoring data integrated into this risk evaluation have either a “high” or “medium” confidence rating, as shown in Table 2-5.

For several conditions of use, EPA modeled exposure in occupational settings. The models were used to either supplement existing exposure monitoring data or to provide exposure estimates where measured data are unavailable. The inhalation exposure models used to assess vapor degreasing, cold cleaning, aerosol degreasing, dry cleaning, and spot cleaning conditions of use were previously developed for, and peer reviewed as part of the [2016 Draft Risk Assessment \(U.S. EPA, 2016c\)](#), and have been subsequently refined to address peer review comments.

Measured or modeled TWA exposure concentrations are then used to calculate the Acute Concentration (AC), Average Daily Concentrations (ADC) and Lifetime Average Daily Concentration (LADC) using the approach and equations described in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019f](#)). In general, AC and ADC were based on a full work-week basis, 8 hr/day and 260 days/year. Therefore, for most OES they are identical. For risk estimation of developmental toxicity endpoints however, Points of Departure (PODs) are identical for acute and chronic exposure scenarios (Section 3.2.8) based on a single workday basis (8hr/day) and ADC is adjusted to account for the number of working days per year out of 365.

Table 2-5. Data Evaluation of Sources Containing Occupational Exposure Data

Source Reference	Data Type	Confidence Rating	Condition of Use
(OSHA, 2013a)	PBZ Monitoring	High	Manufacture
(Enviro Tech International, 2020)	PBZ Monitoring	High	Processing -- Incorporation into Formulation
(Reh and Nemhauser, 2001)	PBZ Monitoring	High	Batch Vapor Degreaser
(Miller, 2019)	PBZ Monitoring	High	Batch Vapor Degreaser
(OSHA, 2013b)	PBZ Monitoring	High	Batch Vapor Degreaser, Spot Cleaner, Adhesive Chemicals (Spray Adhesive), Cold Cleaner
(OSHA, 2019)	PBZ Monitoring	High	Batch Vapor Degreaser, Spot Cleaner
(U.S. EPA, 2006b)	PBZ Monitoring	Medium	Batch Vapor Degreaser, Aerosol Spray Degreaser/Cleaner
(Eisenberg and Ramsey, 2010)	PBZ Monitoring	High	Dry Cleaning
(Blando et al., 2010)	PBZ Monitoring	High	Dry Cleaning
(NIOSH, 2002b)	PBZ Monitoring	High	Adhesive Chemicals (Spray Adhesive)
(Reh et al., 2002)	PBZ Monitoring	High	Adhesive Chemicals (Spray Adhesive)
(NIOSH, 2003b)	PBZ Monitoring	High	Adhesive Chemicals (Spray Adhesive)

2.3.1.3 Consideration of Engineering Control and Personal Protective Equipment

OSHA requires and NIOSH recommends that employers utilize the hierarchy of controls to address hazardous exposures in the workplace. The hierarchy of controls strategy outlines, in descending order of priority, the use of elimination, substitution, engineering controls, administrative controls, and lastly personal protective equipment (PPE). The hierarchy of controls prioritizes the most effective measures first which is to eliminate or substitute the harmful chemical (*e.g.*, use a different process, substitute with a less hazardous material), thereby preventing or reducing exposure potential. Following elimination and substitution, the hierarchy recommends engineering controls to isolate employees from the hazard, followed by administrative controls, or changes in work practices to reduce exposure potential (*e.g.*, source enclosure, local exhaust ventilation (LEV) systems). Administrative controls are policies and procedures instituted and overseen by the employer to protect worker exposures. As the last means of control, the use of PPE (*e.g.*, respirators, gloves) is recommended, when the other control measures cannot reduce workplace exposure to an acceptable level. The impact of respirator use on worker exposure is addressed in Section 4.2, Human Health Risk.

OSHA’s Respiratory Protection Standard (29 CFR 1910.134) provides a summary of respirator types by their assigned protection factor (APF). OSHA defines APF to mean: the workplace level of respiratory protection that a respirator or class of respirators is expected to provide to employees when the employer implements a continuing, effective respiratory protection program according to the requirements of OSHA’s Respiratory Protection Standard. If respirators are necessary in atmospheres that are not immediately dangerous to life or health, workers must use NIOSH-certified air-purifying respirators or NIOSH-approved supplied-air respirators with the appropriate APF. Respirators that meet these criteria include air-purifying respirators with organic vapor cartridges. Respirators must meet or exceed the required level of protection listed in Table 2-6. Based on the APF, inhalation exposures may be reduced by a factor of 5 to 10,000 if respirators are properly worn and fitted.

Table 2-6. Assigned Protection Factors for Respirators in OSHA Standard 29 CFR 1910.134

Type of Respirator	Quarter Mask	Half Mask	Full Facepiece	Helmet/Hood	Loose-fitting Facepiece
1. Air-Purifying Respirator	5	10	50	-	-
2. Power Air-Purifying Respirator (PAPR)	-	50	1,000	25/1,000	25
3. Supplied-Air Respirator (SAR) or Airline Respirator	-	-	-	-	-
• Demand mode	-	10	50	-	-
• Continuous flow mode	-	50	1,000	25/1,000	25
• Pressure-demand or other positive-pressure mode	-	50	1,000	-	-

Type of Respirator	Quarter Mask	Half Mask	Full Facepiece	Helmet/Hood	Loose-fitting Facepiece
4. Self-Contained Breathing Apparatus (SCBA)	-	-	-	-	-
• Demand mode	-	10	50	50	-
• Pressure-demand or other positive-pressure mode (e.g., open/closed circuit)	-	-	10,000	10,000	-

Source: 29 CFR 1910.134(d)(3)(i)(A)

NIOSH and the U.S. Department of Labor’s Bureau of Labor Statistics (BLS) conducted a voluntary survey of U.S. employers regarding the use of respiratory protective devices between August 2001 and January 2002 ([NIOSH, 2001](#)). For additional information, please refer to [Memorandum_NIOSH_BLS Respirator Usage in Private Sector Firms. Docket: EPA-HQ-OPPT-2019-0500].

2.3.1.4 Dermal Exposures Approach and Methodology

Although the inhalation pathway is expected to be the primary exposure for 1-BP, dermal exposure may be important in contributing to the overall exposure. EPA assessed dermal exposure to workers using the *Dermal Exposure to Volatile Liquids Model* (modified version of the peer reviewed *EPA/OPPT 2-Hand Dermal Exposure to Liquids Model*) ([U.S. EPA, 2013a](#)). The model estimates 0.29 percent dermal absorption for non-occluded exposures based on measurements from a 2011 *in vitro* dermal penetration study of 1-BP conducted by Frasch et al. ([2011](#)). The report presents several occupational dermal exposure scenarios, accounting for the potential for evaporation and glove use. The dermal exposure assessment is described in more detail in Section 2.3.1.23.

The occupational dermal exposure model shares a common underlying methodology as the consumer dermal exposure model in Section 2.3.2 but uses different parametric approaches due to different data availability and assessment needs. For example, the occupational approach accounts for glove use using protection factors, while the consumer approach does not consider glove use since consumers are not expected to always use gloves, or use gloves constructed with appropriate materials. The consumer approach factors in time because the duration of product use activities in consumer scenarios have been better characterized, while duration of dermal exposure times for different occupational activities across various workplaces are often not known.

2.3.1.5 Manufacture

Process Descriptions

1-BP is produced by reacting n-propyl alcohol with hydrogen bromide and then removing the excess water that forms in the process ([NTP, 2013b](#)). The reaction product may then be distilled, neutralized with sodium hydrogen carbonate, stored, and packaged ([Ichihara et al., 2004a](#)). The purity of the final product may range from 96 percent ([Li et al., 2010](#)) to over 99.9 percent ([OSHA, 2013a](#)).

The manufacturing process may be either batch or continuous. Based on a site visit in 2013 conducted by PEC, Icarus Environmental, and OSHA representatives, one major U.S. manufacturer of 1-BP operates a continuous, closed production process for 24 hours per day and 7 days per week ([OSHA, 2013a](#)).

Assessment of Inhalation Exposure Based on Monitoring Data

1-BP exposure monitoring data were identified for one manufacturing facility in the U.S. At this facility, workers were observed to spend most of their time in a control room monitoring the production process via a computerized system. QC samples are taken and analyzed inside a laboratory fume hood, and in some cases, in a nitrogen purge dry box. Product loading is controlled using a computerized system; smart-hoses and a vent line are used to minimize leaks and to capture vapors generated during loading. At this facility, employees wear safety glasses, nitrile gloves¹⁸, and steel toe shoes when performing product sampling and laboratory analysis. In addition, operators wear a full chemical suit¹⁹ during truck loading, including a full-face respirator equipped with organic vapor cartridges ([OSHA, 2013a](#)).

Table 2-7 presents the exposure levels from an OSHA site visit to this facility. The purpose of the site visit was to collect information on 1-BP production processes, engineering controls, and potential exposures. OSHA performed personal sampling on one operator during the day shift, one operator during the night shift, and one laboratory technician; the company also collected simultaneous samples for result comparison and verification. EPA used the TWA results to assess worker exposures; EPA assumed the TWA exposures approximate 8-hr TWA because actual sampling time ranged from 429 to 449 minutes (7.2 to 7.5 hour). In the table, the high-end exposure value represents the maximum TWA exposure among the three workers sampled, and the central tendency value represents the median exposure. Exposure was highest during truck loading, which occurs once every 24 hours. The operator wore a full-face respirator during this activity ([OSHA, 2013a](#)).

Additional monitoring data from a Chinese manufacturing facility were identified during systematic review and available in Ichihara et al. ([Ichihara et al., 2004a](#)). None of the workers surveyed at this facility wore PPE, and work practices at this facility may not be representative of U.S. operations. Therefore, data from this study were not integrated into the assessment.

Table 2-7. Summary of 8-hr 1-BP TWA Exposures (AC, ADC and LADC) for Manufacture Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	Central tendency (Median)	High-end (Max)	Central tendency (Median)	High-end (Max)		
Worker ^a	0.09	0.27	0.04	0.14	3	High

¹⁸ Nitrile is not a recommended glove material for protection against 1-BP according to the OSHA/NIOSH Hazard Alert ([OSHA, 2013c](#)).

¹⁹ Chemical resistant pants and jacket with hood, steel-toed rubber boots, chemical resistant gloves, and full-face respirator equipped with organic vapor cartridges.

Source: ([OSHA, 2013a](#))

AC = Acute Concentration; ADC = Average Daily Concentration and LADC = Lifetime Average Daily Concentration.

a – Because OSHA and the company took simultaneous samples, two sets of exposure monitoring data are available for each worker. For the same worker, EPA used the higher of the two TWA exposure results. For the lab technician and the day shift operator, EPA used company results (OSHA experienced a pump malfunction while performing sampling on the lab technician, and OSHA results for the day shift operator were below the reporting limit of 0.007 ppm of OSHA’s sampling and analytical method PV2061). For the night shift operator, EPA used OSHA results. The workers worked 12-hour shifts but were not exposed to 1-BP for the entire shift; exposure data are available as 8-hr TWA exposures.

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data collected at workplaces directly applicable to this condition of use. The data were obtained from one of only two domestic manufacturing facilities and were determined to have a “high” confidence rating through EPA’s systematic review process. Specifically, the data were determined to be highly reliable, representative in geographic scope, and reflective of current operations. The source also provides complete metadata including sample type, sample duration, and exposure frequency.

The three data points come from a detailed site visit report and consider all sources of exposure at that manufacturing facility. EPA has a high level of confidence in the assessed exposures based on the strength of the monitoring data.

2.3.1.6 Import

Process Descriptions

Commodity chemicals such as 1-BP may be imported into the United States in bulk via water, air, land, and intermodal shipments ([Kane, 2015](#)). These shipments take the form of oceangoing chemical tankers, railcars, tank trucks, and intermodal tank containers. Chemicals shipped in bulk containers may be repackaged into smaller containers for resale, such as drums or bottles. The type and size of container will vary depending on customer requirement. In some cases, QC samples may be taken at import sites for analyses. Some import facilities may only serve as storage and distribution locations, and repackaging/sampling may not occur at all import facilities.

1-BP may be imported neat or as a component in a formulation. In the 2016 CDR, most companies reported importing 1-BP at concentrations greater than 90 percent; one company reported importing a formulation containing 1 to 30 percent 1-BP.

Assessment of Inhalation Exposure Based on Modeling

EPA has not identified exposure monitoring data for import. Therefore, EPA assessed exposure using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model*. Based on data reported in the 2016 CDR, the model assumes 1-BP is present at 30 and 100 percent concentration in the import formulation for the central tendency and high-end exposure scenario, respectively. The model provides inhalation exposure estimates to volatile liquid chemicals during outdoor loading and unloading activities at an industrial facility. The model accounts for the emissions of saturated air containing the chemical of interest that remains in the loading arm, transfer hose, and related equipment, and emissions from equipment leaks from processing units such as pumps, seals, and valves. The model assumes industrial facilities use a vapor recovery system to minimize air emissions, such that vapor

losses from displacement of saturated air inside the container is mitigated by the use of such systems. See the *Supplemental Information on Occupational Exposure Assessment* (EPA, 2019f) on model documentation, including detailed description of the model equations and parameters.

For the central tendency scenario, the model assumes the use of a 12-foot transfer hose with two-inch diameter, with an average outdoor wind speed of 9 miles per hour (mph). For the high-end scenario, the model assumes the use of an engineered loading system, such as a loading arm, and that the operation occurs outdoor with a wind speed of 5 mph. For the purpose of this assessment, loading/unloading event is assumed to occur once per work shift. Combining published EPA emission factors and engineering calculations with EPA *Mass Balance Inhalation Model* (peer reviewed), this model estimates central tendency and high-end exposure concentrations for chemical unloading scenarios at industrial facilities. As shown in Table 2-8, the central tendency and high-end exposures are 0.004 ppm and 0.06 ppm as 8-hr TWA, respectively. The model does not estimate exposure levels for ONUs.

Table 2-8. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Import Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	3.83E-3	5.67E-2	1.52E-3	2.91E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgement to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, the model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker exposure. Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.7 Processing as a Reactant

Process Descriptions

Processing as a reactant or intermediate is the use of 1-BP as a raw material in the production of another chemical, in which 1-BP is reacted and consumed. According to the 2016 CDR, 1-BP is used as an intermediate²⁰ in the production of other organic chemicals, inorganic chemicals, pesticides, fertilizers,

²⁰ Pharmaceuticals was erroneously included in the description for this condition of use within the draft risk evaluation. Therefore, it has been removed from the final risk evaluation.

and other agricultural chemicals. The volume of these uses from CDR are CBI ([Enviro Tech International, 2017](#); [HSIA, 2010](#)).

Assessment of Inhalation Exposure Based on Modeling

See Section 2.3.1.6 for the assessment of worker exposure from chemical unloading activities. At industrial facilities, workers are potentially exposed when unloading 1-BP from transport containers into intermediate storage tanks and process vessels. Workers may be exposed via inhalation of vapor or via dermal contact with liquids while connecting and disconnecting hoses and transfer lines. EPA assumes the exposure sources, routes, and exposure levels are similar to those at an import facility. The exposure results are presented in Table 2-9.

Table 2-9. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Processing as a Reactant Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	3.83E-3	5.67E-2	1.52E-3	2.91E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgement to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, this activity may be only a small part of the worker’s day. The model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities that can contribute to a worker’s overall 8-hr daily exposure. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker 8-hr exposure. Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.8 Processing – Incorporation into Formulation, Mixture, or Reaction Product

Process Descriptions

After manufacture, 1-BP may be supplied directly to end-users, or may be incorporated into various products and formulations at varying concentrations for further distribution. Incorporation into a formulation, mixture, or reaction product refers to the process of mixing or blending several raw materials to obtain a single product or preparation. For example, formulators may add stabilizing packages to 1-BP for specialized vapor degreasing uses ([Enviro Tech International, 2017](#)), or mix 1-BP with other additives to formulate adhesives, sealants, and other products. The specific worker activity to unload 1-BP into the system, the type of formulation equipment used, the exact production schedule, and presence of engineering control will likely differ among various formulation facilities.

Assessment of Inhalation Exposure Based on Monitoring Data

For formulation of 1-BP into products, EPA assessed exposure using personal air monitoring data from a formulation facility submitted by Enviro Tech. The facility is dedicated to the production of 1-BP based products; a batch of product containing 80 to 96 percent 1-BP is produced during a single eight-hour shift per year, and production takes place twice per weeks for 50 weeks per year in a closed system with mechanized filling operations. Table 2-10 presents the central tendency and high-end exposure levels for employees at this facility. The worker exposure level represents employee exposure when working as the mixing room operator; the mixing room is where all mixing, decanting, and filling operations occur. Employees at this facility work once during the work week as the mixing room operator, and performs other work for the remainder of the week. Exposure levels for occupational non-user represent employee exposure when performing other job duties, primarily in the warehouse, storage, office, areas of the facility where they do not directly handle 1-BP ([Enviro Tech International, 2020](#)).

In a separate study, Hanley et al. ([Hanley et al., 2010](#)) measured exposure at an adhesive manufacturing facility. The study did not provide detailed data to allow determination of 50th and 95th percentile exposures, but stated that the geometric mean full-shift (8 to 10 hour) TWA measurement was 3.79 ppm for those who handled 1-BP products (workers), and 0.33 ppm for those who did not use 1-BP (*i.e.*, ONUs). The maximum exposure value was 18.9 ppm TWA for those who directly used 1-BP, and 1.59 ppm TWA for those who did not use 1-BP. This facility does not have local exhaust ventilation, but uses high volume general dilution ventilation to provide directional air flow in the production area ([Hanley et al., 2010](#)).

Table 2-10. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Processing/Formulation Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end		
Worker	7.20		2.86		1	High
ONU	0.16	0.28	0.06	0.14	10	

Source: ([Enviro Tech International, 2020](#))

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data collected at one formulation facility. Although the data have a high confidence rating and are directly applicable to this condition of use, the data may not be representative of exposures across the range of facilities that formulate products containing 1-BP. Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.9 Processing – Incorporation into Articles

Process Descriptions

According to EPA’s Use Dossier, 1-BP is present at less than 5 percent concentration in the THERMAX™ brand insulation manufactured by Dow Chemical ([U.S. EPA, 2017c](#)). THERMAX™ is a

polyisocyanurate rigid board insulation for interior and exterior applications, and can be used on walls, ceilings, roofs, and crawl spaces in commercial and residential buildings. The product is marketed to have superior durability and fire performance over generic polyisocyanurate insulations.²¹ EPA does not have information on the exact process for producing THERMAX™ and the function of 1-BP in the insulation material ([DOW, 2018](#)).

Assessment of Inhalation Exposure Based on Modeling

EPA did not find monitoring data for this condition of use. As such, EPA modeled exposure using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model*. The model provides estimates of high-end and central tendency exposure concentration for a chemical unloading scenario. See Section 2.3.1.6 for the assessment of worker exposure from chemical unloading activities. The exposure results are presented in Table 2-11.

Table 2-11. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Processing – Incorporation into Articles Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	3.83E-3	5.67E-2	1.52E-3	2.91E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgment to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, the model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker exposure. Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.10 Repackaging

Process Descriptions

Chemicals shipped in bulk containers may be repackaged into smaller containers for resale, such as drums or bottles. The type and size of container will vary depending on customer requirement. In some cases, QC samples may be taken at repackaging sites for analyses. Repackaging could occur for both

²¹ <https://www.dow.com/en-us/products/thermaxbrandinsulation#sort=%40gtitle%20ascending>

domestic and imported shipments of 1-BP; repackaging activities that occur at import facilities are addressed in Section 2.3.1.6.

Assessment of Inhalation Exposure Based on Modeling

EPA has not identified exposure monitoring data for repackaging. Therefore, EPA assessed exposure using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model*. As shown in Table 2-12, the central tendency and high-end exposures are 0.004 ppm and 0.06 ppm as 8-hr TWA, respectively. The model does not estimate exposure levels for ONUs.

Table 2-12. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Repackaging Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	3.83E-3	5.67E-2	1.52E-3	2.91E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgement to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, the model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker exposure. Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.11 Batch Vapor Degreaser (Open-Top)

Process Descriptions

Vapor degreasing is a process used to remove dirt, grease, and surface contaminants in a variety of industries. 1-BP is often used to replace chlorinated solvents, especially in applications where flammability is a concern ([CRC Industries Inc., 2017](#)). 1-BP is also desirable because of its low corrosivity, compatibility with many metals, and suitability for use in most modern vapor degreasing equipment. Vapor degreasing may take place in batches or as part of an in-line (*i.e.*, continuous) system. In batch machines, each load (parts or baskets of parts) is loaded into the machine after the previous load is completed. With in-line systems, parts are continuously loaded into and through the vapor degreasing equipment as well as the subsequent drying steps. Vapor degreasing equipment can generally be categorized into one of the three categories: (1) batch vapor degreasers, (2) conveyORIZED vapor degreasers and (3) web vapor degreasers.

In batch open-top vapor degreasers (OTVDs), a vapor cleaning zone is created by heating and volatilizing the liquid solvent in the OTVD. Workers manually load or unload fabricated parts directly into or out of the vapor cleaning zone. The tank usually has chillers along the side of the tank to prevent losses of the solvent to the air. However, these chillers are not able to eliminate emissions, and throughout the degreasing process emissions of the solvent to air can occur. Additionally, the cost of replacing solvent lost to emissions can be expensive (NEWMOA, 2001). The use of 1-BP in OTVD has been previously described in EPA's 2016 Draft Risk Assessment (U.S. EPA, 2016c).

OTVDs with enclosures operate the same as standard OTVDs except that the OTVD is enclosed on all sides during degreasing. The enclosure is opened and closed to add or remove parts to/from the machine, and solvent is exposed to the air when the cover is open. Enclosed OTVDs may be vented directly to the atmosphere or first vented to an external carbon filter and then to the atmosphere (U.S. EPA; ICF Consulting, 2004). Figure 2-1 illustrates an OTVD with an enclosure. The dotted lines in Figure 2-1 represent the optional carbon filter that may or may not be used with an enclosed OTVD.

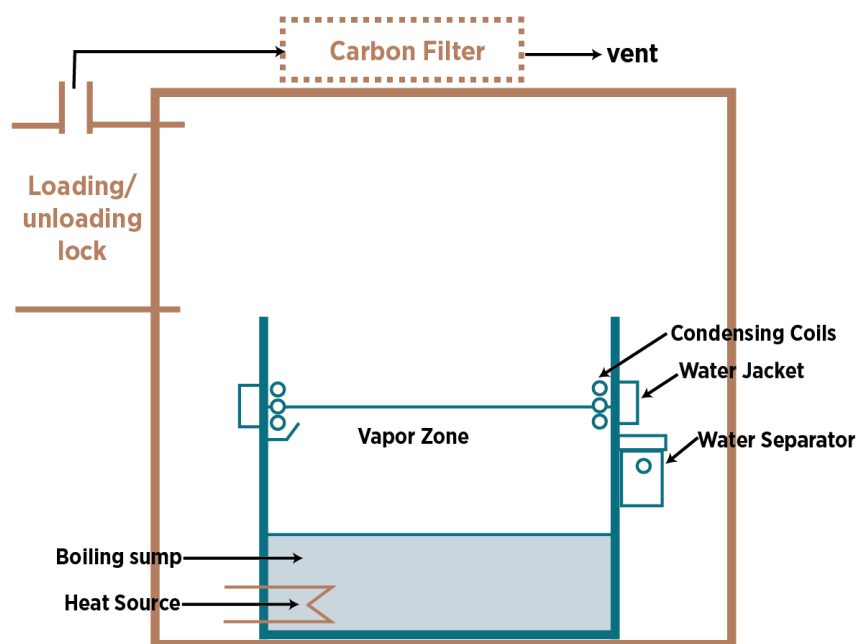


Figure 2-1. Open-Top Vapor Degreaser with Enclosure

Assessment of Inhalation Exposure Based on Monitoring Data

Table 2-13 summarizes the 1-BP exposure data for vapor degreasing operations. EPA obtained exposure monitoring data from several sources, including journal articles, public comments, NIOSH Health Hazard Evaluations (HHEs), the OSHA Chemical Exposure Health Data (CEHD) database, and data submitted to EPA SNAP program. NIOSH HHEs are conducted at the request of employees, employers, or union officials, and provide information on existing and potential hazards present in the workplaces evaluated. OSHA CEHD are workplace monitoring data from OSHA inspections; EPA SNAP program data are collected as part of EPA's effort to identify substitutes for ozone-depleting substances. Some of these data, such as monitoring data conducted during OSHA inspections, are not intended to be representative of typical exposure levels.

Data from these sources cover exposure at a variety of industries that conduct vapor degreasing, including telecommunication device manufacturing, aerospace parts manufacturing, electronics parts manufacturing, helicopter transmission manufacturing, hydraulic power control component manufacturing, metal product fabrication, optical prism and assembly, and printed circuit board manufacturing. It should be noted that sources that only contain a statistical summary of worker exposure monitoring, but exclude the detailed monitoring results, are not included in EPA’s analysis below.

Most of the gathered data were for batch open-top vapor degreasers, except for data from OSHA ([OSHA, 2019, 2013b](#)) and EPA SNAP program, where the type of degreaser is typically not specified. EPA included these data in the analysis despite uncertainty in the degreaser type.

Monitoring data show exposure levels can vary widely depending on several factors, including facility ventilation, degreaser design (e.g., freeboard ratio), or the presence of an enclosure. The 2016 Draft Risk Assessment ([U.S. EPA, 2016c](#)) previously categorized data as either pre- or post-Engineering Control. After further evaluation, EPA removed these categories because EPA determined there is insufficient information on engineering controls at all facilities to accurately characterize the dataset.

EPA defined a vapor degreasing “worker” as an employee who operates or performs maintenance tasks on the degreaser, such as draining, cleaning, and charging the degreaser bath tank. EPA defined “occupational non-user” as an employee who does not directly handle 1-BP but performs work in the surrounding area. Some data sources do not describe their work activities in detail, and the exact proximity of these occupational non-users to the degreaser is unknown. As shown in the table, the 50th and 95th percentile exposure levels for workers are 6.70 ppm and 49.3 ppm as 8-hr TWA, respectively. For occupational non-users, the 50th and 95th percentile exposure levels are below 1 ppm as 8-hr TWA.

Table 2-13. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Vapor Degreaser Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Worker	6.70	49.3	2.66	25.3	155	Medium - High
ONU	0.10	0.46	0.04	0.24	75	

Source: ([OSHA, 2019, 2013b](#); [U.S. EPA, 2006b](#); [Reh and Nemhauser, 2001](#)) ([Miller, 2019](#))

Assessment of Inhalation Exposure Based on Modeling

Figure 2-2 illustrates the near-field / far-field model that can be applied to vapor degreasing ([AIHA, 2009](#)). As the figure shows, volatile 1-BP vapors evaporate into the near-field, resulting in worker exposures at a concentration C_{NF} . The concentration is directly proportional to the evaporation rate of 1-BP, G , into the near-field, whose volume is denoted by V_{NF} . The ventilation rate for the near-field zone (Q_{NF}) determines how quickly 1-BP dissipates into the far-field, resulting in occupational non-user exposures to 1-BP at a concentration C_{FF} . V_{FF} denotes the volume of the far-field space into which the 1-BP dissipates out of the near-field. EPA assumes the far-field volume (V_{FF}) ranges from 300 m³ (10,594 ft³) to 2,000 m³ (70,629 ft³) for degreasing facilities ([Von Grote et al., 2003](#)). The ventilation rate for the

surroundings, denoted by Q_{FF} , determines how quickly 1-BP dissipates out of the surrounding space and into the outside air. See *Supplemental Information on Occupational Exposure Assessment* (EPA, 2019f) for the model equations, model parameters, parameter distributions, and associated assumptions.

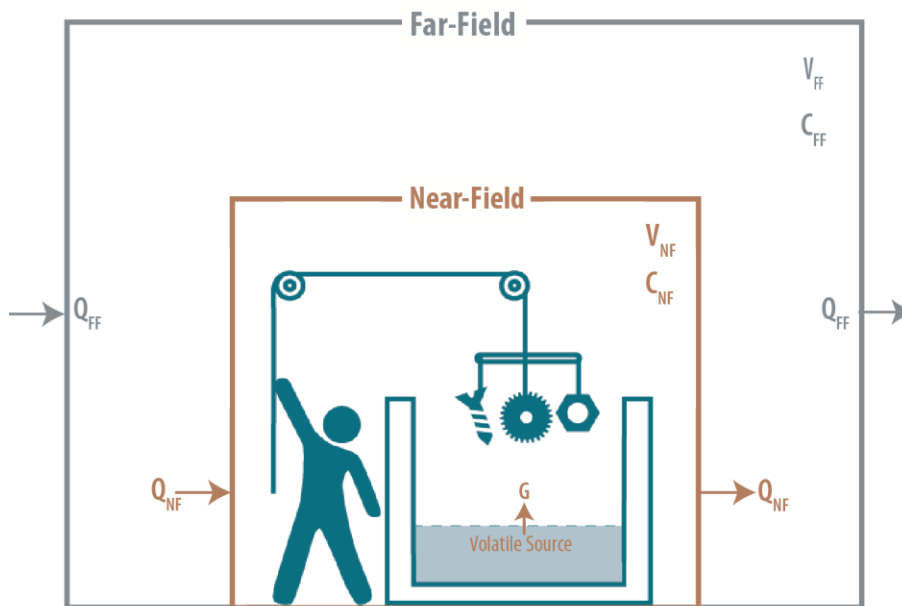


Figure 2-2. Schematic of the Near-Field/Far-Field Model for Vapor Degreasing

To estimate the 1-BP vapor generation rate, the model references an emission factor developed by the California Air Resources Board (CARB) for the California Solvent Cleaning Emissions Inventories (CARB, 2011). CARB surveyed facilities that conduct solvent cleaning operations and gathered site-specific information for 213 facilities. CARB estimated a 1-BP emission factor averaging 10.43 lb/employee-yr, with a standard deviation of 17.24 lb/employee-yr, where the basis is the total number of employees at a facility. The majority of 1-BP emissions were attributed to the vapor degreasing category.

The “vapor degreasing” category in CARB’s study includes the batch-loaded vapor degreaser, aerosol surface preparation process, and aerosol cleaning process. It is not known what percentage, if any, of the 1-BP emission factor is derived from aerosol applications. This modeling approach assumes the 1-BP emission factor is entirely attributed to vapor degreasing applications. The emission factor is expected to represent emissions from batch-loaded degreasers used in California at the time of study. It is not known whether these are specifically open-top batch degreasers, although open-top is expected to be the most common design. The CARB survey data did not include emissions for conveyORIZED vapor degreasers.

The CARB emission factor is then combined with U.S. employment data for vapor degreasing industry sectors from the Economic Census.²² The 2016 1-BP draft Risk Assessment ([U.S. EPA, 2016c](#)) identified 78 NAICS industry codes that are applicable to vapor degreasing. For these industry codes, the Census data set indicates a minimum industry average of 8 employees per site, with a 50th percentile and 90th percentile of 25 and 61 employees per site, respectively. A lognormal distribution is applied to the Census data set to model the distribution of the industry-average number of employees per site for the NAICS codes applicable to vapor degreasing.

These nationwide Census employment data are comparable to the 2008 California employment data cited in CARB's study. According to the CARB study, approximately 90 percent of solvent cleaning facilities in California had less than 50 employees (whereas the national Census data estimate 90 percent of facilities have less than or equal to 61 employees). Census data report an average number of employees per site for each NAICS code. The number of employees for each individual site within each NAICS code is not reported. Therefore, the distribution EPA calculated represents a population of *average* facility size for each NAICS code, and not the population of *individual* facility sizes over all NAICS codes.

The vapor generation rate, G (kg/unit-hr), is calculated *in-situ* within the model, as follows:

Equation 2-1. Equation for Calculating Vapor Degreasing Vapor Generation Rate

$$G = EF \times EMP / (2.20462 \times OH \times OD \times U)$$

Where

EF = emission factor (lb/employee-yr)

EMP = Number of employees (employee/site)

OH = Operating hours per day (hr/day)

OD = Operating days per year (day/yr)

U = Number of degreasing units (unit/site)

2.20462 = Unit conversion from lb to kg (lb/kg)

Batch degreasers are assumed to operate between two and 24 hours per day, based on NEI data on the reported operating hours for OTVD using TCE. EPA performed a *Monte Carlo* simulation with 100,000 iterations and the Latin Hypercube sampling method in [@Risk](#)²³ to calculate 8-hour TWA near-field and far-field exposure concentrations. Near-field exposure represents exposure concentrations for workers who directly operate the vapor degreasing equipment, whereas far-field exposure represents exposure

²² For the purpose of modeling, EPA used data from the 2007 Economic Census for the vapor degreasing NAICS codes as identified in the TCE RA ([U.S. EPA, 2014c](#)). The 2012 Economic Census did not have employment data (average number of employees per establishment) for all vapor degreasing NAICS codes of interest.

²³ A risk analysis software tool (Microsoft Excel add-in) using *Monte Carlo* simulation

concentrations for occupational non-users (*i.e.*, workers in the surrounding area who do not handle the degreasing equipment). Table 2-14 presents a statistical summary of the exposure modeling results. These exposure estimates represent modeled exposures for the workers and occupational non-users. For workers, the baseline (pre-engineering control) 50th percentile exposure is 1.89 ppm 8-hr TWA, with a 95th percentile of 23.9 ppm 8-hr TWA. Compared to literature studies:

- Hanley et al. ([2010](#)) reported a geometric mean of 2.63 ppm 8-hr TWA exposure with a range of 0.078 to 21.4 ppm 8-hr TWA among 44 samples;
- NIOSH ([Reh and Nemhauser, 2001](#)) reported a range of 0.01 to 0.63 ppm 8-hr TWA among 20 samples;
- A 2003 EPA analysis suggested that 87 percent of the samples were less than 25 ppm 8-hr TWA among 500 samples at vapor degreasing facilities ([U.S. EPA, 2003](#)).

The modeled mean near-field exposure is found to be generally comparable to the exposures reported in literature. For occupational non-users, the modeled far-field exposure has a 50th percentile value of 0.99 ppm and a 95th percentile of 13.5 ppm 8-hr TWA. These modeled far-field results are somewhat higher than reported literature values. ([Hanley et al., 2010](#)) reported workers away from the degreasers are exposed at concentrations of 0.077 to 1.69 ppm 8-hr TWA, with a geometric mean of 0.308 ppm 8-hr TWA. The modeled exposures represent the potential exposure associated with batch-loaded degreasers, which could include both OTVD and batch-loaded, closed-loop vapor degreasers.

The model also presents a “post-Engineering Control” (post-EC) scenario by applying a 90 percent emission reduction factor to the baseline, pre-EC scenario. The estimate is based on a Wadden et al. ([1989](#)) study, which indicates a LEV system for an open-top vapor degreaser (lateral exhaust hoods installed on two sides of the tank) can be 90 percent effective ([Wadden et al., 1989](#)). The study covered only reductions in degreaser machine emissions due to LEV and did not address other sources of emissions such as dragout, fresh and waste solvent storage and handling. Furthermore, a caveat in the study is that most LEV likely do not achieve ACGIH design exhaust flow rates, indicating that the emission reductions in many units may not be optimized. Therefore, using this factor likely overestimates control technology efficiency, and underestimates exposures. Actual exposure reductions from added engineering controls can be highly variable.

Table 2-14. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Batch Vapor Degreaser (Open-Top) Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Workers (Near-Field)					
Pre EC	1.89	23.9	0.70	9.19	N/A – Modeled Data
Post EC 90%	0.19	2.39	0.07	0.92	
Occupational non-users (Far-Field)					
Pre EC	0.99	13.5	0.37	5.23	N/A – Modeled Data
Post EC 90%	0.10	1.35	0.04	0.52	

Pre-EC: refers to modeling where no reduction due to engineering controls was assumed

Post-EC: refers to modeling where engineering controls with 90% efficiency were implemented. The percent effectiveness is applied to the pre-EC exposure concentration to calculate post-EC exposure.

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data from several different sources, with confidence rating of the data ranging from medium to high, as determined through EPA’s systematic review process. Some of the data sources do not clearly specify whether the vapor degreaser is a batch, open-top system or another system. Because OTVDs typically have the highest emissions among all vapor degreasers, the inclusion of data for other degreaser types may underestimate exposure for this condition of use.

The exposure data are supplemented with near-field/far-field exposure modeling using a *Monte Carlo* analysis, which incorporates variability in the model input parameters. This model was peer reviewed as part of the 2016 1-BP draft Risk Assessment ([U.S. EPA, 2016c](#)). Although there is some uncertainty on the CARB emission factor used in the model and whether the factor represents emissions exclusively for batch open-top systems, the model results are in general agreement with monitoring data. Based on reasonably available information, EPA has a high level of confidence in the assessed exposure for this condition of use.

2.3.1.12 Batch Vapor Degreaser (Closed-Loop)

Process Descriptions

In closed-loop degreasers, parts are placed into a basket, which is then placed into an airtight work chamber. The door is closed, and solvent vapors are sprayed onto the parts. Solvent can also be introduced to the parts as a liquid spray or liquid immersion. When cleaning is complete, vapors are exhausted from the chamber and circulated over a cooling coil where the vapors are condensed and recovered. The parts are dried by forced hot air. Air is circulated through the chamber and residual solvent vapors are captured by carbon adsorption. The door is opened when the residual solvent vapor concentration has reached a specified level ([Kanegsberg and Kanegsberg, 2011](#)). Figure 2-3 illustrates a standard closed-loop vapor degreasing system.

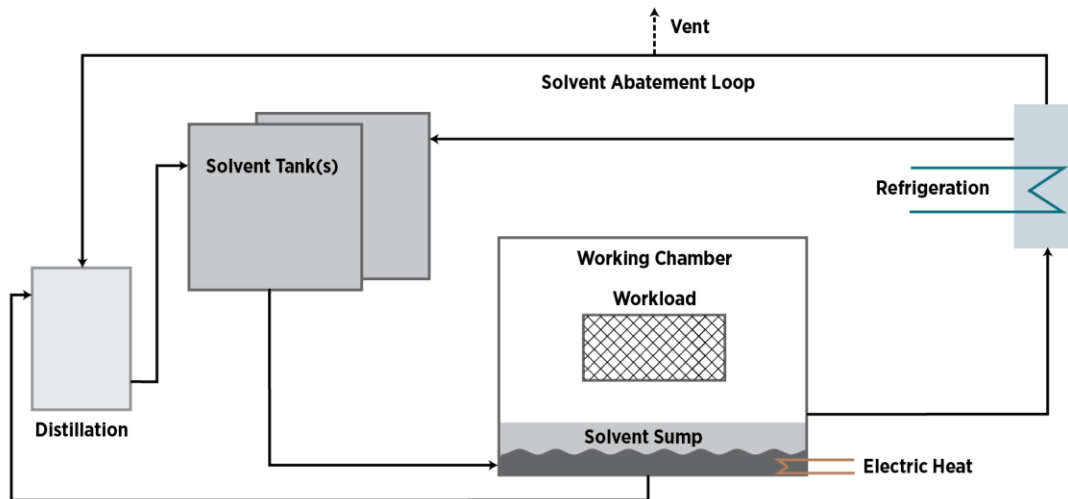


Figure 2-3. Closed-loop/Vacuum vapor Degreaser

Airless degreasing systems are also sealed, closed-loop systems, but remove air at some point of the degreasing process. Removing air typically takes the form of drawing vacuum but could also include purging air with nitrogen at some point of the process (in contrast to drawing vacuum, a nitrogen purge operates at a slightly positive pressure). In airless degreasing systems with vacuum drying only, the cleaning stage works similarly as with the airtight closed-loop degreaser. However, a vacuum is generated during the drying stage, typically below 5 torr (5 mmHg). The vacuum dries the parts and a vapor recovery system captures the vapors ([Kanegsberg and Kanegsberg, 2011](#); [ERG, 2001](#); [NEWMOA, 2001](#)).

Airless vacuum-to-vacuum degreasers are true “airless” systems because the entire cycle is operated under vacuum. Typically, parts are placed into the chamber, the chamber sealed, and then vacuum drawn within the chamber. The typical solvent cleaning process is a hot solvent vapor spray. The introduction of vapors in the vacuum chamber raises the pressure in the chamber. The parts are dried by again drawing vacuum in the chamber. Solvent vapors are recovered through compression and cooling. An air purge then purges residual vapors over an optional carbon adsorber and through a vent. Air is then introduced in the chamber to return the chamber to atmospheric pressure before the chamber is opened ([Durkee, 2014](#); [NEWMOA, 2001](#)). The general design of vacuum vapor degreasers and airless vacuum degreasers is similar as illustrated in Figure 2-3 for closed-loop systems except that the work chamber is under vacuum during various stages of the cleaning process.

Assessment of Inhalation Exposure Based on Modeling

There are no 1-BP monitoring data specific to closed-loop degreasers. A NEWMOA study states air emissions can be reduced by 98 percent or more when a closed-loop degreaser is used instead of an open-top vapor degreaser ([NEWMOA, 2001](#)). This reduction factor is applied to the vapor degreasing model results presented in Section 2.3.1.11 to estimate exposure to batch closed-loop vapor degreasers.

The approach assumes the CARB emission factor primarily represents emissions from OTVDs, rather than other types of batch-loaded degreasers.

Table 2-15 presents the exposure model results for batch closed-loop vapor degreasers. For workers, the 50th and 95th percentile exposure levels are 0.04 ppm and 0.48 ppm as 8-hr TWA. For occupational non-users, the 50th and 95th percentile exposure levels are 0.02 ppm and 0.27 ppm as 8-hr TWA, respectively.

Table 2-15. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Batch Closed-Loop Vapor Degreasing Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Worker	0.04	0.48	0.01	0.18	N/A – Modeled Data
ONU	0.02	0.27	0.01	0.10	

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

For this condition of use, EPA did not identify any exposure monitoring data. Exposure is assessed using the OTVD model and by assuming 98 percent exposure reduction when switching from open-top to closed-loop batch vapor degreasers. The model incorporates variability in the input parameters through a *Monte Carlo* approach, and the model was peer reviewed in 2016. However, the representativeness of the exposure reduction factor used in the model is not known, as actual exposure will likely differ depending on the specific equipment design and work practices. In addition, this model uses the CARB emission factor for batch-loaded degreasers to estimate average baseline emissions from open-top vapor degreasers, which could result in an underestimate. Based on reasonably available information, EPA has a medium level of confidence in the assessed exposure for this condition of use.

2.3.1.13 In-line Vapor Degreaser (Conveyorized)

Process Descriptions

In conveyorized systems, an automated parts handling system, typically a conveyor, continuously loads parts into and through the vapor degreasing equipment and the subsequent drying steps. Conveyorized degreasing systems are usually fully enclosed except for the conveyor inlet and outlet portals.

Conveyorized degreasers are likely used in shops where large number of parts need to be cleaned. There are seven major types of conveyorized degreasers: monorail degreasers; cross-rod degreasers; vibra degreasers; ferris wheel degreasers; belt degreasers; strip degreasers; and circuit board degreasers ([U.S. EPA, 1977](#)). See Supplemental Information on Occupational Exposure Assessment ([EPA, 2019f](#)) for detailed description of each type of conveyorized degreaser.

Continuous web cleaning machines are a subset of conveyorized degreasers but differ in that they are specifically designed for cleaning parts that are coiled or on spools such as films, wires, and metal strips ([Kanegsberg and Kanegsberg, 2011](#); [U.S. EPA, 2006a](#)). In continuous web degreasers, parts are uncoiled and loaded onto rollers that transport the parts through the cleaning and drying zones at speeds

greater than 11 feet per minute ([U.S. EPA, 2006a](#)). The parts are then recoiled or cut after exiting the cleaning machine ([Kanegsberg and Kanegsberg, 2011](#); [U.S. EPA, 2006a](#)).

Assessment of Inhalation Exposure

There are no monitoring data specific to conveyORIZED degreasers that use 1-BP. Additionally, there is not sufficient data to model exposure to 1-BP from these degreasers.

The 2014 NEI contains emission data for dichloromethane (DCM), perchloroethylene (PERC), and trichloroethylene (TCE). Based on comparison of NEI data for OTVD and conveyORIZED vapor degreasers, emissions from conveyORIZED vapor degreasers are generally similar to that from OTVDs. As such, EPA assumed the associated 1-BP worker exposure for conveyORIZED degreasers may be similar to the exposure levels presented in Section 2.3.1.11 Batch Vapor Degreaser (Open-Top).

2.3.1.14 Cold Cleaner

Process Descriptions

Cold cleaners are non-boiling solvent degreasing units. Cold cleaning operations include spraying, brushing, flushing, and immersion. Figure 2-4 shows the design of a typical batch-loaded, maintenance cold cleaner, where dirty parts are cleaned manually by spraying and then soaking in the tank. After cleaning, the parts are either suspended over the tank to drain or are placed on an external rack that routes the drained solvent back into the cleaner. Batch manufacturing cold cleaners could vary widely, but have two basic equipment designs: the simple spray sink and the dip tank. The dip tank design typically provides better cleaning through immersion, and often involves an immersion tank equipped with agitation ([U.S. EPA, 1981](#)). Emissions from batch cold cleaning machines typically result from (1) evaporation of the solvent from the solvent-to-air interface, (2) “carry out” of excess solvent on cleaned parts, and (3) evaporative losses of the solvent during filling and draining of the machine ([U.S. EPA, 2006a](#)). Emissions from cold in-line (conveyORIZED) cleaning machines result from the same mechanisms, but with emission points only at the parts entry and exit ports ([U.S. EPA, 2006a](#)).

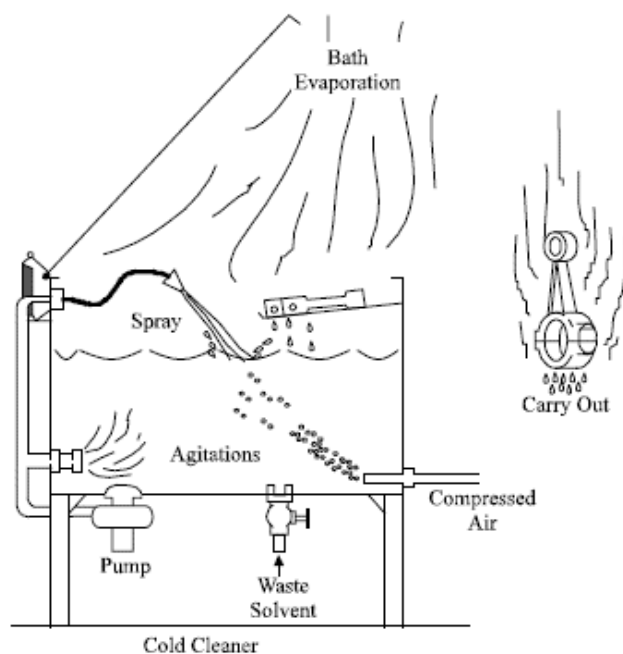


Figure 2-4. Typical Batch-Loaded, Maintenance Cold Cleaner ([U.S. EPA, 1981](#))

Assessment of Inhalation Exposure Based on Monitoring Data

The general worker activities for cold cleaning include placing the parts that require cleaning into a vessel. The vessel is usually something that will hold the parts but not the liquid solvent (*i.e.*, a wire basket). The vessel is then lowered into the machine, where the parts could be sprayed, and then completely immersed in the solvent. After a short time, the vessel is removed from the solvent and allowed to drip or air dry. Depending on the industry and/or company, these operations may be performed manually (*i.e.*, by hand) or mechanically. Sometimes parts require more extensive cleaning; in these cases, additional cleaning is performed including directly spraying, agitation, wiping or brushing ([Reh and Nemhauser, 2001](#); [U.S. EPA, 1997](#)).

Table 2-16 presents OSHA CEHD for two facilities. The first facility uses 1-BP to clean parts in an immersion process in an area with general ventilation. The second facility uses 1-BP in a degreasing tank equipped with a spray nozzle. The degreasing operation is conducted in an area with local exhaust ventilation. Based on the available process description, EPA assumes these facilities operate a cold cleaner, even though the equipment is not described in detail in the OSHA CEHD. For workers, only five data points are available – the median and maximum exposures are 4.30 ppm and 7.40 ppm 8-hr TWA, respectively, from the available dataset. For occupational non-users, the exposure value is based on a single data point for a Chemical Safety and Health Officer (CSHO), who is an official from OSHA or a state plan occupational safety and health program. The exposure for this individual measured 2.60 ppm 8-hr TWA. EPA presents this data point as the potential exposure level for an occupational non-user; however, the exposure level may not be representative because the CSHO is not regularly present in the production area. It should be further noted that CEHD are obtained from OSHA inspections, and not intended to be representative of typical worker exposure.

Table 2-16. Summary of 1-BP Inhalation Exposure Monitoring Data for Cold Cleaner

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	Central tendency	High-end (Max)	Central tendency	High-end (Max)		
Worker	4.30	7.40	1.71	3.79	5	High
ONU	2.60		1.03	1.33	1	

Source: ([OSHA, 2013b, d](#)).

Assessment of Inhalation Exposure Based on Modeling

Detailed description of the Cold Cleaning modeling approach is provided in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019f](#)). The [EPA AP-42, Compilation of Air Emissions Factors](#) contains emission factors and process information developed and compiled from source test data, material balance studies, and engineering estimates ([U.S. EPA, 1981](#)). AP-42 Chapter 4.6 provides generic, non-methane VOC emission factors for several solvent cleaning operations, including cold cleaning and vapor degreasing. These emission factors suggest that cold cleaning emissions range from 3.2 to 57.1 percent of the emissions from a traditional open-top vapor degreaser ([U.S. EPA, 1981](#)). It is not known whether the emission factors derived using VOC data would be representative of 1-BP emissions, or whether the emission reduction when switching from vapor degreasing to cold cleaning would be similar across different chemicals. To model exposures during 1-BP cold cleaning, an exposure reduction factor, RF, with uniform distribution from 0.032 to 0.571 is applied to the vapor generation rate in the vapor degreasing model.

Figure 2-5 presents the model approach for cold cleaning. Except for the exposure reduction factor, the model approach and input parameters for cold cleaning are identical to those previously presented for batch vapor degreasing. EPA performed a *Monte Carlo* simulation with 100,000 iterations and the Latin Hypercube sampling method in [@Risk](#) to estimate 8-hr TWA near-field and far-field exposures, acute exposures, ADCs, and LADCs. The cold cleaning model approach and the underlying data used (*i.e.*, EPA AP-42) do not differentiate between a spray versus immersion cold cleaner.

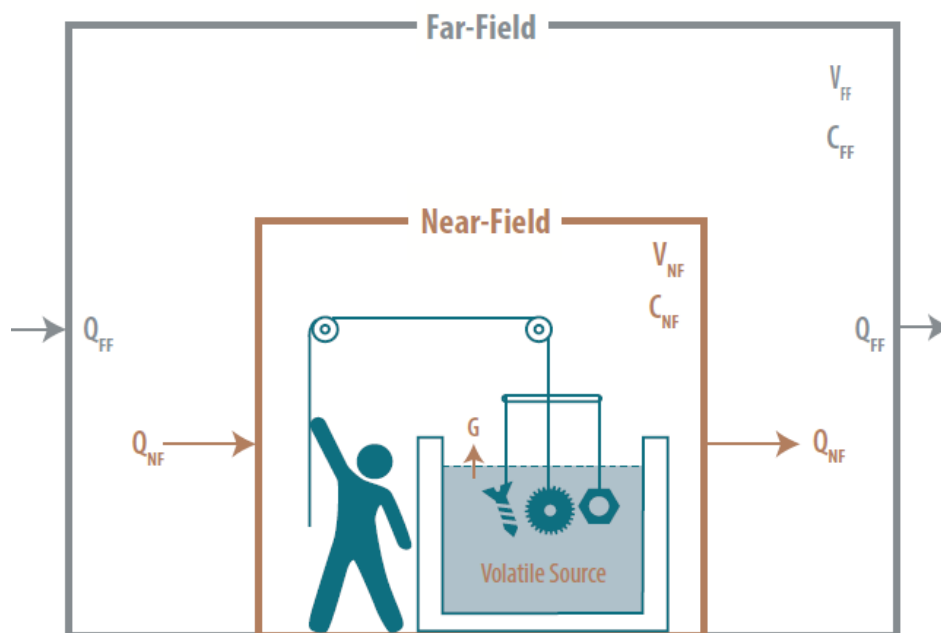


Figure 2-5. The Near-Field/Far-field Model for Cold Cleaning Scenario

Table 2-17 presents a statistical summary of the inhalation exposure modeling results. For workers, the 50th and 95th percentile exposures are 0.55 ppm and 11.91 ppm 8-hr TWA. For occupational non-users, the 50th and 95th percentile exposures are 0.29 ppm and 6.83 ppm 8-hr TWA. The model exposure levels are in good agreement with monitoring data.

Table 2-17. Summary of 1-BP 8-hr TWA Inhalation Exposures (AC, ADC and LADC) for Cold Cleaner Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Worker	0.55	11.91	0.21	4.59	N/A – Modeled Data
ONU	0.29	6.83	0.11	2.63	

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data from OSHA CEHD, and the data were determined to have a high confidence rating through EPA’s systematic review process. However, CEHD data are obtained from OSHA inspections and are not intended to represent typical exposure levels at the workplace. In addition, monitoring data for a CSHO may not be representative of the exposure level for the typical occupational non-users.

The exposure monitoring data is supplemented with near-field/far-field exposure modeling using a *Monte Carlo* approach. The exposure model was peer reviewed as part of the [2016 Draft Risk Assessment \(U.S. EPA, 2016c\)](#). The model references EPA AP-42 emission factors for generic, non-

methane VOC. These emission factors may not be representative of emissions for 1-BP, and could result in either an over- or underestimate. Despite these uncertainties, the model results are in good agreement with the exposure monitoring data. Based on reasonably available information above, EPA has a high level of confidence in the assessed exposure.

2.3.1.15 Aerosol Spray Degreaser/Cleaner

Process Descriptions

Aerosol degreasing is a process that uses an aerosolized solvent spray, typically applied from a pressurized can, to remove residual contaminants from fabricated parts. Based on identified safety data sheets (SDS), 1-BP-based formulations typically use carbon dioxide, liquified petroleum gas (LPG) (*i.e.*, propane and butane), 1,1,1,2-tetrafluoroethane, 1,1-difluoroethane, and pentafluorobutane as the carrier gas ([U.S. EPA, 2017c](#)). The aerosol droplets bead up on the fabricated part and then drip off, carrying away any contaminants and leaving behind a clean surface.

Figure 2-6 illustrates the typical process of using aerosol degreasing to clean components in commercial settings. One example of a commercial setting with aerosol degreasing operations is repair shops, where service items are cleaned to remove any contaminants that would otherwise compromise the service item's operation. Internal components may be cleaned in place or removed from the service item, cleaned, and then re-installed once dry ([U.S. EPA, 2014a](#)). Example uses of aerosol products containing 1-BP include general purpose degreasing, engine degreasing, brake cleaning, and metal product cleaning applications.

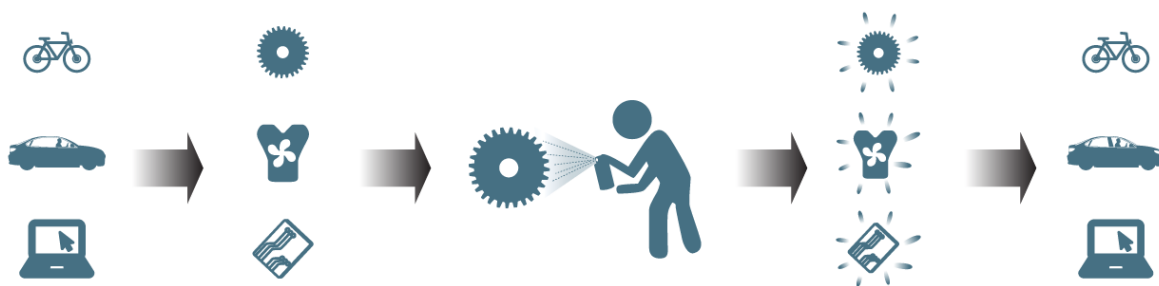


Figure 2-6. Overview of Aerosol degreasing

Assessment of Inhalation Exposure Based on Monitoring Data

Table 2-18 summarizes 8-hr TWA PBZ monitoring data for aerosol degreasing obtained from ([Stewart, 1998](#)) and ([Tech Spray, 2003](#)). The Stewart ([1998](#)) study measured 1-BP worker PBZ during an aerosol spray can application on a test substrate consisting of a small electric motor; the scenario was intended to simulate workers performing typical repair and maintenance work. The Tech Spray ([2003](#)) study measured worker exposure in a test scenario that simulated cleaning of printed circuit boards for the repair of computers and electrical systems. Among the two test studies, the 50th and 95th percentile worker exposures were 16.1 ppm and 31.6 ppm, respectively.

The Tech Spray study tested an exposure scenario where the 1-BP aerosol degreasing occurred inside a non-vented booth. Subsequently, the company tested the same scenario in a vented booth. With a non-

vented booth, worker exposure ranged from 13 to 32 ppm 8-hr TWA. With the vented booth, worker exposure was reduced to 5.50 ppm 8-hr TWA based on a single data point. The representativeness of this single data point as a post-EC scenario is unknown. The vented booth scenario has a constant draw of 0.9 cubic meters per second during the 8-hour test. The data suggest the significance of ventilation and its impact on worker exposure.

Table 2-18. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Aerosol Spray Degreaser/Cleaner Based on Monitoring Data

Category ^a	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Worker, Pre EC	16.1	31.6	6.38	16.2	6	Medium
Worker, Post EC ^b	5.50		2.19	2.82	1	

Source: Stewart (1998); Tech Spray (2003), as cited in (U.S. EPA, 2006b). The vented booth scenario from Tech Spray is used as the post-EC scenario, and the remaining data points are used as the pre-EC scenario.

^a Worker includes operators, technicians, mechanics, and maintenance supervisor. Data are not available for occupational non-users.

^b The 8-hr TWA exposure estimate is combined with 50th and 95th percentile value on the number of working years to calculate LADC. See Appendix B.

In addition to the data summarized above, the Tech Spray study included a test scenario that measured short-term worker exposure that simulated an automotive repair shop. In this test, 1-BP was sprayed continuously over a 15-minute period. In reality, workers are only expected to spray 1-BP for a few minutes at a time; as such, the test was intended to simulate a heavy-usage scenario at this facility. The 15-min short term exposure for operators ranged from 190 to 1,100 ppm. Further, the 15-minute short term exposure for a worker in an adjacent room measured 11 ppm ((Tech Spray, 2003), as cited in (U.S. EPA, 2006b)). The presence of 1-BP in the adjacent room suggests the infiltration of contaminated air into other work areas.

Assessment of Inhalation Exposure Based on Modeling

Aerosol degreasing formulations containing 1-BP can be used at a variety of workplaces. For the purpose of modeling, EPA modeled worker exposure to 1-BP during brake servicing as a representative exposure scenario. EPA chose to model this scenario because the process of brake servicing is well understood and there is sufficient data to construct such a model. EPA believes brake servicing and engine degreasing at automotive maintenance and repair shops is a common application for products containing 1-BP, and the process is a representative aerosol degreasing scenario.

Figure 2-7 illustrates the *Brake Servicing Near-Field/Far-Field Inhalation Exposure Model*. The general model framework was previously included in the [2016 Draft Risk Assessment \(U.S. EPA, 2016c\)](#); however, specific model parameters have been updated with data from a recent CARB study. As the figure shows, 1-BP in aerosolized droplets immediately volatilizes into the near-field, resulting in worker exposures at a concentration C_{NF}. The concentration is directly proportional to the amount of aerosol degreaser applied by the worker, who is standing in the near-field-zone (*i.e.*, the working zone).

The volume of this zone is denoted by V_{NF} . The ventilation rate for the near-field zone (Q_{NF}) determines how quickly 1-BP dissipates into the far-field (*i.e.*, the facility space surrounding the near-field), resulting in occupational non-user exposures to 1-BP at a concentration C_{FF} . V_{FF} denotes the volume of the far-field space into which the 1-BP dissipates out of the near-field. The ventilation rate for the surroundings, denoted by Q_{FF} , determines how quickly 1-BP dissipates out of the surrounding space and into the outside air.

In this scenario, 1-BP vapors enter the near-field in non-steady “bursts,” where each burst results in a sudden rise in the near-field concentration, followed by a more gradual rise in the far-field concentration. The near-field and far-field concentrations then decay with time until the next burst causes a new rise in near-field concentration. The product application rate is based on a 2000 CARB report for brake servicing, which estimates that each facility performs on average 936 brake jobs per year, and that each brake job requires approximately 14.4 ounces of product. For each model iteration, EPA determined the concentration of 1-BP by assuming the formulation could be one of 25 possible aerosol degreasing products identified in the *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane* (U.S. EPA, 2017c). Detailed model parameters and assumptions are presented in the *Supplemental Information on Occupational Exposure Assessment* (EPA, 2019f). EPA did not model a “post-EC” scenario because there is not sufficient information to determine the type and effectiveness of engineering control at automotive and other commercial degreasing facilities.

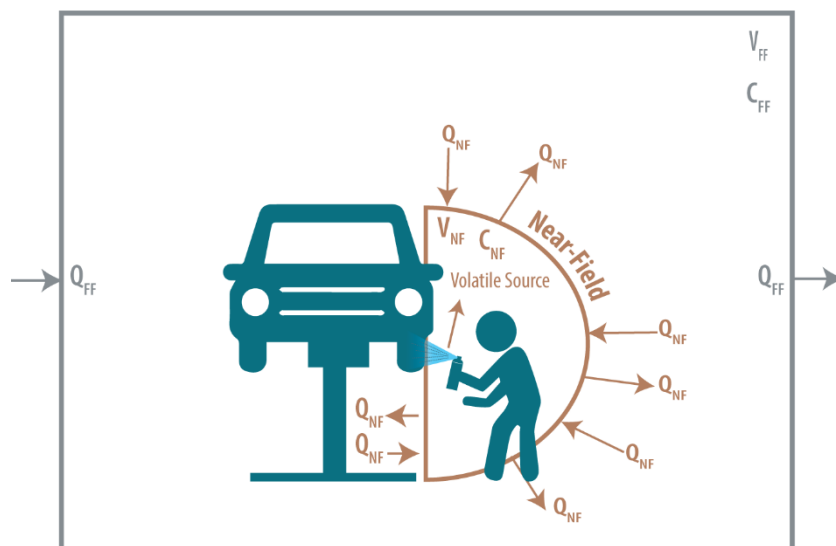


Figure 2-7. Schematic of the Near-Field/Far-Field Model for Aerosol degreasing

EPA performed a *Monte Carlo* simulation with 100,000 iterations and the Latin hypercube sampling method to model near-field and far-field exposure concentrations in the aerosol degreasing scenario. Table 2-19 presents a statistical summary of the exposure modeling results. The 50th and 95th percentile exposures are 6.37 ppm and 22.53 ppm 8-hr TWA for workers, and 0.11 ppm and 0.93 ppm 8-hr TWA for occupational non-users.

Table 2-19. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Aerosol Spray Degreaser/Cleaner Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Worker	6.37	22.53	2.38	9.05	N/A – Modeled Data
ONU	0.11	0.93	0.04	0.36	

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

Exposure is assessed using 1-BP personal breathing zone monitoring data specific to aerosol degreasing. The data come from two studies with “medium” confidence rating.

The exposure monitoring data are supplemented with the Brake Servicing Near-Field/Far-Field Inhalation Exposure Model, which provides exposure estimates for a brake cleaning scenario. The model uses a *Monte Carlo* approach to incorporate variability. Although the model scenario is specific to brake cleaning and may not encompass the full range of aerosol degreasing scenarios, the model results are in good agreement with monitoring data. Based on reasonably available information above, EPA has a high level of confidence in the assessed exposure.

2.3.1.16 Dry Cleaning

Process Descriptions

1-BP is a solvent used in dry cleaning machines. There are two known 1-BP based dry cleaning formulations, DrySolv® and Fabrisolv™ XL, which were introduced beginning in 2006. These formulations are often marketed as “drop-in” replacements for perchloroethylene (PERC), which indicates they can be used in third generation or higher Perc equipment ([TURI, 2012](#)). Third generation equipment, introduced in the late 1970s and early 1980s, are non-vented, dry-to-dry machines with refrigerated condensers. These machines are essentially closed systems and are only open to the atmosphere when the machine door is opened. In third generation machines, heated drying air is recirculated back to the drying drum through a vapor recovery system ([CDC, 1997](#)).

Fourth generation dry cleaning equipment are essentially third-generation machines with added secondary vapor control. These machines “rely on both a refrigerated condenser and carbon adsorbent to reduce the Perc concentration at the cylinder outlet below 300 ppm at the end of the dry cycle,” and are more effective at recovering solvent vapors ([CDC, 1997](#)). Fifth generation equipment have the same features as fourth generation machines, but also have a monitor inside the machine drum and an interlocking system to ensure that the concentration is below approximately 300 ppm before the loading door can be opened ([CDC, 1997](#)).

Dry cleaners who opt to use 1-BP can either convert existing Perc machines or purchase a new dry cleaning machine specifically designed for 1-BP. To convert existing Perc machines to use 1-BP, machine settings and components must be changed to prevent machine overheating and solvent leaks ([Blando et al., 2010](#)). 1-BP is known to damage rubber gaskets and seals. It can also degrade cast

aluminum, which is sometimes used on equipment doors and other dry cleaning machine components. In addition, 1-BP is not compatible with polyurethane and silicone ([TURI, 2012](#)). Enviro Tech International, Inc. (Enviro Tech), a major 1-BP supplier, recently ceased selling DrySolv® to users of converted Perc machines ([Enviro Tech International, 2017](#)).

Figure 2-8 provides an overview of the dry cleaning process. Worker exposure monitoring studies for 1-BP at dry cleaning facilities suggest workers are exposed when 1) adding make-up solvent, typically by manually dumping it through the front hatch, 2) opening the machine door during the wash cycle, and 3) removing loads from the machines ([Blando et al., 2010](#)).

Engineering controls such as local exhaust ventilation (LEV) located at or near the machine door can reduce worker exposure during machine loading, machine unloading, and maintenance activities ([NCDOL, 2013](#)).

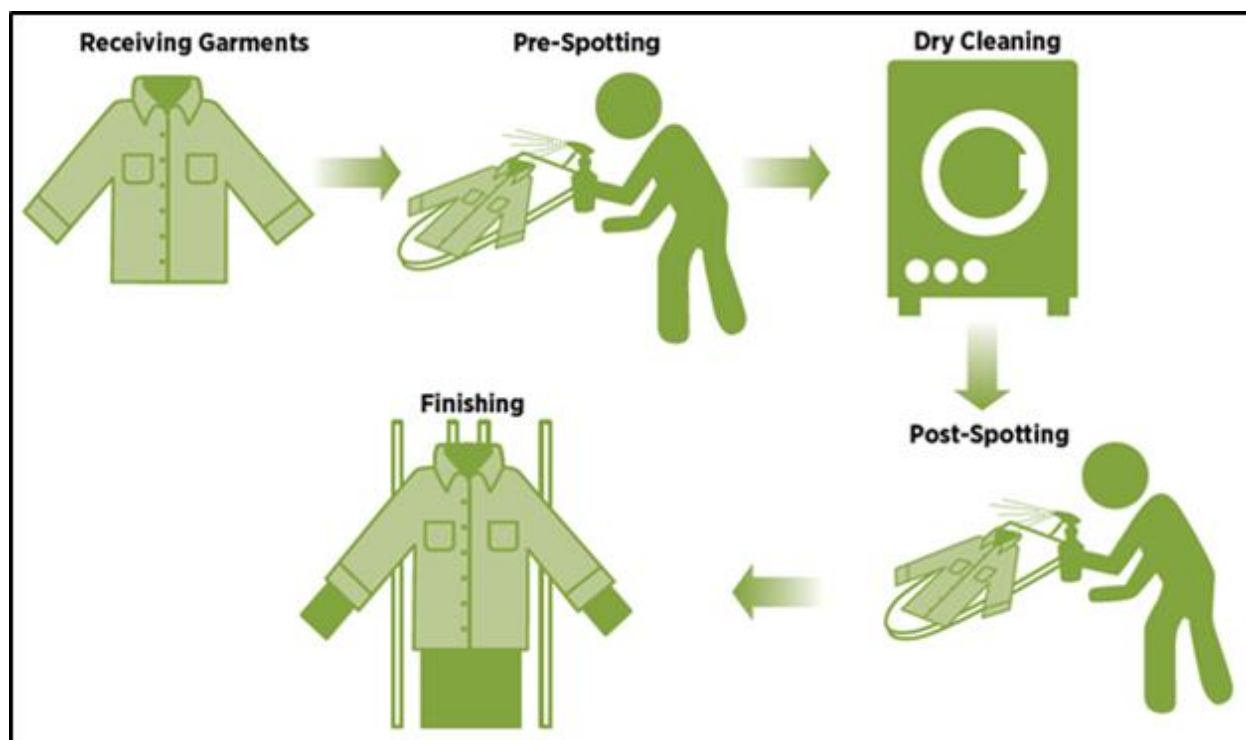


Figure 2-8. Overview of Dry Cleaning

Assessment of Inhalation Exposure Based on Monitoring Data

Table 2-20 presents an analysis of the 8-hr TWA Personal Breathing Zone (PBZ) monitoring data from literature. The data were obtained from two literature studies covering the same four dry cleaning shops in New Jersey. The studies noted that work load and work practices varied greatly among the shops, resulting in variability in 1-BP exposure across these shops. In addition, there was variability in 1-BP exposure across different job titles, and in some cases on different days when the exposure monitoring was conducted. One study ([Eisenberg and Ramsey, 2010](#)) contains additional partial-shift exposure data that are not summarized here. For those data, an 8-hr TWA value was not obtained because owners of the shop requested that NIOSH remove the sampling equipment once they had finished running the dry cleaning machines ([Eisenberg and Ramsey, 2010](#)).

All four shops included in the studies used converted 3rd generation machines ([Blando et al., 2010](#)). The shops dry cleaned one to 14 loads of garments per day. Some shops that converted the machines themselves “cooked” the solvent, a practice that had been performed widely for Perc but is no longer recommended by the manufacturers for 1-BP operation ([Eisenberg and Ramsey, 2010](#)). Only one shop added make-up solvent on Sample Day 1 and Sample Day 2 by manually dumping a 5-gallon can of solvent product through the front hatch of the machine ([Blando et al., 2010](#)). The facilities had general building ventilation, ceiling-mounted or wall-mounted fans, but lacked controls specifically designed to reduce exposure to the dry cleaning solvent.

EPA defined workers as employees who operate dry cleaning machine or who perform dry cleaning activities such as spotting, pressing and finishing. For workers, the 50th and 95th percentile exposures are 29.4 ppm and 50.2 ppm 8-hr TWA, respectively. The exposure level is impacted by the number of loads cleaned, the number of solvent “cooking” (heating the solvent for recovery) cycles used, and whether any make-up solvent was added in that particular shop and on that particular day when the monitoring was conducted ([Blando et al., 2010](#)). The highest 1-BP concentration in air was found when a facility with a converted Perc machine cooked the solvent ([Eisenberg and Ramsey, 2010](#)).

EPA defined occupational non-users as employees who work in the dry cleaning shops but do not perform dry cleaning activities. For occupational non-users, the 50th and 95th percentile exposures are 12.1 ppm and 20.6 ppm 8-hr TWA, respectively. The data suggest that cashiers, clerks, and other employees at the shop are also exposed to 1-BP. In addition to occupational non-users, children may also be present at some small, family-owned dry cleaning shops, and thereby be exposed to 1-BP. The monitoring studies do not contain information on exposure to children.

Table 2-20. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Dry Cleaning Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Worker ^a	29.4	50.2	11.7	25.7	8	High
ONU ^b	12.1	20.6	4.80	10.6	6	

Source: ([Blando et al., 2010](#); [Eisenberg and Ramsey, 2010](#); [NIOSH, 2010](#))

^a Worker refers to dry cleaning machine operators.

^b Occupational non-user refers to cashiers and clerks.

Assessment of Inhalation Exposure Based on Modeling

Because there are multiple activities with potential 1-BP exposure at a dry cleaner, a multi-zone modeling approach is used to account for 1-BP vapor generation from multiple sources. Figure 2-9 illustrates this multi-zone approach, which considers the following three worker activities:

- Spot cleaning of stains on both dirty and clean garments: On receiving a garment, dry cleaners inspect for stains or spots they can remove as much of as possible before cleaning the garment in a dry cleaning machine. Spot cleaning may also occur after dry cleaning if the stains or spots were not adequately removed. Spot cleaning occurs on a spotting board and can involve the use of a spotting

agent containing various solvents, such as 1-BP. Workers are exposed to 1-BP when applying it via squeeze bottles, hand-held spray bottles, or even from spray guns connected to pressurized tanks. Once applied, the worker may come into further contact with the 1-BP if using a brush, spatula, pressurized air or steam, or their fingers to scrape or flush away the stain ([Young, 2012](#); [NIOSH, 1997](#)). For modeling, EPA assumed the near-field is a rectangular volume covering the body of a worker.

- Unloading garments from dry cleaning machines: At the end of each dry cleaning cycle, workers manually open the machine door to retrieve cleaned garments. During this activity, workers are exposed to 1-BP vapors remaining in the dry cleaning machine cylinder. For modeling, EPA assumed that the near-field consists of a hemispherical area surrounding the machine door, and that the entire cylinder volume of air containing 1-BP exchanges with the workplace air, resulting in a “spike” in 1-BP concentration in the near-field, C_D , during each unloading event. This concentration is directly proportional to the amount of residual 1-BP in the cylinder when the door is opened. The near-field concentration then decays with time until the next unloading event occurs.
- Finishing and pressing: The cleaned garments taken out of the cylinder after each dry clean cycle contain residual solvents and are not completely dried ([Von Grote et al., 2003](#)). The residual solvents are continuously emitted into the workplace during pressing and finishing, where workers manually place the cleaned garments on the pressing machine to be steamed and ironed. EPA assumed any residual solvent is entirely evaporated during pressing, resulting in an increase in the near-field 1-BP concentration during this activity. Workers are exposed to 1-BP vapors while standing in vicinity of the press machine. For modeling, EPA assumed the near-field is a rectangular volume covering the body of a worker.

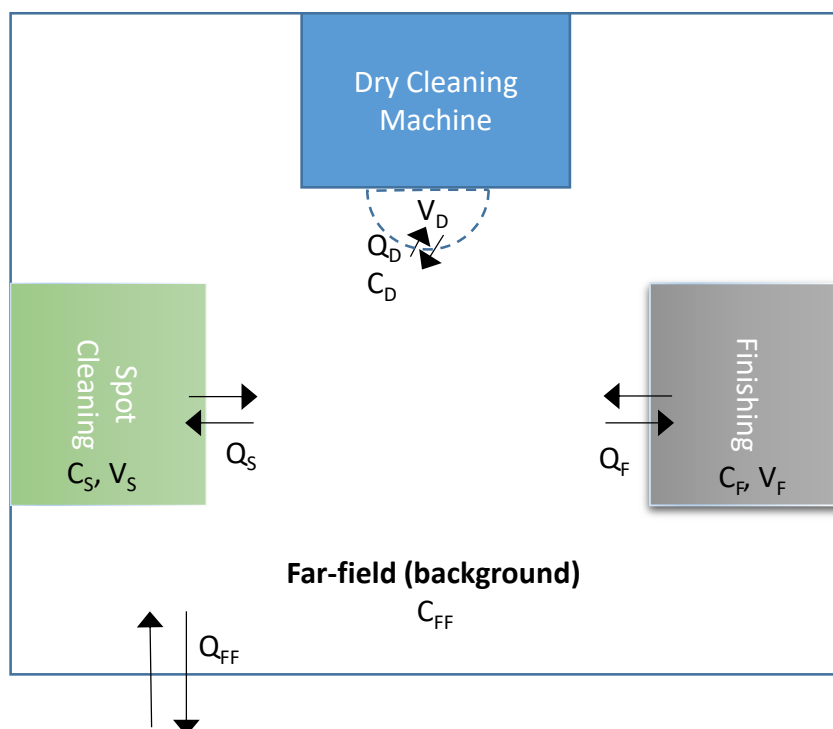


Figure 2-9. Illustration of the Multi-Zone Model

As the figure shows, 1-BP vapor is generated in each of the three near-fields, resulting in worker exposures at concentrations C_S , C_D , and C_F . The volume of each zone is denoted by V_S , V_D , and V_F . The ventilation rate for the near-field zone (Q_S , Q_D , Q_F) determines how quickly 1-BP dissipates into the far-field (*i.e.*, the facility space surrounding the near-fields), resulting in occupational non-user exposures to 1-BP at a concentration C_{FF} . V_{FF} denotes the volume of the far-field space into which the 1-BP dissipates out of the near-field. The ventilation rate for the surroundings, denoted by Q_{FF} , determines how quickly 1-BP dissipates out of the surrounding space and into the outside air. The *Supplemental Information on Occupational Exposure Assessment* (EPA, 2019f) summarizes the parameters and equations for the multi-zone model. The far-field volume, air exchange rate, and near-field indoor wind speed are identical to those used in the 1-BP Spot Cleaning Model (see Section 2.3.1.17). These values were selected using engineering judgment and literature data that EPA believed to be representative of a typical dry cleaner.

Based on recent communication with Enviro Tech, only eight dry cleaning establishments were using 1-BP in 2019 (Enviro Tech International, 2019). EPA assumed these eight dry cleaning shops are small shops that operate up to 12 hours a day and up to 6 days a week. In addition, EPA assumed each shop only has a single machine. The assumption is supported by an industry study conducted in King County, Washington, where 96 percent of 151 respondents reported having only one machine at their facility. Four reported having two machines, and two reported having three machines (Whittaker and Johanson, 2011).

EPA modeled the baseline scenario assuming the facility operates a converted third generation machine, the machine type observed at all three New Jersey dry cleaners in the Blando et al. (2010) study. For the

engineering control scenario, EPA modeled a facility with a fourth generation machine. EPA believes facilities using 1-BP are unlikely to own fifth generation machines ([ERG, 2005](#)).

EPA assessed three types of workers within the modeled dry cleaning facility: 1) a worker who performs spot cleaning; 2) a worker who unloads the dry cleaning machine and finishes and presses the garments; and 3) an occupational non-user. Each worker type is described in further detail below. EPA assumed each worker activity is performed over the full 12-hour operating day.

- EPA assumed spot cleaning occurs for a duration varying from two to five hours in the middle of the twelve-hour day. The worker is exposed at the spot cleaning near-field concentration during this time, and at the far-field concentration for the remainder of the day. Spot cleaning can be performed for both dry cleaned loads and for laundered loads.
- EPA assumed a separate worker unloads the dry cleaning machine, and finishes and presses the garments. After each load, EPA assumed this worker spends five minutes unloading the machine, during which he or she is exposed at the machine near-field concentration. After unloading, the worker spends five minutes in the finishing near-field to prepare the garments. Then, the worker spends another 20 minutes finishing and pressing the cleaned garments. During this 20-minute period of finishing and pressing, the residual 1-BP solvent is off-gassed into the finishing near-field. The amount of residual 1-BP solvent is estimated using measured data presented in ([Von Grote et al., 2003](#)). These unloading and finishing activities are assumed to occur at regular intervals throughout the twelve-hour day. The frequency of unloading and finishing depends on the number of loads dry cleaned each day, which varies from one to 14, where 14 was the maximum number of loads observed in the studies ([Blando et al., 2010](#); [Eisenberg and Ramsey, 2010](#)). When this worker is not unloading the dry cleaning machine or finishing and pressing garments, the worker is exposed at the far-field concentration.
- EPA assumed one occupational non-user is exposed at the far-field concentration for twelve hours a day. The occupational non-user could be the cashier, tailor, or launderer, who works at the facility but does not perform dry cleaning activities.

Table 2-21 presents the *Monte Carlo* results with the Latin hypercube sampling method and 10,000 iterations. Statistics of the 12-hr TWA exposures²⁴ (95th and 50th percentiles) are calculated at the end of the simulation after all iterations have completed. The AC, ADC, and LADC calculations are integrated into the *Monte Carlo* simulation, such that the exposure frequency matches the model input values for each iteration. As shown in the table, the worker who performs unloading and finishing activities have the highest exposure; this exposure can be reduced if the facility switches from a third generation to a fourth generation machine. However, the machine type does not significantly impact exposure level for other persons present at the facility, including the spot cleaner and the occupational non-user. The model values cover a wider distribution of exposure levels when compared to the monitoring data. This is likely due to the wide range of model input parameter values covering a higher number of possible exposure scenarios. However, the modeled occupational non-user exposures are lower than actual

²⁴ The 12-hr TWA values are the model exposure concentration averaged over a 12-hr period. These values do not follow the OSHA extended shift policy.

monitoring results. The model assumes the occupational non-user spends their time entirely in the far-field. In reality, these employees may occasionally perform activities in the near-field, thereby having a higher level of exposure.

Table 2-22 presents the exposure concentration for children who may be present at the dry cleaning facility. Because many dry cleaners are family owned and operated, it is possible that children may be present for a four-hour period (3 – 7pm) after school, during which they may be exposed at similar levels as occupational non-users. The table provides the 4-hr TWA exposure concentration and the 24-hr TWA AC. EPA could not calculate exposure for chronic scenarios (ADC and LADC) due to uncertainty in the exposure frequency and number of years with exposure for children. EPA believes these exposures are unlikely to be chronic in nature.²⁵ In addition, it is unclear whether children are present at any of the remaining eight dry cleaners.

Table 2-21. Summary of 1-BP Dry Cleaning Exposures for Workers and Occupational Non-users Based on Modeling

Machine Type	12-hr TWA Exposures (ppm) C _{1-BP, 12-hr TWA}		Acute, Non-Cancer Exposures (ppm) AC _{1-BP, 24-hr TWA}		Chronic, Non-Cancer Exposures (ppm) ADC _{1-BP, 24-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 24-hr TWA}	
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile
	Workers: Machine Unloading and Finishing (Near-Field)							
3 rd Gen.	14.1	60.5	7.06	30.3	4.98	21.70	1.89	8.57
4 th Gen.	2.38	6.36	1.19	3.18	0.84	2.30	0.31	0.94
Workers: Spot Cleaning (Near-Field)								
3 rd Gen.	2.93	7.93	1.47	3.97	1.03	2.83	0.39	1.14
4 th Gen.	2.40	5.65	1.20	2.83	0.85	2.02	0.32	0.82
Occupational non-users (Far-Field)								
3 rd Gen.	1.82	6.65	0.91	3.33	0.64	2.37	0.24	0.95
4 th Gen.	1.31	4.21	0.65	2.11	0.46	1.49	0.17	0.60

Confidence rating of air concentration data: N/A – modeled data.

Table 2-22. Summary of 1-BP Dry Cleaning Exposures for Children Based on Modeling

Machine Type	4-hr TWA Exposures (ppm) C _{1-BP, 4-hr TWA}		Acute, Non-Cancer Exposures (ppm) AC _{1-BP, 24-hr TWA}		Chronic, Non-Cancer Exposures (ppm) ADC _{1-BP, 24-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 24-hr TWA}	
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile
	Children (Far-Field)							
3 rd Gen.	0.54	4.03	0.09	0.67	N/A	N/A	N/A	N/A
4 th Gen.	0.09	1.02	0.01	0.17	N/A	N/A	N/A	N/A

²⁵ EPA did not calculate risk for children associated with acute exposure at dry cleaners because the acute health domains (developmental effects) are not applicable to children. Further, EPA did not calculate risks for chronic and cancer scenarios for children at dry cleaners because EPA believes exposure to children at workplaces are unlikely to be chronic in nature.

N/A – Not applicable

Confidence rating of air concentration data: N/A – modeled data.

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

For this condition of use, exposure is assessed using 1-BP personal breathing zone monitoring data from three different studies, all of which have a high confidence rating as determined through EPA’s systematic review process. The monitoring data, which were collected from facilities using converted third generation machines, are in good agreement with model results for the same machine type.

The multi-zone Dry Cleaning model (peer reviewed in 2016) uses a *Monte Carlo* approach to incorporate variability in the environmental conditions, worker activity patterns, use rate, and other model input parameters. The model assumes each dry cleaner operates a single machine, and does not represent exposures for larger facilities that may have multiple machines. Based on reasonably available information above, EPA has a high level of confidence in the assessed exposure for these machine types.

2.3.1.17 Spot Cleaner, Stain Remover

Process Descriptions

EPA assessed a separate spot cleaning scenario at dry cleaners. This scenario represents dry cleaners or other shops that use 1-BP-based spot cleaning formulations but do not otherwise use 1-BP in a dry cleaning machine. The extent of such uses is likely limited, as Enviro Tech claimed that while DrySolv spotting products were advertised to the dry cleaning industry, most were never commercialized ([Enviro Tech International, 2017](#)).

On receiving a garment, dry cleaners inspect for stains or spots and remove as much of them as possible before cleaning the garment in a machine. As Figure 2-10 shows, spot cleaning occurs on a spotting board and can involve the use of a spotting agent containing various solvents, such as 1-BP. The spotting agent can be applied from squeeze bottles, hand-held spray bottles, or even from spray guns connected to pressurized tanks. Once applied, the dry cleaner may come into further contact with the 1-BP if using a brush, spatula, pressurized air or steam, or their fingers to scrape or flush away the stain ([Young, 2012](#); [NIOSH, 1997](#)).



Figure 2-10. Overview of Use of Spot Cleaning at Dry Cleaners

Assessment of Inhalation Exposure Based on Monitoring Data

Table 2-23 presents 8-hr TWA PBZ monitoring data from OSHA CEHD for three facilities where spot cleaning is performed. At one facility, workers spray-applied solvent formulation to stained portions of dresses and did not wear any personal protective equipment. It is unclear if there were any engineering controls at the facility to mitigate worker exposure.

The 50th and 95th percentile exposure level for workers were 0.90 ppm and 4.73 ppm 8-hr TWA, respectively. No exposure monitoring data are available for occupational non-users.

Table 2-23. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Spot Cleaner Based on Monitoring Data

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Worker	0.90	4.73	0.36	2.42	6	High

Source: ([OSHA, 2019, 2013b](#))

Assessment of Inhalation Exposure Based on Modeling

Figure 2-11 illustrates the near-field/far-field modeling approach that EPA applied to spot cleaning facilities. The model, including all input parameters, are described in more detail in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019f](#)).

As the figure shows, chemical vapors evaporate into the near-field (at evaporation rate G), resulting in near-field exposures to workers at a concentration C_{NF} . The concentration is directly proportional to the amount of spot cleaner applied by the worker, who is standing in the near-field-zone (*i.e.*, the working zone). The volume of this zone is denoted by V_{NF} . The ventilation rate for the near-field zone (Q_{NF}) determines how quickly the chemical of interest dissipates into the far-field (*i.e.*, the facility space surrounding the near-field), resulting in occupational non-user exposures at a concentration C_{FF} . V_{FF} denotes the volume of the far-field space into which the chemical of interest dissipates out of the near-field. The ventilation rate for the surroundings, denoted by Q_{FF} , determines how quickly the chemical dissipates out of the surrounding space and into the outdoor air.

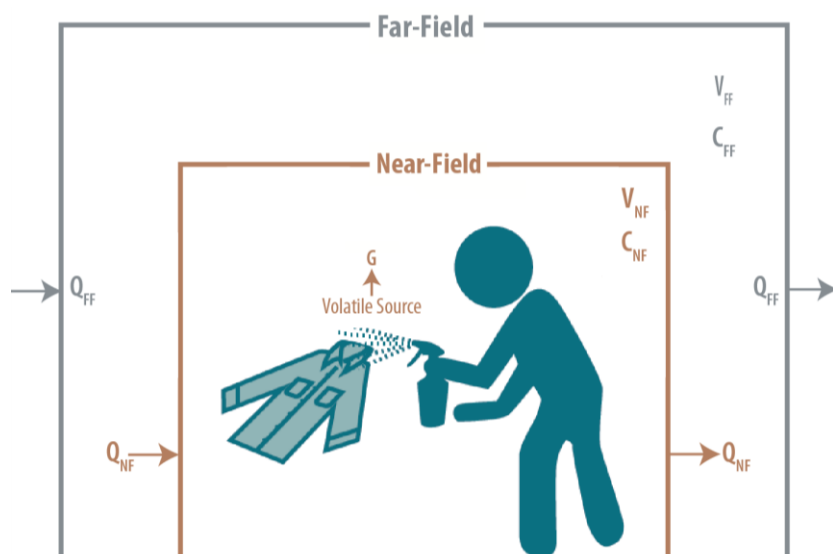


Figure 2-11. Schematic of the Near-Field/Far-Field Model for Spot Cleaning

To determine the 1-BP use rate, EPA references a comparative analysis from the Massachusetts Department of Environmental Protection (MassDEP), which contains case studies of Perc alternatives that can be potentially used at dry cleaners. One case study estimates a dry cleaner spends \$60 per month on spotting agents containing 1-BP. This particular facility dry cleans 100 pieces of garments per day. MassDEP noted that the facility size can vary greatly among individual dry cleaners ([MassDEP, 2013](#)). Blando et al. (2009) estimated that 1-BP solvent products cost \$45 per gallon. Based on this information, EPA calculated a spot cleaner use rate of 1.33 gallons per month, or 16 gallons per year. The Safety Data Sheet for DrySolv, a common 1-BP formulation, indicates the product contains greater than 87 percent 1-BP by weight ([Enviro Tech International, 2013](#)).

EPA performed *Monte Carlo* simulations, applying 100,000 iterations and the Latin hypercube sampling method. Table 2-24 presents a statistical summary of the exposure modeling results. The 50th and 95th percentile exposure for workers (near-field) are 3.24 ppm and 7.03 ppm 8-hr TWA, respectively. These results are generally comparable to the monitoring data. For occupational non-users (far-field), the 50th and 95th percentile exposure levels are 1.63 ppm and 4.68 ppm 8-hr TWA, respectively. The table also presents the AC, ADC, and LADC values, which are integrated into the *Monte Carlo*. EPA assumes no engineering controls (*e.g.*, exhaust hoods) are present at spot cleaning facilities, because controls may not be financially feasible for small shops.

Table 2-24. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Use of Spot Cleaner Based on Modeling

Category	Acute, Non-Cancer Exposures (8-Hour TWAs in ppm)		Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm)		Chronic, Cancer Exposures (ppm)		Confidence Rating of Air Concentration Data
	AC _{1-BP, 8-hr TWA}		ADC _{1-BP, 8-hr TWA}		LADC _{1-BP, 8-hr TWA}		
	50th Percentile	95th Percentile	50th Percentile	95th Percentile	50th Percentile	95th Percentile	
Worker	3.24	7.03	0.76	1.66	0.29	0.68	N/A – Modeled Data
ONU	1.63	4.68	0.38	1.10	0.15	0.45	

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

For this condition of use, the 1-BP personal breathing zone monitoring data have a high confidence rating as determined through EPA’s systematic review process. The data, however, come from OSHA CEHD, which is not intended to represent typical workplace exposure levels.

The monitoring data are supplemented with the near-field/far-field Spot Cleaning exposure model. The model incorporates a *Monte Carlo* simulation to address variability, and the model has been previously peer reviewed in 2016. Although there is uncertainty in the representativeness of the spot cleaner use rate from the MassDEP case study used in modeling, the model results are in good agreement with the monitoring data. Based on reasonably available information above, EPA has a high level of confidence in the assessed exposure.

2.3.1.18 Adhesive Chemicals (Spray Adhesives)

Process Descriptions

1-BP is used in spray adhesives for foam cushion manufacturing and fabrication (*e.g.*, the furniture industry). Figure 2-12 illustrates a typical process of using spray adhesives. During foam cushion manufacturing and fabrication, foam is cut into pieces and then bonded together to achieve the appropriate shape. Spray guns are used to spray-apply an adhesive onto flexible foam surfaces for bonding. Adhesive spraying typically occurs either on an open top workbench with side panels that may have some local ventilation, or in an open workspace with general room ventilation. After the adhesive is applied, workers assemble the cushions by hand-pressing together pieces of cut flexible foam ([NIOSH, 2003b](#), [2002b](#)).

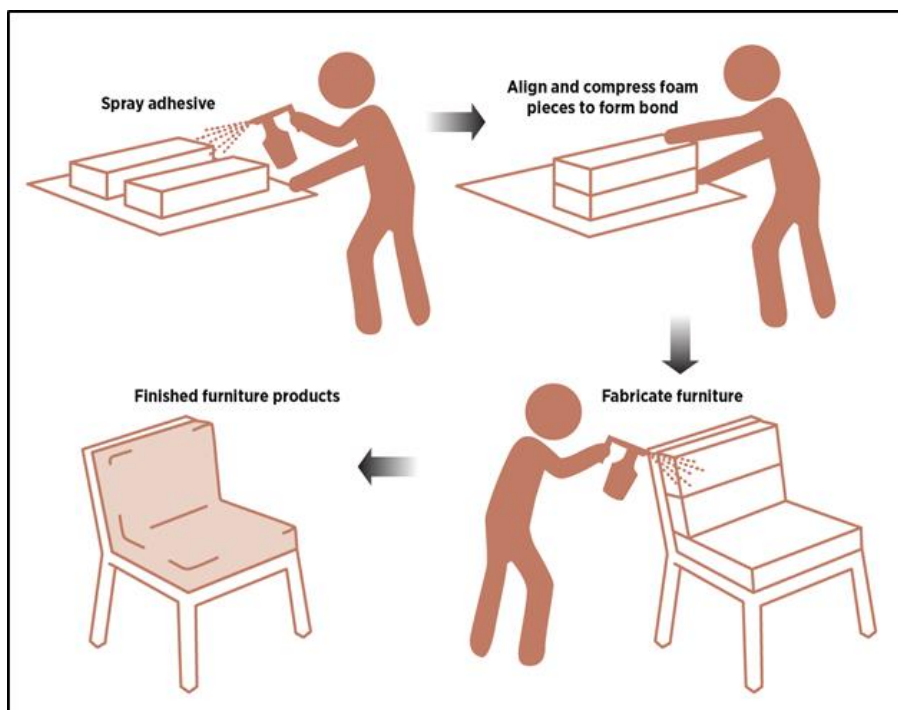


Figure 2-12. Overview of Use of Spray Adhesive in the Furniture Industry

Assessment of Inhalation Exposure Based on Monitoring Data

1-BP exposure monitoring data were identified in several sources, including journal articles, NIOSH HHEs, and OSHA CEHD database. NIOSH HHEs are conducted at the request of employees, employers, or union officials and help inform on potential hazards present at the workplace. HHEs can also be conducted in response to a technical assistance request from other government agencies. OSHA CEHD are workplace monitoring data from OSHA inspections. These inspections can be random or targeted, or can be the result of a worker complaint.

Among these sources, three NIOSH studies provide the most comprehensive information on worker exposure to 1-BP from spray adhesives in foam cushion manufacturing. Two of the three HHEs also compare exposure pre- and post-engineering controls (EC). A summary of these HHEs follows:

- From March 1998 to April 2001, NIOSH investigated a facility in Mooresville, North Carolina to assess 1-BP exposures during manufacturing of foam seat cushions ([Reh et al., 2002](#)). The company had four departments: Saw, Assembly, Sew, and Covers. Workers in Assembly and Covers departments worked directly with the adhesive; however, workers in all four departments were exposed. The spray adhesive used at this facility contained between 60 and 80 percent 1-BP. NIOSH conducted an initial exposure assessment in 1998 and observed that the ventilation exhaust filters were clogged with adhesive. In 2001, NIOSH conducted a follow-up exposure assessment after the facility made improvements to its ventilation system.
- From November 2000 to August 2001, NIOSH investigated workplace exposures to 1-BP during manufacturing of foam seat cushions at another cushion company in North Carolina ([NIOSH, 2002b](#)). This facility used a spray adhesive containing 55 percent 1-BP. NIOSH conducted an initial exposure assessment in 2000, and recommended that the facility reduce worker exposure by enclosing the spray stations to create “spray booths.” Subsequently, in 2001, NIOSH conducted a follow-up assessment after spray station enclosures were installed.
- From April 1999 to May 2001, NIOSH investigated another cushion company in North Carolina ([NIOSH, 2003b](#)). In this study, NIOSH conducted two separate exposure assessments. In the initial assessment, NIOSH measured 1-BP inhalation exposures to workers in and near the adhesive spray operation areas. In the second assessment, NIOSH measured additional 1-BP inhalation exposures at the facility. There were no changes to the facility’s local exhaust ventilation system between the first and second assessment.

Table 2-25 summarizes available 1-BP exposure data from the NIOSH and OSHA sources. The data set includes exposures in pre-EC and post-EC scenarios for each worker job category. EPA defined three job categories for 1-BP spray adhesive use:

- Sprayers: Workers who perform manual spraying of 1-BP adhesive as a regular part of his or her job;
- Non-sprayers: Workers who are not “sprayers,” but either handle the 1-BP adhesive or spend the majority of their shift working in an area where spraying occurs. For example, the NIOSH ([2002](#)) study indicated spraying occurs in the Assembly and Covers departments. EPA assumes workers in these departments who do not perform spraying still work in the vicinity of spraying operations and may be regularly exposed to 1-BP; and
- Occupational non-users: Workers who do not regularly perform work in an area of the facility where spraying occurs. For example, EPA assumes workers in the Saw and Sew departments of the 2002 NIOSH study ([2002](#)) are “occupational non-users.”

For each worker job category (sprayer, non-sprayer or occupational non-user) and exposure scenario (pre-EC or post-EC), EPA calculated the 50th and 95th percentile exposure levels from the observed data set. Pre-EC exposure scenarios suggest that all workers at foam cushion manufacturing facilities that use 1-BP spray adhesives have substantial exposure to 1-BP. Sprayers have the highest levels of exposure because they work directly with the 1-BP adhesive. However, non-sprayers and occupational non-users may also be exposed.

In general, exposure levels for job categories vary widely depending on the worker's specific work activity pattern, individual facility configuration, and proximity to the 1-BP adhesive. For example, workers in the Saw and Sew departments in the NIOSH (2002) study classified as "occupational non-users" are exposed at levels above 100 ppm 8-hr TWA. The high exposure levels are caused by their proximity to spraying operations in other departments, even though no adhesive is used in the Saw and Sew departments (Reh et al., 2002). Additionally, some workers may not have a single assigned role; as such, their exposure level will vary depending on the specific tasks performed.

Post-EC exposure scenarios suggest that engineering controls such as ventilation and spray booth enclosure, if well designed, maintained, and operated, can reduce worker exposures by an order of magnitude. However, engineering controls alone do not reduce exposures for sprayers and non-sprayers to levels below 0.1 ppm, the time-weighted average threshold limit value (TLV) recommended by the American Conference of Governmental Industrial Hygienists (ACGIH).

Additional 1-BP worker exposure monitoring data have been identified in other literature studies such as Hanley et al. (2009; 2006b), Ichihara et al. (2002), and Majersik et al. (2007). However, these studies are not used in EPA's analysis because they either do not provide individual data points or lack specific information on worker job descriptions to adequately categorize the exposure results.

Table 2-25. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Spray Adhesive on Monitoring Data

Category ^a	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP} , 8-hr TWA and ADC _{1-BP} , 8-hr TWA		Chronic, Cancer Exposures (ppm) LADC _{1-BP} , 8-hr TWA		Data Points	Confidence Rating of Air Concentration Data
	50th Percentile	95th Percentile	50th Percentile	95th Percentile		
Sprayer, Pre EC	132.8	253.6	52.8	130.04	83	High
Sprayer, Post EC	17.8	41.9	7.08	21.5	49	
Non-Sprayer ^b , Pre EC	127.2	210.9	50.6	108.1	31	
Non-Sprayer ^b , Post EC	18.0	28.8	7.15	14.8	9	
ONU ^c , Pre EC	3.0	128.7	1.19	66.0	39	
ONU ^c , Post EC	2.0	5.48	0.79	2.81	17	

Sources: (OSHA, 2013b; NIOSH, 2003b, 2002b; Reh et al., 2002)

^a EC = Engineering Controls. Pre-EC = Initial NIOSH visit; Post EC = Follow-up NIOSH visit engineering controls implemented: Enclosing spray tables to create “spray booths” and/or improve ventilation.

^b Non-Sprayer refers to those employees who are not sprayers, but either handle the adhesive or spend the majority of their shift working in an area where spraying occurs.

^c Occupational non-user refers to those employees who do not regularly work in a department/area where spraying occurs (e.g., employees in saw and sew departments).

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

This condition of use assesses exposure using 1-BP personal breathing zone monitoring data from several studies. All data have a high confidence rating as determined through EPA’s systematic review process. The individual data points in these studies are further characterized into either pre- or post-EC scenarios, based on reasonably available information on engineering control. EPA has a high level of confidence in the assessed exposure based on the confidence rating of the underlying monitoring data.

2.3.1.19 THERMAX™ Installation

Process Descriptions

1-BP is used in the production of a polyisocyanurate rigid board insulation produced by Dow Chemical Company that goes by the trade name THERMAX™. THERMAX™ can be used for interior and exterior applications including walls, ceilings, roofs, foundations, basements, and crawl spaces in commercial and residential buildings. After THERMAX™ is installed, seams are typically covered with aluminum foil tape. Additional wallboard, baseboard, or molding may then be installed over the insulation²⁶.

²⁶ <https://www.dupont.com/content/dam/dupont/amer/us/en/performance-building-solutions/public/documents/179-04453.pdf>

Assessment of Inhalation Exposure Based on Modeling

EPA has not identified exposure monitoring data associated with this condition of use. THERMAX™ products comprise a polyisocyanurate foam core with aluminum facers on each side. Because the aluminum facers inhibit the off-gassing of 1-BP, workers are only potentially exposed to 1-BP off-gassed from edges of the insulation.

EPA conducted a screening-level analysis using EPA's Indoor Environment Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU) model to estimate the potential 1-BP concentration from off-gassing of THERMAX™ insulation. The IECCU model is a simulation program that can be used to model indoor chemical air concentrations in buildings with multiple zones and multiple sources and sinks. The IECCU model uses a general mass balance equation for a chemical of interest to calculate the time series of indoor concentrations. The equation combines all processes governing source emissions, convective transfer by bulk air, sorption, and re-emission by indoor sinks, interactions with airborne particles and settled dust and gas-phase chemical reactions. Results of the analysis show that worker and ONU exposure to 1-BP during installation would be below 0.01 ppm 8-hr TWA inside a residential home for the initial work day, and less on subsequent days after install. Additional details of this screening-level analysis can be found in Appendix L of *1-BP Supplemental File: Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019f](#)).

2.3.1.20 Other Uses

Process Descriptions

Based on products identified in EPA's data gathering and information received in public comments, a variety of other aerosol and non-aerosol uses may exist for 1-BP [see Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane, [EPA-HQ-OPPT-2016-0741-0003](#) (U.S. EPA, 2017c)]. Examples of these uses include, but are not limited to ([AIA, 2017](#); [CRC Industries Inc., 2017](#); [Enviro Tech International, 2017](#); [OSHA; NIOSH, 2013](#)):

- Aerosol mold cleaning and release: 1-BP is a carrier solvent in aerosol mold cleaning and release products. These products are used to coat the molds for injection molding, compression molding, blow molding and extrusion applications. The product use rate varies depending on mold size and frequency of re-application. This use is likely limited because 1-BP is not compatible with some mold release applications.
- Asphalt extraction: 1-BP is used for asphalt extraction in centrifuge extractors, vacuum extractors, and reflux extractors. In this process, 1-BP is used to separate asphalt from the aggregate and filler material to allow for determination of asphalt content. This condition of use is expected to make up one percent of the total domestic 1-BP use volume.
- Coin and scissor cleaner: 1-BP is used in product formulations designed to clean collectible coins and scissors.
- General purpose degreaser: General purpose degreasing products containing 1-BP (both aerosol and non-aerosol) are used in industrial settings, with usage varying widely by facility. Refineries and utilities are known to be the largest volume users, with usage being cyclical as 1-BP is used to clean

and maintain equipment primarily during plant shutdowns. 1-BP is also used for heavy duty transportation maintenance, *e.g.*, maintaining buses, trains, trucks, etc.

- High voltage cable cleaner: 1-BP is contained in both aerosol and non-aerosol cleaning products, which are used to clean the semi-conductive cores of high voltage cables when splicing and terminating cables. A few ounces of product are used to clean each splice.
- Refrigerant flush: 1-BP is used to flush oxygen lines in hospitals and in the aerospace industry. 1-BP is also used to clean refrigeration lines in various industries. This condition of use is expected to make up one percent of the total domestic 1-BP use volume.
- Temperature indicator: 1-BP is used in temperature indicating fluids and coatings. These coatings can be applied to fabrics, rubber, plastics, glass, and/or polished metal. When the substrate is heated, the coating will melt at the designated temperature, leaving a mark on the surface. This condition of use is expected to make up less than 0.5 percent of the total domestic 1-BP use volume.
- Other uses: 1-BP has a number of other uses, such as adhesive accelerant, as coating component for pipes and fixtures, and as laboratory chemical for research and development.

Assessment of Inhalation Exposure Based on Monitoring Data

EPA has not identified exposure data associated with these conditions of use. The worker activity, use pattern, and associated exposure will vary for each condition of use. For conditions of use where 1-BP is used in an aerosol application, the exposure levels may be as high as those presented in Section 2.3.1.15. Actual exposure levels for each condition of use will likely vary depending on the use volume, engineering control, and PPE.

2.3.1.21 Disposal, Recycling

Process Descriptions

Each of the conditions of use of 1-BP may generate waste streams that are collected and transported to third-party sites for disposal, treatment, or recycling. Industrial sites that treat or dispose onsite wastes that they themselves generate are assessed in each condition of use assessment in Sections 2.3.1.5 through 2.3.1.20. Wastes containing 1-BP that are generated during a condition of use and sent to a third-party site for treatment, disposal, or recycling may include wastewater, solid wastes, and other wastes.

Solid wastes are defined under RCRA as any material that is discarded by being: abandoned; inherently waste-like; a discarded military munition; or recycled in certain ways (certain instances of the generation and legitimate reclamation of secondary materials are exempted as solid wastes under RCRA). Solid wastes may subsequently meet RCRA's definition of hazardous waste by either being listed as a waste at 40 CFR §§ 261.30 to 261.35 or by meeting waste-like characteristics as defined at 40 CFR §§ 261.20 to 261.24. Solid wastes that are hazardous wastes are regulated under the more stringent requirements of Subtitle C of RCRA, whereas non-hazardous solid wastes are regulated under the less stringent requirements of Subtitle D of RCRA. Solid wastes containing 1-BP may be regulated as a hazardous waste under RCRA waste code D001 for ignitable liquids (40 CFR 261.21). 1-BP may also be commingled with solvent mixtures that are RCRA regulated substances. These wastes would be either

incinerated in a hazardous waste incinerator or disposed to a hazardous waste landfill. Some amount of 1-BP may be improperly disposed as municipal wastes, although they are likely to be a small fraction of the overall waste stream. As stated in the Problem Formulation, releases to RCRA Subtitle C and Subtitle D landfills are not included in this risk evaluation.

Assessment of Inhalation Exposure Based on Modeling

EPA did not identify exposure monitoring data related to waste treatment and disposal sites. To assess worker exposure, EPA assumed wastes containing 1-BP are transported and handled as bulk liquid shipments and modeled exposure using the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* (previously described in Section 2.3.1.6).

Table 2-26 summarizes the model exposures from waste handling activities. The model assumes liquid wastes may contain a range of concentrations for 1-BP. The central tendency scenario assumes a mixture containing 30 percent 1-BP, while the high-end scenario assumes the waste contains 100 percent 1-BP. EPA does not know the typical 1-BP concentration in the waste stream and the model may not be representative of the full distribution of possible exposure levels at waste disposal facilities.

Table 2-26. Summary of 1-BP 8-hr TWA Exposures (AC, ADC and LADC) for Disposal Based on Modeling

Category	Acute and Chronic, Non-Cancer Exposures (8-Hour TWAs in ppm) AC _{1-BP, 8-hr TWA} and ADC _{1-BP, 8-hr TWA}		Chronic, Cancer Exposures (ppm) LADC _{1-BP, 8-hr TWA}		Confidence Rating of Air Concentration Data
	Central tendency	High-end	Central tendency	High-end	
Worker	3.83E-3	5.67E-2	1.52E-3	2.91E-2	N/A – Modeled Data

Strength, Limitation, and Uncertainty of the Inhalation Exposure Assessment

The *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is used to estimate exposure. The model uses a combination of published EPA emission factors and engineering judgement to estimate central tendency and high-end exposures. EPA believes the model exposures are likely to be representative of exposure associated with bulk container loading. However, the model does not account for other potential sources of exposure at industrial facilities, such as sampling, equipment cleaning, and other process activities. The model also assumes only one container is loaded per day, although larger facilities may have higher product loading frequencies. These model uncertainties could result in an underestimate of the worker exposure.

Based on reasonably available information above, EPA has a medium level of confidence in the assessed exposure.

2.3.1.22 Summary of Inhalation Exposure Assessment

Table 2-27 summarizes the inhalation exposure estimates for all occupational exposure scenarios. Where statistics can be calculated, the central tendency estimate represents the 50th percentile exposure level of the available data set, and the high-end estimate represents the 95th percentile exposure level. For most conditions of use, the central tendency and high-end TWA exposures for both workers and ONUs are

above the ACGIH TLV of 0.1 ppm. The TWA exposures are 8-hr TWA, except for the dry cleaning condition of use, where exposures are modeled as 12-hr TWA.

For conditions of use where both monitoring and model data are available, the results were found to be in good agreement with each other (with difference less than one order of magnitude).

Table 2-27. Summary of Occupational Inhalation Exposure Results

Condition of Use	Exposure Scenario	Category	TWA Exposures		Chronic, Cancer Exposures		Statistical Value for Central Tendency and High-end	Data Type
			C ₁ -BP, 8-hr or 12-hr TWA (ppm)		LADC ₁ -BP, 8-hr or 24-hr TWA (ppm)			
			Central Tendency	High-end	Central Tendency	High-end		
Manufacture	-	Worker	9.00E-02	2.70E-01	3.58E-02	1.38E-01	Median, Maximum	Monitoring Data
Import, Processing as a Reactant, Processing – Incorporation into Articles, Repackaging	-	Worker	3.83E-3	5.67E-2	1.52E-3	2.91E-2	N/A – CT and HE ^b	Model (Deterministic)
Processing - Incorporation into Formulation	-	Worker	7.20E+00		2.86E+00		N/A (1 data point)	Monitoring Data
	-	ONU	1.55E-01	2.76E-01	6.16E-02	1.41E-01	50 th and 95 th Percentile	
Batch Vapor Degreaser (Open-Top)	-	Worker	6.70E+00	4.94E+01	2.66E+00	2.53E+01	50 th and 95 th Percentile	Monitoring Data
	-	ONU	2.00E-02	2.15E+00	7.95E-03	1.10E+00		
	Pre-EC	Worker	1.89E+00	2.39E+01	7.04E-01	9.19E+00	50 th and 95 th Percentile	Model (Probabilistic)
	Post-EC	Worker	1.89E-01	2.39E+00	7.04E-02	9.19E-01		
	Pre-EC	ONU	9.93E-01	1.35E+01	3.71E-01	5.23E+00		
	Post-EC	ONU	9.93E-02	1.35E+00	3.71E-02	5.23E-01		
Batch Vapor Degreaser (Closed-loop)	-	Worker	3.78E-02	4.78E-01	1.41E-02	1.84E-01	50 th and 95 th Percentile	Model (Probabilistic)
	-	ONU	1.99E-02	2.70E-01	7.43E-03	1.05E-01		
Cold Cleaner	-	Worker	4.30E+00	7.40E+00	1.71E+00	3.79E+00	Median, Maximum	Monitoring Data
	-	ONU	2.60E+00		1.03E+00	1.33E+00	N/A (1 data point)	
	-	Worker	5.49E-01	1.19E+01	2.06E-01	4.59E+00	50 th and 95 th Percentile	Model (Probabilistic)
	-	ONU	2.89E-01	6.83E+00	1.08E-01	2.63E+00		
Aerosol Spray Degreaser/Cleaner	Pre-EC	Worker	1.61E+01	3.16E+01	6.38E+00	1.62E+01	50 th and 95 th Percentile	Monitoring Data
	Post-EC	Worker	5.50E+00		2.19E+00	2.82E+00	N/A (1 data point)	
	-	Worker	6.37E+00	2.25E+01	2.38E+00	9.05E+00	50 th and 95 th Percentile	Model (Probabilistic)
	-	ONU	1.10E-01	9.30E-01	4.00E-02	3.60E-01		
Adhesive Chemicals (Spray Adhesive)	Pre-EC	Sprayer	1.33E+02	2.54E+02	5.28E+01	1.30E+02	50 th and 95 th Percentile	Monitoring Data
	Post-EC	Sprayer	1.78E+01	4.19E+01	7.08E+00	2.15E+01		

Condition of Use	Exposure Scenario	Category	TWA Exposures		Chronic, Cancer Exposures		Statistical Value for Central Tendency and High-end	Data Type
			C ₁ -BP, 8-hr or 12-hr TWA (ppm)		LADC ₁ -BP, 8-hr or 24-hr TWA (ppm)			
			Central Tendency	High-end	Central Tendency	High-end		
	Pre-EC	Non-Sprayer	1.27E+02	2.11E+02	5.06E+01	1.08E+02		
	Post-EC	Non-Sprayer	1.80E+01	2.88E+01	7.15E+00	1.48E+01		
	Pre-EC	ONU	3.00E+00	1.29E+02	1.19E+00	6.60E+01		
	Post-EC	ONU	2.00E+00	5.48E+00	7.95E-01	2.81E+00		
Dry Cleaning	-	Worker	2.94E+01	5.02E+01	1.17E+01	2.57E+01	50 th and 95 th Percentile	Monitoring Data
	-	ONU	1.21E+01	2.06E+01	4.80E+00	1.06E+01		
	3rd Gen	Spot Cleaner	2.93E+00	7.93E+00	3.94E-01	1.14E+00	50 th and 95 th Percentile	Model ^a (Probabilistic)
	3rd Gen	Machine & Finish	1.41E+01	6.05E+01	1.89E+00	8.57E+00		
	3rd Gen	ONU	1.82E+00	6.65E+00	2.43E-01	9.49E-01		
	3rd Gen	Child	5.41E-01	4.03E+00	N/A	N/A		
	4th Gen	Spot Cleaner	2.40E+00	5.65E+00	3.20E-01	8.22E-01		
	4th Gen	Machine & Finish	2.38E+00	6.36E+00	3.15E-01	9.35E-01		
	4th Gen	ONU	1.31E+00	4.21E+00	1.73E-01	5.96E-01		
	4th Gen	Child	8.96E-02	1.02E+00	N/A	N/A		
Spot Cleaner, Stain Remover	-	Worker	9.00E-01	4.73E+00	3.58E-01	2.42E+00	50 th and 95 th Percentile	Monitoring Data
	-	Worker	3.24E+00	7.03E+00	2.89E-01	6.82E-01		Model (Probabilistic)
	-	ONU	1.63E+00	4.68E+00	1.45E-01	4.45E-01		
Disposal, Recycling	-	Worker	3.83E-3	5.67E-2	1.52E-3	2.91E-2	N/A – CT and HE ^b	Model (Deterministic)

a – For this condition of use, the acute concentration (AC) and chronic, non-cancer exposure (ADC) differ from the TWA exposure. See previous subsections for AC and ADC values.

b – Based on distinct model scenarios that are likely representative of central tendency (CT) and high-end (HE) exposures.

2.3.1.23 Dermal Exposure Assessment

Dermal absorption of 1-BP depends on the type and duration of exposure. Where exposure is non-occluded, only a fraction of 1-BP that comes into contact with the skin will be absorbed as the chemical readily evaporates from the skin (see Section 1.1). However, dermal exposure may be increased in cases of occluded exposure, repeated contacts, or dermal immersion. For example, work activities with a high degree of splash potential may result in 1-BP liquids trapped inside the gloves, inhibiting the evaporation of 1-BP and increasing the exposure duration.

To assess exposure, EPA used the *Dermal Exposure to Volatile Liquids Model* (see following equation) to calculate the dermal retained dose. The equation modifies EPA/OPPT *2-Hand Dermal Exposure to Liquids Model* (peer reviewed) by incorporating a “fraction absorbed (f_{abs})” parameter to account for the evaporation of volatile chemicals and a “protection factor (PF)” to account for glove use:

Equation 2-2. Equation for Calculating Occupational Dermal Exposure

$$D_{exp} = \frac{S \times (Q_u \times f_{abs}) \times Y_{derm} \times FT}{PF}$$

Where:

D_{exp} is the dermal retained dose (mg/kg-day)

S is the surface area of contact (Default: 535 cm² for central tendency and 1,070 cm² for high-end scenario, equivalent to the total surface area of one and two hands, respectively)

Q_u is the quantity remaining on the skin after an exposure event (Default: 1.4 mg/cm²-event for central tendency and 2.1 mg/cm²-event for high-end scenario²⁷)

Y_{derm} is the weight fraction of the chemical of interest in the liquid ($0 \leq Y_{derm} \leq 1$)

FT is the frequency of events (integer number per day)

f_{abs} is the fraction of applied mass that is absorbed (Default for 1-BP: 0.0029)

PF is the glove protection factor (Default: see Table 2-28)

In a 2011 *in vitro* dermal penetration study, Frasch et al. (2011) measured a 1-BP fractional absorption (f_{abs}) of 0.16 percent in a non-occluded, finite dose scenario. The author noted a large standard deviation in the experimental measurement, which is indicative of the difficulty in spreading a small, rapidly evaporating dose of 1-BP evenly over the skin surface. The measurement was performed in an open fume hood with an average air speed of 0.3 m/s (30 cm/s), a wind speed higher than those typically experienced in an indoor workplace. At a more typical indoor wind speed of 12.2 cm/s, the 1-BP fractional absorption can be adjusted to 0.29 percent. Detailed calculations of this adjusted value are provided in Appendix D.

²⁷ Value for Q_u is derived from experimental studies of liquid with varying viscosities. The 50th and 90th percentile value of this distribution correspond to 1.4 and 2.1 mg/cm², respectively, and are the default values for the *Dermal Exposure to Volatile Liquids Model*.

Default glove PF values, which vary depending on the type of glove used and the presence of employee training program, are shown in Table 2-28. 1-BP easily travels through most glove materials. Recommended glove materials for protection against 1-BP are supported polyvinyl alcohol or multiple-layer laminates ([OSHA, 2013c](#)).

Table 2-28. Glove Protection Factors for Different Dermal Protection Strategies

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 available permeation data indicating that the material of construction offers good protection for the substance		5
c. Chemically resistant gloves (<i>i.e.</i> , as <i>b</i> above) with “basic” employee training		10
d. Chemically resistant gloves in combination with specific activity training (<i>e.g.</i> , procedure for glove removal and disposal) for tasks where dermal exposure can be expected to occur	Industrial Uses Only	20

Source: ([Marquart et al., 2017](#))

Table 2-29 presents the estimated dermal retained dose for *workers* in various exposure scenarios, including what-if scenarios for glove use. The exposure estimates assume one exposure event (applied dose) per work day and that 0.29 percent of the applied dose is absorbed through the skin. The exposure estimates are provided for each condition of use, where the conditions of uses are “binned” based on the maximum possible exposure concentration (Y_{derm}) and the likely level of exposure. The exposure concentration is determined based EPA’s review of currently available products and formulations containing 1-BP. For example, EPA found that 1-BP concentration in degreasing formulations such as Solvon PB can be as high as 97 percent:

- Bin 1: Bin 1 covers industrial uses that generally occur in closed systems. For these uses, dermal exposure is likely limited to chemical loading/unloading activities (*e.g.*, connecting hoses) and taking quality control samples.
- Bin 2: Bin 2 covers industrial degreasing uses, which are not closed systems. For these uses, there is greater opportunity for dermal exposure during activities such as charging and draining degreasing equipment, drumming waste solvent, and removing waste sludge.
- Bin 3: Bin 3 covers the use of 1-BP in spray adhesives in foam cushion product manufacturing, which is a unique condition of use. Workers (sprayers) can be dermally exposed when mixing adhesive, charging adhesive to spray equipment, and cleaning adhesive spray equipment. Other workers (non-sprayers) may also have incidental contact with the applied adhesive during subsequent fabrication steps.
- Bin 4: Bin 4 covers commercial activities of similar maximum concentration. Most of these uses are uses at dry cleaners, and/or uses expected to have direct dermal contact with bulk liquids. At dry cleaning shops, workers may be exposed to bulk liquids while charging and draining solvent to/from machines, removing and disposing sludge, and maintaining equipment. Workers can also be exposed to 1-BP used in spot cleaning products at the same shop.

- Bin 5: Bin 5 covers aerosol uses, where workers are likely to have direct dermal contact with film applied to substrate and incidental deposition of aerosol to skin. This bin also covers miscellaneous non-aerosol applications that are typically niche uses of 1-BP.

As shown in the table, the calculated retained dose is low for all non-occluded scenarios as 1-BP evaporates quickly after exposure. Dermal exposure to liquid is not expected for occupational non-users, as they do not directly handle 1-BP.

EPA also considered potential dermal exposure in cases where exposure is occluded. See further discussion on occlusion in the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019f](#)).

Strength, Limitation, and Uncertainty of the Dermal Exposure Assessment

Dermal exposures are assessed using the *Dermal Exposure to Volatile Liquids Model*, which relies on the Frasch et al. ([2011](#)) study to determine fractional absorption in accounting for chemical volatilization. Although the study presents 1-BP specific measurement, the study also noted a large standard deviation in the measured value. In addition, the underlying EPA dermal model assumes one exposure event per day, which likely underestimates exposure as workers often come into repeat contact with the chemical throughout their work day. Based on the uncertainties described above, EPA has a medium level of confidence in the assessed baseline exposure.

Glove protection factors are presented as what-if scenarios to show the potential effect of glove use on exposure levels. The actual frequency, type, and effectiveness of glove use in specific workplaces with 1-BP conditions of use are uncertain.

Table 2-29. Estimated Dermal Retained Dose for Workers in All Conditions of Use

Condition of Use	Bin	Max Y _{derm}	Dermal Exposure (mg/day)			
			No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (Industrial uses, PF = 20)
Manufacture	Bin 1	1.0	2.2 (CT) 6.5 (High-end)	0.4 (CT) 1.3 (High-end)	0.2 (CT) 0.7 (High-end)	0.1 (CT) 0.3 (High-end)
Import, Repackaging						
Processing - Incorporating into formulation						
Processing as a reactant						
Processing - Incorporating into articles						
Recycling						
Disposal						
Use - Batch Vapor Degreaser	Bin 2	0.97	2.1 (CT) 6.3 (High-end)	0.4 (CT) 1.3 (High-end)	0.2 (CT) 0.6 (High-end)	0.1 (CT) 0.3 (High-end)
Use – In-line Vapor Degreaser						
Use - Cold Cleaner						
Use – Adhesive Chemicals (Spray Adhesives)	Bin 3	0.8	1.7 (CT) 5.2 (High-end)	0.3 (CT) 1.0 (High-end)	0.2 (CT) 0.5 (High-end)	N/A
Use - Dry Cleaning	Bin 4	0.94	2.0 (CT) 6.1 (High-end)	0.4 (CT) 1.2 (High-end)	0.2 (CT) 0.6 (High-end)	N/A
Use - Spot Cleaner, Stain Remover						
Use - Other non-aerosol uses	Bin 5	1.0	2.2 (CT) 6.5 (High-end)	0.4 (CT) 1.3 (High-end)	0.2 (CT) 0.7 (High-end)	N/A
Use – Aerosol Spray Degreaser/Cleaner, Other aerosol uses						

2.3.2 Consumer Exposures

EPA evaluated 1-BP exposure resulting from the use of consumer products within a residence. EPA utilized a modeling approach to evaluate exposure because chemical specific personal monitoring data was not identified for consumers during data gathering and literature searches performed as part of systematic review.

Table 2-30 summarizes the consumer conditions of use from Table 1-4 and the associated consumer conditions of use assessed in this evaluation.

Table 2-30. Consumer Conditions of Use Assessed in This Risk Evaluation

Life-Cycle Stage	Category	Subcategory	Assessed Condition of Use	
Consumer Uses	Solvent (for cleaning or degreasing)	Aerosol spray degreaser/cleaner	Section 2.3.2.2.1– Aerosol spray degreaser/cleaner - general	
			Section 2.3.2.2.2– Aerosol spray degreaser/cleaner - electronics	
	Cleaning and furniture care products	Spot cleaner, stain remover	Section 2.3.2.2.3 – Spot cleaner/stain remover	
			Liquid cleaner (e.g., coin and scissors cleaner)	Section 2.3.2.3.1– Coin and scissors cleaner
			Liquid spray/aerosol cleaner	Section 2.3.2.2.4 – Spray cleaner – general
	Other uses	Arts, crafts and hobby materials – adhesive accelerant	Section 2.3.2.2.5 – Adhesive accelerant	
		Automotive care products – refrigerant flush	Section 2.3.2.3.2 – Automobile AC flush	
		Anti-adhesive agents – mold cleaning and release product	Section 2.3.2.2.6 Mold cleaning and release product	
		Building/construction materials not covered elsewhere – insulation	Section 2.3.2.4.1 and Section 2.3.2.4.2 – Insulation (off-gassing)	

2.3.2.1 Consumer Exposures Approach and Methodology

Consumer products containing 1-BP are readily available at retail stores and via the internet for purchase and use. Use of these products can result in consumer exposure to 1-BP during and after product use. This assessment quantitatively evaluates consumer exposure to 1-BP for the consumer user and bystander within a residence. For purposes of this assessment, consumer user is the receptor using a product containing 1-BP within a residence in a specified room of use. The consumer bystander is the receptor within the residence where a product containing 1-BP is used but outside the specified room of use during product use. This assessment qualitatively evaluates consumer exposure for potentially exposed susceptible subpopulations (PESS).

Product Identification

Consumer products containing 1-BP were identified through review and searches of a variety of sources, including the National Institutes of Health (NIH) Household Products Database, various government and trade association sources for products containing 1-BP, company websites for

Safety Data Sheets (SDS), Kirk-Othmer Encyclopedia of Chemical Technology, and the internet in general. These consumer products are summarized in the *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane* document ([U.S. EPA, 2017c](#)), put together by EPA and included in the docket for this final evaluation (Docket Number [EPA-HQ-OPPT-2016-0741-0003](#)). This *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane* document ([U.S. EPA, 2017c](#)) may not be a complete list of all consumer products available at the time of the searches because not all SDS display a complete list of chemical ingredients, therefore some products may contain 1-BP but cannot be confirmed by EPA. This *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane* document ([U.S. EPA, 2017c](#)) is representative of information found at the time of the searches and is considered reasonably available information; but does not take into consideration company-initiated formulation changes, product discontinuation, or other business or market based factors that occurred after the document was compiled.

Models Used and Routes of Exposure Assessed

Three models were used to evaluate consumer inhalation exposure to 1-BP for this assessment, EPA’s Consumer Exposure Model (CEM), EPA’s Multi-Chamber Concentration and Exposure Model (MCCEM), and EPA’s Indoor Environment Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU) model. These models can be found through the following link <https://www.epa.gov/tsca-screening-tools/approaches-estimate-consumer-exposure-under-tsca>.

Two models were used to evaluate consumer dermal exposure to 1-BP for this assessment, EPA’s CEM (Permeability) method and CEM (Fraction Absorbed). Table 2-31 summarizes the assessed consumer conditions of use (COUs), the routes of exposure assessed, and the models used for the assessment of each condition of use.

Table 2-31. Consumer Conditions of Use (COUs) and Routes of Exposure Assessed

Assessed COUs	Routes of Exposure	
	Inhalation	Dermal
Aerosol Spray Degreaser/Cleaner-General	CEM	CEM (Permeability)
Aerosol Spray Degreaser/Cleaner-Electronics	CEM	CEM (Fraction Absorbed)
Spot Cleaner and Stain Remover	CEM	CEM (Permeability)
Coin and Scissors Cleaner	MCCEM	CEM (Permeability)
Spray Cleaner-General	CEM	CEM (Permeability)
Adhesive Accelerant	CEM	CEM (Fraction Absorbed)
Automobile AC Flush	MCCEM	CEM (Fraction Absorbed)
Mold Cleaning and Release Product	CEM	CEM (Fraction Absorbed)
Insulation (Off-gassing)	IECCU	N/A

Inhalation

Reasonably available information on the toxicity profile and physicochemical properties of 1-BP support inhalation as an expected route of exposure for human health associated with consumer product uses. Consumer user and bystander inhalation exposure to 1-BP can occur through direct

inhalation of vapors, mists, and aerosols (*e.g.*, aerosols from spray applications) during product use as well as indirect inhalation of 1-BP following application and evaporation (*e.g.*, as products dry and evaporate from surfaces to which it is applied or a pool of product during use). The magnitude of inhalation exposure depends on a variety of factors including the concentration of 1-BP in products used, use patterns (including frequency, duration, amount of product used, room of use, and local ventilation), and application methods.

While inhalation exposure can be acute or chronic in nature, EPA does not expect consumer exposure to be chronic in nature because product use patterns tend to be infrequent with relatively short durations of use. The one exception, among the nine consumer COUs identified in Table 2-31, is the insulation (off-gassing) scenario which involves both an acute exposure (short duration, high concentration exposure following initial installation) and a chronic exposure (long duration, low concentration exposure for years following initial installation). Therefore, this assessment evaluates acute inhalation exposure for all nine consumer COUs identified in Table 2-31 and chronic inhalation exposure for the insulation (off-gassing) scenario.

Dermal

Dermal exposure is a reasonably foreseeable exposure route associated with consumer product use. Consumer dermal exposure to 1-BP resulting from product use occurs via liquid, vapor or mist deposition onto the skin or direct contact with material during product use or after application (*e.g.*, immersion of a body part into a pool of product or placing an unprotected body part on a surface prior to the surface fully drying following product application to that surface). The magnitude of dermal exposure depends on several factors including skin surface area, product volume, concentration of 1-BP in products used, and dermal exposure duration. The potential for dermal exposure to 1-BP is limited by several factors including physical-chemical properties of 1-BP, high vapor pressure, and expected quick volatilization of product containing 1-BP from surfaces.

There is limited toxicological data available for the dermal route of exposure, and no toxicokinetic information is available to develop physiologically-based pharmacokinetic models. While dermal exposure can be acute or chronic in nature, EPA does not expect consumer dermal exposure to be chronic in nature because product use patterns tend to be infrequent with relatively short durations of use. Although 1-BP is volatile, EPA evaluated dermal exposure for all consumer COUs identified in Table 2-31 except the Insulation (off-gassing) COU since dermal exposure is not expected to occur from rigid insulation board off-gassing. EPA used the CEM (Permeability) model to evaluate dermal exposure for those COUs where there is the possibility of a continuous supply of chemical against the skin with inhibited or prohibited evaporation potential due to a barrier or direct immersion of body parts into a product during use. EPA used the CEM (Fraction Absorbed) model for the remaining COUs where evaporation is expected to be uninhibited and no direct immersion of body parts into a product occurs during use.

Populations Evaluated

This assessment quantitatively evaluates inhalation and dermal exposures to 1-BP for the consumer user and inhalation exposures to 1-BP for the bystander within a residence. Consumer users, for

this evaluation, are assumed to be male and female youth (between 11 and 21 years of age) and male and female adults (21 years of age and greater). Consumer users include men and women of reproductive age. The consumer user is the individual using a product containing 1-BP within a residence in a specified room of use. The consumer user remains within the specified room of use during product use. Following product use, a consumer user may remain in the room of use for a certain period of time, leave the room of use, or go in and out of the room of use for the remainder of the day depending on their activity pattern.

Bystanders, for this evaluation, can be male or female individuals in any age group ranging from infants (less than one year of age) to adults. Bystanders include men and women of reproductive age as well as infants, toddlers, children at various developmental stages in life, and elderly. The consumer bystander is the receptor within the residence where a product containing 1-BP is used but remains outside the specified room of use during product use. Following product use, a bystander may remain outside the room of use for a certain period of time or go in and out of the room of use for the remainder of the day depending on their activity pattern.

2.3.2.2 Consumer Exposure Model (CEM) - Overview, Approach, Inputs, and Results

Overview

The CEM predicts indoor air concentrations from consumer product use through a deterministic, mass-balance calculation derived from emission calculation profiles within the model. It is a peer reviewed EPA model which relies on user provided input parameters, various assumptions, and several default inputs to generate exposure estimates. The defaults within CEM are a combination of high-end and mean/central tendency values from published literature, other studies, and values taken from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)). The CEM has built in flexibility which allows the modeler to modify certain default values when chemical specific information is available. The CEM also allows the modeler to select, if desired, an option for CEM to provide a time series air concentration profile (intermediate concentration values produced prior to applying pre-defined activity patterns) for each run. The CEM does not require chemical - specific emissions data, which may be required to run more complex consumer models, but does provide the modeler the opportunity to input certain chemical-specific emissions data (like background concentrations) when desired. Readers can learn more about the CEM, equations within the models, detailed input and output parameters, pre-defined scenarios, default values used, and supporting documentation by reviewing the CEM user guide ([U.S. EPA, 2019a](#)) and CEM user guide appendices ([U.S. EPA, 2019b](#)).

Approach and Inputs

There are six emission calculation profiles (E1-E6), three inhalation models (P_INH1, P_INH2, and A_INH1), and seven dermal models (P_DER1, P_DER2a, P_DER2b, P_DER3, A_DER1, A_DER2, and A_DER3) within CEM. There are also seventy-three specific product and article categories and several generic product categories with pre-defined default values within CEM. All consumer COUs for which exposure was assessed with the CEM utilized the Generic Product E3

(+ Vapor to Skin) product category except the coin and scissors cleaner COU which used the Generic Product E5 (+ Vapor to Skin) product category. All six of the consumer COUs for which inhalation exposure was assessed with the CEM utilized the P_INH2 inhalation model. All consumer COUs identified in Table 2-31 for which dermal exposure was assessed with the CEM (Permeability) model utilized the P_DER2b dermal model. The consumer COUs identified in Table 2-31 for which dermal exposure was assessed with the CEM (Fraction Absorbed) model utilized the P_DER2a model.

E3 (Emission from Product Sprayed): This profile assumes a small percentage of a product is aerosolized (e.g., overspray) and therefore immediately available for uptake by inhalation. The remainder of product is assumed to contact the target surface and later volatilize at a rate that depends on the chemical's molecular weight and vapor pressure. The aerosolized portion of product is treated using a constant emission rate model. The remaining portion of the product (non-aerosolized) is treated in the same manner as products applied to a surface (combining a constant application rate with an exponentially declining rate for each instantaneously applied segment).

E5 (Emission from Product Placed in Environment): This model assumes emission at a constant rate over a duration that depends on the chemical's molecular weight and vapor pressure. If this duration exceeds the user specified duration of use, then the chemical emissions are truncated at the end of the product use period, because the product is assumed to be removed from the house after the use period.

P_INH2 (Inhalation of Product Used in Environment; Near Field/Far Field): This model predicts indoor air concentrations from product use utilizing the associated emission profile (E1-E5) and a two-zone representation of the building of use (Zone 1 and Zone 2). Zone 1 represents the room where the consumer product is used while Zone 2 represents the remainder of the building of use. This model further divides Zone 1 into Zone 1 near-field and Zone 1 far-field to accommodate situations where a higher concentration of product is expected very near the product user during product use. The Zone 1 near-field can be represented as a bubble around the product user which moves throughout the room of use with the product user. The Zone 1 far-field represents the remainder of the room of use (Zone 1). Product users inhale airborne concentrations estimated within the Zone 1 near-field during product use and Zone 1 far-field following product use while the product user remains in the room of use.

P_DER2a (Dermal Dose from Product Applied to Skin, Fraction Absorbed Model): This model uses an absorption coefficient to estimate dermal exposure based on the absorbed dose of a chemical from a thin film applied onto the skin. This methodology assumes the application of the chemical of concern (or product containing the chemical of concern) occurs once to a specific film thickness. Utilizing an assumption that the entire mass of the chemical in the thin film enters the skin, this model then estimates the absorbed dose by applying the absorption coefficient to the entire mass of chemical within the skin. This model essentially measures two competing processes, evaporation of the chemical from the skin and penetration of the chemical deeper into the skin, and therefore is more applicable to conditions of use where evaporation is uninhibited and full immersion of body parts does not occur during use.

P_DER2b (Dermal Dose from Product Applied to Skin, Permeability Model): This model uses a skin permeability coefficient to estimate dermal exposure based on potential or absorbed doses for products that come in direct contact with the skin. The permeability coefficient can be a user defined value (if available for the chemical of concern) or estimated using the built in permeability estimator within CEM. This model is based on the ability of a chemical to penetrate the skin layer once contact occurs. This model assumes a constant supply of chemical, directly in contact with the skin, throughout the exposure duration. This model does not consider evaporative losses in its estimates of dermal exposure and therefore is more representative of a dermal exposure condition where evaporation is limited or prohibited due to direct immersion of skin into a product or use of a product soaked rag or other barrier that is in direct contact with unprotected skin during product use.

EPA utilized the time-series indoor air concentration option within the CEM. This provided concentrations in 30-second increments across the entire time period simulated in each run (72 hours). EPA also utilized the near-field/far-field option within the CEM. Use of these two options together provided EPA with zone specific concentrations (Zone 1 near-field, Zone 1 far-field, and Zone 2) to which a stay-at-home activity pattern was applied for the user and bystander during post-processing within Microsoft Excel. A rolling 24-hour time-weighted average (TWA) concentration was calculated for each personal exposure time series (user and bystander). The maximum 24-hour time-weighted average (TWA) was then identified and extracted as the exposure concentration.

Numerous input parameters are required to generate exposure estimates within the CEM. These parameters include physical-chemical properties of the chemical of concern, product information (*e.g.*, density, water solubility, vapor pressure), model selection and scenario inputs (*e.g.*, pathways, emission model(s), emission rate, activity pattern), product or article property inputs (*e.g.*, frequency of use, fraction of product aerosolized), environmental inputs (*e.g.*, building volume, room of use, air exchange rates), and receptor exposure factor inputs (*e.g.*, body weight, exposure duration, inhalation rate).

To characterize a potential range of consumer user and bystander exposures, modeling efforts involved varying select parameters across a range of values found in the literature. EPA identified parameters to vary based on the sensitivity of the CEM to the parameters, the parameters representativeness of consumer behavior patterns for product use, and availability of a range of values within published literature.

A sensitivity analysis was conducted on the CEM and is provided in the CEM User Guide Appendices ([U.S. EPA, 2019b](#)). EPA reviewed the sensitivity analysis to identify key parameters to which the CEM is both sensitive to and representative of consumer behavior patterns for product use. EPA then cross referenced these key parameters with those found in literature and other sources (captured and evaluated as part of the systematic review process) to identify the availability of a range of values for those parameters. Based on this effort, EPA identified the following three key parameters to vary for modeling purposes:

- 1) Duration of use per event (minutes/use),

- 2) Mass of product used per event (gram(s)/use), and
- 3) Amount of chemical in the product (weight fraction).

Each of these three parameters were modeled at three points across the range of values found in the literature. More specifically, duration of use per event and mass of product used per event were modeled at the 10th, 50th, and 95th percentile values extracted from an EPA directed survey of consumer behavior patterns in the United States titled Household Solvent Products: A National Usage Survey ([EPA, 1987](#)) (Westat Survey). This survey is a nationwide survey which provides information on product usage habits for thirty-two different product categories. The information for this survey was collected via questionnaire or telephone from 4,920 respondents across the United States. The Westat Survey was rated as a high quality study during data evaluation within the systematic review process.

The amount of chemical in the product(s) was modeled at the minimum, mid, and maximum values extracted from product specific Safety Data Sheets (SDS). Modeling three key parameters across three range values results in a maximum of twenty-seven different iterations for each condition of use assessed with the CEM in this evaluation [See Appendix F for a table summarizing the 27 iterations].

Additional input parameters for the consumer COUs evaluated with the CEM are discussed below. Detailed tables of all input parameters for each use evaluated with the CEM are provided in the 1-BP Supplemental File: Information on Consumer Exposure Assessment Model Input Parameters ([EPA, 2019a](#)).

Non-Varied Input Parameters

Physical-chemical properties of 1-BP were kept constant across all conditions of use modeled and all iterations. The vapor pressure of 1-BP applied for modeling was 110.8 Torr. The saturation concentration of 1-BP in air was estimated by the CEM as 9.66E+05 milligrams per cubic meter (mg/m³).

A neat-based, chemical-specific, skin permeability coefficient was calculated from literature and experimental data identified and evaluated as part of EPA's systematic review process ([Frasch et al., 2011](#)) and the 1992 EPA Dermal Exposure Assessment: Principles and Applications ([U.S. EPA, 1992](#)). The calculated skin permeability coefficient of 4.62E-04 centimeters per hour (cm/hr) was utilized for all COUs evaluated using the CEM (Permeability) model for dermal exposure.

A measured experimental fraction absorbed term was identified within the literature ([Frasch et al., 2011](#)) and evaluated as part of EPA's systematic review process. The measured fraction absorbed term was adjusted for air speed due to experimental conditions under which it was obtained. The adjusted value of 0.0029 was utilized for all COUs evaluated using the CEM (Fraction Absorbed) model for dermal exposure.

The activity pattern selected for modeling consumer user and bystander exposures in this evaluation was stay-at-home with a start time for product use of 9:00 AM. Frequency of use for acute exposure calculations was held constant at one event per day. The building volume used for

all conditions of use modeled for all iterations was the CEM default value of 492 m³ from the 2011 U.S. EPA Exposure Factors Handbook ([U.S. EPA, 2011](#)). The near-field volume selected for all conditions of use modeled for all iterations was one cubic meter to represent the immediate breathing zone of the consumer user. The aerosol fraction (overspray fraction) immediately available for uptake via inhalation was set at six percent based on a review of the literature. The background concentration of 1-BP was assumed to be negligible and therefore set at zero.

Conditions of Use Specific Input Parameters

Certain input parameters were varied across different conditions of use modeled, but kept constant for all iterations run for that particular condition of use. These condition of use specific input parameters include, product densities, room of use, and volume of room of use. Product densities were extracted from product-specific SDS and varied by product type. The room of use was extracted from the Westat Survey ([EPA, 1987](#)) based on a cross-walk EPA developed between each 1-BP condition of use modeled and comparable Westat Survey product categories. This crosswalk is summarized in Table 2-32.

Table 2-32. Crosswalk Between 1-BP Conditions of Use and Westat Product Category

1-BP Condition of Use	Representative Westat Product Category
1. Aerosol Spray Degreaser/Cleaner-General	Engine Degreasers
2. Aerosol Spray Degreaser/Cleaner-Electronics	Specialized Electronics Cleaners (TV, VCR, Razor, etc.)
3. Spot Cleaner and Stain Remover	Spot Removers
4. Coin and Scissors Cleaner	Not Applicable
5. Spray Cleaner-General	Solvent Type cleaning Fluids or Degreasers
6. Adhesive Accelerant	Contact Cement, Super Glues, and Spray Adhesives
7. Automobile AC Flush	Not Applicable
8. Mold Cleaning and Release product	Solvent Type Cleaning Fluids or Degreasers
9. Insulation (Off-gassing)	Not Applicable

The room of use selected for each condition of use modeled for this evaluation is based on the room in which the Westat Survey results reported the highest percentage of respondents last used a product within the room. When the Westat Survey identified the room of use where the highest percentage of respondent last used the product as “other inside room,” the utility room was selected within the CEM for modeling purposes. The volume of the selected room of use varied based on the room of use selected and ranged from 20 to 90 m³. The volume of the selected room is based on default volumes within the CEM.

Scenario Specific Input Parameters

Three key input parameters were varied across both conditions of use modeled and all iterations run for that particular condition of use. The duration of use per event and mass of product used per event were extracted from the Westat Survey based on the associated condition of use to which it is cross-walked. The extracted data represents the tenth, fiftieth (median), and ninety-fifth percentile data, as presented in the Westat Survey ([EPA, 1987](#)). The amount of chemical in the product (weight fraction) was extracted from product-specific SDS. This parameter was varied across the

given range of products within the same condition of use modeled. The values represent the minimum, mid/mean, and maximum weight fractions across the set of products identified for each condition of use. Under this approach, if three products were identified for a single condition of use with the following 1-BP weight fraction(s) or ranges [50%, 50-80%, 90%], then the “minimum” weight fraction would be represented by 50%, the “mid/mean” weight fraction would be represented by $(50+90)/2$ or 70%, and the “maximum” weight fraction would be represented by 90%. Where SDS were only available for a single product with a single weight fraction or very small range, or multiple products which only provided a single weight fraction or very small range, a single weight fraction was used for modeling purposes. Table 2-33 summarizes the scenario specific varied input parameters for the six conditions of use for which the CEM was used to model inhalation exposure to 1-BP.

Table 2-33. Scenario Specific Varied Input Parameters for the CEM Inhalation Modeling

Consumer Use	Duration of Use			Mass of Product Used			Amount of Chemical In Product		
	(minutes/use)			(gram(s)/use)			(weight fraction)		
	10 th	50 th	95 th	10 th	50 th	95 th	Low	Mean	High
Aerosol Spray Degreaser/Cleaner-General	5	15	120	111.86	445.92	1845.17	0.109	0.505	0.9505
Aerosol Spray Degreaser/Cleaner-Electronics	0.5	2	30	1.56	19.52	292.74	0.496	0.72	0.972
Spot Cleaner and Stain Remover	0.5	5	30	9.76	51.91	434.43	0.276	0.58	0.922
Spray Cleaner-General	2	15	120	21.86	126.86	1249.04		0.94 (Single)	
Adhesive Accelerant	0.5	4.25	60	1.20	9.98	172.45		0.99 (Single)	
Mold Cleaning and Release Product	0.5	2	30	3.84	21.14	192.21	0.32	0.6	0.915

Results

Modeling results for inhalation and dermal exposures evaluated with the CEM are summarized and discussed below. Results are presented by condition of use. All results for all iterations modeled are provided in the 1-BP Supplemental File: Information on Consumer Exposure Assessment Model Outputs ([EPA, 2019b](#)).

Results are presented in this section for three of the 27 possible iterations run for each condition of use. Inhalation concentrations are presented in parts per million (ppm) while dermal doses are presented as average daily doses (ADD) in milligrams of 1-BP per kilogram body weight per day (mg/kg-day). The three iterations selected provide a range of exposure concentrations across each condition of use modeled. Three descriptors are used in the results tables to represent the three iterations presented. These descriptors are based on the three key input parameters varied during

modeling (duration of use per event, mass of product used per event, and amount of chemical in product (weight fraction)) as follows:

High Intensity Use: Refers to the model iteration which utilizes the 95th percentile duration of use per event and mass of product used per event (as presented in the Westat Survey ([EPA, 1987](#))) and the maximum amount of chemical in product (weight fraction) extracted from product specific SDS.

Moderate Intensity Use: Refers to the model iteration which utilizes the median (50th percentile) duration of use per event and mass of product used per event (as presented in the Westat Survey ([EPA, 1987](#))) and the mid/mean amount of chemical in product (weight fraction) extracted from product specific SDS.

Low Intensity Use: Refers to the model iteration which utilizes the 10th percentile duration of use per event and mass of product used per event (as presented in the Westat Survey ([EPA, 1987](#))) and the minimum amount of chemical in product (weight fraction) extracted from product specific SDS.

Inhalation exposure is presented for two receptors (consumer user and bystander) utilizing a 24 hour time-weighted average. Dermal exposure is only presented for the consumer user as a bystander is not expected to receive a dermal dose. Dermal exposure is presented for three age groups Adult, Youth A, and Youth B utilizing an average daily dose.

- Adult: Male and female individuals 21 years of age and older.
- Youth A: Male and female individuals from 16 years of age through 20 years of age.
- Youth B: Male and female individuals from 11 years of age through 15 years of age.

These three age groups were evaluated because the CEM separates the Youth category into two age brackets due to variability of exposure factors (like respiration rates, body weight, skin surface area, and other factors) which can vary or change considerably during this developmental age range. Although the Youth B age group includes individuals between 11 and 15 years of age, the lower end of this age group (11-13) is a possible, but not necessarily reasonably foreseeable user of these high solvent products, with the exception of the coin cleaner. However, the upper end of this age group (14-15) is a possible and reasonably foreseeable user of all products whether it is using cleaning products to complete chores within the residence, or learning basic automotive care or other shop-type work like cleaning/degreasing items. Additionally, while certain products within a general arts and crafts condition of use may include products like school glue, the only 1-BP containing product identified within the arts and crafts condition of use for this evaluation is a specialized, solvent-based adhesive accelerant. This product is not associated with a common school glue and expected to be utilized by older, dedicated hobbyists for select projects where a quicker curing of a separate adhesive is required or desired. Therefore, EPA does not include an evaluation of dermal exposure to infants, toddlers, or children below the age of 11 for the arts and crafts condition of use within this evaluation as they are not expected or intended users of such a product.

2.3.2.2.1 Aerosol Spray Degreaser/Cleaner-General

This condition of use represents consumer uses of product as a solvent for cleaning or degreasing in the form of an aerosol spray degreaser or cleaner. The products are used to dissolve oils, greases, and similar materials from textiles, glassware, metal surfaces, and other articles. These products are available to consumers with 1-BP concentrations ranging from 10 percent to 95 percent by weight based on a review of product specific SDS. The room of use is the garage, based on the results from the Westat Survey ([EPA, 1987](#)) product category cross-walked with this condition of use. The duration of product use per event for these products ranges from 5 minutes to 120 minutes based on the Westat Survey.

Table 2-34. Aerosol Spray Degreaser/Cleaner-General (Inhalation Exposure Concentrations)

Source Description	Parameters Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Mass Used (grams)	Weight Fraction (percent)		
High Intensity Use	95 th (120)	95 th (1845.17)	Maximum (95.05)	User	141
				Bystander	41
Moderate Intensity Use	50 th (15)	50 th (445.92)	Mean (50.5)	User	19
				Bystander	5
Low Intensity Use	10 th (5)	10 th (111.86)	Minimum (10.9)	User	1.0
				Bystander	0.25

Table 2-34 shows the inhalation exposure concentrations found for the low, moderate, and high intensity use categories for this condition of use. The 24-hour TWA air concentrations of 1-BP for the user varies from 1 ppm to 141 ppm. The 24-hour TWA air concentrations of 1-BP for the bystander varies from 0.25 ppm to 41 ppm.

Dermal exposure was evaluated for this condition of use utilizing the CEM (Permeability) model due to the possibility of a continuous supply of product on the skin and expected inhibited or prohibited evaporation resulting from wiping with a product soaked rag during use. EPA used inside of one hand as the area and body part exposed.

Table 2-35. Aerosol Spray Degreaser/Cleaner-General (Dermal Exposure Doses)

Source Description	Parameter Varied			Exposed Receptor	ADD (mg/kg-day)
	Duration (min)	Mass Used (grams)	Weight Fraction (Percent)		
High Intensity Use	95 th (120)	95 th (1845.17)	Maximum (95.05)	Adult	3.5
				Youth A	3.3
				Youth B	3.6
Moderate Intensity Use	50 th (15)	50 th (445.92)	Mean (50.5)	Adult	0.23
				Youth A	0.22
				Youth B	0.24
Low Intensity Use	10 th (5)	10 th (111.86)	Minimum (10.9)	Adult	1.7E-02
				Youth A	1.6E-02
				Youth B	1.7E-02

Table 2-35 shows the dermal exposure dose found for the low, moderate, and high intensity use categories for this condition of use. The ADD of 1-BP for adults varies from 1.7E-02 mg/kg-day to 3.5 mg/kg-day. The ADD of 1-BP for Youth A varies from 1.6E-02 mg/kg-day to 3.3 mg/kg-day. The ADD of 1-BP for Youth B varies from 1.7E-02 mg/kg-day to 3.6 mg/kg-day.

2.3.2.2.2 Aerosol Spray Degreaser/Cleaner-Electronics

This condition of use represents consumer uses of product as a solvent for cleaning or degreasing in the form of an aerosol spray degreaser or cleaner for a more specialized category of electronic degreasers. The products are used to dissolve oils, greases, and similar materials from textiles, glassware, metal surfaces, and other articles. These products are available to consumers with 1-BP concentrations ranging from 49 percent to 97 percent by weight based on a review of product specific SDS. The room of use is the living room, based on the results from the Westat Survey product category cross-walked with this condition of use. The duration of product use per event for these products ranges from 0.2 minutes to 30 minutes based on the Westat Survey (EPA, 1987). However, due to a limitation on the minimum value available for duration of use within the CEM, the low end value used for modeling this condition of use is 0.5 minutes.

At the time the Westat Survey (EPA, 1987) was conducted, this type of product would typically be used to clean consumer items like VCRs, cassette tape players, or early generation CD players. There is an expectation that use of these types of degreasers/cleaners continues today, although the consumer items cleaned may be more represented by DVD players or game consoles/cassettes/cartridges contact areas. Items could also include computers and computer motherboards, although some of these materials may be sensitive to such high solvent consumer cleaning products. While water-based products are likely available, the high solvent consumer cleaning products are still available for purchase and use.

Table 2-36. Aerosol Spray Degreaser/Cleaner-Electronics (Inhalation Exposure Concentrations)

Source Description	Parameters Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Mass Used (grams)	Weight Fraction (percent)		
High Intensity Use	95 th (30)	95 th (292.74)	Maximum (97.2)	User	30
				Bystander	8.7
Moderate Intensity Use	50 th (2)	50 th (19.52)	Mean (72)	User	1.4
				Bystander	0.35
Low Intensity Use	10 th (0.5)	10 th (1.56)	Minimum (49.6)	User	6.7E-02
				Bystander	1.9E-02

Table 2-36 shows the inhalation exposure concentrations found for the low, moderate, and high intensity use categories for this condition of use. The 24-hour TWA air concentrations of 1-BP for the user varies from 6.6E-02 ppm to 30 ppm. The 24-hour TWA air concentrations of 1-BP for the bystander varies from 1.9E-02 ppm to 8.7 ppm.

Dermal exposure was evaluated for this condition of use utilizing the CEM (Fraction Absorbed) model due to the expectation of uninhibited evaporation and no full immersion of body parts into the product during use. EPA used 10% of one hand as the area and body part exposed.

Table 2-37. Aerosol Spray Degreaser/Cleaner-Electronics (Dermal Exposure Doses)

Source Description	Parameter Varied			Exposed Receptor	ADD (mg/kg-day)
	Duration (min)	Mass Used (grams)	Weight Fraction (Percent)		
High Intensity Use	95 th (30)	95 th (292.74)	Maximum (97.2)	Adult	4.6E-02
				Youth A	4.3E-02
				Youth B	4.7E-02
Moderate Intensity Use	50 th (2)	50 th (19.52)	Mean (72)	Adult	3.4E-02
				Youth A	3.2E-02
				Youth B	3.5E-02
Low Intensity Use	10 th (0.5)	10 th (1.56)	Minimum (49.6)	Adult	2.4E-02
				Youth A	2.2E-02
				Youth B	2.4E-02

Table 2-37 shows the dermal exposure dose found for the low, moderate, and high intensity use categories for this condition of use. The ADD of 1-BP for adults varies from 2.4E-02 mg/kg-day to 4.6E-02 mg/kg-day. The ADD of 1-BP for Youth A varies from 2.2E-02 mg/kg-day to 4.3E-02 mg/kg-day. The ADD of 1-BP for Youth B varies from 2.4E-02 mg/kg-day to 4.7E-02 mg/kg-day.

2.3.2.2.3 Spot Cleaner and Stain Remover

This condition of use represents consumer uses of a solvent product for cleaning and furniture care in the form of spot cleaners or stain removers. The products are used to remove dirt, grease, stains, and foreign matter from furniture and furnishings, or to cleanse, sanitize, or improve the appearance of surfaces. These products are available to consumers with 1-BP concentrations ranging from 27.6 percent to 92.2 percent by weight based on a review of product specific SDS. The room of use is the utility room, based on the results from the Westat Survey product category cross-walked with this condition of use. The duration of product use per event for these products ranges from 0.3 minutes to 30 minutes based on the Westat Survey ([EPA, 1987](#)). However, due to a limitation on the minimum value available for duration of use within the CEM, the low-end value used for modeling this condition of use is 0.5 minutes.

Table 2-38. Spot Cleaner and Stain Remover (Inhalation Exposure Concentrations)

Source Description	Parameters Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Mass Used (grams)	Weight Fraction (percent)		
High Intensity Use	95 th (30)	95 th (434.43)	Maximum (92.2)	User	47
				Bystander	7.2
Moderate Intensity Use	50 th (5)	50 th (51.91)	Mean (58)	User	3.4
				Bystander	0.54
Low Intensity Use	10 th (0.5)	10 th (9.76)	Minimum (27.6)	User	0.26
				Bystander	4.8E-02

Table 2-38 shows the inhalation exposure concentrations found for the low, moderate, and high intensity use categories for this condition of use. The 24-hour TWA air concentrations of 1-BP for the user varies from 0.26 ppm to 47 ppm. The 24-hour TWA air concentrations of 1-BP for the bystander varies from 4.8E-02 ppm to 7.2 ppm.

Dermal exposure was evaluated for this condition of use utilizing the CEM (Permeability) model due to the possibility of a continuous supply of product on the skin and expected inhibited or prohibited evaporation resulting from wiping with a product soaked rag during use. EPA used inside of one hand as the area and body part exposed.

Table 2-39. Spot Cleaner and Stain Remover (Dermal Exposure Doses)

Source Description	Parameter Varied			Exposed Receptor	ADD (mg/kg-day)
	Duration (min)	Mass Used (grams)	Weight Fraction (Percent)		
High Intensity Use	95 th (30)	95 th (434.43)	Maximum (92.2)	Adult	0.87
				Youth A	0.81
				Youth B	0.89
Moderate Intensity Use	50 th (5)	50 th (51.91)	Mean (58)	Adult	9.1E-02
				Youth A	8.5E-02
				Youth B	9.3E-02
Low Intensity Use	10 th (0.5)	10 th (9.76)	Minimum (27.6)	Adult	4.3E-03
				Youth A	4.1E-03
				Youth B	4.4E-03

Table 2-39 shows the dermal exposure dose found for the low, moderate, and high intensity use categories for this condition of use. The ADD of 1-BP for adults varies from 4.3E-03 mg/kg-day to 0.87 mg/kg-day. The ADD of 1-BP for Youth A varies from 4.1E-03 mg/kg-day to 0.81 mg/kg-day. The ADD of 1-BP for Youth B varies from 4.4E-03 mg/kg-day to 0.89 mg/kg-day.

2.3.2.2.4 Spray Cleaner-General

This condition of use represents consumer uses of solvent product for cleaning and furniture care in the form of liquid spray and aerosol cleaners. The products are available to consumers as a general purpose spray cleaner. These products are used to remove dirt, grease, and stains, or to cleanse, , scour, polish, protect, or improve the appearance of surfaces. These products are

available to consumers, to be used as is, with 1-BP concentration of 94 percent by weight based on a review of product specific SDS. The room of use is the utility room, based on the results from the Westat Survey product category cross-walked with this condition of use. The duration of product use per event for these products ranges from 2 minutes to 120 minutes based on the Westat Survey.

Table 2-40. Spray Cleaner-General (Inhalation Exposure Concentrations)

Source Description	Parameters Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Mass Used (grams)	Weight Fraction (percent)		
High Intensity Use	95 th (120)	95 th (1249.04)	Single (94)	User	133
				Bystander	33
Moderate Intensity Use	50 th (15)	50 th (126.86)	Single (94)	User	14
				Bystander	2.7
Low Intensity Use	10 th (2)	10 th (21.86)	Single (94)	User	2.3
				Bystander	0.44

Table 2-40 shows the inhalation exposure concentrations found for the low, moderate, and high intensity use categories for this condition of use. The 24-hour TWA air concentrations of 1-BP for the user varies from 2.3 ppm to 133 ppm. The 24-hour TWA air concentrations of 1-BP for the bystander varies from 0.44 ppm to 33 ppm.

Dermal exposure was evaluated for this condition of use utilizing the CEM (Permeability) model due to the possibility of a continuous supply of product on the skin and expected inhibited or prohibited evaporation resulting from wiping with a product soaked rag during use. EPA used inside of one hand as the area and body part exposed.

Table 2-41. Spray Cleaner-General (Dermal Exposure Doses)

Source Description	Parameter Varied			Exposed Receptor	ADD (mg/kg-day)
	Duration (min)	Mass Used (grams)	Weight Fraction (Percent)		
High Intensity Use	95 th (120)	95 th (1249.04)	Single (94)	Adult	3.6
				Youth A	3.3
				Youth B	3.6
Moderate Intensity Use	50 th (15)	50 th (126.86)	Single (94)	Adult	0.44
				Youth A	0.42
				Youth B	0.45
Low Intensity Use	10 th (2)	10 th (21.86)	Single (94)	Adult	5.9E-02
				Youth A	5.5E-02
				Youth B	6.1E-02

Table 2-41 shows the dermal exposure dose found for the low, moderate, and high intensity use categories for this condition of use. The ADD of 1-BP for adults varies from 5.9E-02 mg/kg-day to 3.6 mg/kg-day. The ADD of 1-BP for Youth A varies from 5.5E-02 mg/kg-day to 3.3 mg/kg-day. The ADD of 1-BP for Youth B varies from 6.1E-02 mg/kg-day to 3.6 mg/kg-day.

2.3.2.2.5 Adhesive Accelerant

This condition of use represents consumer uses of product as a solvent for adhesive accelerant for arts, crafts, and hobby activities. The products are aerosol sprays used to accelerate the time it takes for adhesives to dry. These products are available to consumers with 1-BP concentrations of 99 percent by weight based on a review of product specific SDS. The room of use is the utility room, based on the results from the Westat Survey (EPA, 1987) product category cross-walked with this condition of use. The duration of product use per event for these products ranges from 0.3 minute to 60 minutes based on the Westat Survey (EPA, 1987). However, due to a limitation on the minimum value available for duration of use within the CEM, the low-end value used for modeling this condition of use is 0.5 minutes.

Table 2-42. Adhesive Accelerant (Inhalation Exposure Concentration)

Source Description	Parameters Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Mass Used (grams)	Weight Fraction (percent)		
High Intensity Use	95 th (60)	95 th (172.45)	Single (99)	User	18
				Bystander	4.5
Moderate Intensity Use	50 th (4.25)	50 th (9.98)	Single (99)	User	1.1
				Bystander	0.2
Low Intensity Use	10 th (0.5)	10 th (1.2)	Single (99)	User	0.12
				Bystander	2.5E-02

Table 2-42 shows the inhalation exposure concentrations found for the low, moderate, and high intensity use categories for this condition of use. The 24-hour TWA air concentrations of 1-BP for the user varies from 0.12 ppm to 18 ppm. The 24-hour TWA air concentrations of 1-BP for the bystander varies from 2.5E-02 ppm to 4.5 ppm.

Dermal exposure was evaluated for this condition of use utilizing the CEM (Fraction Absorbed) model due to the expectation of uninhibited evaporation and no full immersion of body parts into the product during use. EPA used 10% of one hand as the area and body part exposed.

Table 2-43. Adhesive Accelerant (Dermal Exposure Doses)

Source Description	Parameter Varied			Exposed Receptor	ADD (mg/kg-day)
	Duration (min)	Mass Used (grams)	Weight Fraction (Percent)		
High Intensity Use	95 th (60)	95 th (172.45)	Single (99)	Adult	4.8E-02
				Youth A	4.5E-02
				Youth B	4.9E-02
Moderate Intensity Use	50 th (4.25)	50 th (9.98)	Single (99)	Adult	4.8E-02
				Youth A	4.5E-02
				Youth B	4.9E-02
Low Intensity Use	10 th (0.5)	10 th (1.2)	Single (99)	Adult	4.8E-02
				Youth A	4.5E-02
				Youth B	4.9E-02

Table 2-43 shows the dermal exposure dose found for the low, moderate, and high intensity use categories for this condition of use. The ADD of 1-BP for adults across all intensities of use (high, moderate, low) is 4.8E-02 mg/kg-day. The ADD of 1-BP for Youth A across all intensities of use is 4.5E-02 mg/kg-day. The ADD of 1-BP for Youth B across all intensities of use is 4.9E-02 mg/kg-day. The ADD for each age group across all use conditions is 0.05 mg/kg-day. The identical ADD is due to the availability of only a single weight fraction for products in this condition of use and the use of a published experimental absorption fraction value (independent of duration) rather than an estimated value (reliant on duration).

2.3.2.2.6 Mold Cleaning and Release Product

This condition of use represents consumer uses of product as solvents for mold cleaning and release. The products are used as anti-adhesive agents intended to prevent bonding between other substances by discouraging surface attachments. The products are available to consumers with 1-BP concentrations ranging from 32 percent to 91.5 percent by weight based on a review of product specific SDS. The room of use is the utility room, based on the results from the Westat Survey (EPA, 1987) product category cross-walked with this condition of use. The duration of product use per event for these products ranges from 0.1 minute to 30 minutes based on the Westat Survey (EPA, 1987). However, due to a limitation on the minimum value available for duration of use within the CEM, the low-end value used for modeling this condition of use is 0.5 minutes.

Table 2-44. Mold Cleaning and Release Product (Inhalation Exposure Concentration)

Source Description	Parameters Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Mass Used (grams)	Weight Fraction (percent)		
High Intensity Use	95 th (60)	95 th (192.21)	Maximum (91.5)	User	21
				Bystander	4.2
Moderate Intensity Use	50 th (2)	50 th (21.14)	Mean (60)	User	1.4
				Bystander	0.27
Low Intensity Use	10 th (0.5)	10 th (3.84)	Minimum (32)	User	0.12
				Bystander	2.6E-02

Table 2-44 shows the inhalation exposure concentrations found for the low, moderate, and high intensity use categories for this condition of use. The 24-hour TWA air concentrations of 1-BP for the user varies from 0.12 ppm to 21 ppm. The 24-hour TWA air concentrations of 1-BP for the bystander varies from 2.6E-02 ppm to 4.2 ppm.

Dermal exposure was evaluated for this condition of use utilizing the CEM (Fraction Absorbed) model due to the expectation of uninhibited evaporation and no full immersion of body parts into the product during use. EPA used 10% of one hand as the area and body part exposed.

Table 2-45. Mold Cleaning and Release Product (Dermal Exposure Doses)

Source Description	Parameter Varied			Exposed Receptor	ADD (mg/kg-day)
	Duration (min)	Mass Used (grams)	Weight Fraction (Percent)		
High Intensity Use	95 th (60)	95 th (192.21)	Maximum (91.5)	Adult	4.3E-02
				Youth A	4.0E-02
				Youth B	4.4E-02
Moderate Intensity Use	50 th (2)	50 th (21.14)	Mean (60)	Adult	2.8E-02
				Youth A	2.6E-02
				Youth B	2.9E-02
Low Intensity Use	10 th (0.5)	10 th (3.84)	Minimum (32)	Adult	1.5E-02
				Youth A	1.4E-02
				Youth B	1.5E-02

Table 2-45 shows the dermal exposure dose found for the low, moderate, and high intensity use categories for this condition of use. The ADD of 1-BP for adults ranges from 1.5E-02 mg/kg-day to 4.3E-02 mg/kg-day. The ADD of 1-BP for Youth A ranges from 1.4E-02 mg/kg-day to 4.0E-02 mg/kg-day. The ADD of 1-BP for Youth B across all intensities of use is 1.5E-02 mg/kg-day to 4.4E-02 mg/kg-day.

2.3.2.3 Multi-Chamber Concentration and Exposure Model (MCCEM)

Overview

The MCCEM predicts indoor air concentrations of, and inhalation exposure to, chemicals released from products used or materials installed in a residence through a deterministic, mass-balance approach. It is a peer reviewed EPA model which relies on user provided input parameters, various assumptions, and several default inputs to generate exposure estimates. The defaults within MCCEM are a combination of high-end and mean/central tendency values from published literature, other studies, and values taken from U.S. EPA’s Exposure Factors Handbook ([U.S. EPA, 2011](#)). The MCCEM has built in flexibility which allows the modeler to modify certain default values when chemical specific information is available. The MCCEM provides a time series air concentration profile (intermediate concentration values produced prior to applying pre-defined activity patterns) for each run. Readers can learn more about the model by reviewing the MCCEM user guide ([U.S. EPA, 2019d](#)).

Approach and Inputs

There are four types of source models for inhalation exposure available within the MCCEM, including: constant source, single-exponential source, incremental source, and a special cases or expressions source not otherwise addressed by the first three source models (referred to in the MCCEM as data entry form). Both conditions of use identified in Table 2-31 (coin and scissors cleaner and automobile AC flush) for which inhalation exposure was assessed with the MCCEM utilized the constant source model. Since the MCCEM does not have a dermal component, dermal exposure from these two conditions of use was evaluated with CEM as shown in Table 2-31 [Coin

and Scissors Cleaner CEM (Permeability) model (P_DER2b) and Automobile AC Flush CEM (Fraction Absorbed) model (P_DER2a).

Constant Source Model (MCCEM): This model assumes the emission source emits at a constant rate for the entire period during which it is active. This model requires the user to specify the constant emission rate for the emission source as one of the inputs.

P_DER2a (Dermal Dose from Product Applied to Skin, Fraction Absorbed Model): This model uses an absorption coefficient to estimate dermal exposure based on the absorbed dose of a chemical from a thin film applied onto the skin. This methodology assumes the application of the chemical of concern (or product containing the chemical of concern) once to a specific film thickness. Utilizing an assumption that the entire mass of the chemical in the thin film enters the skin, this model then estimates the absorbed dose by applying the absorption coefficient to the entire mass of chemical within the skin. This model essentially measures two competing processes, evaporation of the chemical from the skin and penetration of the chemical deeper into the skin, and therefore is more applicable to conditions of use where evaporation is uninhibited and full immersion of body parts does not occur during use.

P_DER2b (Dermal Dose from Product Applied to Skin, Permeability Model) (CEM): This model uses a skin permeability coefficient to estimate dermal exposure based on potential or absorbed doses for products that come in direct contact with the skin. The permeability coefficient can be a user defined value (if available for the chemical of concern) or estimated using the built in permeability estimator within CEM. This model is based on the ability of a chemical to penetrate the skin layer once contact occurs. This model assumes a constant supply of chemical, directly in contact with the skin, throughout the exposure duration. This model does not consider evaporative losses in its estimates of dermal exposure and therefore is more representative of a dermal exposure condition where evaporation is limited or prohibited due to direct immersion of skin into a product or use of a product soaked rag or other barrier that is in direct contact with unprotected skin during product use.

EPA obtained time-varying indoor concentrations across the entire time period simulated in each model run (72 hours for both MCCEM and CEM). EPA also utilized the near-field/far-field option within MCCEM. Use of these two options together provided EPA with zone specific concentrations (Zone 1 near-field, Zone 1 far-field, and Zone 2) to which a stay-at-home activity pattern was applied for the users and bystanders during post-processing within Microsoft Excel. Post-processing involved calculating a rolling 24-hour time weighted average (TWA) concentration for each personal exposure time series (user and bystander). The maximum 24-hour TWA was then identified and extracted as the exposure concentration.

Identification of the inhalation exposure scenario to be evaluated for the coin and scissors cleaner and automobile AC flush conditions of use began with a general internet search and investigation into these uses. The search and investigation found the coin cleaning process typically involved placing the coin cleaner product into a small, open top dish or bowl. Coins to be cleaned are then placed within the pool of product, soaked, scrubbed/wiped, and then removed for drying. The automobile AC flush process involved directly spraying the flush product into the opened

automobile AC system. The product is transferred through the system by pressure to the opposite end and expelled into an open top bucket where it is collected. Both of these processes involve an open top container, of certain dimensions, which contains a pool of the product being evaluated. Inhalation exposure then occurs as a result of 1-BP evaporation from a pool of liquid product in each container.

Dermal exposure for the coin and scissors cleaner condition of use is possible as a result of immersion of the users hand into the product being evaluated. Dermal exposure for the automobile AC flush condition of use is possible during connection of the product container to the automobile AC system (at head and shoulder level), spraying from an incorrect connection, splashing from the material expelling from the automobile AC system, and splashing during transport/clean-up of the product from the open top container.

Numerous input parameters are required to generate exposure estimates within the MCCEM. These parameters help define various aspects of the model run, exposure scenario, activity patterns, and receptor specific information. Inputs include run time, house/residence information (*e.g.*, number of zones, building volumes, air flows), emissions information (emission rate, zone of emissions source location, start/end time, and source model), activity pattern information, dose information, and receptor information (*e.g.*, inhalation rate, body weight).

The inputs needed for the MCCEM include: (1) the emission rate; (2) product amount and duration of use; (3) house and zone volumes; and (4) airflows to and from each zone. Each of these input categories are discussed below. Detailed tables of all input parameters for each use evaluated with the MCCEM are provided in the 1-BP Supplemental File: Information on Consumer Exposure Assessment Model Input Parameters ([EPA, 2019a](#)).

Emission Rate

The emission rate of 1-BP from the pool of liquid product for the two conditions of use evaluated using the MCCEM was estimated outside of the MCCEM. A study by Guo ([Guo, 2002](#)), compiled and briefly discussed fifty-two indoor emission source models. Two of the models compiled (M32 and M33) can be applied to estimate an emission rate from a pool of liquid.

The M32 model ([Jayjock, 1994](#)), applies to an evaporating solvent pool with a fixed surface area. At a given temperature, the emission rate calculated using the M32 model is determined by (1) the gas-phase mass transfer coefficient, (2) the vapor pressure, and (3) the back pressure effect. The M33 model ([Chang and Krebs, 1992](#)), was developed for sublimation of p-dichlorobenzene from moth cakes. However, sublimation and evaporation of pure compounds share similar mechanisms and therefore the M33 model can also be applied to emissions from solvent pools ([Guo, 2002](#)).

The M33 model ([Chang and Krebs, 1992](#)) was utilized to estimate the emission rate for both the coin and scissors cleaner and automobile AC flush conditions of use. This model is represented as follows:

$$E = k_g (C_v - C)$$

Where:

E= the emission rate (mg/m²/hr)

K_g= the gas-phase mass transfer coefficient (m/hr)

C_v= the saturation concentration for a pure compound (mg/m³)

C= the prevailing indoor air concentration (mg/m³)

EPA assumed zero for the prevailing indoor air concentration when determining the emission rate for these two scenarios. This assumption therefore makes the emission rate in the M33 model product of three quantities: (1) mass-transfer coefficient; (2) saturation concentration; and (3) exposed surface area. The exposed surface area of the two reservoirs is needed to both estimate the characteristic length of the reservoir (needed to determine the gas phase mass transfer coefficient) as well as converting the emission rate from the M33 model (mg/m²/hr) into the correct units needed for the MCCEM (mg/hr).

To estimate the mass-transfer coefficient, EPA used the program PARAMS (<https://www.epa.gov/air-research/parameters-params-program-version-11-indoor-emission-source-modeling>), which involves the following components:

- Air Density, calculated at 23 C and 50% RH;
- Viscosity of Air, calculated at 23 C;
- Velocity, the midpoint of the recommended range of 5-10 cm/s;
- Diffusivity in air, calculated using the Wilke Lee (WL) method (see input screen below); and
- Characteristic length – PARAMS describes this parameter as follows:
“Characteristic length is often approximated by the square root of the source area.”

The saturation concentration for 1-BP is 731,535 mg/m³ (732 g/m³). For the coin cleaner reservoir, EPA chose a small bowl with a 4-inch diameter, giving a source area of 81 cm², a characteristic length of 9 cm, and an estimated mass-transfer coefficient of 6.01 m/hr. For the automobile AC flush reservoir, EPA chose a bucket with a 12-inch diameter, giving a source area of 730 cm², a characteristic length of 27.0 cm, and an estimated mass-transfer coefficient of 3.47 m/h.

The emission rate for the coin cleaner utilized as the input for the MCCEM was obtained by multiplying the estimated mass transfer coefficient (6.01 m/hr) by the saturation concentration for 1-BP (731,535 mg/m³), and the source area (0.0081 m²). This gives an estimated emission rate for 1-BP from the coin cleaner reservoir of 35,612 mg/hr (36 g/hr). Similarly, the emission rate for the automobile AC flush utilized as the input for the MCCEM was obtained by multiplying the estimated mass transfer coefficient (3.47 m/hr) by the saturation concentration of 1-BP (731,535 mg/m³), and the source area (0.073 m²). This gives an estimated emission rate for 1-BP from the automobile AC flush reservoir of 185,305 mg/hr (185 g/hr).

Product Amount and Duration of Use

To characterize a potential range of consumer user and bystander exposures, modeling efforts involved identifying appropriate parameters to vary across a range of values representative of the expected conditions of use evaluated. Unlike the scenarios modeled with the CEM, involving an immediate uptake of the overspray fraction and exponential decay rate for the material contacting the surface, the two scenarios modeled with the MCCEM assumed only a constant rate of material evaporating from the surface of the liquid pool which is in effect until all available 1-BP mass is evaporated. This approach results in the emission rate being governed by the surface area of the liquid pool and not dependent on chemical mass, provided the duration of use is less than the time it takes for all 1-BP mass to evaporate. For both the coin and scissors cleaner and automobile AC flush conditions of use, the time it takes for all 1-BP mass to evaporate from the products is longer than the durations of use by the consumer evaluated for this analysis. Since emission rate is not dependent on chemical mass for the two MCCEM scenarios, the only parameter varied for the coin and scissors cleaner and automobile AC flush conditions of use was duration of use. This results in three exposure scenarios per condition of use.

EPA chose three durations of use for inhalation exposure (15, 30, and 60 minutes) for the coin and scissors cleaner condition of use. Coin cleaning is expected to be a somewhat passive activity where coins may remain undisturbed within the pool for an extended period of time. As a result, EPA expects dermal exposure will occur for a shorter period of time consisting of when coins are placed into the product, potentially scrubbed/wiped within the product, and taken out for drying. Outside of these activities, dermal exposure is not expected to occur although the user will remain within the room inhaling the vapors expelled from the pool. For dermal exposure EPA chose three durations (2, 4, and 6 minutes) which represent the total duration of dermal exposure during use.

EPA chose three durations of use for inhalation exposure (5, 15, and 30 minutes) for the automobile AC flush condition of use. Unlike coin cleaning, automobile AC flushing is an active process where material is constantly sprayed into the system, flushed through, and exits the system. Inhalation exposure occurs for the entire period of time and since it is an active process, dermal exposure can also occur for the entire period of time. As a result, for dermal exposure EPA also presents the exposure values representing 5, 15, and 30 minutes of ongoing dermal exposure.

House and Zone Volumes and Airflows

The zone volumes and airflow rates for the coin and scissors cleaner and automobile AC flush condition of use are discussed below and summarized in two tables in Appendix D. For the coin and scissors cleaner condition of use, EPA is assuming the room of use to be the utility room, with a volume of 20 m³ that is further split into near-field and far-field zones for which the respective volumes (1 m³ and 19-m³) are consistent with CEM defaults. The assumed house volume is 446 m³, resulting in a volume of 426 m³ for the third zone, termed the “rest of house” or ROH.

The air exchange rate for the house (0.45) is the same as the CEM default. EPA used an interzonal airflow rate of 100 m³/h between the near field and far-field. EPA assumed that there was no air

flow between the near field and outdoors (Zone 0). For the interzonal airflow rate between the utility room and ROH, the CEM default rate of 107.1 m³/h was used.

For the auto AC flush scenario, EPA assumed the room of use to be the garage with a volume of 118 m³. This volume is the average for 15 single-family homes with attached garages as reported by Batterman et al. ([Batterman et al., 2007](#)). The garage was further split into a 4-m³ near field and a 114-m³ far field. Zone 3 was defined as the entire house volume of 446 m³, which did not include the garage.

The air exchange rate for the house (0.45) is the same as the CEM default. Relatively few measurements have been taken of garage air exchange rates. Emmerich et al. ([Emmerich et al., 2003](#)) used a blower door to measure the airtightness of garages under induced-pressurization conditions for a limited sample of homes but with a range of house ages, styles, and sizes. The average airtightness measured was 48 air changes per hour at 50 Pa (ACH50), which corresponds to an air exchange rate of ~ 2.5 air exchanges/h (giving an airflow rate of 295 m³/h) under naturally occurring conditions. EPA also assumed an airflow rate of 107.1 m³/h between the garage and house as well as an airflow rate of zero between the near field and outdoors.

Results

Modeling results for inhalation exposures evaluated with the MCCEM are summarized and discussed below. Modeling results for dermal exposures for the coin and scissors cleaner and automobile AC flush conditions of use with the CEM are also summarized and discussed below. Results are presented by condition of use. All results for all iterations modeled are provided in the 1-BP Supplemental File: Information on Consumer Exposure Assessment Model Outputs ([EPA, 2019b](#)).

Results are presented in this section for all three iterations run with the MCCEM for the coin and scissors cleaner and automobile AC flush condition of use. Inhalation concentrations are presented in parts per million (ppm) while dermal doses are presented as average daily doses (ADD) in milligrams of 1-BP per kilogram body weight per day (mg/kg-day). The three iterations presented provide a range of exposure concentrations across each condition of use modeled. The three descriptors utilized for the MCCEM iterations are the same as those used for the CEM results. However, since only one parameter was varied for the two conditions of use evaluated with the MCCEM, the descriptors are only based on the duration of use per event.

High Intensity Use: Refers to the model iteration which utilizes the highest duration of use per event.

Moderate Intensity Use: Refers to the model iteration which utilizes the median duration of use per event.

Low Intensity Use: Refers to the model iteration which utilizes the lowest duration of use per event.

2.3.2.3.1 Coin and Scissors Cleaner

This condition of use represents consumer uses of product as a solvent for cleaning in the form of liquid cleaner. The products are used to dissolve oils, greases, stains, or to cleanse, sanitize, scour, polish, protect or improve the appearance of surfaces. These products are available to consumers with a 1-BP concentration of 50 to 100 percent by weight based on a review of product specific SDS. The room of use is assumed to be the utility room. The duration of use per event evaluated for these products ranged from 15 minutes to 60 minutes.

Inhalation Exposure

Table 2-46. Coin and Scissors Cleaner (Inhalation Exposure Concentration)

Source Description	Parameters Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Mass Used (grams)	Weight Fraction (percent)		
High Intensity Use	High (60)	Maximum (624.5)	Maximum (100)	User	2.0
				Bystander	1.0
Moderate Intensity Use	Median (30)	Mean (312.3)	Mean (75)	User	1.5
				Bystander	0.47
Low Intensity Use	Low (15)	Minimum (126.9)	Minimum (50)	User	1.2
				Bystander	0.22

Table 2-46 shows the inhalation exposure concentrations found for the low, moderate, and high intensity use categories for this condition of use. The 24-hour TWA air concentrations of 1-BP for the user varies from 1.2 ppm to 2.0 ppm. The 24-hour TWA air concentrations of 1-BP for the bystander varies from 0.22 ppm to 1.0 ppm.

Dermal Exposure

Dermal exposure was evaluated for this condition of use utilizing the CEM (Permeability) model due to the possibility of a continuous supply of product on the skin and expected inhibited or prohibited evaporation resulting from wiping with a product soaked rag during use. EPA used 10% of one hand as the area and body part exposed.

Table 2-47. Coin and Scissors Cleaner (Dermal Exposure Doses)

Source Description	Parameter Varied			Exposed Receptor	ADD (mg/kg-day)
	Duration (min)	Mass Used (grams)	Weight Fraction (Percent)		
High Intensity Use	High (6)	Maximum (624.5)	Maximum (100)	Adult	7.6E-02
				Youth A	7.1E-02
				Youth B	7.7E-02
Moderate Intensity Use	Median (4)	Median (312.3)	Median (75)	Adult	3.8E-02
				Youth A	3.5E-02
				Youth B	3.9E-02
Low Intensity Use	Low (2)	Minimum (126.9)	Minimum (50)	Adult	1.3E-02
				Youth A	1.2E-02
				Youth B	1.3E-02

Table 2-47 shows the dermal exposure dose found for the low, moderate, and high intensity use categories for this condition of use. The ADD of 1-BP for adults varies from 1.3E-02 mg/kg-day to 7.6E-02 mg/kg-day. The ADD of 1-BP for Youth A varies from 1.2E-02 mg/kg-day to 7.7E-02 mg/kg-day. The ADD of 1-BP for Youth B varies from 1.3E-02 mg/kg-day to 7.7E-02 mg/kg-day.

2.3.2.3.2 Automobile AC Flush

This condition of use represents consumer uses of product as an automotive care product in the form of a liquid cleaner. The product is used to dissolve and flush out foreign materials from the coils of an automobile AC coil. These products are available to consumers with 1-BP concentrations greater than 90 percent by weight based on a review of product specific SDS. The room of use is assumed to be the garage. The duration of product use per event evaluated for this product ranges from 5 minutes to 30 minutes.

Inhalation Exposure

Table 2-48. Automobile AC Flush (Inhalation Exposure Concentration)

Source Description	Parameters Varied			Exposed Receptor	24-hour TWA (ppm)
	Duration (min)	Mass Used (grams)	Weight Fraction (percent)		
High Intensity Use	High (30)	Maximum (573)	Single (90)	User	0.80
				Bystander	0.51
Moderate Intensity Use	Median (15)	Mean (286)	Single (90)	User	0.53
				Bystander	0.24
Low Intensity Use	Low (5)	Minimum (143)	Single (90)	User	0.37
				Bystander	7.5E-02

Table 2-48 shows the inhalation exposure concentrations found for the low, moderate, and high intensity use categories for this condition of use. The 24-hour TWA air concentrations of 1-BP for the user varies from 0.37 ppm to 0.80 ppm. The 24-hour TWA air concentrations of 1-BP for the bystander varies from 7.5E-02 ppm to 0.51 ppm.

Dermal Exposure

Dermal exposure was evaluated for this condition of use utilizing the CEM (Fraction Absorbed) model due to the expectation of uninhibited evaporation and no full immersion of body parts into the product during use. EPA used the full area of face, hands, and arms as the area and body parts exposed.

Table 2-49. Automobile AC Flush (Dermal Exposure Doses)

Source Description	Parameter Varied			Exposed Receptor	ADD (mg/kg-day)
	Duration (min)	Mass Used (grams)	Weight Fraction (Percent)		
High Intensity Use	High (30)	Maximum (573)	Single (90)	Adult	0.50
				Youth A	0.47
				Youth B	0.52

Moderate Intensity Use	Median (15)	Median (286)	Single (90)	Adult	0.50
				Youth A	0.47
				Youth B	0.52
Low Intensity Use	Low (5)	Minimum (143)	Single (90)	Adult	0.50
				Youth A	0.47
				Youth B	0.52

Table 2-49 shows the dermal exposure dose found for the low, moderate, and high intensity use categories for this condition of use. The ADD of 1-BP for adults across all intensities of use (high, moderate, low) is 0.50 mg/kg-day. The ADD of 1-BP for Youth A across all intensities of use is 0.47 mg/kg-day. The ADD of 1-BP for Youth B across all intensities of use is 0.52 mg/kg-day. The identical ADD is due to the availability of only a single weight fraction for products in this condition of use and the use of a published experimental absorption fraction value (independent of duration) rather than an estimated value (reliant on duration).

2.3.2.4 Indoor Environmental Concentrations in Buildings with Conditioned and Unconditioned Zones Model (IECCU)

Overview

The IECCU predicts indoor air concentrations of chemicals released from products used or materials installed in a building through a deterministic, mass-balance approach. It is a peer reviewed EPA model which relies on user provided input parameters and various assumptions to generate exposure estimates. The IECCU can be used as (1) a general-purpose indoor exposure model in buildings with multiple zones, multiple chemicals, and multiple sources and sinks or (2) a special purpose concentration model for simulating the effects of sources in unconditioned zones on the indoor environmental concentrations in conditioned zones. Readers can learn more about the IECCU by reviewing the IECCU user guide ([U.S. EPA, 2019c](#)).

Approach and Inputs

The IECCU was utilized in this evaluation as a general purpose indoor exposure model to estimate time-series indoor air concentrations within a residence where THERMAX™ insulation boards are installed. THERMAX™ insulation board is a non-structural, rigid board insulation consisting of a glass-fiber-infused polyisocyanurate foam core laminated between 1.0 mm smooth, reflective aluminum facers on both sides. While rigid insulation would typically be installed in walls and encapsulated under drywall or other material, a general internet search identified the availability of certain pre-finished products which can be installed without the need to “finish” it with drywall provided applicable building or other codes allow. Based on a review of available products and public comments included in the Docket for this evaluation, THERMAX™ insulation boards are the only U.S. made rigid insulation board which includes 1-BP within its formulation.

The evaluation of the insulation (off-gassing) condition of use was expanded in this risk evaluation to include two building configurations as well as chronic exposure. The first building configuration consisted of an attic/living space/crawlspace configuration where the insulation board was installed in the attic (roof and floor) and crawlspace (ceiling). The second building configuration consisted of an attic/living space/full basement configuration where the insulation board was installed in the attic (roof and floor) and basement (walls). Once the rigid insulation board is installed, there is an

initial spike in 1-BP concentration due to off-gassing. Following the initial spike, 1-BP concentrations due to off-gassing quickly fall to lower, more stable but decreasing levels which may be maintained for months or even years, potentially resulting in a longer term exposure to lower concentrations. This long-term, lower concentration exposures lend itself to the possibility of a longer-term chronic exposure. While spray foam insulation is a consumer product, EPA did not identify any consumer spray foam products which identified 1-BP as a component of its formulation. As a result, this risk evaluation only considered 1-BP exposure from the THERMAX™ rigid insulation board product.

Other changes to the approach for the insulation (off-gassing) condition of use incorporated into this evaluation include a smaller surface area from which 1-BP may off-gas. This change was made because it is expected the aluminum facing applied to the front and back surfaces of the full insulation board is impermeable to 1-BP, therefore the area from which 1-BP may off-gas was limited for this evaluation to all four edges of each insulation board installed. Additionally, since the amount of a chemical of concern off-gassing is sensitive to temperature (especially in unconditioned zones like the attic and crawlspace, and possibly to some degree a full basement), this evaluation modeled short-term concentrations based on four installation times (February 1st, May 1st, August 1st, and November 1st). These values address initial spikes in concentration immediately following installation and seasonal variation of concentrations resulting from the effects of temperature. A representative concentration for exposure estimation purposes was then calculated by averaging the results from all four installation dates for each zone.

The general mass balance equation used by the IECCU to determine the change in the concentration of a chemical of concern in air within a given zone is determined by six factors: (1) the emissions from the sources in the zone, (2) the rate of chemical removal from the zone by the ventilation and interzonal air flows, (3) the rate of chemical carried into the zone by the infiltration and interzonal air flows, (4) the rate of chemical sorption by interior surfaces, (5) the rate of chemical sorption by airborne particles, and (6) the rate of chemical sorption by settled dust. Since 1-BP is highly volatile, once it is in the vapor phase, 1-BP is expected to remain in the vapor phase. As a result, EPA only considered the first three factors listed above when evaluating inhalation exposure to 1-BP for the insulation off-gassing condition of use. Dermal exposure is not expected from off-gassing and therefore was not evaluated.

Input parameters for running the IECCU were obtained from published literature, including U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)), or estimated with either empirical or QSAR models. A discussion of some specific inputs are included below and summarized in Table 2-50 and Table 2-51. Detailed tables of all input parameters for the IECCU are provided in the 1-BP Supplemental File: Information on Consumer Exposure Assessment Model Input Parameters ([EPA, 2019a](#)).

A three-zone configuration described by Bevington et al. in ([Sebroski, 2017](#)) was used to represent a generic residential building for both building configurations. The assumed location of installed insulation for the attic/living space/crawlspace building configuration was the floor and rafters within the attic and the ceiling of the crawlspace area which spans the entire blue print of the

building floor area. The assumed location of installed insulation for the attic/living space/full basement building configuration was the floor and rafters within the attic and all four walls in the basement. The baseline ventilation and interzonal air flows for the two building configurations are shown in Figure 2-13 and Figure 2-14.

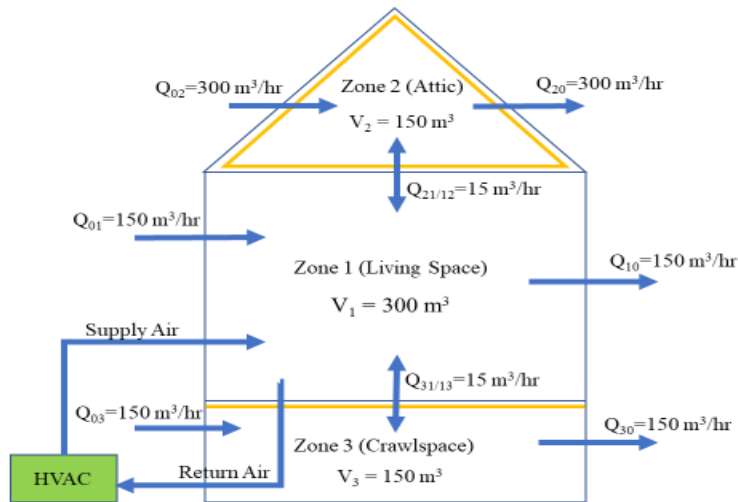


Figure 2-13. The Three-Zone Configuration for a Residential Setting and Baseline Ventilation and Interzonal Air Flows for the Attic/Living Space/Crawlspace Building Configuration.

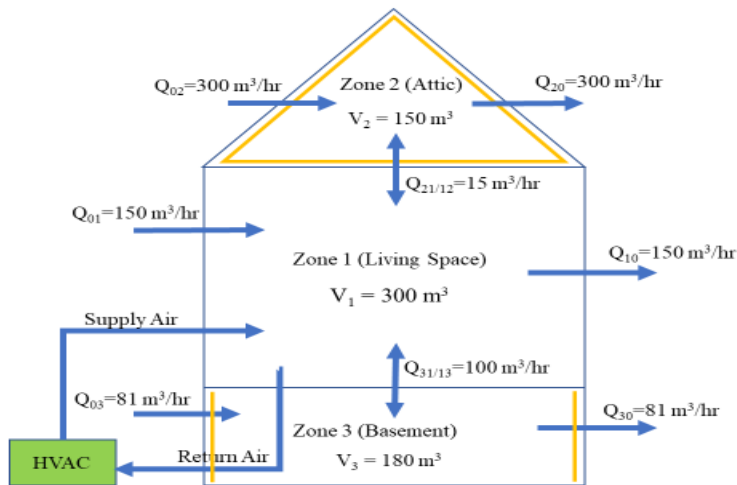


Figure 2-14. The Three-Zone Configuration for a Residential Setting and Baseline Ventilation and Interzonal Air Flows for the Attic/Living Space/Full Basement Building Configuration.

Table 2-50 summarizes general inputs utilized in the IECCU modeling runs for the two building configurations. Insulated area is based on the available surface area where insulation was installed. This includes an assumption that a ¼ inch gap exist between adjacent panels and the ceiling and floor. Number of panels is based on the area needing insulation and a product size of four feet wide by eight feet long by two inches thick. Source area is calculated by multiplying the number of panels needed for each area by the total area of all four edges of the insulation board shown in Table 2-51. Since EPA assumes insulation is only installed in the attic and crawlspace/attic and basement, there is no insulated area in the living space.

Table 2-50. Zone Names, Volumes, and Baseline Ventilation Rates

Zone name	Zone volume (m ³)	Insulated Area (m ²)	Number of Panels needed	Source Area	Ventilation Rate (h ⁻¹)
Living space	300	N/A	N/A	N/A	0.5
Attic	150	180	60	22.3	2.0
Crawlspace	150	120	40	14.9	1.0
Basement	180	75	30	11.2	0.45

Table 2-51. Parameters for the 1-BP Sources

Property	Value
Total Area four board edges (m ²)	0.372

Board thickness (cm)	5.1
1-BP content	0.5%
Density (g/cm ³)	0.03
Partition coef. (K) at 21 °C	3.3
K as a function of temp.	$a = 0.9$ $\Delta H_v = 8.14 \times 10^4$
Diffusion coef. (D) at 20 °C	1.88E-11

Results

Sensitivity Analysis: A sensitivity analysis was conducted to see the impact of installation date and temperature on the off-gassing of 1-BP from rigid insulation board. These results are presented in Figure 2-15 and Figure 2-16 for the attic/living space/crawlspace and attic/living space/basement building configurations, respectively.

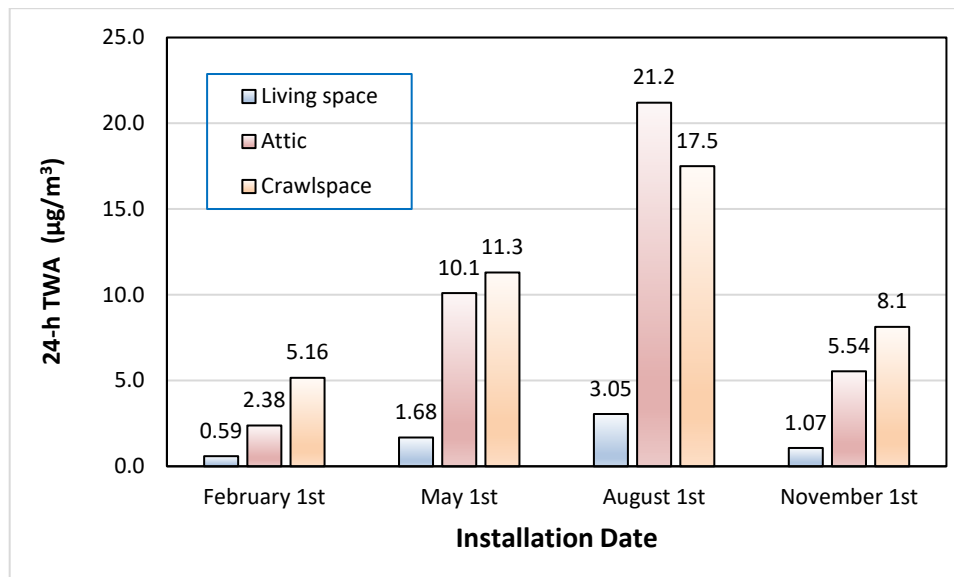


Figure 2-15. 24-Hour TWA Concentrations for Attic/Living Space/Crawlspace Building Configuration Across Four Different Installation Dates

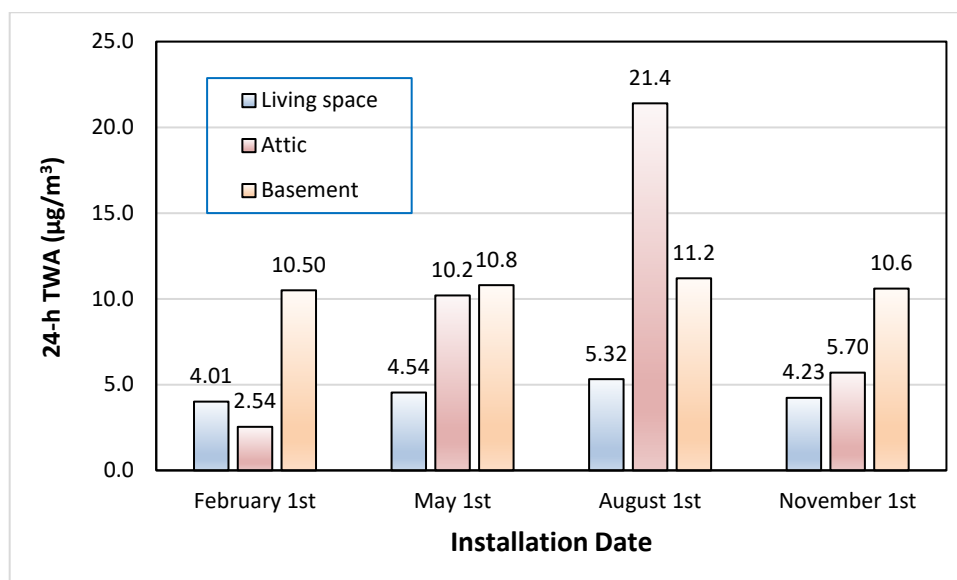


Figure 2-16. 24-Hour TWA Concentrations for Attic/Living Space/Full Basement Building Configuration Across Four Different Installation Dates

Figure 2-15 and Figure 2-16 show the variation in concentrations based on the date when initial installation of the rigid insulation board occurs. These figures demonstrate that off-gassing is sensitive to temperature and the highest estimated concentrations occur in August. The seasonal fluctuation is particularly sensitive in unconditioned zones like the attic or crawlspace. Concentrations in the basement are also impacted.

Inhalation Exposure: Modeling results for acute and chronic inhalation exposures evaluated with the IECCU are summarized and discussed below. Results are presented for both building configurations.

2.3.2.4.1 Insulation (Off-Gassing): Acute Inhalation Exposure

This condition of use represents consumer use of insulation material as building and construction materials in the form of rigid board insulation for interior applications. The product evaluated is assumed to contain 0.5 percent by weight of 1-BP. The rooms of use where the product is installed are assumed to include the attic and either the crawlspace or the basement of a residential home.

The acute inhalation exposure evaluation considers short-term exposure to 1-BP resulting from an initial spike in the air concentration of 1-BP from newly installed rigid insulation board. It incorporates a higher initial air concentration for a short duration.

To obtain representative short-term inhalation exposure concentrations, EPA calculated the average 24-hour TWA concentration across all four installation dates utilized for the sensitivity analysis for each zone in both building configurations. Table 2-52 summarizes the calculated average 24-hour TWA concentrations for each zone. The IECCU provides concentrations in micrograms per cubic meter ($\mu\text{g}/\text{m}^3$). These were converted to ppm with the following equation:

$$C_{\text{ppm}} = ((C_{\mu\text{g}/\text{m}^3}/1000) \times 24.45)/\text{MW}$$

Where:

C_{ppm} is concentration of 1-BP in units of ppm

$C_{\mu g/m^3}$ is concentration of 1-BP in units of micrograms per cubic meter

24.45 is a conversion factor representing molar volume (L)

MW is the molecular weight of 1-BP (122.99 g/mol)

Table 2-52. Average 24-Hour TWA Concentration of 1-BP by Zone in Two Building Configurations

	Avg. 24-Hour TWA ($\mu\text{g}/\text{m}^3$)			Avg. 24-Hour TWA (ppm)		
	Attic	Living Space	Crawlspace/Basement	Attic	Living Space	Crawlspace/Basement
Attic/Living Space/Crawlspace	9.8	1.6	11	2.0E-03	3.2E-04	2.1E-03
Attic/Living Space/Basement	10	4.5	11	2.0E-03	9.0E-04	2.1E-03

Table 2-52 shows the inhalation exposure concentrations found for the attic/living space/crawlspace and the attic/living space/basement building configuration. The 24-hour TWA air concentration of 1-BP in the attic of both building configurations is 2.0E-03 ppm. The 24-hour TWA air concentration of 1-BP in the crawlspace and basement is 2.1E-03 ppm. The 24-hour TWA air concentrations of 1-BP in the living space of each building configuration varies by a factor of approximately 3 (3.2E-04 ppm for the attic/living space/crawlspace and 9.0E-04 ppm for the attic/living space/basement building configuration).

2.3.2.4.2 Insulation (Off-Gassing): Chronic Inhalation Exposure

The chronic inhalation exposure evaluation considers longer-term exposure to 1-BP. This evaluation modeled chronic inhalation exposure concentrations over a seven year period. The seven year simulation assumed the insulation boards are installed on May 1st. The seven year period captures the initial spike in the air concentration of 1-BP from newly installed rigid insulation board, the rapid decrease in the air concentration of 1-BP following initial installation, and relatively stable but lower air concentrations of 1-BP over an extended period of time.

Table 2-53 and Table 2-54 summarize the calculated annual TWA concentrations for each zone for each year for the attic/living space/crawlspace and attic/living space/basement building configurations, respectively. To obtain a representative long-term concentration, EPA calculated a seven year average for each zone by adding each individual annual concentration together and dividing by seven.

Table 2-53. Predicted 1-Year TWA Concentrations by Zone for the Attic/Living Space/Crawlspace Building Configuration

	Annual TWA ($\mu\text{g}/\text{m}^3$)			Annual TWA (ppm)		
	Attic	Living Space	Crawlspace	Attic	Living Space	Crawlspace
Year 1	6.3E-01	1.0E-01	6.0E-01	1.2E-04	2.0E-05	1.2E-04
Year 2	2.7E-01	4.4E-02	2.6E-01	5.3E-05	8.7E-06	5.2E-05
Year 3	2.1E-01	3.4E-02	2.0E-01	4.1E-05	6.7E-06	3.9E-05
Year 4	1.7E-01	2.8E-02	1.7E-01	3.5E-05	5.7E-06	3.3E-05
Year 5	1.5E-01	2.5E-02	1.5E-01	3.0E-05	5.0E-06	2.9E-05
Year 6	1.4E-01	2.3E-02	1.3E-01	2.7E-05	4.5E-06	2.6E-05
Year 7	1.3E-01	2.1E-02	1.2E-01	2.5E-05	4.1E-06	2.5E-05
7-Year Avg.	2.4E-01	4.0E-02	2.3E-01	4.8E-05	7.9E-06	4.6E-05

Table 2-54. Predicted 1-Year TWA Concentrations by Zone for the Attic/Living Space/Basement Building Configuration

	Annual TWA ($\mu\text{g}/\text{m}^3$)			Annual TWA (ppm)		
	Attic	Living Space	Crawlspace	Attic	Living Space	Crawlspace
Year 1	6.4E-01	2.5E-01	5.7E-01	1.3E-04	5.0E-05	1.1E-04
Year 2	2.7E-01	1.1E-02	2.5E-01	5.4E-05	2.2E-05	4.9E-05
Year 3	2.1E-01	8.4E-02	1.9E-01	4.2E-05	1.7E-05	3.8E-05
Year 4	1.8E-01	7.1E-02	1.6E-01	3.5E-05	1.4E-05	3.2E-05
Year 5	1.6E-01	6.2E-02	1.4E-01	3.1E-05	1.2E-05	2.8E-05
Year 6	1.4E-01	5.6E-02	1.3E-01	2.8E-05	1.1E-05	2.5E-05
Year 7	1.3E-01	5.2E-02	1.2E-01	2.6E-05	1.0E-05	2.4E-05
7-Year Avg.	2.5E-01	9.8E-02	2.2E-01	4.9E-05	2.0E-05	4.4E-05

The 7-year average TWA air concentrations of 1-BP in the attic for both building configurations is approximately the same (4.8E-05 and 4.9E-05 ppm). The 7-year average TWA air concentrations of 1-BP in the crawlspace and basement for both building configurations is also approximately the same (4.6E-05 and 4.4E-05 ppm). The 7-year average TWA air concentrations of 1-BP in the living space of each building configuration varies by a factor of approximately 2.5 (7.9E-06 ppm for the attic/living space/crawlspace and 2.0E-05 ppm for the attic/living space/basement building configuration).

2.3.2.5 Summary of Consumer Exposure Assessment

Consumer exposure was evaluated for nine consumer conditions of use summarized in Table 2-31 (aerosol spray degreaser/cleaner-general, aerosol spray degreaser/cleaner-electronics, spot cleaner and stain remover, coin and scissors cleaner, spray cleaner-general, adhesive accelerant, automobile AC flush, mold cleaning and release product, insulation (off-gassing)). All nine consumer uses were evaluated for inhalation and dermal exposure, excluding the insulation (off-gassing) COU which was only evaluated for inhalation exposure.

The results for all conditions of use and exposure routes presented in Sections 2.3.2.2 and 2.3.2.3 are summarized in Table 2-55 (Inhalation) and Table 2-56 (Dermal). The results for the insulation (off-gassing) condition of use are shown in Table 2-57.

Table 2-55. Inhalation Results Summary

Condition of Use	Scenario Description	24-hour TWA (ppm)		Model Used
		User	Bystander	
Aerosol Spray Degreaser/Cleaner-General	High Intensity Use	141	41	CEM
	Moderate Intensity Use	19	5.0	
	Low Intensity Use	1.0	0.25	
Aerosol Spray Degreaser/Cleaner-Electronics	High Intensity Use	30	8.7	CEM
	Moderate Intensity Use	1.4	0.35	
	Low Intensity Use	6.7E-02	1.9E-02	
Spot Cleaner and Stain Remover	High Intensity Use	47	7.2	CEM
	Moderate Intensity Use	3.4	0.54	
	Low Intensity Use	0.26	4.8E-02	
Coin and Scissors Cleaner	High Intensity Use	2.0	1.0	MCCEM
	Moderate Intensity Use	1.5	0.47	
	Low Intensity Use	1.2	0.22	
Spray Cleaner-General	High Intensity Use	133	33	CEM
	Moderate Intensity Use	14	2.7	
	Low Intensity Use	2.3	0.44	
Adhesive Accelerant	High Intensity Use	18	4.5	CEM
	Moderate Intensity Use	1.1	0.20	
	Low Intensity Use	0.12	2.5E-02	
Automobile AC Flush	High Intensity Use	0.8	0.51	MCCEM
	Moderate Intensity Use	0.53	0.24	
	Low Intensity Use	0.37	7.5E-02	
Mold Cleaning and Release Product	High Intensity Use	21	4.2	CEM
	Moderate Intensity Use	1.4	0.27	
	Low Intensity Use	0.12	2.6E-02	

Table 2-56. Dermal Results Summary

Condition of Use	Scenario Description	Average Daily Dose (mg/kg-day)			Model Used
		Adult	Youth A	Youth B	
Aerosol Spray Degreaser/Cleaner-General	High Intensity Use	3.5	3.3	3.6	CEM (Permeability)
	Moderate Intensity Use	0.23	0.22	0.24	
	Low Intensity Use	1.7E-02	1.6E-02	1.7E-02	
Aerosol Spray Degreaser/Cleaner- Electronics	High Intensity Use	4.6E-02	4.3E-02	4.7E-02	CEM (Fraction Absorbed)
	Moderate Intensity Use	3.4E-02	3.2E-02	3.5E-02	
	Low Intensity Use	2.40E-02	2.20E-02	2.40E-02	
	High Intensity Use	0.87	0.81	0.89	

Spot Cleaner and Stain Remover	Moderate Intensity Use	9.1E-02	8.5E-02	9.3E-02	CEM (Permeability)
	Low Intensity Use	4.3E-03	4.1E-03	4.4E-03	
Coin and Scissors Cleaner	High Intensity Use	7.6E-02	7.1E-02	7.7E-02	CEM (Permeability)
	Moderate Intensity Use	3.8E-02	3.5E-02	3.9E-02	
	Low Intensity Use	1.3E-02	1.2E-02	1.3E-02	
Spray Cleaner-General	High Intensity Use	3.6	3.3	3.6	CEM (Permeability)
	Moderate Intensity Use	0.44	0.42	0.45	
	Low Intensity Use	5.9E-02	5.5E-02	6.1E-02	
Adhesive Accelerant	High Intensity Use	4.8E-02	4.5E-02	4.9E-02	CEM (Fraction Absorbed)
	Moderate Intensity Use	4.8E-02	4.5E-02	4.9E-02	
	Low Intensity Use	4.8E-02	4.5E-02	4.9E-02	
Automobile AC Flush	High Intensity Use	0.50	0.47	0.52	CEM (Fraction Absorbed)
	Moderate Intensity Use	0.50	0.47	0.52	
	Low Intensity Use	0.50	0.47	0.52	
Mold Cleaning and Release Product	High Intensity Use	4.3E-02	4.0E-02	4.4E-02	CEM (Fraction Absorbed)
	Moderate Intensity Use	2.8E-02	2.6E-02	2.9E-02	
	Low Intensity Use	1.5E-02	1.4E-02	1.5E-02	

The maximum inhalation concentration modeled for the consumer user and bystander occurred under the high intensity use scenario for an aerosol spray degreaser/cleaner-general condition of use. The minimum inhalation concentration modeled for the consumer user and bystander both occurred under the low intensity use scenario for the aerosol spray cleaner/degreaser-electronics condition of use.

Across all consumer uses modeled for dermal exposure, the maximum ADD for the Adult user occurred under the high intensity use scenario for the spray cleaner-general condition of use. The maximum ADD for the Youth A and Youth B users occurred under the high intensity use scenario of both the spray cleaner-general condition of use and the aerosol spray degreaser/cleaner-general condition of use. The minimum ADD for all three users (Adult, Youth A, and Youth B), occurred under the low intensity use scenario for the spot cleaner/stain remover condition of use.

Insulation Results

EPA evaluated the insulation (off-gassing) condition of use for both acute and chronic exposures. Unlike the other conditions of use summarized above, which cause a short-term, higher-level exposure, installation of the rigid installation board causes both a short-term, higher-level exposure (initial spike in concentrations from off-gassing for the first few days) and a long-term, lower-level exposure (rapid decrease in concentration from off-gassing reaching a relatively consistent concentration after the first few months). This can be seen in Figure 2-17 and Figure 2-18.

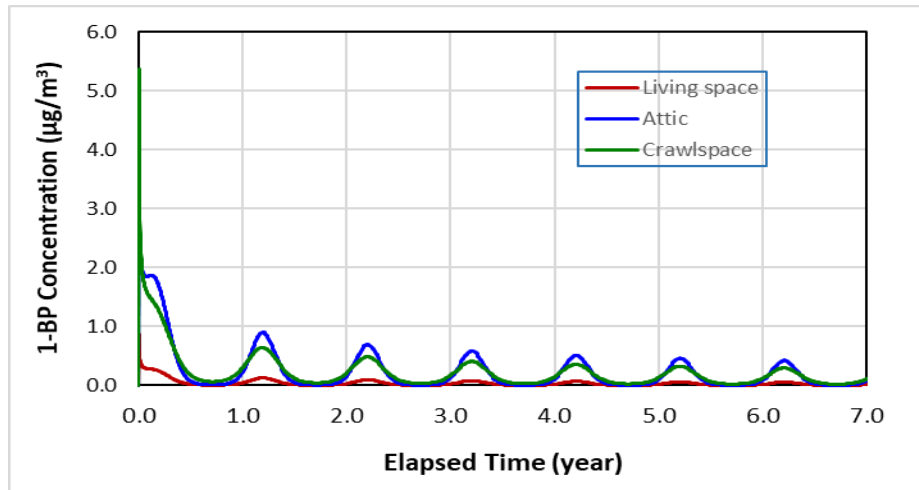


Figure 2-17 Predicted Gas-Phase 1-BP Concentration (Mg/M^3) in Three Locations Within the Attic/Living Space/Crawlspace Building Configuration.

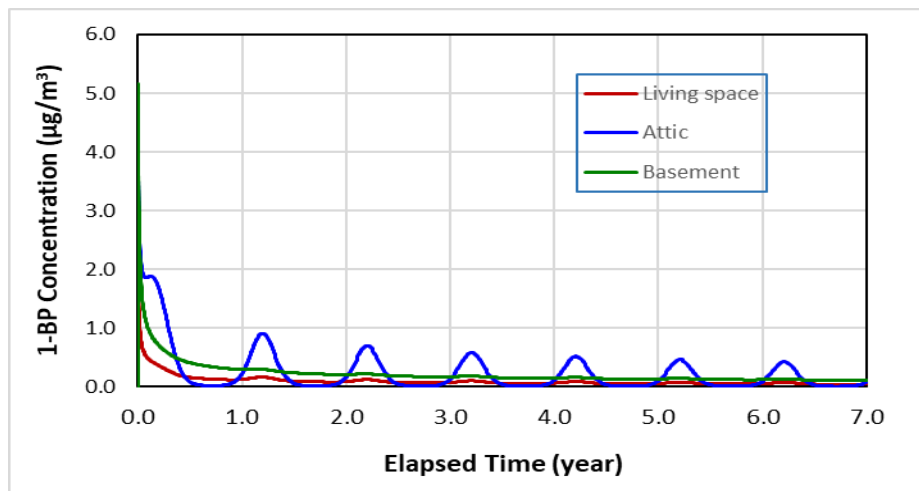


Figure 2-18. Predicted Gas-Phase 1-BP Concentrations (Mg/M^3) in Three Locations Within the Attic/Living Space/Crawlspace Building Configuration.

Figure 2-17 and Figure 2-18 show the predicted 1-BP concentration in each of the three areas modeled for each building configuration for the seven year concentration profile. Each figure shows the spike in concentration from off-gassing following initial installation of the rigid board insulation evaluated followed by the rapid decrease in concentrations over the first few months. In each building configuration, the living area has less fluctuations in concentrations after the initial concentration spike following installation compared to other areas. Similarly, the basement in the attic/living space/basement building configuration has less fluctuations in concentrations after the initial concentration spike following installation. The higher variability in concentrations seen in the attic of both building configurations and the crawlspace of the attic/living space/crawlspace building configuration reflect the sensitivity of off-gassing to temperature in unconditioned zones within the two building configurations.

Table 2-57. Inhalation Results Summary-Insulation (Off-Gassing)

Condition of Use	Scenario Description	Bystander Exposure Concentration (ppm)		Model Used
		24-hour TWA	7-Year Average TWA	
Insulation (Off-gassing) Attic/Living Space/Crawlspace	Attic	2.0E-03	4.9E-05	IECCU
	Living Space	9.0E-04	2.0E-05	
	Crawlspace	2.1E-03	4.4E-05	
Insulation (Off-gassing) Attic/Living Space/Basement	Attic	2.0E-03	4.8E-05	IECCU
	Living Space	3.2E-04	7.9E-06	
	Basement	2.1E-03	4.6E-05	

Considering the likely locations where an individual may spend most of their time within a residence, the concentrations within the living space of both building configurations and the basement of the attic/living space/basement building configuration are of particular interest for both short-term and long-term inhalation exposures. Concentrations within the attic can be a factor to consider for short-term and long-term inhalation exposures if the attic was converted to a living space, play area, or bedroom, as was sometimes done in older residences or some modern renovations to garner more usable space. Outside of conversion of the attic to a usable space, the 7-year average values for the attic and crawlspace would be more representative of a short-term exposure to individuals entering the area for a short period of time to remove items stored, do some other applicable repair work, or clean out the area beginning several months after initial installation of the rigid insulation board.

2.3.2.6 Key Assumptions, Uncertainties, and Confidence

Modeling was used to evaluate consumer exposure concentrations under the conditions of use summarized in Table 2-31. This modeling required a variety of inputs when data were available. In the absence of available data, this modeling relied on certain default data values and certain assumptions. As with any risk evaluation, there are uncertainties associated with the data used, assumptions made, and approaches used. An overall review of these three factors can help develop a qualitative description of the confidence associated with these factors and results obtained.

Key Assumptions and Uncertainties

Consumer exposure for this risk evaluation is based on the assumption that the product used under the conditions of use (Table 2-31) was only used once per day. This assumption considers a single use event occurring over a certain period of time and represents an expected consumer use pattern. This assumption applies to all conditions of use evaluated (except for the insulation (off-gassing) condition of use). There is a low uncertainty associated with this assumption because most consumer products are used for a single use over a short-period of time. Additional uses which may occur within a given year are expected to occur well after the first use and typically would occur after the concentration from the original use decreases to background levels.

Exposure for the insulation (off-gassing) condition of use assumes the rigid board insulation is installed in each location (attic and crawlspace/basement) within a single day and remains installed for an extended period of time. This assumption considers short-term initial exposure from off-gassing due to the initial spike in 1-BP concentrations immediately following installation as well as long-term exposure from off-gassing following the initial spike in 1-BP concentrations. There is a low uncertainty associated with this assumption because the rigid board insulation's intended use is a permanent installation over an extended period of time. Unlike the other conditions of use evaluated, however, off-gassing of 1-BP is continuous for years after initial installation.

Consumer exposure for this evaluation is also based on the assumption that a single product is used for a single day under a specific condition of use. There is a medium-low uncertainty associated with this assumption because certain consumer activities (like cleaning) may entail the use of more than one cleaning product within a particular condition of use. However, there remains some uncertainty because even if more than one cleaning product is used, to impact the estimated exposure in this evaluation, each product used would have to contain 1-BP and therefore result in a higher overall exposure.

This evaluation assumes consumer exposure under each condition of use (excluding insulation (off-gassing)) is not chronic in nature due to the infrequent use and short duration of use for a given product. There is a medium uncertainty associated with this assumption because, although information found during EPA's systematic review process supports infrequent use and short durations of use, there is a growing consumer practice to do-it-yourself projects or activities which could lead to increased frequencies of use and the possibility of more than one product containing a chemical of concern within a given day.

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-chemical properties of the chemical of concern which is the high vapor pressure and expected quick dissipation of the chemical of concern. There is a low uncertainty associated with this assumption.

Selection of Models Used

Inhalation Models: Three peer reviewed EPA models were used to estimate inhalation exposure to the consumer user or bystander (CEM, MCCEM, and IECCU) in this evaluation. These models were selected as fit-for-purpose models which had pre-defined exposure scenarios comparable to the expected consumer use exposure scenarios. Each model has certain limitations and uncertainties within the model or associated with inputs or default values utilized by the models.

Limitations of the models were considered as part of the selection process for each condition of use. For example, neither CEM nor IECCU have a scenario designed for a pool of liquid (coin and scissors cleaner or automobile AC flush), but MCCEM had two applicable models. Similarly, IECCU is an indoor air pollution transport model which can consider seasonal variation while CEM and MCCEM do not have that capability.

The selection and use of these models, even considering limitations, inherently have some uncertainty. Applying fit-for-purpose concepts and considering limitations of each model helps to

reduce uncertainties and increase confidence in the overall model selected. EPA has an overall low uncertainty in the models utilized for estimating inhalation exposure.

Dermal Models: Three models were considered for estimating dermal exposure to the consumer user (CEM (Fraction Absorbed), CEM (Permeability), and a full transient exposure model based on a published paper from Frasch ([Frasch and Bunge, 2015](#))) in this evaluation. EPA evaluated each model, the inputs and outputs associated with each model, the applicability of each model to the expected consumer dermal exposure scenarios for each condition of use, and applied a fit-for-purpose approach to selecting the final models used to estimate consumer dermal exposures. A comparison and sensitivity analysis of all three models (including results) is provided in Appendix F.

Utilizing the process described above, EPA selected two models for estimating dermal exposure to the consumer user (CEM (Fraction Absorbed) and CEM (Permeability)) for this evaluation. The CEM (Fraction Absorbed) model was selected for those COUs where evaporation is uninhibited and where full immersion of body parts is not expected during use. The basis for this selection is that CEM (Fraction Absorbed) is a mass limited model which considers evaporation from the skin and only the fraction absorbed portion of the total exposure occurring during product use. To minimize uncertainty, this model was run utilizing the assumption that the entire mass of chemical in the thin film enters the stratum corneum. With this assumption, the CEM (Fraction Absorbed) model correctly applies the fraction absorbed component to the chemical retained within the skin rather than on the skin. Additionally, while the estimated absorption coefficient (K_p) within the CEM (Fraction Absorbed) model is based on an aqueous vehicle, a neat K_p was obtained from literature and incorporated into the model. The use of the neat K_p is more representative of the products identified within the various COUs for which this model was utilized as most products were not aqueous (in water) but rather in other carbon based solvent media and had a chemical specific weight fraction of 50 to 100 percent.

The CEM (Permeability) model was selected for those COUs where evaporation is inhibited/prohibited or where full immersion of body parts is expected during use. The basis for this selection is that CEM (Permeability) does not consider evaporation from the skin and assumes a constant supply of product against the skin during the entire duration of use. Similar to CEM (Fraction absorbed), the CEM (Permeability) model estimates the permeability coefficient based on an aqueous vehicle. To minimize uncertainty, the CEM (Permeability) model was run utilizing a neat (K_p) value obtained from published literature and evaluated in accordance with EPA's systematic review process. The use of the neat K_p is more representative of the products identified within the various COUs for which this model was utilized as most products were not aqueous (in water) but rather in other carbon based solvent media and had a chemical specific weight fraction of 50 to 100 percent.

While the model presented in ([Frasch and Bunge, 2015](#)) is mathematically more complete than CEM (Fraction Absorbed), it is not applicable to splash or similar dermal exposure scenarios expected for the COUs where CEM (Fraction Absorbed) is utilized. Additionally, the published model in ([Frasch and Bunge, 2015](#)) has certain variables which are based on aqueous vehicles of

delivery. To utilize this model for solvent-based vehicles of delivery would require modifications to the published method which are not necessary when utilizing the CEM (Fraction Absorbed) or CEM (Permeability) model.

The selection and use of the two CEM models, even considering limitations, inherently have some uncertainty. Applying fit-for-purpose concepts and considering limitations of each model helps to reduce uncertainties and increase confidence in the overall model selected. EPA has an overall low confidence in the models utilized for estimating dermal exposure based primarily on the uncertainties associated with aqueous/solvent-based vehicles, revisions to model approaches with neat K_p values vs. aqueous K_p values as well as other factors identified in Appendix F.

Inputs and Uncertainties

Inputs for modeling in this evaluation were a combination of physical-chemical properties of 1-BP, default values within the models used, values from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)), Westat Survey ([EPA, 1987](#)), and other data found in the literature as part of the systematic review process. Physical-chemical properties of 1-BP are pre-defined and well-established in the literature. These properties do not change under standard conditions and therefore have very low uncertainty 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 U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)). The models used have a variety of default values as well as some estimation methodologies which were relied upon as part of this evaluation. There is a medium-low uncertainty associated with these values due to the number of parameters where defaults are available.

Values from U.S. EPA's 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 low uncertainty associated with the values in U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)).

Multiple aspects of the Westat Survey ([EPA, 1987](#)) were utilized in this evaluation including cross-walking conditions of use evaluated with one of the thirty-two product categories within the survey; frequency of use, duration of use, and room of use for cross-walked product categories; and other information utilized to inform approaches taken. Most of the consumer uses summarized in Table 2-31 aligned well with one of the thirty-two product categories within the Westat Survey. There is a medium-low uncertainty associated with the cross-walking of consumer uses with the Westat product categories.

The representativeness of the information extracted for modeling from the cross-walked product categories within the Westat Survey ([EPA, 1987](#)) aligns well with expected modern day consumer patterns. However, there is uncertainty associated with the age of the Westat Survey in that it may not be fully representative of modern day consumer activities and products like do-it-yourself hobbyists, modified uses, more concentrated formulations, ease of access to products, or similar

changes which have occurred. There is a medium uncertainty associated with the representativeness of the consumer use patterns described within the Westat Survey and modern 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 personal protective equipment or natural/engineered controls.

As described in Section 2.3.2.1, EPA's Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane document ([U.S. EPA, 2017c](#)) included in the docket for this risk evaluation (Docket Number [EPA-HQ-OPPT-2016-0741-0003](#)), is based on information available at that time. It does not take into consideration company-initiated formulation changes, product discontinuation, or other business or market based factors that occurred after the document was compiled. There is a medium uncertainty associated with the information included in the document.

There are multiple model specific factors to which a level of uncertainty may apply including user groups (age groups) evaluated, building characteristics, and default model parameters. There is a medium level of uncertainty associated with the appropriateness of considering all three age groups (Adult, Youth A and Youth B) as users for dermal exposure in this evaluation. As discussed in Section 2.3.2.2, the lower end of the Youth B age group (11-13 years of age) are possible users but not necessarily reasonably foreseeable users of high solvent products identified in the conditions of use evaluated, with the exception of perhaps the coin and scissors cleaner condition of use. However, the upper end of the age group (14-15 years of age) are possible and reasonably foreseeable users of the same products in the context of cleaning chores or learning general automobile care from parents, friends, shop classes, or hobbyist activities like dirt bikes or go carts.

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, EPA relied on default values within the models for these parameters. These default values were primarily obtained from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)). There is a low uncertainty associated with these parameters.

Room size varied for this evaluation based on room of use obtained from the Westat Survey ([EPA, 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 and 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 low uncertainty 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 low uncertainty 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 low uncertainty associated with building size.

EPA assumes consumers will not wear personal protective equipment (PPE) and will not use complex engineering controls like hoods, baghouses, or incineration devices during product use. Even if basic PPE like gloves or eye protection is used, EPA cannot assume the appropriate PPE will be selected or that consumers will use the PPE correctly. There is low uncertainty associated with these assumptions as 1-BP requires highly specialized gloves to adequately protect against exposure, and neither gloves nor eye protection protects against inhalation exposure.

Confidence

Inhalation Models and Results: There is an overall high confidence in the three models used to evaluate inhalation exposure and the inhalation results found for the conditions of use identified in Table 2-31. 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.

All three models used for this evaluation are peer reviewed models. The models themselves were used for this evaluation as they were developed and designed to be used. The equations within the models 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 models (and retained for this evaluation) are a combination of central tendency and high-end estimates from both peer reviewed literature and U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)). The approaches taken for this evaluation cover a spectrum of modeling results representative of expected consumer use patterns. Even though some default values have high-end values (like building size or ventilation rates), it should be recognized that the sensitivity of these parameters are actually negative and the "higher" building sizes or higher ventilation rates would

result in more mixing and dissipation leading to lower exposure concentrations and therefore a less conservative exposure estimate.

The data used in lieu of default values within the model are a combination of low, central tendency, and high-end values from the Westat Survey ([EPA, 1987](#)) which was rated as a high quality study as part of the systematic review process. The nine conditions of use evaluated align well with specific scenarios within the Westat Survey ([EPA, 1987](#)), pre-defined model scenarios, and other approaches taken. The deterministic approach taken for consumer inhalation exposure in this evaluation varies three parameters which are highly sensitive, representative of consumer use patterns, or both. The three parameters varied also provide 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.

Dermal Models and Results: There is an overall low confidence in the two models used to evaluate dermal exposure and the dermal results found for the conditions of use identified in Table 2-31. This confidence derives from the limitations and uncertainties inherent within the two dermal models, including aqueous delivery vehicles and the use of solubility rather than density in several sub-equations within the models. These limitations were minimized by using a neat-based Kp and experimental absorption coefficient where allowed. The assumptions necessary to correctly apply the two models used for dermal modeling tend to result in an overestimation of exposure for a typical consumer user (single product, infrequent use, shorter duration of use), although absent monitored data, a more conservative estimate is preferred to ensure potential risks are captured.

2.4 Potentially Exposed or Susceptible Subpopulations

TSCA § 6(b)(4)(A) 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 § 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.”

For occupational exposures, EPA assessed exposures to workers and ONUs from all 1-BP conditions of use. Table 2-58 presents the percentage of employed workers and ONUs who may be susceptible subpopulations within select industry sectors relevant to 1-BP conditions of use. The percentages were calculated using Current Population Survey (CPS) data for 2017. CPS is a monthly survey of households conducted by the Bureau of Census for the Bureau of Labor Statistics (BLS) and provides a comprehensive body of data on the labor force characteristics. Statistics for the following subpopulations of workers and ONUs are provided: individuals age 16

to 19, men and women of reproductive age,²⁸ and the elderly. For the purpose of this risk evaluation, EPA considers “reproductive age” as age 16 to 54. As shown in Table 2-58, men make up the majority of the workforce in manufacturing sectors. In other sectors, women (including those of reproductive age and elderly women) make up nearly half of the workforce.

Adolescents (16 to <21 years old) appear to be generally a small part of the total workforce based on CPS data for employed individuals between 16 and 19 years of age. Table 2-59 presents further breakdown on this subset of adolescents employed by industry subsectors. As shown in the table, they comprise less than two percent of the workforce, with the exception of repair and maintenance subsector where 1-BP may be used in aerosol degreasing, and the dry cleaning subsector where 1-BP may be used for dry cleaning and spot cleaning. These data do not cover all adolescents in the 1-BP workforce because of the different age range used by the BLS.

Table 2-58. Percentage of Employed Persons by Age, Sex, and Industry Sector

Age group	Sex	Manufacturing	Wholesale and retail trade	Professional and business services	Other services
16-19 years	Male	0.8%	3.0%	0.7%	1.4%
	Female	0.4%	3.2%	0.5%	1.7%
Reproductive age (16-54 years)	Male	52.9%	42.8%	44.4%	35.2%
	Female	22.2%	35.4%	32.8%	38.4%
Elderly (55+)	Male	17.5%	12.3%	13.4%	13.1%
	Female	7.3%	9.6%	9.4%	13.3%

Source: ([U.S. BLS, 2017](#)). Percentage calculated using CPS table 14, “Employed persons in nonagricultural industries by age, sex, race, and Hispanic or Latino ethnicity.”

Table 2-59. Percentage of Employed Persons Age 16-19 Years by Detailed Industry Sector

Sector	Subsector	Age: 16-19 years
Manufacturing	All	1.2%
Wholesale and retail trade	Wholesale trade	1.4%
Professional and business services	Waste management and remediation services	0.9%
Other services	Repair and maintenance	3.1%
	Drycleaning and laundry services	3.7%

Source: ([U.S. BLS, 2017](#)). Percentage calculated using CPS table 18b, “Employed persons by detailed industry and age.”

²⁸ While statistics on pregnant women are not available, CPS provides data on the number of employed female workers by age group, which allows for determination of the number of employed women of reproductive age.

The CPS uses 2012 Census industry classification, which was derived from the 2012 NAICS. The Census classification uses the same basic structure as NAICS but is generally less detailed. 1-BP conditions of use fall under the following Census industry sectors:

- Manufacturing – The Manufacturing sector comprises establishments engaged in the mechanical, physical, or chemical transformation of materials, substances, or components into new products. Establishments in the sector are often described as plants, factories, or mills. For 1-BP, this sector covers most conditions of use that occur in an industrial setting, including: Manufacturing, Processing as a reactant, Processing – Incorporation into formulation, mixture, or reaction product, Incorporation into Articles, Spray adhesives, and the vast majority of facilities likely engaged in Vapor Degreasing (all degreaser types) and Cold Cleaning. This sector also covers cement manufacturing facilities that may burn waste containing 1-BP for energy recovery.
- Wholesale and retail trade – The wholesale trade sector comprises establishments engaged in wholesaling merchandise, generally without transformation, and rendering services incidental to the sale of merchandise. Wholesalers normally operate from a warehouse or office. This sector likely covers facilities that are engaged in the importation of 1-BP or products and formulations containing 1-BP. The retail trade sector comprises establishments engaged in retailing merchandise and rendering services incidental to the sale of merchandise.
- Professional and business services – This sector comprises establishments that specialize in a wide range of services. This sector covers waste management and remediation services, which includes establishments that may handle, dispose, treat, and recycle wastes containing 1-BP.
- Other services – This sector comprises establishments engaged in providing services not specifically provided for elsewhere in the classification system. For 1-BP, this sector covers the vast majority of commercial repair and maintenance facilities that are likely to use 1-BP for aerosol degreasing. The sector also covers the use of 1-BP in dry cleaning and spot cleaning.

For consumer exposures, EPA assessed exposures to users and bystanders. EPA assumes, for this evaluation, consumer users are male or female individuals (between 11 and 21 years of age and greater than 21 years of age). Bystanders could be any age group ranging from infants to adults (Section 2.3.2.1).

This assessment qualitatively evaluates consumer exposure for potentially exposed susceptible subpopulations (PESS). PESS can include reproductive age females who may be or become pregnant; lactating women; reproductive age males; infants, toddlers, children at various developmental stages in life, and elderly; individuals of any age with health issues or concerns including suppressed immune systems, asthma, chemical sensitivity, heart disease, or other health issues or concerns. PESS can be a consumer user or bystander depending on the individuals age and location during product use.

Additional PESS groups include people with implantable prosthetics because 1-BP is an available cleaner for implantable prosthetic devices (<https://www.albemarle.com/businesses/bromine-specialties/bromine-&-derivatives/specialty-chemicals>).

3 HAZARDS (Effects)

3.1 Environmental Hazards

3.1.1 Approach and Methodology

In the Problem Formulation ([U.S. EPA, 2018c](#)), EPA performed quantitative and qualitative screening-level analysis to determine which pathways to include in the scope of the risk evaluation.

The qualitative aspect of the assessment considered the physical-chemical properties of 1-BP as well as the conditions of use within the scope of the risk evaluation to determine whether potential exposures to terrestrial species from air releases, water releases or land application of biosolids could present a risk concern. This qualitative assessment indicated that exposures and risks to terrestrial receptors are not expected and no further analysis is necessary ([U.S. EPA, 2018c](#)). Similarly, potential concerns for aquatic sediment-dwelling species were assessed by considering the potential for exposure given the physical chemical properties of 1-BP in water, which indicated that risks are not expected. Consistent with the analysis plan of the Problem Formulation ([U.S. EPA, 2018c](#)), no further analysis of hazards to sediment-dwelling aquatic or terrestrial species was carried out as part of this evaluation and the results presented below are brought forward from the problem formulation to make a risk determination for these species because the initial evaluation was sufficient to make a risk determination for these organisms.

The quantitative aspect of this risk evaluation compared hazard threshold concentrations for water column-dwelling aquatic species (calculated using an acute fish study identified during the literature search for 1-BP as well as environmental hazard endpoints estimated using the Ecological Structure Activity Relationships (ECOSAR, v.2.0²⁹) modeling program) with estimated environmental exposure concentrations in the water column resulting from discharges of 1-BP to surface water. This aspect of the analysis has been updated in this final risk evaluation due to uncertainties about the data presented in the Problem Formulation and draft risk evaluation which utilized hazard data summaries presented in the European Chemical Health Agency (ECHA) REACH registration page for 1-BP. The results presented in these ECHA summaries are not utilized in this final risk evaluation, as EPA was unable to identify a US-based data owner and could not obtain the full study reports for these summaries. The results of this updated quantitative analysis for aquatic species indicated that risks to aquatic species are unlikely and no further analysis is necessary.

EPA identified environmental hazard data through a literature search for 1-BP as outlined in *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, [EPA-HQ-OPPT-2016-0741-0047](#). As described below, a total of one on-topic environmental hazard study (acute fish study; ([Geiger et al., 1988](#))) was identified and reviewed according to the systematic review criteria described in *Application of Systematic Review in TSCA*

²⁹ More information about the ECOSAR program can be found at: <https://www.epa.gov/tsc-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model>

Risk Evaluations (U.S. EPA, 2018a) and *Strategy for Assessing Data Quality in TSCA Risk Evaluations* (U.S. EPA, 2017e). This study was determined to be high quality following data quality evaluation; the full study quality evaluation is presented in the systematic review data evaluation document for ecological hazard studies (EPA, 2019k).

Five robust data summaries were identified in the European Chemicals Agency (ECHA) database to characterize the environmental hazards of 1-BP to aquatic receptors (ECHA, 2017). These data summaries were not utilized in the final risk evaluation because the full study reports could not be obtained by the EPA and reviewed for data quality. To reduce uncertainties about relying on a single acute toxicity study with fish to draw conclusions about the environmental risks across all species, EPA utilized the Ecological Structure Activity Relationships (ECOSAR, v.2.0³⁰) program to estimate the acute (short-term) toxicity and chronic (long-term or delayed) toxicity to aquatic organisms from exposure to 1-BP. This utilizes quantitative structure activity relationships (QSARs) to predict the aquatic toxicity based on a similarity of the structure to chemicals for which the aquatic toxicity has been previously measured. ECOSAR relies on a linear mathematical relationship between the predicted log Kow values and the corresponding log of the measured toxicity values within the training set of chemicals for each class of interest (in the case of 1-BP, this class is neutral organics). The results of this modeling is presented in Table 3-1 and the modeling output is presented in Appendix G.

3.1.2 Hazard Identification- Toxicity to Aquatic Organisms

Two notable updates to the analysis of environmental hazard were made to the environmental hazard conclusions of this document. First, EPA evaluated reasonably available environmental hazard data for 1-BP for data quality (EPA, 2019k). Second, EPA was unable to obtain the full study reports for the data summaries identified in the ECHA Database and presented in the draft risk evaluation so these data could not be evaluated according to the systematic review criteria and were not included in the final risk evaluation. To assess aquatic toxicity from acute exposures, acute exposure toxicity data for fish were identified. The results of these studies are discussed below and summarized in Table 3-1. The acute fish toxicity study by (Geiger et al., 1988), was conducted with fathead minnows (*Pimephales promelas*) over a 96 hour exposure period. This study was conducted as part of a multi-investigator effort, led by the U.S. EPA Environmental Research Laboratory in Duluth, MN and the University of Wisconsin-Superior in Superior, WI. The goal of this effort was to generate a systematic database of acute toxicity data for a variety of organic chemicals for use by regulatory and academic communities to support advances in the development of quantitative structure-activity relationship (QSAR) models. This effort resulted in a multi-volume report. In addition to toxicity data for 1-BP, the cited volume contained acute fish toxicity data for several dozen organic chemicals across 24 chemical classes, all of which were conducted according to procedures which are outlined in the introduction of the publication. The experimental procedures used in this effort represent the best practices for conducting acute

³⁰ More information about the ECOSAR program can be found at: <https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model>

toxicity testing with fathead minnows and are consistent with the test guidelines currently recommended by EPA and international regulatory partner organizations for conducting ecological risk assessment purposes for fish. Because this effort was funded and led by EPA, it was conducted according to the editing, quality assurance and peer review procedures set forth by EPA as a requirement for the publication of empirical test data to be used in regulatory science. An LC₅₀ value of 67.3 mg/L (based on measured test concentrations) was reported based on mortality observed in the test organisms ([Geiger et al., 1988](#)). The study authors reported sublethal effects that included a loss of schooling behavior, hypoactivity, underreactivity to external stimuli, increased respiration, dark coloration and loss of equilibrium prior to death. This study was evaluated by EPA under EPA's TSCA Systematic Review Process for data quality and determined to be high quality ([EPA, 2019k](#)). In addition, ECOSAR (v2.0) predicted toxicity value for fish is 72.9 mg/L. The acute toxicity estimate for aquatic invertebrates predicted by ECOSAR (v.2.0) is 42.0 mg/L, while the algae EC₅₀ value predicted by ECOSAR is 33.2 mg/L. The ECOSAR-predicted toxicity values for acute and chronic exposure to fish, aquatic invertebrates and algae also available in Table 3-1, which supports EPA's weight of scientific evidence conclusions.

The vapor pressure of 1-BP is 110 mm Hg at 20°C and the Henry's law constant is calculated to be over 700 Pa.M³/mol. These physical-chemical properties input to the WVol model in EPISuite indicate that 1-BP will volatilize from a model river with a half-life on the order of an hour and from a model lake on the order four days. Although volatilization is expected to be rapid, a Level III Fugacity model predicts that when 1-BP is continuously released to water, 80% of the mass will be in water 19% in air due in part to its water solubility. Intermittent releases of 1-BP are not expected to result in long-term presence in the aquatic compartment. Chronic exposure is only a likely scenario for environments near continuous direct release sites. As no data were available to characterize the hazards of chronic exposure to aquatic species, EPA estimated hazards from chronic exposure using an acute-to-chronic ratio (ACR). The most sensitive species following acute exposure, freshwater fish reported a 96-hr LC₅₀ of 67.3 mg/L the value ([Geiger et al., 1988](#)) was divided by an ACR of 10 to estimate the toxicity to fish following chronic exposure. This results in a fish chronic value (ChV) of 67.3 mg/L/ 10= 6.73. The chronic toxicity value for fish predicted by ECOSAR is 7.24 mg/L, while the chronic toxicity value for aquatic invertebrates is 4.26 mg/L. The ECOSAR predictions for 1-BP are summarized below in Table 3-1.

3.1.3 Hazard Identification- Toxicity to Terrestrial Organisms

1-BP is expected to be present at limited concentrations in terrestrial ecosystems. As a result of high volatility (Vapor Pressure= 110 mm Hg at 20°C; Henry's Law constant of 7.3×10^{-3} atm-m³/mole; see Table 1-1) and conditions of use of the chemical, it is expected that 1-BP will only be present in terrestrial environmental compartments as a transient vapor. No specific conditions of use (*i.e.*, systematic application to land) were identified that resulted in systematic, significant airborne exposures that overlap with terrestrial habitats, so this is not a relevant route of exposure for 1-BP under the conditions of use of this risk evaluation. Additionally, 1-BP is not expected to bioaccumulate (BAF=12; BCF=11, see Table 2-1) which means that exposures to terrestrial species through oral routes is limited. This preliminary conclusion, which was presented in the Problem Formulation, is confirmed in this final risk evaluation; no further analysis of hazards to

terrestrial receptors was carried out as part of this evaluation, as exposure to terrestrial species is not expected.

3.1.4 Weight of the Scientific Evidence

During the data integration stage of EPA's systematic review, EPA analyzed, synthesized, and integrated reasonably available data/information. This involved weighing scientific evidence for quality and relevance, using a Weight of the Scientific Evidence (WoE) approach ([U.S. EPA, 2018a](#)). The ecological risk assessor decided if data/information were relevant based on whether it has biological, physical-chemical, and environmental relevance ([U.S. EPA, 1998a](#)):

- Biological relevance: correspondence among the taxa, life stages, and processes measured or observed and the assessment endpoint.
- Physical-chemical relevance: correspondence between the chemical or physical agent tested and the chemical or physical agent constituting the stressor of concern.
- Environmental relevance: correspondence between test conditions and conditions in the region of concern. ([U.S. EPA, 1998a](#))

A single acute fish toxicity study was used to conduct a screening-level characterization of the environmental hazards of 1-BP. EPA was unable to obtain the full environmental hazard studies that were summarized in the ECHA database and these studies could not be evaluated for data quality, so EPA chose not to include these study summaries in the final risk assessment (The studies were in French and Japanese with no U.S.A. sponsor). As a result, only a single acute fish toxicity study identified during the literature search process ([Geiger et al., 1988](#)) has been evaluated according to the systematic review criteria in The Application of Systematic Review in TSCA Risk Evaluations and was determined to be of high quality ([Geiger et al., 1988](#)) ([U.S. EPA, 2018a](#)). While this peer reviewed study was determined to be of high quality, the lack of data for other aquatic species led to some uncertainty about whether this single study was appropriate to estimate environmental hazards across species. To reduce uncertainty about the lack of environmental hazard data, QSAR modeling outputs provided by ECOSAR (v2.0) ([EPA, 2017](#)) were used in the assessment. The acute toxicity study and ECOSAR modeling outputs both indicate that 1-BP presents a moderate hazard to aquatic environmental receptors³¹. While empirical data are not available to characterize the hazards of 1-BP to aquatic invertebrates and algae, ECOSAR modeling is appropriate for 1-BP. ECOSAR-predictions for 1-BP are based on the neutral organics chemical class. Of the 120 chemical classes within ECOSAR, this class is the largest and most robust. The dataset used to generate the regression equation to predict hazards of acute exposure to chemicals within the neutral organics chemical class contains 296 data points for fish, 147 for aquatic invertebrates, and 66 for algae. The dataset used to generate the regression

³¹ Hazard concern levels for acute exposure: Low >100mg/L; Moderate >1.0 mg/L and <100 mg/L; High <1.0. Hazard concern levels for chronic exposure: Low >10 mg/L; Moderate >0.1 mg/L and <10 mg/L; High <0.1 ([U.S. EPA, 2012e](#)).

equation used to predict hazards from chronic exposure contains 46 data points for fish, 26 for daphnia and 34 for algae. In addition, the majority of the data that comprise the QSAR training set in the neutral organics chemical class were generated as part of the same research effort as the high confidence acute fish toxicity test for 1-BP ([Geiger et al., 1988](#)). While the acute toxicity data for 1-BP are not specifically included in the QSAR training set for neutral organic chemicals in ECOSAR, there are several organic chemicals with a similar log K_{ow} and molecular weight that are in the training set such as analogous chemicals N,N-Dimethylaniline (MW 121, Log K_{ow}=2.31) and 6-Methyl-5-hepten-2-one (MW=126, LogK_{ow}=2.1) with similar measured toxicity values for fish that indicate 1-BP is well-characterized by the neutral organics chemical class. The acute toxicity study and ECOSAR modeling outputs both indicate that 1-BP presents a moderate hazard to aquatic environmental receptors.

3.1.5 Concentrations of Concern (COCs)

The acute and chronic concentrations of concern (COCs) for aquatic species were calculated based on the results of the high quality study ([Geiger et al., 1988](#)). An uncertainty factor (UF; also referred to as an assessment factor (AF)) is applied according to EPA methods ([Suter, 2016](#)) ([U.S. EPA, 2012e](#)) ([U.S. EPA, 2013b](#)). 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 also account for differences in inter- and intra-species variability, as well as laboratory-to-field variability. These assessment factors are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group. The assessment factors are often standardized in risk assessments conducted under TSCA, since the data available for most industrial chemicals are limited. For fish and aquatic invertebrates (*e.g.*, daphnia), the acute COC values are divided by an AF of 5. For chronic COCs, and to calculate a COC for algae, where multiple generations can be present over the course of a standard toxicity test, an AF of 10 is used.

3.1.5.1 Acute COC:

As described above, the 96-hour LC₅₀ value for 1-BP that was reported in the high quality study is 67.3 mg/L ([Geiger et al., 1988](#)). This high quality value was then divided by the AF of 5 for fish and then multiplied by 1,000 to convert from mg/L to µg/L, or ppb. To reduce uncertainty related to the lack of data available to characterize the hazard of 1-BP to aquatic species, a COC was also calculated using the ECOSAR-predicted endpoints for acute exposure, as presented in Table 3-1.

- The acute COC for 1-BP, based on 96-hour fish toxicity LC₅₀ is: (67.3 mg/L) / AF of 5 x 1,000 = 13,460 µg/L or ppb.
- To provide additional characterization of potential risks from acute exposure to 1-BP, a COC based on the most sensitive species for acute exposure as predicted by ECOSAR, which is algae: (33.2 mg/L) / AF of 10 x 1,000 = 3,320 µg/L or ppb.

3.1.5.2 Chronic COC:

Since there are no long-term chronic studies for 1-BP, the fish 96-hr LC₅₀ of 67.3 mg/L (the value in the dataset derived from the high quality toxicity study; is divided by an acute-to-chronic ratio (ACR) of 10 to obtain a chronic value (ChV) for fish ([Geiger et al., 1988](#)). The fish ChV is then divided by an AF (10), and then multiplied by 1,000 to convert from mg/L to µg/L, or ppb to obtain a chronic COC. The ECOSAR modeling results indicate that the relationship between predicted acute and chronic hazard is close to 10 for 1-BP (ECOSAR-estimated Fish 96 hr LC₅₀=72.9 mg/L, Fish ChV=7.24 mg/L; Daphnid 48 hr LC₅₀=42.0 mg/L, Daphnid ChV=4.26 mg/L). This supports the use of an ACR of 10 to estimate hazards from chronic exposure to 1-BP.

- The Chronic COC for 1-BP, based on an estimate of the chronic hazard to fish is (67.3 mg/L) / 10 (ACR) / AF of 10 x 1000 = 0.673 mg/L or 673 µg/L or ppb.
- To provide additional characterization of potential risks from chronic exposure to 1-BP, a COC based on the most sensitive species for chronic exposure as predicted by ECOSAR, which are aquatic invertebrates: (4.26 mg/L) / AF of 10 x 1,000 = 426 µg/L or ppb.

3.1.6 Hazard Summary

1-BP presents a moderate hazard (according to the concern levels outlined in U.S. EPA ([2012e](#))³²) to aquatic species based on data characterizing the effects of acute exposure to fish and ECOSAR predictions for acute and chronic exposure to fish, aquatic invertebrates and algae. Sublethal effects reported following acute exposure to fish included darkened pigmentation, and loss of orientation were observed in test organisms at lower concentrations, but specific concentrations where these were observed were not reported ([Geiger et al., 1988](#)). Acute to chronic extrapolation indicates that effects in fish following chronic exposure to 1-BP are estimated to occur at 6.73 mg/L.

This conclusion of moderate environmental hazard is supported by QSAR modeling outputs provided by ECOSAR (v2.0) ([EPA, 2017](#)) where moderate hazard was reported for all aquatic taxa following acute and chronic exposure. This is similar to the predicted hazard from chronic exposure based on the application of an acute to chronic ratio to acute toxicity endpoint for fish. ECOSAR modeling is commonly utilized for the environmental risk assessment of new chemical substances.

After evaluating all available 1-BP test data for data quality, EPA has high confidence in the results of the acute fish toxicity test as explained in Section 3.1.2, but as data were not available for other aquatic taxa such as aquatic invertebrates and algae, EPA bolstered the overall dataset using Structure-Activity Relationship (SAR) predictions for 1-BP provided by ECOSAR (v.2.0) ([EPA, 2017](#)). While empirical data are not available to characterize the hazards of 1-BP to aquatic

³² Hazard concern levels for acute exposure: Low >100mg/L; Moderate >1.0 mg/L and <100 mg/L; High <1.0. Hazard concern levels for chronic exposure: Low >10 mg/L; Moderate >0.1 mg/L and <10 mg/L; High <0.1 ([U.S. EPA, 2012e](#)).

invertebrates and algae, ECOSAR modeling is appropriate for 1-BP. ECOSAR-predictions for 1-BP are based on the neutral organics chemical class. Of the 120 chemical classes within ECOSAR, this class is the largest and most robust. The dataset used to generate the regression equation to predict hazards of acute exposure to chemicals within the neutral organics chemical class contains 296 data points for fish, 147 for aquatic invertebrates, and 66 for algae. The dataset used to generate the regression equation used to predict hazards from chronic exposure contains 46 data points for fish, 26 for daphnia and 34 for algae. In addition, the majority of the data that comprise the QSAR training set in the neutral organics chemical class were generated as part of the same research effort as the high quality acute fish toxicity test for 1-BP ([Geiger et al., 1988](#)). While the acute toxicity data for 1-BP are not specifically included in the QSAR training set for neutral organic chemicals in ECOSAR, there are several organic chemicals with a similar log K_{OW} and molecular weight that are in the training set such as N,N-Dimethylaniline (MW 121, Log K_{OW}=2.31) and 6-Methyl-5-hepten-2-one (MW=126, LogK_{OW}=2.1) with similar measured toxicity values for fish that indicate 1-BP is well-characterized by the neutral organics chemical class. As a result, EPA has medium confidence that the data incorporates the most conservative (highest toxicity)/environmentally-protective acute and chronic concentrations of concern.

As discussed above, COCs were calculated to provide a conservative estimate for a screening level comparison with estimated surface water concentrations to identify potential concerns to aquatic species. The analysis of the environmental COCs are based on EPA methods ([U.S. EPA, 2012e](#)). To calculate acute COCs, the acute 96-hour fish toxicity values were divided by an assessment factor of 5, while chronic COCs were calculated using an AF of 10. Therefore, based on available fish data the acute COCs for 1-BP are 13,640 ppb; $LC_{50} (67.3 \text{ mg/L}) / \text{AF of } 5 = 13,460 \text{ } \mu\text{g/L}$ or ppb. To reduce uncertainty resulting from a lack of data, an acute COC of 3,640 ppb was also calculated based on the most sensitive endpoint predicted by ECOSAR modeling for acute exposure. Based on estimated chronic hazard endpoint for fish, best available data indicate a chronic COC of 673 ppb ($\text{fish } 96\text{-hr } LC_{50} (67.3 \text{ mg/L}) / 10 (\text{ACR}) / \text{AF of } 10 = 673 \text{ } \mu\text{g/L}$ or ppb. Similarly to the approach for acute exposure, a chronic COC of 430 ppb was calculated by using the most sensitive endpoint for chronic exposure as predicted by ECOSAR. These endpoints and the resulting COC values are presented in Table 3-1. 1-BP is expected to be present at low concentrations in the terrestrial ecosystems and the sediment compartment of aquatic ecosystems therefore, no further analysis of hazards to these environmental receptors is necessary.

Table 3-1. Ecological Hazard Characterization of 1-BP

Duration	Test organism	Endpoint	Measured Hazard value (mg/L) ¹	Effect Endpoint	ECOSAR-predicted hazard value (mg/L) ²
Acute	Fish	LC ₅₀	67.3	Mortality	72.9
	Aquatic invertebrates	EC ₅₀	N/A	N/A	42.0
	Algae	EC ₅₀	N/A	N/A	33.2³
	Acute COC		13.46		3.32
Chronic	Fish	ChV	6.73	N/A, calculated with an ACR of 10	7.24
	Aquatic invertebrates	ChV	N/A	N/A	4.26³
	Algae	ChV	N/A	N/A	8.98
	Chronic COC		0.673		0.426

¹ Values in the tables are presented as reported by the study authors in [Geiger et al., 1988](#).

² Predictions were made with ECOSAR v2.0 ([EPA, 2017](#)). More information on the use of this tool is available at: <https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model>. Model outputs are available in Appendix G.

³ Bolded values indicate the most sensitive species for acute or chronic exposure as indicated by ECOSAR modeling. These values are used to calculate a COC.

3.2 Human Health Hazard

3.2.1 Background on the Process of Systematic Review

EPA gathered and evaluated information on the human health hazards associated with 1-BP exposure according to the process described in the *Application of Systematic Review in TSCA Risk Evaluations* ([U.S. EPA, 2018a](#)). EPA identified hazard data for 1-BP through an extensive literature search, as described in EPA's *Strategy for Conducting Literature Searches for 1-Bromopropane (1-BP): Supplemental Document to the TSCA Scope Document* ([U.S. EPA, 2017e](#)). Published and non-published data sources, including key and supporting studies identified in previous assessments, were evaluated during this process. EPA also relied heavily on the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016c](#)) to inform hazard characterization. EPA has high confidence in the toxicological studies used to support risk estimation.

Although EPA conducted a comprehensive search and screening process as described in section 1.5, EPA generally used previous chemical assessments, such as the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016c](#)), to identify key and supporting information that would be influential in the risk evaluation, including information supporting key analyses, arguments, and/or conclusions in the risk evaluation. Where applicable, EPA also considered newer information not considered in the

previous chemical assessments. Using this pragmatic approach, EPA evaluated the quality of the key and supporting data sources from these authoritative sources (including studies considered for dose-response analysis and genotoxicity studies considered for contribution to the mode of action (MOA) analysis) instead of evaluating all the underlying evidence published on the human health hazards of 1-BP exposure. This allowed EPA to maximize 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. The influential information sources used to support quantitative analyses represents a smaller pool of studies that were ultimately subjected to the TSCA systematic review process to ensure that the risk evaluation uses the best available science in the overall weight of the scientific evidence. Whether data sources were obtained from prior assessments or more recently published literature, all studies were considered of equal importance and were evaluated together independent of any previous EPA review.

EPA assessed the quality of the key and supporting studies identified in the 2016 Draft Risk Assessment ([U.S. EPA, 2016c](#)) based on the data quality criteria described in the [Application of Systematic Review in TSCA Risk Evaluations](#) ([U.S. EPA, 2018a](#)); these key and supporting studies were determined to be of high quality (*i.e.*, high confidence). The comprehensive results of the study evaluations can be found in the *Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies*. EPA-HQ-OPPT-2019-0235 ([EPA, 2019o](#)). Section 3.2 and Appendix J may also cite other data sources as part of the reasonably available information on the human health hazards of 1-BP. EPA did not subject these other data sources to the later phases of the systematic review process (*i.e.*, data evaluation and integration). Only the key and supporting studies in the [2016 Draft Risk Assessment for 1-BP](#) ([U.S. EPA, 2016c](#)) (*e.g.*, dose-response studies and genotoxicity assays) were carried forward for dose-response analysis; because these studies were considered to be useful and relevant for hazard identification, EPA skipped the screening step and entered them directly into the data evaluation step. Any new studies published since that time, were subjected to the full TSCA systematic review process.

3.2.2 Approach and Methodology

Development of the 1-BP hazard and dose-response assessment considered principles set forth in various risk assessment guidance and guidelines issued by the National Research Council and EPA. Figure 3-1 depicts the process EPA used to evaluate, extract and integrate 1-BP's human health hazard and dose-response information.

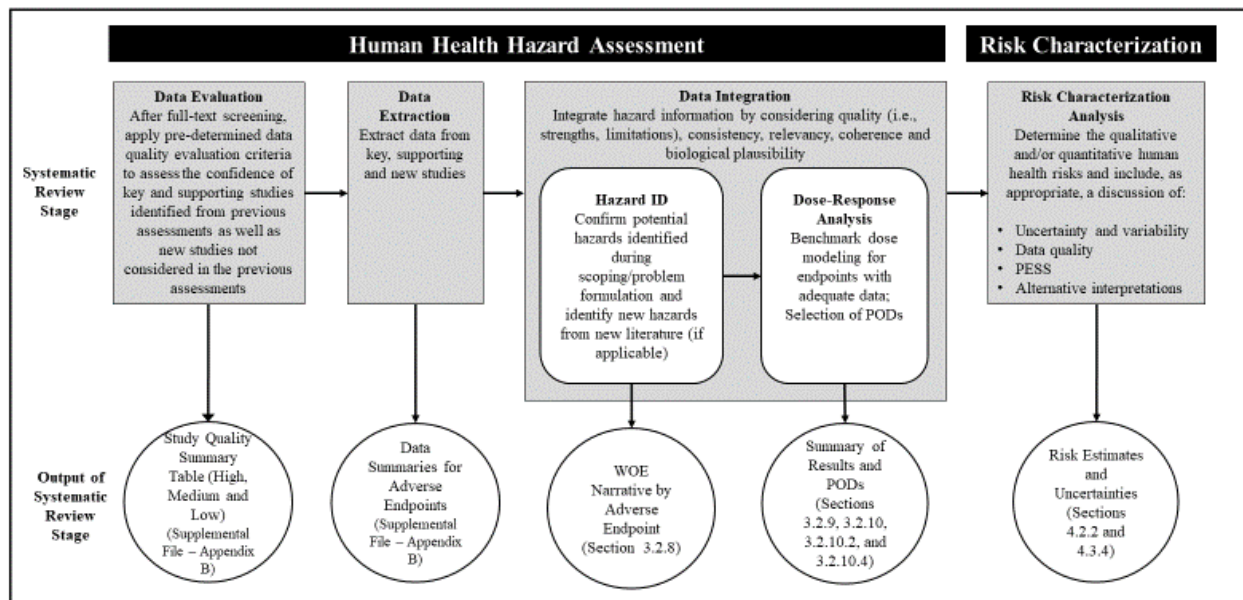


Figure 3-1. EPA Approach to Hazard Identification, Data Integration, and Dose-Response Analysis for 1-BP

1-BP does not have an existing EPA Integrated Risk Information System (IRIS) Toxicological Review; however, 1-BP has been the subject of numerous health hazard reviews including the Agency for Toxic Substances and Disease Registry’s (ATSDR’s) Toxicological Profile (2017), and the National Institute for Occupational Safety and Health (NIOSH) Draft Criteria Document (2016), in addition to the peer-reviewed 2016 Draft Risk Assessment (U.S. EPA, 2016c). During the analysis phase of the risk evaluation, EPA conducted a systematic review of the available literature, using these existing assessments as a starting point. Only the references identified as “on topic” and any new literature published since these existing assessments were considered relevant data/information sources in this risk evaluation, as described in EPA’s *Strategy for Conducting Literature Searches for 1-BP (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0741-0047). These studies were screened against inclusion criteria in the PECO statement and the studies deemed suitable for dose-response analysis were further evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

EPA evaluated the quality of the key and supporting information that would be influential in the risk evaluation using the data evaluation criteria for human, animal, and in vitro studies described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). A summary of the relevant endpoints carried forward for dose-response assessment can be found in Table 3-2, including the no-observed- or lowest-observed-adverse-effect levels (NOAEL and LOAEL) for health endpoints by target organ/system, the corresponding benchmark concentration/dose lower confidence limits (BMCLs/BMDLs), when available, and the

corresponding human equivalent concentrations/doses (HECs/HEDs), and uncertainty factors (UFs). EPA has not developed data quality criteria for all types of hazard information such as toxicokinetics and many types of mechanistic data. Despite the lack of formal criteria, for 1-BP, EPA did review these data informally for quality and used the data to qualitatively support the risk evaluation. For example, many supplemental studies were considered while investigating the 1-BP mode of action (MOA). These findings were considered in synthesizing the evidence and integrated as appropriate, into the relevant health effect sections in Section 3.2.4.

EPA's literature search results for 1-BP human health hazards yielded 813 studies (Section 1.5.1). This included 14 key and supporting studies that were identified from previous EPA assessments. Of the 799 new studies screened for relevance, 784 were excluded based on PECO (off topic). The remaining 15 new studies and 14 key and supporting studies were put through data evaluation; 24 studies were carried forward to data extraction/data integration. Toxicological information was extracted from studies deemed relevant and suitable for dose response analysis.

For this risk evaluation, all of the known human health hazards of 1-BP were described and reviewed. Section 3.2.4 (Hazard Identification) discusses the body of studies for relevant health domains. EPA considered studies of low, medium or high data quality for hazard identification. Based on this review, EPA narrowed the focus of the 1-BP hazard characterization to liver toxicity, kidney toxicity, reproductive/developmental toxicity, neurotoxicity, and cancer (brief summaries are presented for each hazard endpoint in Section 3.2.4; detailed summaries are presented in Appendix J). The weight of the scientific evidence analysis (Section 3.2.5) included integrating information from toxicokinetic and toxicodynamic studies for each health domain described in Section 3.2.4. In particular, data integration considered consistency among the data, data quality, biological plausibility and relevance (although this was also considered during data screening). For each health domain, EPA determined whether the body of scientific evidence was adequate to consider the domain for dose-response modeling. EPA identified or calculated points of departure (PODs) within each of these health domains.

The POD is used as a starting point for subsequent dose-response (or concentration-response) extrapolations and analyses. 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 (*e.g.*, benchmark dose or BMD), a NOAEL value, or a lowest observed adverse effect level (LOAEL) for an observed incidence, or a change in the level (*i.e.*, severity) of a given response ([U.S. EPA, 2002](#)). PODs were adjusted as appropriate to conform to the specific exposure scenarios evaluated (*e.g.*, to account for differences in the duration of inhalation exposure between humans and laboratory animals). Section 3.2.8 provides the dose-response assessment including the selection of PODs for cancer and non-cancer endpoints and the benchmark dose analysis used in the risk evaluation.

Only the inhalation and dermal routes of exposure were evaluated in this assessment. Insufficient toxicological data is available via the oral route. In accordance with EPA guidance, the exposure concentrations used in animal studies were adjusted according to the ratio of the blood:air partition coefficients, where a default ratio of 1 is applied when the partition coefficient for rats is greater

than that of humans ([U.S. EPA, 2002, 1994](#)). For HEC/dermal HED derivations, these exposure concentrations were further adjusted from the exposure durations used in animal studies to durations deemed relevant for human exposure scenarios (e.g., 8-hours/day and 5 days/week for occupational exposures). The majority of exposures occur via inhalation, which is considered the primary route of exposure; however, the CSAC (Chemical Safety Advisory Committee) Peer Review of the [2016 Draft Risk Assessment \(U.S. EPA, 2016c\)](#) recommended that dermal exposures might be an important contributor to overall exposure and recommended that an estimate for dermal exposure also be included in the evaluation, with gaps/limitations clearly stated to address another potential workplace exposure pathway. Since there is limited toxicological data available by the oral and dermal routes, physiologically based pharmacokinetic/pharmacodynamic (PBPK/PD) models that would facilitate route-to-route extrapolation have not been identified, and there are no relevant kinetic or metabolic information for 1-BP that would facilitate development of dosimetric comparisons, EPA chose to derive dermal HEDs by extrapolating from the inhalation PODs. The strengths and limitations of this approach are discussed Section 3.2.8.5 and Section 4.3.

EPA followed the recommendations in EPA's [Guidelines for Developmental Toxicity Risk Assessment](#) when making the decision to use developmental toxicity studies to evaluate risks that may be associated with acute exposure to 1-BP during occupational or consumer use of spray adhesive, dry cleaning or degreasing products that contain 1-BP. This decision is based on EPA's assumption that a single exposure during a critical window of fetal development may be sufficient to produce adverse developmental effects ([Guidelines for Developmental Toxicity Risk Assessment](#)).

3.2.3 Toxicokinetics

This section describes the available information on absorption, distribution, metabolism and excretion (ADME). For additional details, see Appendix I.

As discussed above in Section 3.2.2, EPA has not published systematic review criteria applicable to toxicokinetic studies, however all relevant toxicokinetic information was either obtained from previous regulatory and non-regulatory chemical assessments and/or was informally evaluated for overall data quality and relevance. Studies in humans and laboratory animals show that 1-BP may be absorbed following oral, inhalation or dermal exposure; however, dermal and inhalation pathways are expected to be more relevant for occupational and consumer exposures ([Frasch et al., 2011](#); [Hanley et al., 2009](#); [NIOSH, 2007](#); [Garner et al., 2006](#); [Jones and Walsh, 1979](#)). The extent of absorption via the inhalation route depends on the rate of transfer from pulmonary capillaries to blood (*i.e.*, blood/air partition coefficient), and the rate of metabolism in various tissue compartments.

The blood:air partition coefficients calculated for 1-BP in rats (11.7) and humans (7.08) indicate that it is readily absorbed ([Meulenberg and Vijverberg, 2000](#)). Upon uptake, 1-BP distribution via the systemic circulation follows the individual tissue/blood partition coefficients for respective tissue compartments. The fat:blood partition coefficient (calculated as the ratio of fat:air and blood:air partition coefficients) for 1-BP in rats (20) and humans (18) suggests that it may partition

to fat ([Meulenberg and Vijverberg, 2000](#)). Higher partitioning to muscle, liver and fat has been predicted for 1-BP in female versus male rats ([ECHA, 2012](#)).

Metabolism studies in rats and mice have shown that 1-BP can directly conjugate with glutathione forming N-acetyl-S-propyl cysteine, or be oxidized via cytochrome P450 enzymes (primarily CYP2E1) to reactive metabolites that can be further oxidized and/or conjugated with glutathione ([Jones and Walsh, 1979](#); [Barnsley et al., 1966](#)) (Figure 3-2). Glutathione conjugates formed via the glutathione-S-transferase catalyzed pathway are eventually excreted as mercapturic acid derivatives in urine. Although both pathways remain operative, the CYP2E1 pathway generally predominates at lower exposure concentrations ([Garner et al., 2006](#)).

1-BP may also be converted to either of two epoxide metabolites, glycidol and propylene oxide (see Appendix H and Figure 4.1 of IARC ([2018](#)))

Further evidence for the specific contribution of CYP2E1 to 1-BP metabolism is provided by studies with Cyp2e1^{-/-} knockout mice ([Garner et al., 2007](#)) which show the elimination half-life in these animals to be more than twice that seen in wild type mice (3.2 vs. 1.3 hours, respectively) following 1-BP inhalation exposure. The ratio of glutathione conjugation to 2-hydroxylation reactions increased 5-fold in Cyp2e1^{-/-} versus wild-type mice. Earlier work from this laboratory has shown that administration of 1-aminobenzotriazole (a general suicide inhibitor of P450) caused nearly complete elimination of 1-BP oxidative metabolism, and a compensatory shift toward GSH conjugation in rats ([Garner et al., 2006](#)).

In humans and laboratory animals, 1-BP is rapidly eliminated from the body primarily via exhalation, with lesser amounts excreted in urine and feces ([Garner and Yu, 2014](#); [Garner et al., 2006](#); [Ishidao et al., 2002](#)). In gas uptake studies with male and female rats, the elimination half-times calculated for 1-BP decreased with increasing air concentrations ([Garner and Yu, 2014](#)). Terminal elimination half-times in male and female mice following 1-BP inhalation exposure at ≤ 800 ppm ranged from 0.5 to 2 hrs ([Garner and Yu, 2014](#); [Garner et al., 2006](#)). ([Garner et al., 2006](#)) investigated the metabolism of 1-BP in male F344 rats and B6C3F1 mice following inhalation or tail vein injection and determined that the proportion of 1-BP metabolized via CYP2E1 oxidation versus glutathione conjugation was inversely proportional to dose in rats, but independent of dose in mice.

Occupational exposure studies have consistently identified significant correlations between 1-BP concentrations in ambient air and the levels of 1-BP or its metabolites in urine ([Ichihara et al., 2004b](#); [Kawai et al., 2001](#)). N-acetyl-S-(n-propyl)-L-cysteine (AcPrCys), produced via direct glutathione conjugation of 1-BP, was the primary urinary metabolite detected in exposed workers ([Hanley et al., 2010, 2009](#); [NIOSH, 2007](#); [Valentine et al., 2007](#); [Hanley et al., 2006b](#)).

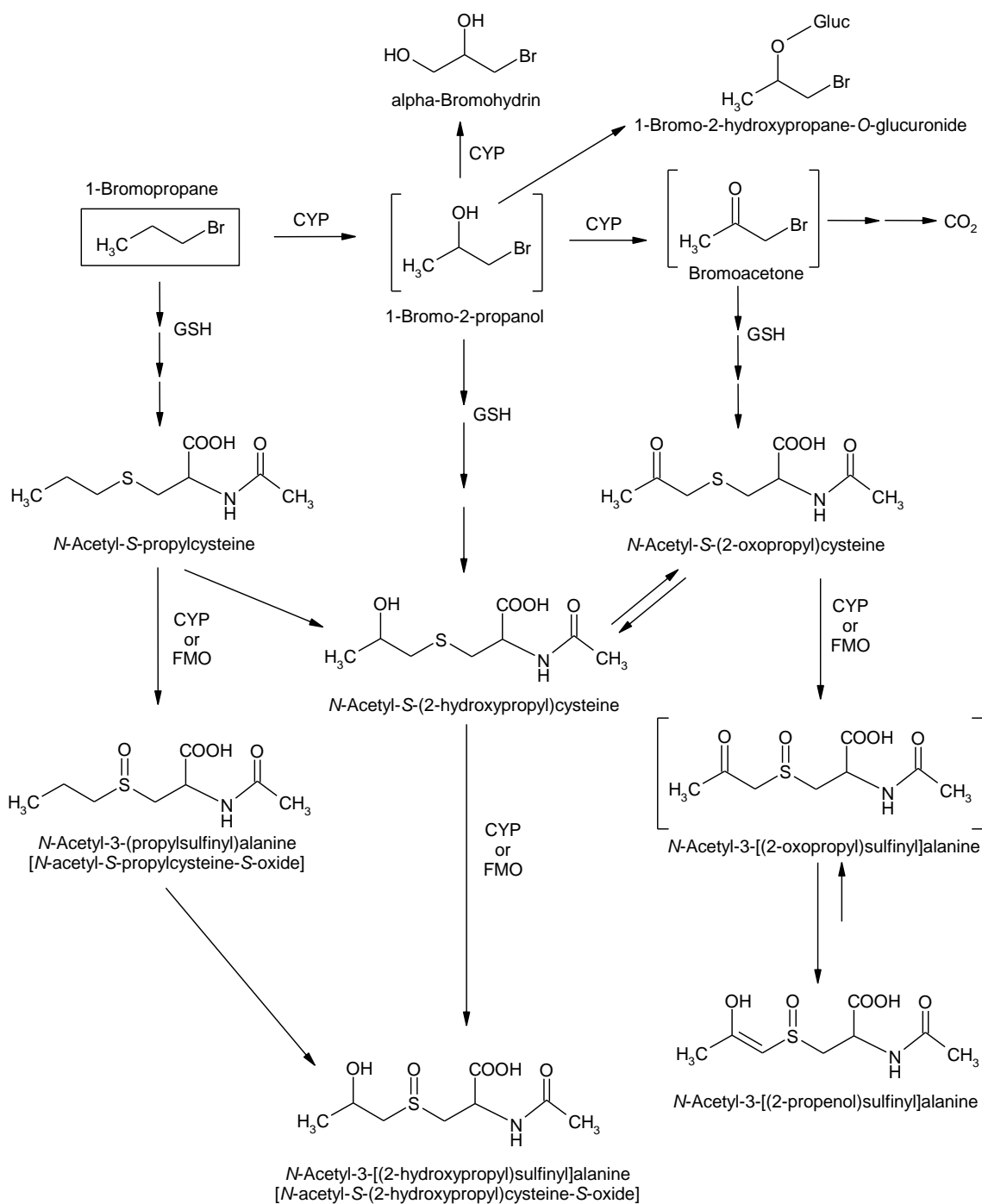


Figure 3-2. Metabolism of 1-Bromopropane in Male F-344 Rats and B6C3F1 Mice Following Inhalation Exposure or Tail Vein Injection*

*Structures in brackets are proposed intermediates and were not isolated in urine.

CYP = cytochrome P450 monooxygenase; FMO = flavin-containing monooxygenase;
GSH = glutathione

Sources: Adapted from ([NTP, 2013a](#); [Garner et al., 2007](#); [Garner et al., 2006](#))

3.2.3.1 Biomarkers of Exposure

Several human and laboratory animal studies have investigated the utility of urinary biomarkers of 1-BP exposure ([Mathias et al., 2012](#); [Hanley et al., 2009](#); [Valentine et al., 2007](#); [Hanley et al., 2006b](#); [B Hymer and Cheever, 2005](#); [Ichihara et al., 2004a](#); [Kawai et al., 2001](#)). Bromide ion and N-acetyl-S-(n-Propyl)-L-Cysteine (AcPrCys) have shown the most promise as biomarkers of exposure to occupationally-relevant concentrations.

1-BP is metabolized rapidly, via glutathione conjugation and cytochrome P-450 mediated oxidation, producing many metabolites which are subsequently excreted in urine. Glutathione conjugation leads to bromide ion release and formation of mercapturic acid derivatives. Bromide ion levels have been used as an internal biomarker of 1-BP exposure. They are slowly excreted from the body; the elimination half-life of bromide ions in blood generally ranges from 10.5 to 14 days ([Mathias et al., 2012](#); [Hanley et al., 2006b](#)). N-acetyl-S-(n-propyl)-L-cysteine (AcPrCys) is the primary urinary metabolite found in 1-BP exposed workers (see below); it also is considered to be a valid biomarker for 1-BP exposure ([Mathias et al., 2012](#); [Valentine et al., 2007](#)).

Both Kawai ([2001](#)) and Ichihara ([2004a](#)) have shown a correlation between urinary 1-BP levels and 1-BP occupational exposure; however, the degree of correlation varied between studies. Kawai et al. ([2001](#)) reported a correlation coefficient of 0.9 for 1-BP concentrations in air and urine; the highest 1-BP concentration in air was 27.8 ppm (geometric mean = 1.42 ppm). Ichihara et al. ([2004a](#)) also reported a statistically significant correlation between 1-BP air concentrations and urinary levels measured on the same day ($r^2 = 0.39$; $p < 0.05$). NIOSH has suggested that urinary 1-BP levels may be a more suitable biomarker than urinary bromide concentrations; however, to ensure accuracy, samples must be tested immediately after collection using gas chromatography-mass spectrometry, which may be unfeasible or cost prohibitive ([NIOSH, 2003a](#)).

Both urine and serum bromide ion levels have been used as biomarkers of 1-BP exposure in workers. Toraason et al. ([2006](#)) found a high correlation ($p < 0.0001$) between 1-BP exposure and bromide ion concentrations in serum ($r^2 = 0.7$ to 0.8), and urine ($r^2 = 0.6$ to 0.9) when evaluating personal breathing zone samples from approximately 50 workers. Workplace exposures ranged from 0.2 to 270 ppm (TWA), and the correlation coefficient for 1-BP air levels and urinary bromide levels was 0.5. Using gas chromatography with electron capture detection to evaluate samples taken from Japanese workers ($n=33$) following 1-BP exposure during an 8-hour shift of cleaning and painting, ([Kawai et al., 2001](#)) reported a good correlation ($r^2 = 0.5$) between bromide levels in urine and 1-BP levels in air; however, control subjects exhibited high background levels of urinary bromide, which were subsequently linked to dietary exposure ([Zhang et al., 2001](#)). Hanley et al. ([2006b](#)) reported 30 workers who were exposed to 1-BP spray adhesives to make polyurethane foam seat cushions. Personal breathing zone samples indicated a geometric mean exposure of 92 ppm (range = 45-200 ppm) for sprayers and 11 ppm for workers in other parts of

the plant. The composite (48-hour) urinary bromide concentrations for sprayers (n=12) ranged from 119 to 250 mg/g creatinine and for non-sprayers (n=17) ranged from 5.5 to 149 mg/g creatinine. The composite bromide concentration in unexposed control subjects (n=7) ranged from 2.6 to 5.9 mg/g creatinine. Daily bromide excretion was approximately four times greater for sprayers than non-sprayers. Based on these results, urinary bromide concentration appears to be a useful index of 1-BP exposure.

Given the confounding factors identified ([Kawai et al., 2001](#)), a search for biomarkers of 1-BP exposure that are not influenced by dietary (or other non-occupational exposures) was initiated. Valentine et al. ([2007](#)), Mathias et al. ([2012](#)) and Hanley et al. ([2009](#)) demonstrated that the mercapturic acid derivative, AcPrCys, could be used as a urinary biomarker of 1-BP exposure. Both the availability of sensitive methods with an acceptable limit of detection (LOD) for this metabolite, and its demonstrated persistence in urine suggest that it may serve as a reliable biomarker of exposure. In addition, 1-BP volatility and rapid elimination in exhaled breath suggests that the measurement of mercapturic acid derivatives in urine may be preferable to 1-BP measurements. Valentine et al. ([2007](#)) sampled blood and urine from women in a 1-BP production facility in China ([Ichihara et al., 2004b](#)). A significant increase in AcPrCys adducts on human globin was demonstrated using LC/MS/MS to evaluate samples taken from 26 1-BP exposed workers and 32 non-exposed controls. Worker exposures ranged from 0.34 ppm to 49.2 ppm, and urinary AcPrCys levels analyzed using GC/MS, increased with increasing 1-BP exposure (n=47) ([Toraason et al., 2006](#)). Hanley et al. ([2009](#)) used aliquots from the urine specimens from those same workers who were exposed to 1-BP spray adhesives ([Hanley et al., 2006a](#)) who applied spray adhesives to foam cushions as described above, to determine the utility of AcPrCys as a biomarker for 1-BP exposure. Higher levels of urinary AcPrCys were observed in sprayers than non-sprayers (geometric mean was approximately four times higher in sprayers). AcPrCys and bromide levels were highly correlated ($p < 0.0001$) in the same urine samples, and both showed statistically significant Spearman's correlation coefficients based on 1-BP TWA exposure concentrations. Mathias et al. ([2012](#)) evaluated the same cohort of workers, reporting the results of Hanley et al. ([2009](#)) and 3-bromopropionic acid (3-BPA), which was evaluated for its potential to induce mutagenic effects and tumor formation in toxicological studies. When urine samples were analyzed for 3-BPA, it was not detected in 50 samples (LOD = 0.01 $\mu\text{g/mL}$). In a study of workers exposed to 1-BP based vapor degreasing solvent, Hanley et al. ([2010](#)) found AcPrCys in urine analyses were sensitive enough to measure exposure from these workers with much lower air exposures and AcPrCys was statistically associated with 1-BP TWAs.

At the time of the CSAC Peer Review for the 2016 Draft Risk Assessment ([U.S. EPA, 2016c](#)), NHANES data was released on selected urinary metabolites of VOCs, primarily associated with tobacco smoking. Although it is not associated with smoking, AcPrCys (or BPMA) was included in the list of 28 VOC metabolites based on its similarity in chemistry to the other tobacco metabolites. NHANES data indicated that BPMA was detected in urine samples of children and adults from NHANES 2005-2006, 2011-2012, and 2013-2014 at approximately 3-4 $\mu\text{g/L}$ (geometric mean) ([CDC, 2019](#)). Several papers describing the summary statistics of the exposures were published at this time, with one reporting a 99% detection of BPMA in 488 pregnant women in the National Childrens Study (2.6 ng/mL , 50th percentile) (([Boyle et al., 2016](#); [Jain, 2015](#); [Alwis](#)

[et al., 2012](#)). These data were discussed during the CSAC Peer Review and the reviewers stated that "...the measurement of BPMA levels by Boyle et al. (2016) suggests the possibility of low level, but very widespread, non-occupational exposures to 1-BP; however, the Committee recognizes that there are some questions regarding the specificity of the biomarker used." The literature does not contain any additional information on the specificity of this biomarker since the last peer review. In addition, CDC has no further information on this biomarker. Therefore, it can still be assumed that the specificity of N-acetyl-S-(n-propyl)-L-cysteine as a biomarker for the U.S. population is questionable ([ATSDR, 2017](#)) and not informative for use in dose-response analysis.

3.2.3.2 PBPK Models

A PBPK model for 1-BP in rats was developed by ([Garner et al., 2015](#)). The model simulates 1-BP exposures via inhalation wherein distribution of 1-BP to tissues is assumed to be flow-limited. Metabolism of 1-BP was simulated with Michaelis-Menten kinetics for oxidative metabolism by cytochrome P450 and first order kinetics for GSH conjugation; parameters were fit to the time course data of chamber concentrations for 1-BP used in rat inhalation studies. Additional metabolic parameters were fit to time course data of chamber concentrations of 1-BP for rat inhalation studies when female rats were pretreated with either the cytochrome P450 inhibitor 1-aminobenzotriazole (ABT) or the GSH synthesis inhibitor D,L-buthionine (S,R)-sulfoximine (BSO). These results show the relative contributions of oxidative metabolism via cytochrome P450 and conjugation with GSH in female rats. Confidence in the PBPK model predictions for 1-BP concentrations in blood and tissues are limited by the lack of comparison of model predictions with measured data. The PBPK model was further extended to simulate human exposures by scaling the physiological parameters to humans, assuming the partition coefficients are the same in rats and humans and scaling metabolic parameters by $BW^{3/4}$. Cross species and route to route extrapolations with the Garner et al. (2015) model are precluded by the lack of data to inform a model of a species other than rat and a route other than inhalation.

3.2.4 Hazard Identification

This section summarizes the available cancer and non-cancer hazard information for 1-BP. A comprehensive summary table (Table_Apx J-2) which includes all endpoints considered for this assessment, as well as detailed summaries for each health effect domain, are presented in Appendix J. The 1-BP database includes epidemiological studies, experimental animal studies, and in vitro studies. Human studies (case-control studies, industrial surveys, and case reports) corroborate that the nervous system is a sensitive target of 1-BP exposure in humans. Certain characteristics of the evaluation of 1-BP human studies are discussed throughout this section. Experimental animal studies of 1-BP consist of studies that evaluated liver toxicity, kidney toxicity, immunotoxicity, reproductive toxicity, developmental toxicity, neurotoxicity, genetic toxicity, and carcinogenicity. The following sections also describe several in vitro and some animal studies that evaluated biochemical and other endpoints used to consider the evidence related to modes of action.

EPA considered many of the studies as informative and useful for characterizing the health hazards associated with exposure to 1-BP. EPA extracted the results of key and supporting studies from the [2016 Draft Risk Assessment \(U.S. EPA, 2016c\)](#) and studies identified in the updated literature search.

EPA reviewed the 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 in Section 3.2.4.1 and included in the data extraction summary tables in the supplementary files accompanying this document. As a result, EPA narrowed the focus of this assessment to six adverse health effect domains: (1) liver toxicity, (2) kidney toxicity, (3) reproductive toxicity, (4) developmental toxicity, (5) neurotoxicity, and (6) carcinogenicity. For non-cancer endpoints, emphasis was placed on acute/short term inhalation, and repeated-dose inhalation studies identified as most appropriate for hazard characterization and dose-response analysis.

The weight of the scientific evidence Section 3.2.5 identifies any study evaluation concerns that may have meaningfully influenced the reliability or interpretation of the results. Studies with high confidence for hazard identification and considered for dose-response assessment are discussed in Section 3.2.8 and included in Table 3-2.

3.2.4.1 Non-Cancer Hazard Identification

Toxicity Following Acute Exposure

Studies in animals following acute exposures are limited to acute lethality studies only. In animals, deaths from acute inhalation exposure to 1-BP occurred only at high exposure concentrations. LC₅₀ values in rats ranged from 7,000 to 14,374 ppm for 4-hour inhalation exposure ([Kim et al., 1999a](#); [Elf Atochem, 1997](#)). Deaths were associated with an acute inflammatory response and alveolar edema ([Elf Atochem, 1997](#)). Similarly, for oral exposure, the LD₅₀ was >2,000 mg/kg ([Elf Atochem, 1993a](#)). No information on 1-BP toxicity following acute exposure in humans was located.

Liver Toxicity

Data from animal studies suggest the liver is a target for 1-BP. Reported effects include liver histopathology (e.g., hepatocellular vacuolation, swelling, degeneration and necrosis), increased liver weight, and clinical chemistry changes indicative of hepatotoxicity ([Wang et al., 2012](#); [NTP, 2011a](#); [Liu et al., 2009](#); [Lee et al., 2007](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Kim et al., 1999a](#); [Kim et al., 1999b](#); [ClinTrials, 1997a, b](#)).

Hepatotoxicity was not directly evaluated in any of the human studies identified in the literature; however, one study evaluated liver function indirectly in a cohort of 86 Chinese workers exposed to 1-BP (median exposure levels up to 22.6 ppm) for an average of approximately 40 months ([Li et al., 2010](#)) and no statistically significant clinical chemistry changes indicative of liver damage were observed.

Kidney Toxicity

Laboratory animal studies have provided evidence of renal toxicity following 1-BP exposure. Reported kidney effects include increased organ weight, histopathology (pelvic mineralization, tubular casts) and associated clinical chemistry changes (*e.g.*, increased blood urea nitrogen) ([NTP, 2011a](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Kim et al., 1999a](#); [ClinTrials, 1997a, b](#)).

No studies that directly evaluated 1-BP induced renal effects in humans were identified in the published literature; however, no significant clinical chemistry changes indicative of kidney damage were observed in a cohort of 86 Chinese workers exposed to 1-BP (median exposure levels up to 22.58 ppm) for an average of approximately 40 months ([Li et al., 2010](#)) or in 45 workers exposed to a geometric mean concentration of 81.2 ppm for an average of 29 months ([NIOSH, 2003a](#)).

Immunotoxicity

There is limited evidence for immune effects of 1-BP in animal studies. Two independent studies of immune function showed that 1-BP can suppress immune responses in rodents ([Anderson et al., 2013](#); [Lee et al., 2007](#)). Anderson et al. ([2010](#)) reported a decreased IgM plaque-forming response to immunization with sheep red blood cells (sRBC) in splenocytes harvested from female rats and mice following subchronic inhalation exposure to 1-BP (NOAEL = 500 ppm in rats; LOAEL [no NOAEL identified] = 125 ppm in mice). Associated effects in both species included decreases in T cells and increases in natural killer cells in the spleen; other effects reported in mice include reduced splenic cellularity and decreased absolute spleen weight. ([Lee et al., 2007](#)) also reported a decreased antibody response to sRBC and reduced splenic cellularity in female mice after a single oral dose of 1-BP (LOAEL [no NOAEL identified] = 200 mg/kg). Investigation of immune endpoints in other studies (limited to organ weights and histopathology of spleen, thymus, and other lymphoreticular tissues) showed no effects at concentrations as high as 1000 ppm in rats and 500 ppm in mice following subchronic inhalation exposure, and 500 ppm in rats and 250 ppm in mice following chronic inhalation exposure ([NTP, 2011a](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Ichihara et al., 2000a](#); [Kim et al., 1999b](#); [ClinTrials, 1997a, b](#)). No information regarding 1-BP immunotoxicity in humans was located.

Reproductive Toxicity

Animal studies suggest that the reproductive system is a target of concern for 1-BP exposure. A two-generation reproduction inhalation (via whole-body exposure) study in rats reported adverse effects on male and female reproductive parameters ([WIL Research, 2001](#)). The majority of these effects exhibited a dose-response beginning at 250 ppm, with statistical significance observed at 500 ppm. Significant increases in the number of 'former' or 'unaccounted' implantation sites (*i.e.*, the difference between the total number of implantation sites counted and the number of pups born) were reported by ([WIL Research, 2001](#)). EPA considers this finding to be indicative of post-implantation loss (pre-implantation loss could not be determined because of a lack of data on the number of primordial follicles at 100, 250 and 500 ppm). F₀ females experienced a 48% reduction in fertility at 500 ppm and complete infertility at 750 ppm. Other effects reported in this study include dose-related decreases in mating indices, increased estrous cycle length, and a significant

trend of increasing numbers of F₀ females with evidence of mating without delivery (a Cochran Armitage trend test conducted by EPA calculated a *p*-value <0.0001).

Statistically significant changes in reproductive endpoints in F₀ males include decreased absolute prostate and epididymal weights at exposures ≥ 250 and 500 ppm respectively, as well as decreased sperm motility, and decreased mating (500 ppm) and fertility indices (750 ppm) ([WIL Research, 2001](#)). The findings described above are supported by similar reports of reproductive toxicity from independent laboratory studies with rats and mice, including spermatogenic effects (decreased sperm count, altered sperm morphology and decreased sperm motility) and organ weight changes in males (decreased epididymis, prostate and seminal vesicle weights) as well as estrous cycle alterations and decreased numbers of antral follicles in females ([NTP, 2011a](#); [Qin et al., 2010](#); [Liu et al., 2009](#); [Yu et al., 2008](#); [Banu et al., 2007](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Ichihara et al., 2000b](#)).

No data were located on the reproductive effects of 1-BP exposure in humans.

Developmental Toxicity

The developmental effects of 1-BP exposure have been evaluated on the basis of standard prenatal developmental toxicity studies, and a two-generation reproductive toxicity study in rats exposed via whole-body inhalation. No standard developmental neurotoxicity studies are available.

Evidence supporting fetal development as a sensitive target of 1-BP exposure is provided by a number of laboratory animal studies. The current database consists of developmental toxicity testing that shows severe effects resulting from prenatal exposure during gestation and postnatal exposure studies showing adverse developmental effects that manifest at various stages of development, and span multiple generations ([WIL Research, 2001](#)). Reported adverse developmental effects following 1-BP exposure include dose-related decreases in live litter size ([WIL Research, 2001](#)), postnatal survival ([Furuhashi et al., 2006](#)), and pup body weight, brain weight and skeletal development ([Huntingdon Life Sciences, 1999](#)), ([Huntingdon Life Sciences, 2001](#)); ([WIL Research, 2001](#)). ([WIL Research, 2001](#)) also reported decreases in the number of implantation sites, and increases in ‘unaccounted’ implants for corresponding ovulatory events, reported as the difference between the total number of implantation sites counted and the number of pups born. Additional qualitative evidence of impaired development is provided by results from dominant lethal assays with 1-BP which show increased implantation loss (at week 8) in rats subjected to five days of oral 1-BP exposure at 400 mg/kg ([Saito-Suzuki et al., 1982](#)) and in mice (at week 5) following 1-BP exposure via gavage administration at 600 mg/kg for ten days prior to mating ([Yu et al., 2008](#)).

No data were located on the developmental effects of 1-BP exposure in humans.

Neurotoxicity

Data from studies in humans and animals demonstrate that the nervous system is a sensitive target of 1-BP exposure. Both the central and peripheral nervous systems are affected. In animal inhalation studies, the degree or severity of neurotoxicity produced by 1-BP depends on the

concentration as well as duration of exposure, with lower concentrations being effective at longer exposures. Most inhalation studies using concentrations of ≥ 1000 ppm reported ataxia progressing to severely altered gait, hindlimb weakness to loss of hindlimb control, convulsions, and death (*e.g.*, ([Banu et al., 2007](#); [Ishidao et al., 2002](#); [Yu et al., 2001](#); [Fueta et al., 2000](#); [Ichihara et al., 2000a](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997a, b](#)). Concentrations of 400-1000 ppm produced neuropathological changes including peripheral nerve degeneration, myelin sheath abnormalities, and spinal cord axonal swelling ([Wang et al., 2002](#); [Yu et al., 2001](#); [Ichihara et al., 2000a](#)). Brain pathology has also been reported in several studies, including white and gray matter vacuolization, degeneration of Purkinje cells in the cerebellum and decreased noradrenergic but not serotonergic axonal density in frontal cortex and amygdala at exposures ≥ 400 ppm ([Mohideen et al., 2013](#); [Mohideen et al., 2011](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997a, b](#)). Decreased brain weight has been reported in adult and developmental studies ([Subramanian et al., 2012](#); [Wang et al., 2003](#); [WIL Research, 2001](#); [Ichihara et al., 2000a](#); [Kim et al., 1999a](#); [ClinTrials, 1997b](#)). In a two-generation study ([WIL Research, 2001](#)), the NOAEL for decreased brain weight in F1-generation males was 100 ppm (BMD modeling did not produce an acceptable fit); this value is brought forward for risk assessment representing neuropathological changes.

Physiological, behavioral, and biochemical measures have been used to characterize and develop dose-response data for neurological effects. Motor nerve conduction velocity and latency measured in the rat tail nerve were altered at concentrations ≥ 800 ppm with progressive changes from 4 to 12 weeks of exposure ([Yu et al., 2001](#); [Ichihara et al., 2000a](#)). In the brain, electrophysiological changes in hippocampal slices were seen at concentrations of 400 ppm and above ([Fueta et al., 2002a](#); [Fueta et al., 2002b](#); [Fueta et al., 2000](#)); [Fueta et al., 2004](#); [Fueta et al., 2007](#); [Ueno et al., 2007](#)). Behavioral tests such as hindlimb grip strength, landing foot splay, traction (hang) time, gait assessment, motor activity, and water maze performance provide dose-response data and tend to be more sensitive than neuropathology or physiological changes, with effects at concentrations as low as 50-200 ppm ([Banu et al., 2007](#); [Honma et al., 2003](#); [Ichihara et al., 2000a](#)). Exposures to concentrations ≥ 50 ppm produce changes in neurotransmitters, biomarkers, and proteome expressions suggesting alterations in the function and maintenance of neural and astrocytic cell populations ([Huang et al., 2015](#); [Mohideen et al., 2013](#); [Zhang et al., 2013](#); [Huang et al., 2012](#); [Subramanian et al., 2012](#); [Huang et al., 2011](#); [Mohideen et al., 2009](#); [Suda et al., 2008](#); [Yoshida et al., 2007](#); [Wang et al., 2003](#); [Wang et al., 2002](#)). Although less extensively tested, oral or subcutaneous dosing of 1-BP resulted in similar findings as for inhalation exposure, with effects at ≥ 200 mg/kg-day ([Guo et al., 2015](#); [Zhong et al., 2013](#); [Wang et al., 2012](#); [Zhao et al., 1999](#)). Neurological endpoints selected for dose-response analysis were datasets for decreased time hanging from a suspended bar (traction time) in rats in a 3 -week inhalation study ([Honma et al., 2003](#)) and decreased hind limb grip strength in rats in a 12 -week inhalation study ([Ichihara et al., 2000a](#)). These functional measures are relevant to peripheral neurotoxicity reported in human studies.

Human studies (case-control studies, industrial surveys, and case reports) corroborate that the nervous system is a sensitive target of 1-BP exposure in humans. Clinical signs of neurotoxicity (including headache, dizziness, weakness, numbness in lower extremities, ataxia, paresthesia, and changes in mood) and motor and sensory impairments were noted in the case reports of workers

occupationally exposed to 1-BP for 2 weeks to 3 years at estimated concentrations exceeding averages of 100 ppm ([Samukawa et al., 2012](#); [Majersik et al., 2007](#); [Raymond and Ford, 2007](#); [Ichihara et al., 2002](#); [Sclar, 1999](#)), and in industrial surveys with average exposures greater than 81 ppm (ranging from 2 weeks to 9 years) ([NIOSH, 2003a, 2002a, c](#)). Cross-sectional studies of Chinese workers reported increased distal latency and decreased sural nerve conduction velocity in female workers. Statistically significant decreased vibration sense in toes was observed across all exposure groups (0.07-106.4 ppm) compared to controls ([EPA, 2019e](#); [Li et al., 2010](#); [Ichihara et al., 2004b](#)). There were several methodological limitations in these studies, discussed in depth in Appendix J.4; however, these studies provide evidence of neurotoxicity in workers exposed to 1-BP.

3.2.4.2 Genotoxicity and Cancer Hazards: Weight of the Scientific Evidence Integration and Mode of Action

Genetic Toxicity

Barber ([1981](#)) and BioReliance ([2015](#)) both performed bacterial reverse mutation studies of 1-BP using test systems characterized as ‘closed’, but yielded different results for mutagenicity. In the study by Barber ([1981](#)), a positive mutagenicity result was observed for 1-BP in *Salmonella typhimurium* strains TA 1535 and TA 100 (but not TA 1537, TA 1538, or TA 98) in the presence and absence of metabolic activation. In contrast, the study by BioReliance ([2015](#)) found no evidence of mutagenicity in *S. typhimurium* strains TA 98, TA 100, TA 1535, and TA 1537 or *Escherichia coli* strain WP2 uvrA (a DNA repair-deficient strain) in the presence or absence of metabolic activation. The major differences in experimental design between the two studies are the method of test substance application (vapor exposure of plated bacteria versus aqueous preincubation exposure) and the methods used to achieve a ‘closed’ system to account for the inherent volatility of 1-BP (fully enclosed test chamber versus preparation of solutions in screw-capped tubes). It is therefore likely the varied mutagenicity results from the two studies (*i.e.*, positive results in the Barber ([1981](#)) study and negative results in the BioReliance ([2015](#)) study) are due to differences in the methods used for exposure and to compensate for the volatility of 1-BP in the bacterial reverse mutation assay. This assumption is supported by the fact that in the BioReliance ([2015](#)) study, analytical concentrations of 1-BP in preincubation tubes during the confirmatory assays were far below target, with 4-37% of target concentrations at the beginning of the preincubation period and 2-5% of target concentrations by the end of the preincubation period (see Appendix J.5.6 for more details). Other tests for mutagenicity in bacteria were negative ([NTP, 2011a](#); [Kim et al., 1998](#)). While these tests may not have been conducted in closed systems, the occurrence of cytotoxicity at high concentrations in the ([NTP, 2011a](#); [Kim et al., 1998](#)) study suggests that sufficient quantities of 1-BP were present to induce that effect, and therefore, that the lack of observed mutagenicity in the study did not result from lack of 1-BP in the test medium, but rather from lack of mutagenic activity of 1-BP.

In mammalian cells tested in vitro, increased mutation frequency was observed in mouse lymphoma cells exposed to 1-BP with or without activation ([Elf Atochem, 1996a](#)). Using the comet assay, ([Toraason et al., 2006](#)) found evidence of DNA damage in human leukocytes exposed

to 1-BP *in vitro*, but only equivocal evidence of damage in leukocytes from workers exposed to 1-BP on the job. Tests conducted *in vivo* were mostly negative, including assays for dominant lethal mutations and micronuclei induction in rats and mice (NTP, 2011a; Yu et al., 2008; Kim et al., 1998; Elf Atochem, 1995; Saito-Suzuki et al., 1982). Negative results were found for mutagenicity in inhalation studies in the Big Blue® mouse model (Stelljes et al., 2019); (Young, 2016); while these results do not support a mutagenic mode of action (MMOA), they also do not provide sufficient evidence against mutagenicity of 1-BP based on several conceptual, methodological, and study comprehensiveness uncertainties (see Appendix J.5.6).

DNA binding studies have shown that 1-BP can produce N⁷-propyl guanine adducts in calf thymus DNA *in vitro* and in multiple tissues in rats treated *in vivo*, that the degree of adduct formation increases with dose of 1-BP, and that metabolic activation is not needed for adduct formation *in vitro* (Thapa et al., 2016) (Nepal et al., 2019). However, these specific DNA adducts are not known to lead to mutations.

Positive results have been observed in several genotoxicity tests using known or postulated metabolites of 1-BP (including glycidol, propylene oxide, α -bromohydrin, 3-bromo-1-propanol, and 1-bromo-2-propanol) (NTP, 2014; IARC, 2000, 1994). Epoxide intermediates such as propylene oxide and glycidol are expected to have more mutagenic activity than 1-BP (IARC, 2018, 2000, 1994).

Carcinogenicity

Evidence from chronic cancer bioassays in rats and mice suggests that 1-BP may pose a carcinogenic hazard to humans. Significant increases in the incidence of skin tumors (keratoacanthoma/squamous cell carcinomas) in male F344 rats, rare large intestine adenomas in female F344 rats, and alveolar/bronchiolar adenomas or carcinomas (combined) in female B6C3F1 mice were observed following exposure to 1-BP via inhalation for two years (NTP, 2011a). NTP concluded that these data show some evidence for carcinogenicity in male rats, clear evidence for carcinogenicity in female rats, no evidence for carcinogenicity in male mice, and clear evidence for carcinogenicity in female mice. No other laboratory animal or human data were located on the carcinogenicity of 1-BP. IARC (2018) concluded that 1-BP “is *possibly carcinogenic to humans (Group 2B)*” based on inadequate evidence in humans and sufficient evidence in experimental animals for the carcinogenicity of 1-BP, noting there is: (a) strong evidence that 1-BP is electrophilic or can be metabolically activated to reactive intermediates; (b) strong evidence that 1-BP induces oxidative stress, induces chronic inflammation, and is immunosuppressive; and (c) moderate evidence that 1-BP modulates receptor-mediated effects and is genotoxic. By the criteria presented in EPA’s *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a), 1-BP may be considered “*Likely to be Carcinogenic in Humans*” based on the positive findings for carcinogenicity in more than one test species together with positive findings for the direct reactivity of 1-BP with DNA and suggestive but inconclusive evidence for genetic toxicity.

As noted above, 1-BP has been shown to be a multi-site carcinogen in rats and mice. The mode of action for 1-BP carcinogenesis has not been established; however, there is data supporting a mutagenic mode of action (MMOA):

- a. Ames test: 1-BP was mutagenic with and without metabolic activation in the Ames *Salmonella* assay in one (Barber,([1981](#)) of two studies when testing was conducted in closed systems designed for testing volatile chemicals.
- b. Mammalian cells and tissues: 1-BP caused mutations in cultured mammalian cells with or without metabolic activation in one study ([Elf Atochem, 1996a](#)) and DNA damage in human leukocytes exposed *in vitro* without metabolic activation in another study ([Toraason et al., 2006](#)).
- c. Evidence was equivocal, however, for DNA damage in leukocytes collected from workers exposed to 1-BP on the job ([Toraason et al., 2006](#)).
- d. Metabolic activation to mutagenic intermediates: Rodent metabolic studies have indicated that 1-BP can be activated by CYP2E1 to at least five different mutagenic intermediates ([NTP, 2014](#); [IARC, 2000, 1994](#)), including two clearly mutagenic and carcinogenic chemicals (glycidol and propylene oxide) IARC ([2018](#)), which are listed in the NTP Report on Carcinogens as “reasonably anticipated to be human carcinogens” ([2013a](#)). Glycidol has been shown to induce tumors in the intestines ([NTP, 1990](#)), one of the carcinogenic targets of 1-BP. Propylene oxide inhalation has been shown to induce tumors at multiple sites including the thyroid, adrenal gland, and mammary gland ([IARC, 1994](#)). The available evidence suggests similar metabolic pathways for 1-BP in humans and rodents. The role of epoxides as proximate carcinogens should be explored with regard to the mode of 1-BP carcinogenicity.
- e. Structure-Activity Relationship (SAR) consideration: SAR may be used as a criterion for consideration in EPA’s Guidelines for Carcinogen Risk Assessment ([U.S. EPA, 2005a](#)). From the SAR point of view, 1-BP is a low molecular weight alkyl bromide that is electrophilic ([IARC, 2018](#); [NTP, 2013a](#)) and generally known to possess alkylating potential (1-BP has been shown to bind to DNA *in vitro* and *in vivo*, although the specific adducts that have been found, N⁷-propyl guanine adducts, are not known to lead to mutations). Bromoethane and 1-bromobutane, two analogs of 1-BP, both produced positive results in the Ames assay when tested in closed systems. Bromoethane is a known carcinogen via the inhalation route of exposure ([NTP, 1989a](#)), whereas 1-bromobutane has not been tested for carcinogenic activity.

In contrast, other lines of evidence do not provide clear support for a MMOA for 1-BP carcinogenicity including:

- a. With the exception of the one closed study noted above, results are negative for 1-BP in the Ames assay ([NTP, 2011a](#); [Kim et al., 1998](#)), including in the other closed study ([BioReliance, 2015](#)).
- b. While the high volatility of 1-BP is a complication for tests conducted using open systems, at least one of the negative open studies ([NTP, 2011](#)) observed cytotoxicity at high 1-BP concentrations, indicating the presence of 1-BP in the test medium and consequently suggesting that this was a valid test of 1-BP mutagenicity.
- c. *In vivo* micronucleus assays in bone marrow and circulating erythrocytes of mice and rats were negative, as were dominant lethal assays in mice and rats ([NTP, 2011a](#); [Yu et al., 2008](#); [Kim et al., 1998](#); [Elf Atochem, 1995](#); [Saito-Suzuki et al., 1982](#)).

- d. As with other types of genotoxicity data, it is uncertain how predictive the results of in vivo micronucleus assays are for carcinogenicity; Benigni (2012) found a low correlation between in vivo micronucleus assay results and carcinogenicity.
- e. 1-BP did not induce mutations at the *cII* gene of female B6C3F1 transgenic Big Blue® mice following whole-body inhalation exposure to 1-BP vapor concentrations of 62.5, 125, or 250 ppm for 5 days/week (Stelljes et al., 2019; Weinberg, 2016) or 7 days/week over a 28-day period (Young, 2016). These studies do not provide definitive evidence against a MMOA, however, due to limitations in test design, as discussed in Appendix J.5.8.
- f. Other possible MOAs: NTP (2013a) suggested that in addition to mutagenicity, at least three other mechanisms, including oxidative stress, immunosuppression, and cell proliferation can contribute to the multi-stage process of carcinogenesis for 1-BP.

Following EPA's *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a), the evidence for a MMOA for 1-BP induced carcinogenicity is suggestive but inconclusive. Given the lack of a clearly defined MOA or information on the shape of the dose-response curve in the low dose region, linear extrapolation from the point of departure is recommended per EPA's *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a).

3.2.5 Evidence Integration and Evaluation of Human Health Hazards

This section integrates and evaluates both the non-cancer and cancer human health hazard endpoints from the health hazard domains discussed in Section 3.2.4. This evidence integration and evaluation uses a weight of the scientific evidence approach wherein the strengths, limitations and relevance of the hazard data were analyzed and summarized across studies, taking into consideration consistency and coherence among animal studies, quality of the studies (such as whether studies exhibited design flaws that made them unacceptable) and biological plausibility. Relevance of data was considered primarily during the screening process but may also have been considered when weighing the scientific evidence.

The best available human health hazard information was selected for benchmark dose modeling based on an integration of the data quality evaluation results, MOA information and overall weight of scientific evidence. Based on this approach, liver toxicity, kidney toxicity, reproductive toxicity, developmental toxicity, and neurotoxicity are the primary (non-cancer) health effects associated with 1-BP exposure. Emphasis on acute/short term inhalation, and repeated-dose inhalation studies were considered most appropriate for hazard characterization and dose-response analysis.

3.2.5.1 Weight of the Scientific Evidence for Liver Toxicity

Hepatic effects, including increases in liver weight, liver histopathology and associated clinical chemistry changes, were widely reported in animal studies of 1-BP (Wang et al., 2012; NTP, 2011a; Liu et al., 2009; Lee et al., 2007; Yamada et al., 2003; WIL Research, 2001; Kim et al., 1999a; Kim et al., 1999b; ClinTrials, 1997a, b). Human data were available from a single study (Li et al., 2010) that found no clinical chemistry changes indicative of liver toxicity. Overall, based on limited human evidence and evidence in multiple animal species from highly rated studies, there is

evidence to support non-cancer liver effects following 1-BP exposure. Therefore, this hazard endpoint was carried forward for dose-response analysis.

3.2.5.2 Weight of the Scientific Evidence for Kidney Toxicity

Several animal studies of 1-BP reported effects on the kidneys, including increases in kidney weight, renal histopathology and associated clinical chemistry changes ([NTP, 2011a](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Kim et al., 1999a](#); [ClinTrials, 1997a, b](#)). Human data were limited to two studies of workers that showed no clinical chemistry changes indicative of renal toxicity ([Li et al., 2010](#); [NIOSH, 2003a](#)). Overall, the evidence from high-quality animal studies supports kidney toxicity as a consequence of 1-BP exposure, and this hazard endpoint was carried forward for dose-response analysis.

3.2.5.3 Weight of the Scientific Evidence for Immunotoxicity

Two studies were located that found functional evidence of immunosuppressive effects of 1-BP in animals, with corresponding decreases in splenic cellularity and spleen weight ([Anderson et al., 2013](#); [Lee et al., 2007](#)). Other animal studies did not evaluate immune function but found no effects on spleen weight or histopathology ([NTP, 2011a](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Ichihara et al., 2000a](#); [Kim et al., 1999b](#); [ClinTrials, 1997a, b](#)). No human data were located. Overall, the sparse data provide suggestive but inconclusive evidence of an association between 1-BP exposure and immune-related outcomes. Therefore, immune effects were not considered for dose-response analysis.

3.2.5.4 Weight of the Scientific Evidence for Reproductive and Developmental Toxicity

Reproductive and developmental toxicity were identified as critical targets for 1-BP exposure based on a constellation of effects reported across studies, including a two-generation reproduction study ([WIL Research, 2001](#)), which showed adverse effects on male and female reproductive parameters, and the developing conceptus. Additional details can be found in Appendix J.1.

Quantitative and qualitative evidence of 1-BP reproductive toxicity in F0 males include decreases in sperm motility, changes in normal sperm morphology, decreases in mating and fertility indices ([WIL Research, 2001](#)), and decreases in epididymal, prostate, and seminal vesicle weights following 1-BP (whole-body) inhalation exposure ([NTP, 2011a](#); [WIL Research, 2001](#); [Ichihara et al., 2000b](#)). Evidence of reproductive toxicity in F0 females include decreased numbers of corpora lutea, antral follicles, and implantation sites ([NTP, 2011a](#); [Yamada et al., 2003](#); [WIL Research, 2001](#)). Other reported reproductive effects in females include a significant upward trend in increased estrous cycle length, and evidence of mating without delivery ([WIL Research, 2001](#)). Reported impairments in male and female reproductive function resulted in a 48% reduction in fertility at 500 ppm and complete infertility at 750 ppm in F0 mating pairs ([WIL Research, 2001](#)). Although the adverse reproductive effects of 1-BP exposure have not been directly evaluated in humans, the results from laboratory animal studies suggest that it may impair reproductive function.

Evidence supporting fetal development as a sensitive target of 1-BP exposure is provided by a number of laboratory animal studies. The current database consists of developmental toxicity testing that shows severe effects resulting from prenatal exposure during gestation and postnatal exposure studies showing adverse developmental effects that manifest at various stages of development, and span across multiple generations ([WIL Research, 2001](#)). Overall, the general consistency of findings indicative of impaired development across species, as reported in multiple studies from independent laboratories is taken as evidence of a causative association between 1-BP exposure and developmental toxicity. Reported adverse developmental effects following 1-BP exposure include dose-related decreases in live litter size ([WIL Research, 2001](#)), postnatal survival ([Furuhashi et al., 2006](#)), and pup body weight, brain weight and skeletal development ([Huntingdon Life Sciences, 1999](#)), ([Huntingdon Life Sciences, 2001](#)); ([WIL Research, 2001](#)). ([WIL Research, 2001](#)) also reported decreases in the number of implantation sites, and increases in ‘unaccounted’ implants for corresponding ovulatory events, reported as the difference between the total number of implantation sites counted and the number of pups born. EPA interpreted this finding as an indication of post-implantation loss (pre-implantation loss could not be determined due to insufficient data on the number of primordial follicles). Additional qualitative evidence of impaired development is provided by results from dominant lethal assays with 1-BP which show increased implantation loss (at week 8) in rats subjected to five days of oral 1-BP exposure at 400 mg/kg ([Saito-Suzuki et al., 1982](#)) and in mice (at week 5) following 1-BP exposure via gavage administration at 600 mg/kg for ten days prior to mating ([Yu et al., 2008](#)). These findings are supported by consistent reports of 1-BP induced adverse developmental effects from independent laboratory studies with rats and mice. No corresponding epidemiological studies have been identified; however, the concordance of reported results across species and test laboratories is taken as evidence of a causative association between 1-BP exposure and developmental toxicity.

Overall, there is evidence in high-quality animal studies to support adverse reproductive and developmental effects following 1-BP exposure. Therefore, these endpoints were carried forward for dose-response analysis.

3.2.5.5 Weight of the Scientific Evidence for Neurotoxicity

Neurotoxicity has been identified as a critical effect for 1-BP based on over 15 years of behavioral, neuropathological, neurochemical, and neurophysiological studies in rodents as well as cross-sectional studies and case reports in humans (Appendices J.1, J.3, and J.4). Overall, there is considerable support for the finding of peripheral neurotoxicity, and consistency in reports of impaired peripheral nerve function (sensory and motor) and adverse neuromuscular impacts. The effects are progressive in terms of exposure duration and concentration, and range from subtle changes in nervous system function and neurochemistry progressing to physiological manifestations of neuron damage to structural evidence of neuronal pathology.

This spectrum of adverse manifestations of peripheral neurotoxicity is reproducible across almost all of the experimental studies, with a few notable exceptions. In addition, symptoms in humans, such as peripheral weakness, numbness, ataxia, and paraparesis, are concordant with the signs seen in many rodent studies. At high concentrations (≥ 1000 ppm), toxicological reports in rodents

include observations such as hindlimb weakness, ataxia, altered gait, and other signs typical of peripheral neuropathy ([Mohideen et al., 2013](#); [Zhang et al., 2013](#); [Banu et al., 2007](#); [Honma et al., 2003](#); [Fueta et al., 2002a](#); [Fueta et al., 2002b](#); [Ishidao et al., 2002](#); [Yu et al., 2001](#); [Fueta et al., 2000](#); [Ichihara et al., 2000a](#); [Kim et al., 1999a](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997a, b](#)).

However, in a chronic bioassay ([NTP, 2011a](#)) these signs were reported at 2000 ppm but not 1000 ppm; differences in timing and specificity of observations as well as training and blinding of personnel to dose assignment could account for the relative insensitivity of those specific outcomes. A number of papers that did not report any information about the general appearance and health of the animals were mostly mechanistic studies focused only on ex vivo endpoints ([Huang et al., 2015](#); [Huang et al., 2012](#); [Subramanian et al., 2012](#); [Huang et al., 2011](#); [Mohideen et al., 2011](#); [Mohideen et al., 2009](#); [Suda et al., 2008](#); [Fueta et al., 2007](#); [Ueno et al., 2007](#); [Yoshida et al., 2007](#); [Fueta et al., 2004](#); [Wang et al., 2003](#); [Wang et al., 2002](#)). In human reports, severe neurological effects in workers occurred at relatively high exposures (>100 ppm) over a period of time of exposure ranging from weeks to months ([Samukawa et al., 2012](#); [CDC, 2008](#); [Majersik et al., 2007](#); [Raymond and Ford, 2007](#); [Ichihara et al., 2002](#); [Sclar, 1999](#)).

There is general agreement between the 1-BP neurotoxic effects observed across studies using measures of peripheral nerve integrity evaluated by electrophysiological and behavioral tests. Nerve conduction velocity and distal latency in motor neurons are decreased in animals via subcutaneous exposure ([Yu et al., 2001](#); [Ichihara et al., 2000a](#); [Zhao et al., 1999](#)). These experimental findings corroborate the studies of factory workers that describe decreased nerve conduction and/or peripheral sensory impairment ([Li et al., 2010](#); [Ichihara et al., 2004a](#)). The epidemiological studies are, however, somewhat limited by poorly defined exposures as well as concerns about the sensitivity and implementation of the vibration sense test methods used to assess motor and sensory deficits. Using an objective measure of grip strength in rats, decreased function that worsens with continued oral exposure has been reported in several laboratories ([Wang et al., 2012](#); [Banu et al., 2007](#); [Ichihara et al., 2000a](#)), except one ([ClinTrials, 1997a](#)).

A number of animal studies report histopathology of the nervous system (brain, spinal cord, and/or peripheral nerves) at concentrations as low as 400 ppm ([Mohideen et al., 2013](#); [Subramanian et al., 2012](#); [Mohideen et al., 2011](#); [Wang et al., 2002](#); [Yu et al., 2001](#); [Ichihara et al., 2000a](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997b](#)), but not in other studies that used even at higher concentrations ([NTP, 2011a](#); [Fueta et al., 2004](#); [Sohn et al., 2002](#); [WIL Research, 2001](#); [Kim et al., 1999a](#)). There are a few conflicting reports from the same laboratory in 4 week vs 13 week studies ([ClinTrials, 1997a, b](#)), ([Sohn et al., 2002](#); [Kim et al., 1999a](#)). Such differences may be attributable to a number of experimental factors, including tissue preparation, fixation, staining, and sampling, measurement methodology, and training and blinding of personnel to dose group assignment.

Additional experimental animal studies report changes in brain weight, which is considered indicative of neurotoxicity even in cases where other histopathological changes are not evident ([U.S. EPA, 1998b](#)); however, several studies do describe corresponding neuropathology ([Wang et al., 2002](#); [WIL Research, 2001](#); [Kim et al., 1999a](#)). Decreased brain weight was reported with subacute to subchronic exposures in adult rats ([Subramanian et al., 2012](#); [Wang et al., 2003](#); [Ichihara et al., 2000a](#); [Kim et al., 1999a](#); [ClinTrials, 1997b](#)), and in offspring from a multi-

generational reproductive toxicity study with lifetime exposures ([WIL Research, 2001](#)). Only two studies have measured brain weight and reported no effects: 1) ([Wang et al., 2002](#)), in which the duration of exposure (7 days) may not have been sufficient, and 2) the 13-wk study of ([ClinTrials, 1997a](#)), even though the same laboratory reported decreased brain weight at the same concentration with only 4 weeks of exposure (ClinTrials did not provide explanations for this contradictory finding).

Several studies report alterations in central nervous system neuronal communication, neurotransmitter levels, proteins, and oxidative stress markers, all of which are markers of neurotoxicity ([U.S. EPA, 1998b](#)). It is notable that database consistency is partially a function of multiple studies from a few laboratories ([Huang et al., 2015](#); [Mohideen et al., 2013](#); [Zhang et al., 2013](#); [Huang et al., 2012](#); [Subramanian et al., 2012](#); [Huang et al., 2011](#); [Mohideen et al., 2011](#); [Mohideen et al., 2009](#); [Suda et al., 2008](#); [Fueta et al., 2007](#); [Ueno et al., 2007](#); [Fueta et al., 2004](#); [Wang et al., 2003](#); [Fueta et al., 2002a](#); [Fueta et al., 2002b](#); [Fueta et al., 2000](#)). Other studies have reported cognitive deficits following 1-BP inhalation exposure ([Guo et al., 2015](#); [Zhong et al., 2013](#); [Honma et al., 2003](#)).

Overall, the experimental studies, supported by the epidemiological studies, reporting clinical and neurophysiological signs provide strong evidence for peripheral neuropathology. Where quantifiable endpoints that are sensitive to relatively low exposures have been measured, there is generally good consistency in outcomes across laboratories, with only a few notable exceptions. There is also agreement in findings of central nervous system dysfunction in laboratory rodents, but there are no corresponding studies available for comparison in humans. There is evidence in high-quality animal studies to support functional measures of neurotoxicity following 1-BP exposure. Therefore, these endpoints were carried forward for dose-response analysis.

3.2.5.6 Weight of the Scientific Evidence for Cancer

Evidence from chronic cancer bioassays in rats and mice suggests that 1-BP may pose a carcinogenic hazard to humans ([IARC, 2018](#)). Significant increases in the incidence of skin tumors (keratoacanthoma/squamous cell carcinomas) in male F344 rats, rare large intestine adenomas in female F344 rats, and alveolar/bronchiolar adenomas or carcinomas (combined) in female B6C3F1 mice were observed following exposure to 1-BP via whole-body inhalation for two years ([NTP, 2011a](#)). The exact mechanism/mode of action of 1-BP carcinogenesis is not established. Evidence for a MMOA is suggestive but inconclusive. Other potential mechanisms that may contribute to the multi-stage process of carcinogenesis by 1-BP include oxidative stress, immunosuppression, and cell proliferation. Overall, there is evidence in high-quality animal studies to support carcinogenicity following 1-BP exposure. Therefore, these endpoints were carried forward for dose-response analysis.

3.2.6 Possible Mode of Action for 1-BP Toxicity

A definitive mode of action (MOA) has not been clearly established for 1-BP toxicity. Based on the Hard and Soft Acid Base theory classification scheme ([Pearson, 1990](#)) however, 1-BP is expected to induce adduct formation in vivo.

The primary metabolic pathways identified for 1-BP involve cytochrome P450 mediated oxidation (CYP2E1) and glutathione conjugation reactions which can produce numerous reactive intermediates (see Figure 3-3). Over 20 metabolites have been identified in rodent studies, including the four metabolites detected in urine samples taken from workers exposed to 1-BP ([Hanley et al., 2009](#)). These metabolites can react with critical cysteine, histidine and lysine residues, and thereby impact the structural and functional integrity of the cell ([Lopachin et al., 2009](#)).

Various reactive metabolites (*e.g.*, glycidol, α -bromohydrin, bromoacetone) and potential targets for cellular binding interactions (*e.g.*, DNA, mitochondria) have been identified for 1-BP ([NTP, 2013a](#)). Some 1-BP metabolites may exhibit alkylating activity. For example, further metabolism of bromoacetone in a manner analogous to acetone ([Casazza et al., 1984](#)), would result in formation of 1-hydroxy-1-bromoacetone, which yields pyruvate and CO₂, or 3-bromo-1-hydroxypropanone (BOP). BOP has been shown to inhibit sperm energetics and motility via its conversion to bromolactaldehyde and bromopyruvaldehyde, ultimately yielding 3-bromopyruvate ([Garner et al., 2007](#); [Porter and Jones, 1995](#)).

3-Bromopyruvate (3-BP) has been shown to produce many untoward effects, including lowered cell viability via production of reactive oxygen species ([Qin et al., 2010](#)) mitochondrial depolarization ([Macchioni et al., 2011](#)) and activation of mitochondrial apoptosis ([Ko et al., 2004](#)). It is a strong alkylating agent, and a known inhibitor of numerous enzymes, including glutamate decarboxylase ([Fonda, 1976](#)), glutamate dehydrogenase ([Baker and Rabin, 1969](#)), the mitochondrial pyruvate transporter ([Thomas and Halestrap, 1981](#)) and the pyruvate dehydrogenase complex ([Apfel et al., 1984](#); [Lowe and Perham, 1984](#)). 3-BP induced alkylation and inhibition of glyceraldehyde-3-phosphate dehydrogenase can impair energy production via glycolysis ([Da Silva et al., 2009](#); [Ganapathy-Kanniappan et al., 2009](#)) and induce apoptosis or necrosis as a result of ATP depletion due to impaired mitochondrial function ([Kim et al., 2008](#)).

The precise mechanism of action, specific molecular targets, and precursor events (*e.g.*, oxidative stress response) that precede 1-BP toxicity is not clearly understood, but likely relates to structural or functional modification of key signaling proteins as a result of cellular binding interactions induced by 1-BP or its metabolites. Since 1-BP can induce adverse effects in multiple organs acting directly as an alkylating agent, or indirectly via formation of reactive metabolites, different mechanisms may be operative in different organ systems. At least four possible mechanisms (*e.g.*, genotoxicity, oxidative stress, immunosuppression, and cell proliferation) have been proposed ([NTP, 2013a](#)).

Several pathological conditions (*e.g.*, alcoholism, diabetes), as well as chronic drug administration can induce CYP2E1 activity, and numerous cellular targets exist for 1-BP metabolites generated via CYP2E1 mediated oxidative metabolism. Interindividual variability in the expression and function of CYP2E1 has been observed ([Neafsey et al., 2009](#)) and genetic polymorphisms in CYP2E1 expression have been linked to altered disease susceptibility ([Trafalis et al., 2010](#)). Though inconsistencies exist in the available data, it is suggested that chronic exposure to CYP2E1 inducers such as solvents (*e.g.*, ethanol) and pharmaceuticals (*e.g.*, isoniazid), may increase the

probability of developing malignancy, especially for carriers of certain CYP2E1 alleles ([Trafalis et al., 2010](#)).

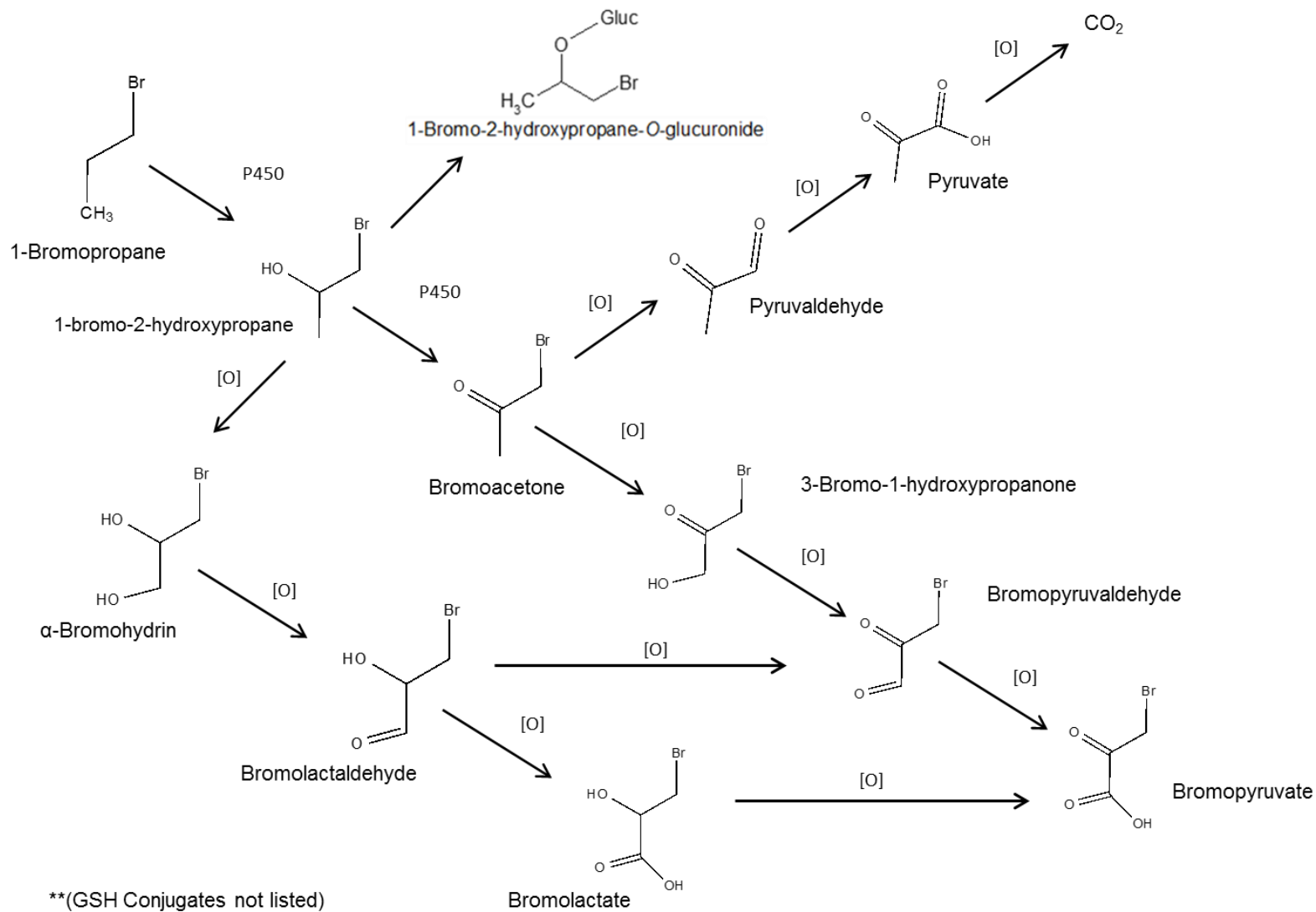


Figure 3-3. Proposed Intermediary Metabolism for 1-BP

Source: ([Garner et al., 2007](#); [Garner et al., 2006](#))

3.2.7 Summary of Hazard Studies Used to Evaluate Acute and Chronic Exposures

EPA considered adverse effects for 1-BP across organ systems and a comprehensive summary table is in Appendix J (Table_Apx J-2). The full list of effects was screened to those that are relevant, sensitive and found in multiple studies which include the following types of effects: liver toxicity, kidney toxicity, developmental/reproductive toxicity, neurotoxicity, and cancer as described above. Immune effects were not considered further, as the weight of the scientific evidence was not conclusive. In general, adverse effects were observed in all of these systems in rats exposed to 1-BP by inhalation in the range of 100 – 1000 ppm (LOAELs). Using principles of systematic review, EPA selected endpoints from the highest quality studies with the least limitations for both non-cancer and cancer that were amenable to quantitative analysis for dose-response assessment as discussed in more detail below in Section 3.2.8. In the following sections, EPA identifies the appropriate toxicological studies to be used for acute and chronic exposure scenarios.

3.2.8 Dose-Response Assessment

EPA evaluated data from studies described above (Section 3.2.4) to characterize the dose-response relationships of 1-BP and selected studies and endpoints to quantify risks for specific exposure scenarios. One of the additional considerations was that the selected key studies had adequate information to perform dose-response analysis for the selected 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.*, BMD), a NOAEL or a LOAEL for an observed incidence or change in the level of response.

3.2.8.1 Selection of Studies for Non-Cancer Dose-Response Assessment

The non-cancer dose-response analysis in this assessment commenced with the review and selection of high quality toxicity studies that went through systematic review that reported both adverse non-cancer health effects and quantitative dose-response data (Table 3-2). The inhalation PODs selected (identified in earlier steps) were considered the most adverse, sensitive and biologically relevant endpoints from among these high quality key and supporting studies. As a result, the non-cancer dose-response assessment was organized into five health effect domains: (1) liver; (2) kidney; (3) reproductive; (4) developmental and (5) nervous system. HEC values were calculated for the inhalation and PODs identified within each health effect domain; dermal HED values were extrapolated from inhalation PODs. Endpoint and study-specific UFs were selected based on EPA guidance ([U.S. EPA, 2002](#)) and used as the benchmark MOEs for risk calculations. These UFs were applied to the PODs to account for (1) variation in susceptibility among the human population (*i.e.*, inter-individual or intraspecies variability); (2) uncertainty in extrapolating animal data to humans (*i.e.*, interspecies uncertainty); (3) uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure (*i.e.*, extrapolating from subchronic to chronic exposure); and (4) uncertainty in extrapolating from a LOAEL rather than from a NOAEL, with default values of 10 applied for each ([U.S. EPA, 2002](#)) with two exceptions, explained further in Section 3.2.8.1.3.

Table 3-2 summarizes the hazard studies and health endpoints by target organ/system that EPA considered suitable for carrying forward for dose-response analysis for the risk evaluation of the exposure scenarios identified in this work plan risk assessment. These equally high quality key and supporting studies in Table 3-2 are briefly described in the Section 3.2.4. Table 3-8 lists the most sensitive and biologically relevant PODs (and corresponding HECs/dermal HEDs) from among these studies by study type and duration (*i.e.*, acute vs. chronic) that were selected to be carried forward for risk estimations.

Benchmark dose (BMD) modeling was applied to these endpoints in a manner consistent with EPA [Benchmark Dose Technical Guidance](#). When the models were adequate, the model results were used as PODs. For studies in which BMD modeling did not achieve an adequate fit to the data, the NOAEL or LOAEL value was used for the POD. Details regarding BMD modeling can be found in the *Supplemental File: Information on Human Health Benchmark Dose Modeling* ([EPA, 2019d](#)). The PODs applied a duration adjustment to convert the air concentrations in laboratory animals for the study duration to exposure durations for workers (*i.e.*, 8 hours/day, 5 days/week) and exposures of 24 hours per day for consumer exposure scenarios. Following EPA's *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* ([U.S. EPA, 1994](#)), EPA converted the adjusted POD to a human equivalent concentration (HEC) by calculating a dosimetric adjustment factor (DAF) based on the ratio between the animal and human blood:air partition coefficients, as shown below. For 1-BP, the blood:air partition coefficient for rats is greater than that for humans, so a default ratio of 1 was applied ([U.S. EPA, 1994](#)). HECs/dermal HEDs were rounded to two significant figures.

BMRs were selected for each endpoint. In cases where biologically relevant BMRs were not available the BMR was 10% for dichotomous endpoints and 1 standard deviation for continuous endpoints consistent with EPA [Benchmark Dose Technical Guidance](#). The liver and kidney endpoints were dichotomous (*i.e.*, incidence) and a BMR of 10% was used in absence of a biologically relevant BMR. The reproductive effects that were able to be BMD modeled (see Table 3-2) were continuous and a BMR of 1 standard deviation was used in absence of a biologically relevant BMR. For pup body weight changes, a BMR of 5% relative deviation from control mean was applied under the assumption that it represents a minimal biologically significant response. In adults, a 10% decrease in body weight in animals is generally recognized as a biologically significant response associated with identifying a maximum tolerated dose; during development, however, identification of a smaller (5%) decrease in body weight is consistent with the assumptions that development represents a susceptible lifestage and that the developing animal is more adversely affected by a decrease in body weight than the adult. In humans, reduced birth weight is associated with numerous adverse health outcomes, including increased risk of infant mortality as well as heart disease and type II diabetes in adults ([Barker, 2007](#); [Reyes and Mañalich, 2005](#)). For these reasons, a BMR of 5% relative deviation was selected for decreased pup weight. For post-implantation loss, a dichotomous endpoint, a BMR of 1% relative deviation was used based on the relative severity of this endpoint considering it is similar to fetal mortality. For decreased live litter size, a BMR of 5% relative deviation was used considering this is possibly a combination of reproductive effects (BMR of 10% relative deviation) and developmental effects including post-implantation loss similar to mortality (BMR of 1% relative deviation) for an overall

BMR of 5% relative deviation. A 1% BMR could potentially be justified for this endpoint as well, however EPA believes that the 5% BMR is the most appropriate selection based on being a mix of a reproductive and developmental effect. For decreased brain weight in F1 and F2 offspring, a BMR of 1% relative deviation was used considering the severity of this effect and the developmental context (*e.g.*, could result in irreversible damage). For developmental endpoints, BMCLs for alternative BMRs are also shown in parentheses for comparison. Alternative BMRs were 1 standard deviation for continuous endpoints and a 10% relative deviation for dichotomous endpoints (except for post-implantation loss the alternative BMR was a 5 % relative deviation because of the severity of this endpoint). For functional nervous system effects, the endpoints were continuous and a BMR of 5% ER or 1 standard deviation was used. When BMD modeling was successful, the PODs were the BMCLs determined for each endpoint. The PODs for endpoints selected following dose-response analysis were calculated either by benchmark dose (BMD) modeling (when the model fit was adequate) or a NOAEL/LOAEL approach based on the endpoint evaluated (see Section 3.2.8.1 and Table 3-2 for all of the PODs).

Given the different exposure scenarios considered (both acute and chronic for spray adhesives, dry cleaning, and degreasing activities for occupational exposure scenarios; and only acute for spot cleaners for consumer exposure scenarios), different endpoints were used based on the expected exposure durations. For non-cancer effects, and based on a weight of the scientific evidence analysis of toxicity studies from rats and humans, risks for developmental effects that may result from a single exposure were evaluated for acute (short-term) exposures, whereas risks for other adverse effects (*e.g.*, toxicity to liver, kidney, reproduction, development and nervous system) were evaluated for repeated (chronic) exposures to 1-BP. The rationale for using the range of toxic effects for chronic scenarios is based on the fact that relatively low dose and short term/sub-chronic exposures can result in long-term adverse consequences.

3.2.8.1.1 PODs for Acute Exposure

Acute exposure was defined for occupational settings as exposure over the course of a single work shift 8 hours and for consumers as a single day. Developmental toxicity (*i.e.*, post-implantation loss; ([WIL Research, 2001](#))) was the endpoint selected as most relevant for calculating risks associated with acute occupational or consumer exposure. Table 3-2 summarizes the hazard studies and health endpoints by target organ/system that EPA considered suitable for the risk evaluation of acute exposure scenarios.

The WIL Research ([2001](#)) study scored a High in systematic review data quality criteria ranking. The POD (post-implantation loss) was considered the most sensitive and biologically relevant developmental toxicity endpoint and is considered to be representative of a robust dataset, representing a continuum of adverse developmental outcomes. EPA considers the general consistency of the effects reported across studies to be supportive of the robustness of the developmental endpoint which exists along a continuum of adverse treatment effects, including mortality.

The acute scenario covers exposures incurred during a single day, with varying time intervals assumed for worker (an 8 hour work shift), and consumer (a 24 hour day) exposure scenarios. Usually, the daily dose is not adjusted for duration of exposure because appropriate toxicokinetic data are not available to support a more granular adjustment. In cases where such data are available, adjustments may be made to provide an estimate of equal average concentration at the site of action for the human exposure scenario of concern. The short half-life for 1-BP suggests there will not be increasing body burden over multiple exposure days, therefore, effects following single-day acute exposure can be reasonably expected to occur at the same dose as repeated exposures and no duration adjustment is needed. Further support for using the post-implantation loss endpoint for acute (short-term) exposures is the fact that the male and female reproductive effects (in the F₀ males and females) collectively contributed to related decreases in live litter size, and these all occurred within a short window of exposure between ovulation and implantation. In addition, decreased live litter size occurred at relatively low exposures, suggesting that this was a sensitive and relevant endpoint, suitable for use in the risk assessment. A BMR of 5% was used to address the severity of this endpoint ([U.S. EPA, 2012a](#)). This BMR choice reflects the intermediate between reproductive effects (where a BMR of 10% would be used) and, developmental effects of post implantation loss, (which is considered a severe effect like mortality where a BMR of 1% would be used) inherent to the endpoint. As previously discussed, EPA acknowledges that the severity of the endpoint, since indicating earlier prenatal mortality, could also potentially warrant a 1% BMR. The POD for the decreased live litter size was a BMCL of 31 ppm.

Additional modeling was performed using the nested dichotomous models (NCTR and NLogistic) within BMDS version 2.7.0.4. Use of nested models is preferred for analysis of developmental toxicity data when suitable data are available. In developmental toxicity studies, exposures are to the dams but observations are made in the fetuses or pups, a situation in which the data are said to be “nested.” For both genetic and environmental reasons, pups in the same litter tend to be more similar to each other than to pups in different litters (litter effect). Models for nested data incorporate two parameters to address litter effect: a litter-specific covariate (*e.g.*, litter size, dam weight, etc) that takes into account the condition of the dam prior to exposure and intra-litter correlation that statistically describes the similarity of responses to exposure among pups of the same litter. The Nested models can only be applied to increases in effects, and therefore, increased post-implantation loss was the endpoint selected as most relevant for calculating risks associated with developmental toxicity following acute exposures ([WIL Research, 2001](#)) using nested modeling.

Significant increases in the number of ‘former’ or ‘unaccounted’ implantation sites (*i.e.*, the difference between the total number of implantation sites counted and the number of pups born) were reported by ([WIL Research, 2001](#)). EPA considers this finding to be indicative of post-implantation loss (pre-implantation loss could not be determined because of a lack of data on the number of primordial follicles at 100, 250 and 500 ppm). F₀ females experienced complete infertility at 750 ppm and therefore these exposures were not included in the post-implantation loss modeling. F₀ females experienced a 48% reduction in fertility at 500 ppm and the post-implantation loss modeling was conducted both with and without this exposure group. After comparing the model fits the results without the 500 ppm exposure group were selected (see the *Supplemental*

File: Information on Human Health Benchmark Dose Modeling ([EPA, 2019d](#)). A BMR of 1% was used to address the severity of this endpoint which is considered a severe effect like mortality ([U.S. EPA, 2012a](#)). Results from the NCTR and Nlogistic models demonstrated similar model fit. The NLogistic model result was therefore selected for resulting in the lowest BMCL, however the results were identical when rounding (22.7 ppm vs 23 ppm). The resulting POD for the increased post-implantation loss was a BMCL of 23 ppm.

Among the two related reproductive/developmental endpoints of decreased live litter size and post-implantation loss, the POD for post-implantation loss based on Nlogistic nested BMD modeling will be used for risk estimation. In addition to the uncertainty over the appropriate BMR for the decreased live litter size endpoint, the post-implantation loss endpoint allowed for nested BMD modeling, which can capture intra-litter variability. PODs for both endpoints are shown for comparison in Table 3-8.

3.2.8.1.2 PODs for Chronic Exposure

Chronic exposure was defined for occupational settings as exposure reflecting a 40-hour work week. Non-cancer endpoints selected as most relevant for calculating risks associated with chronic (repeated) occupational exposures to 1-BP included toxicity to the liver, kidney, reproductive system, developmental effects, and the nervous system.

Table 3-2 summarizes the hazard studies and health endpoints by target organ/system that EPA considered suitable for the risk evaluation of chronic exposure scenarios. The high quality key and supporting studies in Table 3-2 are briefly described in the Section 3.2.4, along with other toxicity and epidemiological studies. BMD modeling was performed for these endpoints in a manner consistent with EPA [Benchmark Dose Technical Guidance](#). BMRs were selected for each endpoint.

Hepatic endpoints selected for dose-response analysis include datasets for histopathology (*e.g.*, hepatocellular vacuolation) from subchronic inhalation studies in rats ([ClinTrials, 1997a, b](#)) and ([WIL Research, 2001](#)). Benchmark dose modeling determined BMCL values of 143, 226 and 322 ppm for the three datasets modeled from these studies.

Renal endpoints selected for dose-response analysis include an increased incidence of pelvic mineralization in male and female rats from a subchronic inhalation study ([WIL Research, 2001](#)). Benchmark dose modeling determined BMCL values for increase of pelvic mineralization of 386 ppm in male rats, and 174 ppm in female rats.

Decreased epididymal weight, decreased prostate weight, decreased seminal vesicle weight, altered sperm morphology and decreased sperm motility were the male reproductive endpoints selected for dose-response analysis ([WIL Research, 2001](#); [Ichihara et al., 2000b](#)). Increased estrous cycle length and decreased antral follicle count were the female reproductive endpoints selected for dose-response analysis ([Yamada et al., 2003](#); [WIL Research, 2001](#)). The PODs for endpoints selected following dose-response analysis were calculated either by benchmark dose (BMD) modeling (when the model fit was adequate) or when BMD modeling did not find an adequate model fit a NOAEL/LOAEL approach was used and this occurred for the reproductive endpoint evaluated (see Section 3.2.8.1 and Table 3-2 for all of the PODs). The PODs were 38, 327, 250,

313 and 338 ppm for decreased relative seminal vesicle weight (use of absolute seminal vesicle weight produced the same BMCL), decreased percent normal sperm, decreased percent motile sperm, and absolute left and right cauda epididymal weights respectively, in males. The PODs were 200 and 250 ppm for decreased antral follicle count and increased estrous cycle length respectively, in females.

Decreased live litter size (*i.e.*, reduced number of live pups per litter) was the endpoint selected as most relevant for calculating risks associated with developmental toxicity following chronic, exposures ([WIL Research, 2001](#)). In addition, decreased live litter size occurred at relatively low exposures, suggesting that this was a sensitive and relevant endpoint, suitable for use in the risk assessment. A BMR of 5% was used to address the severity of this endpoint ([U.S. EPA, 2012a](#)). The POD for the decreased live litter size was a BMCL of 43 ppm. EPA acknowledges that the severity of the endpoint, since indicating prenatal mortality, could also potentially warrant a 1% BMR.

As discussed above for acute exposure, EPA used the BMDS nested dichotomous model (NLogistic) to model data for increased post-implantation loss while accounting for litter effects. Again, a BMR of 1% was used to address the severity of this endpoint ([U.S. EPA, 2012a](#)). The POD for the increased post-implantation loss was a BMCL of 23 ppm.

Neurological endpoints selected for dose-response analysis for chronic, repeated exposures were datasets for decreased time hanging from a suspended bar (traction time) in rats in a 3-week inhalation study ([Honma et al., 2003](#)), decreased hind limb grip strength in rats in a 12-week inhalation study ([Ichihara et al., 2000a](#)) and decreased brain weight in adult (F0) rats ([WIL Research, 2001](#)). The functional measures (decreased time hanging and decreased hind limb strength) are relevant to peripheral neurotoxicity reported in human studies. Benchmark dose modeling for these continuous endpoints used a BMR of 1 standard deviation and determined BMCL values of 18 and 147 ppm, respectively, for these datasets. A BMR of 5% was used to address the severity of the decreased brain weight in adult (F0) rats endpoint ([U.S. EPA, 2012a](#)).

3.2.8.1.3 Uncertainty Factor Determinations

The benchmark MOE used to evaluate risks for each use scenario represents the product of all UFs used for each non-cancer POD. These UFs accounted for various uncertainties including:

1. **Animal-to-human extrapolation (UF_A):** The UF_A accounts for the uncertainties in extrapolating from rodents to humans. In the absence of data, the default UF_A of 10 is adopted which breaks down to a factor of 3 for toxicokinetic variability and a factor of 3 for toxicodynamic variability. There is no PBPK model for 1-BP to account for the interspecies extrapolation using rodent toxicokinetic data in order to estimate internal doses for a particular dose metric. In this assessment, a portion of the toxicokinetic uncertainty may be accounted for by the calculation of an HEC accounting for the relative blood/air partition coefficients across species and application of a dosimetric adjustment factor as outlined in the RfC methodology ([U.S. EPA, 1994](#)); however, an UF_A of 10 is retained to account for additional toxicokinetic differences that remain unaccounted for. 1-BP is irritating to the respiratory tract and rodents exhibit physiological responses (such as reflex bradypnea) that

differ from humans and may alter uptake due to hyper- or hypoventilation, resulting in decreased internal dose in rodents relative to the applied concentration. Therefore, an UF_A of 10 is retained to account for toxicokinetic differences ([OECD 39](#)).

2. **Inter-individual variation (UF_H):** The UF_H accounts for the variation in sensitivity within the human population. In the absence of data, the default UF_H of 10 is adopted which breaks down to a factor of 3 for toxicokinetic variability and a factor of 3 for toxicodynamic variability. Since there is no PBPK model for 1-BP to reduce the human toxicokinetic/toxicodynamic variability, the total UF_H of 10 was retained.
3. **Extrapolation from subchronic to chronic (UF_S):** The UF_S accounts for the uncertainty in extrapolating from a subchronic to a chronic POD. Typically, a UF_S of 10 is used to extrapolate a POD from a less-than-chronic study to a chronic exposure, except for reproductive/developmental endpoints where a study may cover the full duration of relevant developmental or reproductive processes. However, with few exceptions, the vast majority of the five health effect domains (liver, kidney, reproductive, developmental and nervous system), were observed in the multi-generational reproductive toxicity study with lifetime exposures ([WIL Research, 2001](#)); other studies, [ClinTrials, 1997a, b \(for liver effects\)](#), and [Ichihara et al., 2000b and Yamada et al., 2003 \(for reproductive effects\)](#) were longer-term studies. The only exception was for nervous system effects observed in the 3-week study by [Honma et al., 2003](#). However, the totality of information in animal studies support nervous system effects at similar concentrations following chronic exposures to 1-BP. In addition, longer term (2 weeks up to 9 years) exposures in humans (case-control studies, industrial surveys, and case reports) also corroborate the nervous system as a sensitive target of 1-BP exposure ([Samukawa et al., 2012](#); [Majersik et al., 2007](#); [Raymond and Ford, 2007](#); [Ichihara et al., 2002](#); [Sclar, 1999](#)); ([NIOSH, 2003a, 2002a, c](#)). Since exposures in the longer-term animal studies are not reasonably expected to cause equivalent nervous system effects at a lower concentration than the 3-week study by [Honma et al., 2003](#), a UF_S of 1 was used for all of the HECs discussed in EPA's risk evaluation.
4. **LOAEL-to-NOAEL extrapolation (UF_L):** The UF_L accounts for the uncertainty in extrapolating from a LOAEL to a NOAEL. A value of 10 is the standard default UF_L value (when a LOAEL was used as the POD), although lower values (*e.g.*, 3) can be used if the effect is considered minimally adverse at the LOAEL or is an early marker for an adverse effect ([U.S. EPA, 2002](#)). Typically, UF_L ranging from 3 to 30 (*i.e.*, 3, 10, or 30) are used in the HECs. A LOAEL was used as the POD in only two instances; one reproductive POD ([Yamada et al., 2003](#)) and one developmental POD ([WIL Research, 2001](#)). For these PODs, the default UF_L value of 10 was used, resulting in a total UF of 1000. For all other PODs, a UF_L of 1 was used and the total UF was 100.

All endpoints evaluated for dose-response modeling and their associated UFs are provided in Table 3-2.

Table 3-2. Endpoints Selected for the Inhalation Non-Cancer Dose-Response Analysis of 1-BP

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Liver	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL ₁₀ = 143	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	150	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Liver	Rat (male) (n=15/group)	100 to 600	6 hours/day, 5 days/week for 13 weeks	BMCL ₁₀ = 226	Increased incidence of cytoplasmic vacuolization	170	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(ClinTrials, 1997a)	High (1.5)
Liver	Rat (female) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21) for F ₀	BMCL ₁₀ = 322	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	340	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Kidney	Rat (female) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21) for F ₀	BMCL ₁₀ = 174	Increased incidence of pelvic minerali- zation (F ₀)	180	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Kidney	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL ₁₀ = 386	Increased incidence of pelvic minerali- zation (F ₀)	405	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Reproductive System	Rat (male) (n=8-9/group)	200 to 800	8 hours/day, 7 days/week for 12 weeks	BMCL _{1SD} = 38	Decreased absolute/ relative seminal vesicle weight	53	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(Ichihara et al., 2000b)	High (1.7)
Reproductive System	Rat (female) (n=22- 25/group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL _{1SD} = 188	Decreased number of implantation sites	200	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (male) (n=15- 25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	NOAEL* = 250	Decreased percent motile sperm (F ₀)	260	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (female) (n=22- 25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21) for F ₀	NOAEL* = 250	Increase in estrous cycle length (F ₀)	260	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (female) (n=10/ group)	200 to 800	8 hours/day, 7 days/week for 7 or 12 weeks	LOAEL* = 200	Decreased number of antral follicles (F ₀)	280	UF _S =1; UF _A =10; UF _H =10; UF _L =10; Total UF=1000	(Yamada et al., 2003)	High (1.6)

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Reproductive System	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL _{1SD} = 313	Decreased left cauda epididymis absolute weight (F ₀)	330	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (male) (n=24- 25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL _{1SD} = 223	Decreased percent normal sperm morphology (F ₀)	234	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL _{1SD} = 338	Decreased right cauda epididymis absolute weight (F ₀)	350	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Reproductive System	Rat (n=25/group)	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice for F ₀	BMCL ₁₀ = 356	Decreased Male and Female Fertility Index (F ₀)	370	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects (BMDS nested dichotomous model, NLogistic)	Rat (n=25/ group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20 for the F ₁ litters	BMCL ₁ = 23 (BMCL ₅ =89)	Post- implantation loss in F ₀ females	Acute ⁶ : 17 Chronic ⁶ : 17	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects (BMD modeling)	Rat (n=25/group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20 for the F ₁ litters	BMCL ₅ = 41 (BMCL _{1SD} =158)	Decreased live litter size (F ₁) at PND 0	Acute ⁶ : 31 Chronic ⁶ : 31	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Developmental Effects	Rat (female) (n=15- 22/group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	BMCL ₁ = 50 (BMCL _{1SD} =260)	Decreased brain weight in F ₂ females at PND 21	53	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects	Rat (female) (n=25/group)	100 to 500	6 hours/day during gestation plus ≥ 21 weeks after PND21	BMCL ₁ = 82 (BMCL _{1SD} =327)	Decreased brain weight in adult F ₁ females	86	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects	Rat (male) (n=15- 22/group)	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	BMCL ₁ = 98 (BMCL _{1SD} =395)	Decreased brain weight in F ₂ males at PND 21	100	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
Developmental Effects	Rat (male) (n=24- 25/group)	100 to 500	6 hours/day during gestation plus ≥ 21 weeks after PND21	LOAEL* = 100	Decreased brain weight in adult F ₁ males	110	UF _S =1; UF _A =10; UF _H =10; UF _L =10; Total UF=1000	(WIL Research, 2001)	High (1.3)
Developmental Effects	Rat (male) (n=15- 22/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₂	BMCL ₅ = 116 (BMCL _{1SD} =249)	Decreased pup body weights on PND 21 (F ₂ males)	120	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)

Target Organ/ System	Species, sex (#animals/ dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Developmental Effects	Rat (male) (n=10- 24/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₁	BMCL ₅ = 123 (BMCL _{1SD} =229)	Decreased pup body weights on PND 28 (F ₁ males)	130	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Developmental Effects	Rat (female) (n=15- 22/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₂	NOAEL * = 250	Decreased pup body weights on PND 14 (F ₂ females)	260	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Developmental Effects	Rat (male) (n=15- 22/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₂	BMCL ₅ = 136 (BMCL _{1SD} =290)	Decreased pup body weights on PND 14 (F ₂ males)	300	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Developmental Effects	Rat (female) (n=15- 22/group)	100 to 500	6 hours/day during gestation until GD 20 and from PND 5 until weaning (~PND 21) for F ₂	BMCL ₅ = 148 (BMCL _{1SD} =300)	Decreased pup body weights on PND 21 (F ₂ females)	320	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)
Nervous System	Rat (male) (n=5/group)	10 to 1000	8 hours/day, 7 days/week for 3 weeks	BMCL _{1SD} = 18	Decreased time hanging from a suspended bar (traction time)	25	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(Honma et al., 2003)	High (1.6)
Nervous System	Rat (male) (n=25/group)	100 to 750	6 hours/day during pre-mating, throughout mating, and until GD 20 (≥ 16 weeks)	NOAEL * = 100	Decreased brain weight in F ₀ males	110	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)

Target Organ/System	Species, sex (#animals/dose)	Range of Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC (ppm) ⁴	Uncertainty Factors (UFs) for Benchmark MOE ⁵	Reference	Data Quality Ranking ⁷
Nervous System	Rat (male) (n=8-9/group)	200 to 800	8 hours/day, 7 days/week for 12 weeks	BMCL _{1SD} = 147	Decreased hind limb grip strength	206	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(Ichihara et al., 2000a)	High (1.3)
Nervous System	Rat (female) (n=25/group)	100 to 750	6 hours/day during pre-mating, throughout mating, and until GD 20 (≥ 16 weeks)	BMCL ₅ = 584 (BMCL _{1SD} = 509)	Decreased brain weight in F ₀ females	610	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.3)

¹Control concentrations are not included in the table.

² Acute exposures defined as those occurring within a single day. Chronic exposures defined as 10% or more of a lifetime ([U.S. EPA, 2011](#)).

³POD type can be NOAEL, LOAEL, or BMCL. For BMCLs, the subscript indicates the associated BMR. The BMRs are a percentage relative deviation (e.g., 10% relative deviation BMCL₁₀) or 1 standard deviation change (BMCL_{1SD}) from the mean for continuous data. Post-implantation loss was modeled with nested modeling to account for intra-litter correlations and litter-specific covariates. The dam weight litter specific covariate and without intra-litter correlations for the NLogistic model was the selected model based on lowest AICs and lowest BMCL.

⁴HECs are calculated by duration adjustment and a human equivalent DAF. The adjusted POD is the POD x duration adjustment. The HEC_{EXRESP} = adjusted POD × DAF where the DAF is the ratio of blood:gas partition coefficients (animal:human). For 1-BP, the blood:air partition coefficient for rats is greater than that for humans, so a default ratio of 1 is applied ([U.S. EPA, 1994](#)). The baseline used for the duration adjustment was an 8 hours/day exposure for occupational exposure scenarios and 24 hours/day exposure for consumer exposure scenarios. For acute exposure the duration adjustment was (hours per day exposed ÷ 8) and for chronic exposure (occupational scenarios) was (hours per day exposed ÷ 8) × (days per week exposed ÷ 5) to reflect a 40-hour work week. All of the endpoints used the chronic exposure duration adjustment except for the decreased live litter size (F₁) at PND 0 and post implantation loss as described above in Section 3.2.8.1. HECs are rounded to two significant digits.

⁵UF_S = subchronic to chronic UF (default value = 10); UF_A = interspecies UF (default value of 10); UF_H = intraspecies UF (default value = 10); UF_L = LOAEL to NOAEL UF (default value = 10) ([U.S. EPA, 2002](#)). Rationale for selection of specific UF values used to calculate the benchmark MOE for the key studies used in risk is presented in Section 4.2.1. Narratives explaining overall UF determinations are provided in Section 3.2.8.1.

⁶The HEC for decreased live litter size and post-implantation loss were adjusted for acute and chronic occupational exposures as described in footnote 4.

* BMD modeling did not adequately fit the variance in the data so the NOAEL or LOAEL is presented.

⁷ Data Quality Criteria Ranking: High >= 1 and < 1.7; Medium >= 1.7 and < 2.3; Low >=2.3 and <=3; The numbers in parentheses reflect the score associated with the ranking. Lower scores reflect higher quality studies. Higher scores, reflect lower quality studies.

3.2.8.2 Selection of Studies for Carcinogenic Dose-Response Assessment

No data were located on the carcinogenicity of 1-BP in humans. In animals, the carcinogenicity of 1-BP was evaluated in well-designed studies conducted in rodents ([NTP, 2011a](#)). Male and female rats and mice were exposed to 1-BP via whole-body inhalation 6 hours/day, 5 days/week for 2 years. Cancer findings included significant increases in the incidences of: 1) skin tumors (keratoacanthoma/squamous cell carcinomas) in male F344 rats, 2) rare large intestine adenomas in female F344 rats, and 3) alveolar/bronchiolar adenomas and carcinomas (combined) in female B6C3F1 mice.

3.2.8.2.1 Cancer Dose-Response Modeling

Benchmark dose-response modeling of the ([NTP, 2011a](#)) cancer data was performed for all three statistically significantly increased tumor types from the NTP study (*i.e.*, skin tumors in male rats, intestinal tumors in female rats, and lung tumors in female mice). A brief summary of the methodology is presented here and more details are available in the *Supplemental File: Information on Human Health Benchmark Dose Modeling* ([EPA, 2019d](#)). Three approaches were applied; multistage modeling, frequentist model-averaging and Bayesian model averaging. The three approaches include the approach under EPA's 2005 cancer guidelines (*i.e.*, multistage modeling) and two model averaging methods. The model averaging methods allow for an assessment of model uncertainty as described further below. Two options for BMR (0.1% and 10%) added or extra risk were both modeled for comparison with EPA's 2005 cancer guidelines and comparison with the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016c](#)) and the 2016 NIOSH draft criteria document.

In agreement with EPA's long-standing approach, all three tumor types from the NTP study ([NTP, 2011a](#)) were modeled with the cancer model in EPA's BMDS ([U.S. EPA, 2012a](#)). EPA prefers to use the multistage model with constrained model coefficients ≥ 0 for dose-response modeling of cancer bioassay data. The multistage model is a family of different stage polynomial models. The multistage model is preferred because it is sufficiently flexible for most cancer bioassay data, and its use provides consistency across cancer dose-response analyses. There is precedent and some biological support for use of multistage models for cancer. Under U.S. EPA's 2005 cancer guidelines ([U.S. EPA, 2005a](#)), quantitative risk estimates from cancer bioassay data were calculated by modeling the data in the observed range to estimate a BMCL for a BMR of 10% extra risk, which is generally near the low end of the observable range for standard cancer bioassay data. The BMCs and BMCLs are shown in Table 3-3 in the Multistage columns for each of the three cancer datasets. Also, the results for a BMR of 0.1% added risk are presented for comparison.

In addition to the multistage modeling, model averaging methods were applied, frequentist ([Wheeler and Bailer, 2007](#)) and Bayesian (USEPA 2018 [BMDS](#) software) to assess the impact of model uncertainty. In the [2016 Draft Risk Assessment](#) ([U.S. EPA, 2016c](#)), all dichotomous models in the BMD software (gamma, logistic, log-logistic, multistage, probit, log-probit, quantal-linear, and Weibull in [BMDS](#) Version 2.6) were fit to the incidence data for each of the three tumor types. The benchmark response level (BMR) used was 0.1% added risk (corresponding to a 1-in-1,000 working lifetime added risk of cancer) consistent with the 2016 NIOSH draft criteria document. A

model-averaging (MA) technique ([Wheeler and Bailer, 2007](#)) was applied using 3 models that performed better in bias and coverage than other combinations of models (the multistage, log-probit and Weibull models) and applied statistics (bootstrapping technique) to weigh, based on fit, the models providing acceptable fit to the experimental dataset ([Wheeler and Bailer, 2007](#)). Model-averaging software was restricted to avoid supralinear models, which exhibit properties at the low dose that are not considered biologically plausible. The resulting model-average benchmark concentrations (MA BMCs) associated with 0.1% added risk and their 95% lower confidence limits (MA BMCLs) are shown in Table 3-3 in the Frequentist Model-Average (BMDS 2.6) column for each of the three cancer datasets.

Since the 2016 Draft Risk Assessment ([U.S. EPA, 2016c](#)), EPA has conducted an additional third type of modeling, using the BMDS (Version 3.0) and more details are available in the *Supplemental File: Information on Human Health Benchmark Dose Modeling* ([EPA, 2019d](#)). In this third modeling approach all dichotomous frequentist and Bayesian³³ models in the BMD software (BMDS Version 3.0), were fit to the incidence data for each of the three tumor types and the Bayesian model averaging approach was applied (see the for more description [BMDS 3.0 User Guide](#)). To compare with the modeling in the 2016 Draft Risk Assessment ([U.S. EPA, 2016c](#)) which used 0.1% added risk (AR), in this modeling used BMR levels of 0.1% and 10% added and extra risk (ER). The BMR of 10% ER which is generally near the low end of the observable range for standard cancer bioassay data is the approach under EPA’s 2005 cancer guidelines. The resulting model-average benchmark concentrations (MA BMCs) associated with 0.1% added risk (AR) and 10% extra risk (ER) and their 95% lower confidence limits (BMCLs), are shown in Table 3-3 in the Bayesian Model-Average (BMDS 3.0) column for each of the three cancer datasets.

Table 3-3. MultiStage Model, Model-Average (BMDS Version 2.6), and Model-Average (BMDS Version 3.0) BMC and BMCL Estimates of 1-BP Inhalation Exposure Associated with a 0.1% Added Risk and 10% Extra Risk of Tumors in Rodents

		Multistage Model		Frequentist Model-Average (BMDS 2.6)		Bayesian Model-Average (BMDS 3.0)	
Species; Tumor Type	BMR	BMC (ppm) ¹	BMCL (ppm) ¹	BMC (ppm)	BMCL (ppm)	BMC (ppm)	BMCL (ppm)
Male F344 rats; keratoacanthoma/squamous cell carcinoma (combined)	0.1% AR	2.96	1.78	3.73	2.25	9.81	1.47
	10% ER	303.8	185.2	--	--	433.5	220.6
Female F344 rats; large intestine adenoma	0.1% AR	5.27	3.10	13.5	4.85	23.8	7.98
	10% ER	555.3	326.7	--	--	601.5	392.4
	0.1% AR	0.77	0.52	0.85	0.64	1.51	0.085

³³ The Bayesian dichotomous models used in BMDS 3.0 are identical to the frequentist parametric models but incorporate prior information (e.g., parameter distributions) that is used in the model fit (cite BMDS 3.0 User Guide for details; <https://www.epa.gov/bmds/benchmark-dose-software-bmds-version-30-user-guide-readme>).

Female B6C3F1 mice; alveolar/bronchiolar adenoma or carcinoma (combined)	10% ER	78.6	54.1	--	--	104.6	39.4
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¹ First degree Multistage model was selected for all tumor datasets.

Extrapolation to Humans

The human equivalent values shown in Table 3-4 and Table 3-5 are extrapolated from the BMC and BMCL results to generate the target response in rodents exposed 6 hours/day for 5 days/week. The BMC and BMCL values are extrapolated to BMC_{HEC} and BMCL_{HEC} and shown in Table 3-4 based on occupational inhalation exposure to 1-BP during a 40-hour work week (8 hours/day, 5 days/week) or continuous 24 hours/day and 7 days/week. The dermal BMD_{HED} and BMDL_{HED} from the BMC and BMCL values are shown in Table 3-5.

These data were extrapolated to humans based on occupational exposure to 1-BP during a 40-hour work week (8 hours/day, 5 days/week) using the following methodology:

1. Conversion of BMC/BMCLs (ppm) to benchmark dose values (BMD/BMDL in mg/kg-day) by adjusting for the animal breathing rate and experimental exposure duration 6 hours/day³⁴;
2. Conversion of BMD/BMDLs in rodents to human equivalent BMD/BMDLs on the basis of the mg/kg-day dose scaled by body weight to the 0.75 power³⁵ and assuming dermal absorption is equivalent to inhalation absorption the BMD is the dermal HED; and
3. Adjustment of the human equivalent BMD/BMDLs (mg/kg-day) to BMC/BMCLs (ppm) that reflect exposure for either an 8-hour work day or 24-hour continuous exposure³⁶.

The human equivalent BMC and BMCL (BMC_{HEC} and BMCL_{HEC}) estimates using all three modeling approaches are shown in Table 3-4. Three combinations of modeling inputs are shown - the multistage BMR 10% extra risk (ER) *i.e.*, the approach under EPA's 2005 cancer guidelines, frequentist model averaging BMR 0.1% added risk for comparison with the [2016 Draft Risk Assessment \(U.S. EPA, 2016c\)](#) and the 2016 NIOSH draft criteria document and Bayesian Model

³⁴BMD/BMDL (mg/kg-day) = BMC/BMCL (ppm) x (6 hours/24 hours) x (5.031 mg/m³ per ppm) x default inhalation rate (m³/day) ÷ default body weight (kg); where the default inhalation rate and body weight values are 0.36 m³/day and 0.380 kg for male F344 rats, 0.24 m³/day and 0.229 kg for female F344 rats, and 0.06 m³/day and 0.0353 kg for female B6C3F1 mice in chronic studies ([U.S. EPA, 1988](#)).

³⁵Human equivalent BMD/BMDL (mg/kg-day) = BMC/BMCL (mg/kg-day) x default body weight in rats or mice [kg] x (default body weight in humans [kg] ÷ default body weight in rats or mice [kg])^{0.75} ÷ default body weight in humans [kg]; where default body weight values are 0.380 kg for male F344 rats, 0.229 kg for female F344 rats, 0.0353 kg for female B6C3F1 mice, and 70 kg for humans ([U.S. EPA, 1988](#); [ICRP, 1975](#)).

³⁶BMC/BMCL (ppm) = (1 ppm per 5.031 mg/m³) x (default body weight in humans [kg]/default minute volume for human occupational exposure based on an 8-hour shift [m³/day] or a continuous exposure for 24-hours); where default body weight and minute volume values are 70 kg and 9.6 m³/8-hr day or 15 m³/24-hr day ([U.S. EPA, 1994](#)).

averaging BMR 10% ER as the latest modeling approach in BMDS. Since these BMCLs are for different BMRs they are not directly comparable.

Table 3-4. BMC_{HEC} and BMCL_{HEC} Estimates of 1-BP Inhalation Exposures in Humans Exposed 40 hours/week (8 hours/day, 5 days/week) (ppm) or 24 hrs/day 7 days/week (ppm)

		Multistage Model BMR 10% ER		Frequentist Model- Average (BMDS 2.6) BMR 0.1% AR		Bayesian Model- Average (BMDS 3.0) BMR 10% ER	
Species; Tumor Type	Exposure duration	BMC _{HEC} (ppm)	BMCL _{HEC} (ppm)	BMC _{HEC} (ppm)	BMCL _{HEC} (ppm)	BMC _{HEC} (ppm)	BMCL _{HEC} (ppm)
Male F344 rats; keratoacanthoma/squamous cell carcinoma (combined)	40 hrs/wk	141	86	1.73	1.04	200	102
	24 hrs/day	90	55	1.01	0.67	128	65
Female F344 rats; large intestine adenoma	40 hrs/wk	254	149	6.17	2.22	275	179
	24 hrs/day	162	96	3.95	1.42	176	115
Female B6C3F1 mice; alveolar/bronchiolar adenoma or carcinoma (combined)	40 hrs/wk	36	25	0.39	0.30	49	18
	24 hrs/day	23	16	0.25	0.19	31	12

Table 3-5. BMD_{HED} and BMDL_{HED} Estimates of 1-BP Dermal Exposures Extrapolated from BMC and BMCL (mg/kg-day)

		Multistage Model BMR 10% ER		Frequentist Model- Average (BMDS 2.6) BMR 0.1% AR		Bayesian Model- Average (BMDS 3.0) BMR 10% ER	
Species; Tumor Type		BMD _{HED} (mg/kg/d)	BMDL _{HED} (mg/kg/d)	BMD _{HED} (mg/kg/d)	BMDL _{HED} (mg/kg/d)	BMD _{HED} (mg/kg/d)	BMDL _{HED} (mg/kg/d)
Male F344 rats; keratoacanthoma/squamous cell carcinoma (combined)		97	59	1.19	0.72	138	70
Female F344 rats; large intestine adenoma		175	103	4.26	1.53	190	124
Female B6C3F1 mice; alveolar/bronchiolar adenoma or carcinoma (combined)		25	17	0.27	0.21	34	13

Derivation of Inhalation Unit Risk Applying Age-Dependent Adjustment Factors (ADAFs)

Using the mode of action framework, age-dependent adjustment factors (ADAFs) are applied when developing cancer risk estimates when early-life susceptibility is assumed (ages 0-15) and when there is evidence of a MMOA in animal studies (EPA’s Guidelines for Carcinogen Risk Assessment ([U.S. EPA, 2005a](#)); Supplemental Guidance for Assessing Susceptibility from Early Life Exposure to Carcinogens ([U.S. EPA, 2005b](#))). For 1-BP, the weight of the scientific evidence is suggestive but inconclusive that 1-BP is carcinogenic by a MMOA (see Appendix K); and early-

life chronic exposure scenarios are assumed only for the inhalation route, and only for occupational scenarios for worker populations. ADAFs were not applied for any occupational scenarios in this risk evaluation because there is insufficient evidence to definitively conclude that 1-BP is carcinogenic by a MMOA and because worker populations are considered to be 16 years of age and older, ages not covered by the ADAF application guidance ([U.S. EPA, 2005b](#)). ADAFs also were not applied for younger-aged children spending time in the workplace (*e.g.*, family owned businesses) because a MMOA has not been established and because it is unlikely their exposures are chronic in nature.

Derivation of Inhalation Unit Risk and Dermal Slope Factor

The data for lung tumors based on the combined incidence of alveolar/bronchiolar adenoma or carcinoma in female mice (as shown in Section 3.2.8.2) was selected for derivation of the inhalation unit risk (IUR) and for the dermal slope factor. This POD is considered protective for the other tumor types. The BMCL_{HEC} values for both a 40 hours/week (8 hours/day, 5 days/week; and 24 hours/day) using all three modeling approaches (Multistage modeling and both Model Averaging approaches Frequentist Version 2.6 and Bayesian Version 3.0) are depicted in Table 3-6. These BMCL_{HEC} values represent the 95% lower confidence limit estimate of the occupational exposure concentration expected to produce a 1-in-10 (*i.e.*, 10% BMR) or 1-in-1,000 (*i.e.*, 0.1% BMR) lifetime extra (ER) or added risk (AR) of lung cancer, due to the different BMR values they are not directly comparable. The BMCL values were selected as the POD for the inhalation unit risk (IUR) value and the dermal slope factor because they reflect the statistical variability of the data and in consistent with EPA BMD Guidance ([U.S. EPA, 2012a](#)). Although data suggest a MMOA, the exact mode of action of 1-BP-induced tumorigenesis is not known. In the absence of more definitive knowledge regarding the MOA of 1-BP, the inhalation unit risk and dermal slope factor were calculated using the default linear approach *i.e.*, $IUR = BMR \div BMCL$ and rounded to 1 significant figure. The IURs are shown in Table 3-6 and the dermal cancer slope factors are shown in Table 3-7. While the BMCLs are not directly comparable because of different BMRs the IUR incorporate the BMR and can be compared.

Table 3-6. Inhalation Unit Risk (IUR) for Humans Exposed via Inhalation Based on Combined Alveolar/Bronchiolar Adenomas or Carcinomas Observed in Female Mice

Modeling Approach	BMR	BMCL _{HEC} (ppm)	IUR (per ppm)	IUR (per µg/m ³)
Human Exposures 40 hours/week (8 hours/day, 5 days/week)				
Multistage Model, ER	10%	25	4 x 10 ⁻³	8 x 10 ⁻⁷
Frequentist Model-Averaging, Version 2.6, AR	0.1%	0.3	3 x 10 ⁻³	7 x 10 ⁻⁷
Bayesian Model-Averaging, Version 3.0, ER	10%	18	6 x 10 ⁻³	1 x 10 ⁻⁶
Human Exposures 24 hours/day				
Multistage Model, ER	10%	16	6 x 10 ⁻³	1 x 10 ⁻⁶
Frequentist Model-Averaging, Version 2.6, AR	0.1%	0.19	5 x 10 ⁻³	1 x 10 ⁻⁶
Bayesian Model-Averaging, Version 3.0, ER	10%	12	9 x 10 ⁻³	2 x 10 ⁻⁶

Table 3-7. Cancer Slope Factor for Humans Exposed via Dermal Contact Extrapolated from Combined Alveolar/Bronchiolar Adenomas or Carcinomas Observed in Female Mice

Modeling Approach	BMR	BMDL _{HED} (mg/kg-day)	Slope Factor (per mg/kg-day)
Multistage Model, ER	10%	17	6 x 10 ⁻³
Frequentist Model-Averaging, Version 2.6, AR	0.1%	0.21	5 x 10 ⁻³
Bayesian Model-Averaging, Version 3.0, ER	10%	13	8 x 10 ⁻³

Overall, the IURs and dermal slope factors calculated by all three modeling approaches (Multistage modeling and both Model Averaging approaches Frequentist Version 2.6 and Bayesian Version 3.0) are nearly the same. The model averaging approaches can be used to assess the impact of model uncertainty and the similar results suggest model uncertainty is not significantly impacting the IUR or the slope factor. Therefore the IURs and cancer slope factor using the multistage modeling are used in cancer risk estimate calculations below consistent with EPA guidance EPA’s Guidelines for Carcinogen Risk Assessment ([U.S. EPA, 2005a](#)).

The IUR and dermal slope factor were used in EPA’s risk evaluation to estimate extra cancer risks for the inhalation and dermal occupational exposure scenarios. There is high confidence in the IUR and the dermal slope factor because they were based on high quality animal data. EPA did not use the IUR or dermal slope factor to calculate the theoretical cancer risk associated with a single (acute) inhalation/or dermal exposure to 1-BP. Published methodology for extrapolating cancer risks from chronic to short-term exposures includes the caveat that extrapolation of lifetime theoretical extra cancer risks to single exposures has great uncertainties ([NRC, 2001](#)).

As [NRC \(2001\)](#) explains, “There are no adopted state or federal regulatory methodologies for deriving short-term exposure standards for workplace or ambient air based on carcinogenic risk, because nearly all carcinogenicity studies in animals and retrospective epidemiologic studies have entailed high-dose, long-term exposures. As a result, there is uncertainty regarding the extrapolation from continuous lifetime studies in animals to the case of once-in-a-lifetime human exposures. This is particularly problematical, because the specific biologic mechanisms at the molecular, cellular, and tissue levels leading to cancer are often exceedingly diverse, complex, or not known. It is also possible that the mechanisms of injury of brief, high-dose exposures will often differ from those following long-term exposures. To date, U.S. federal regulatory agencies have not established regulatory standards based on, or applicable to, less than lifetime exposures to carcinogenic substances.”

Thus, EPA risk evaluation for 1-BP does not estimate extra cancer risks for acute exposures because the relationship between a single short-term exposure to 1-BP and the induction of cancer in humans has not been established in the current scientific literature.

3.2.8.3 Potentially Exposed or Susceptible Subpopulations

Factors affecting susceptibility examined in the available studies on 1-BP include lifestage, gender, genetic polymorphisms, race/ethnicity, preexisting health status, lifestyle factors, and nutrition

status. The PECO statement in the problem formulation in June, 2018 ([U.S. EPA, 2018c](#)) includes “potentially exposed or susceptible subpopulations such as infants, children, pregnant women, lactating women, women of child bearing age” as “subpopulations” for the 1-BP Risk Evaluation. These susceptible subpopulations were considered against the available 1-BP specific data. Women of reproductive age, pregnant women and their offspring (fetal and postnatal) were identified as susceptible subpopulations based on the non-cancer effects associated with 1-BP exposure in rodent studies ([WIL Research, 2001](#)). A prenatal developmental toxicity study and a two-generation reproductive toxicity study in rats exposed to 1-BP via the inhalation route reported decreased live litter size ([WIL Research, 2001](#)), postnatal survival ([Furuhashi et al., 2006](#)), pup body weight, brain weight and skeletal development ([Huntingdon Life Sciences, 1999](#)), ([Huntingdon Life Sciences, 2001](#)); ([WIL Research, 2001](#)). No epidemiological studies on the developmental effects of 1-BP exposure were identified in the literature. Since effects were observed in animals after gestational and postnatal exposure, pregnant women, and their offspring were identified as susceptible subpopulations; however, there is some uncertainty about the critical window for increased susceptibility to 1-BP exposure.

Other data on the noncancer effects of 1-BP exposure were reviewed to identify potential susceptible subpopulations. A two-generation reproduction study in rats reported adverse effects on male and female reproductive parameters ([WIL Research, 2001](#)) such as, significant increases in post-implantation loss (pre-implantation loss could not be determined because of a lack of data on the number of primordial follicles), reduced fertility in F0 females, and decreased mating indices, and increased estrous cycle length and pregnancy loss. In F0 males, statistically significant changes in reproductive endpoints included decreased absolute prostate and epididymal weights, decreased sperm motility, and decreased mating and fertility indices ([WIL Research, 2001](#)). These findings are supported by other studies ([NTP, 2011b](#); [Qin et al., 2010](#); [Liu et al., 2009](#); [Yu et al., 2008](#); [Banu et al., 2007](#); [Yamada et al., 2003](#); [WIL Research, 2001](#); [Ichihara et al., 2000a](#)), suggesting that males of reproductive age represent another susceptible subpopulation for 1-BP exposure.

The primary metabolic pathways identified for 1-BP involve cytochrome P450 mediated oxidation (CYP2E1) and glutathione conjugation reactions. Genetic polymorphisms and interindividual variability in the expression and function of CYP2E1 have been linked to altered disease susceptibility ([Neafsey et al., 2009](#)) ([Trafalis et al., 2010](#)). Although there are uncertainties in the available data, chronic exposure to CYP2E1 inducers (*e.g.*, ethanol, isoniazid), may increase the probability of developing malignancy, especially for carriers of certain CYP2E1 alleles ([Trafalis et al., 2010](#)). Pre-existing health conditions, including alcoholism and diabetes also induce CYP2E1 activity, thereby enhancing susceptibility to the adverse effects of 1-BP exposure.

Additional susceptibility factors not explicitly quantified in the hazard assessment are expected to be accounted for through the use of a 10x UF to account for human variability, although EPA acknowledges that certain subpopulations with particular disease states or genetic predispositions may fall outside of the range covered by this UF. EPA can also not rule out that certain subpopulations, whether due to very elevated exposure or biological susceptibility, may be at risk for hazards that were not fully supported by the weight of the scientific evidence or could not be quantified (*e.g.*, immune and blood effects). However, in these circumstances, EPA assumes that

these effects are unlikely to occur at a lower dose than those more robust and sensitive endpoints that underwent dose response analysis.

3.2.8.4 Points of Departure for Human Health Hazard Endpoints

Table 3-2 summarizes the hazard studies, health endpoints (PODs) by target organ/system, HECs and UFs that are relevant for the risk evaluation of acute and chronic exposure scenarios. Table 3-8 lists the selected HECs/dermal HEDs by study type and duration category (acute vs. chronic) carried forward for risk estimation. 0 contains a comprehensive summary table of adverse effects.

Inhalation HECs were converted to dermal HEDs using the following equation:

$$\text{Dermal HED (mg/kg-day)} = \text{inhalation POD (ppm)} \times 5.031 \text{ mg/m}^3 / \text{ppm} \times \text{duration adjustment} \times \text{ventilation rate (m}^3) \div \text{body weight (kg)}$$

where the inhalation HEC used was for a 40 hr work week (8 hrs / day, 5 days / week), the duration adjustment was (6 hours / 8 hours \times 7 days / 5 days) to account for differences between animal exposure durations and expected human exposure durations, ventilation rate was 10 m³ (*i.e.*, 1.25 m³ per hour for 8 hours) and the body weight was 80 kg. The dermal exposure estimates account for the fraction of 1-BP that is absorbed (see Section 2.3.1.23), therefore, an absorption adjustment is not applied in the route-to-route extrapolation.

Table 3-8. HECs/Dermal HEDs Selected for Non-Cancer Effects for 1-BP

Exposure Duration for Risk Analysis	Target Organ/System	Species	Route of Exposure	Range of Doses or Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC ⁴ Occupational (ppm)	HEC ⁵ Consumers (ppm)	Dermal HED (mg/kg-day) ⁶	Uncertainty Factors (UFs) for Benchmark MOE ⁷	Reference	Data Quality Ranking ⁸
CHRONIC OCCUPATIONAL & CONSUMER	Liver	Rat (male) (n=25/group)	Inhalation	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice	BMCL ₁₀ = 143.5	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	150	36	95	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
	Kidney	Rat (female) (n=25/group)	Inhalation	100 to 750	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	BMCL ₁₀ = 174	Increased incidence of pelvic mineralization (F ₀)	180	44	115	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
	Reproductive System	Rat (male) (n=8-9)/group	Inhalation	200 to 800	8 hours/day, 7 days/week for 12 weeks	BMCL _{1SD} = 38	Decreased absolute/relative seminal vesicle weight	53	13	33	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(Ichihara et al., 2000b)	High (1.7)
	Developmental Effects (BMDS nested dichotomous model, NLogistic)	Rat (n=25/group)	Inhalation	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20 for the F ₁ litters	BMCL ₁ = 23	Post-implantation loss in F ₀ females	17	6	15	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
	Developmental Effects (BMD modeling)	Rat (n=25/group)	Inhalation	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until GD 20 for the F ₁ litters	BMCL ₅ = 41	Decreased live litter size (F ₁) at PND 0	31	10	27	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)

	Nervous System	Rat (male) (n=5/group)	Inhalation	10 to 1000	8 hours/day, 7 days/week for 3 weeks	BMCL _{1SD} = 18.2	Decreased time hanging from a suspended bar (traction time)	25	6	16	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(Honma et al., 2003)	High (1.6)
Exposure Duration for Risk Analysis	Target Organ/System	Species	Route of Exposure	Range of Doses or Conc. ¹ (ppm)	Duration ²	POD Type (ppm) ³	Effect	HEC ⁴ Occupational (ppm)	HEC ⁵ Consumer (ppm)	Dermal HED (mg/kg-day) ⁶	Uncertainty Factors (UFs) for Benchmark MOE ⁷	Reference	Data Quality Ranking ⁸
ACUTE OCCUPATIONAL & CONSUMER	Developmental Effects (BMDS nested dichotomous model, NLogistic)	Rat (male) (n=24-25/group)	Inhalation	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until 27weaning of offspring (~PND 21) in females	BMCL ₁ = 23	Post-implantation loss in F ₀ females	17	6	11	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)
	Developmental Effects (BMD modeling)	Rat (male) (n=24-25/group)	Inhalation	100 to 500	6 hours/day during pre-mating (≥ 70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	BMCL ₅ = 41	Decreased live litter size (F ₁)	31	10	19	UF _S =1; UF _A =10; UF _H =10; UF _L =1; Total UF=100	(WIL Research, 2001)	High (1.2)

¹Control concentrations are not included in the table.

² Acute exposures defined as those occurring within a single day. Chronic exposures defined as 10% or more of a lifetime ([U.S. EPA, 2011](#)).

³POD type can be NOAEL, LOAEL, or BMCL. For BMCLs, the subscript indicates the associated BMR. The BMRs are a percentage relative deviation (e.g., 10% relative deviation BMCL₁₀) or 1 standard deviation change (BMCL_{1SD}) from the mean for continuous data. Post-implantation loss was modeled using the NLogistic model.

⁴ HECs/dermal HEDs are adjusted from the study conditions by the equation $HEC_{EXRESP} = POD \times \text{duration adjustment} \times DAF$. The DAF is the ratio of blood:gas partition coefficients (animal:human). For 1-BP, the blood:air partition coefficient for rats is greater than that for humans, so a default ratio of 1 is applied ([U.S. EPA, 1994](#)). For chronic exposure the duration adjustment was $(\text{hours per day exposed} \div 8) \times (\text{days per week exposed} \div 5)$ to reflect a 40-hour work week and for acute exposure the duration adjustment was $(\text{hours per day exposed} \div 8)$. All endpoints used the chronic exposure duration adjustment except for the acute developmental endpoints of decreased live litter size (F₁) at PND 0 and post-implantation loss as described above in Section 3.2.8.1. The differences in the HECs between the

occupational and consumer exposures are due to the baseline used for the duration adjustment of acute occupational and consumer exposures; occupational exposures was 8 hours/day, and consumer exposures was 24 hours/day (see next footnote). HECs/dermal HEDs are rounded to two significant digits.

⁵HEC for chronic consumer exposures is adjusted to 24 hours per day, 7 days per week and HEC for acute consumer exposures is adjusted to 24 hours per day.

⁶The dermal HEDs for dermal exposures were extrapolated from the inhalation PODs in mg/kg-day using a duration adjustment, human ventilation rate and human body weight.

⁷UF_S = subchronic to chronic UF (default value = 10); UF_A = interspecies UF (default value of 10); UF_H = intraspecies UF (default value = 10); UF_L = LOAEL to NOAEL UF (default value = 10) ([U.S. EPA, 2002](#)). Rationale for selection of specific UF values used to calculate the benchmark MOE for the key studies used in risk is presented in Section 4.2.1. Narratives explaining overall UF determinations are provided in Section 3.2.8.1.

* BMD modeling did not adequately fit the variance in the data so the LOAEL is presented

⁸Data Quality Criteria Ranking: High >= 1 and < 1.7; Medium >= 1.7 and < 2.3; Low >=2.3 and <=3; The numbers in parentheses reflect the score associated with the ranking. Lower scores reflect higher quality studies. Higher scores, reflect lower quality studies.

3.2.8.5 Strength, Limitation, and Uncertainty of the Hazard Identification and Selection of PODs for Dose-Response Assessment

Limited toxicological data is available by the oral route, and no repeated-dose toxicity studies by the dermal route were identified on 1-BP. Although the oral repeated-dose toxicity studies are insufficient for a quantitative dose-response assessment, data from these studies were used as qualitative support in the weight of the scientific evidence for nervous system effects (see Section 3.2.5.5 and Appendix J), suggesting that, at least for the nervous system endpoints, the delivery of 1-BP via the inhalation- (*i.e.*, pulmonary/systemic circulation) and oral- (*i.e.*, portal circulation) routes of exposure results in comparable toxic endpoints. EPA chose to derive dermal HEDs for dermal exposures by extrapolating from the inhalation route for systemic endpoints (*i.e.*, not point of contact effects). None of the key endpoints for 1-BP (liver, kidney, reproductive, developmental and nervous system effects) were considered point of contact therefore, all were used for route-to-route extrapolation. The route-to-route extrapolations enabled EPA to estimate applied dermal PODs. Since physiologically based pharmacokinetic/ pharmacodynamic (PBPK/PD) models that would facilitate route-to-route extrapolation have not been identified, there is no relevant kinetic or metabolic information for 1-BP that would facilitate development of dosimetric comparisons, and the studies by the oral route were insufficient for quantitative dose-response assessment, EPA chose to derive dermal HEDs for dermal exposures by extrapolating from the inhalation PODs. However, the inhalation studies were performed by whole body exposure, rather than nose only exposure, which may have led to additional dosing by the oral and dermal routes of exposure, due to deposition on fur and the grooming behavior of rodents, resulting in uncertainty of actual dose received. It should be noted that EPA was unable to conclude with certainty that comparable toxic endpoints would be associated with the dermal route of exposure, considering the expected quantitative ADME differences and the absence of an adequate PBPK model. Notwithstanding these uncertainties, EPA considered this approach appropriate considering the comparable toxic endpoints identified in the available repeated-dose oral/inhalation toxicity studies and the uncertainty with the putative toxicant (*i.e.*, 1-BP or a metabolite(s)).

Overall there is high confidence in all endpoints selected as PODs for both acute and chronic exposure. Endpoints selected for PODs for both acute and chronic exposure scenarios were derived from three studies, ([WIL Research, 2001](#)), ([Ichihara et al., 2000b](#)), and ([Honma et al., 2003](#)). These studies were selected because they all scored High in data evaluation, followed OECD guidance and Good Laboratory Practice, and were of longer duration with effects observed more consistently than other high-quality studies that were evaluated. In addition, these endpoints were identified as the most robust and sensitive endpoints relevant to acute and chronic exposures and were incidentally, also the lowest available PODs. The NOAEC or LOAECs from these studies were refined with BMD modeling in order to obtain more precise POD values that were used to derive corresponding HECs/dermal HEDs and uncertainty factors. BMD modeling results always contain some level of uncertainty, and various factors such as model fit and BMR selection may have a large effect on the final POD value. The PODs from all three studies could be fit into BMD modeling, thereby reducing the uncertainty factors (*i.e.*, $UF_L = 1$) used in deriving the benchmark MOE. EPA believes that the selected PODs best represent the hazards associated with 1-BP for quantitative risk estimation.

EPA considers some developmental toxicity endpoints observed in a repeat dose developmental toxicity study applicable to acute exposures. While there is some uncertainty surrounding this consideration because the precise critical exposure window is unknown, multiple publications suggest that some developmental effects (*e.g.*, decreased live litter size and increased post-implantation loss) may result from a single exposure during a critical window of development. In this risk evaluation, effects following acute exposures to 1-BP included decreased live litter size and increased post implantation loss ([WIL Research, 2001](#)). These specific developmental effects were considered the most sensitive HECs/dermal HEDs derived for an acute exposure duration, and are considered to be biologically relevant to the potentially exposed or susceptible subpopulation (*i.e.*, adults of reproductive age and their offspring). Further support for using this endpoint for acute (short-term) exposures is the fact that the male and female reproductive effects (in the F₀ males and females) collectively contributing to the decreases in live litter size, all occurred within a short window of exposure between ovulation and implantation. While exposures during other lifestages (such as in childhood) may cause similar or related effects, without specific information on the mechanism of action or developmental windows of sensitivity for these specific developmental effects, there are uncertainties in extrapolating these effects for other lifestages in order to refine dose estimates for these additional lifestages.

4 RISK CHARACTERIZATION

4.1 Environmental Risk

EPA integrated relevant pathways of environmental exposure with available environmental hazard data to estimate risk to environmental receptors. EPA used estimated exposure values calculated from E-FAST and monitored data from TRI, as well as aquatic hazard values based on reasonably available hazard data to perform a quantitative screening-level determination of risks to aquatic species from acute and chronic exposures to 1-BP using the RQ method. EPA's approach is expected to represent a high-end estimate of aquatic exposure.

High volatility (Vapor Pressure= 110 mm Hg and Henry's Law constant of 7.3×10^{-3} atm- m^3 /mole), and a consideration of the conditions of use of the chemical, indicates that 1-BP will only be present in terrestrial environmental compartments as a transient vapor. No specific conditions of use were identified that resulted in systematic, significant airborne exposures that overlap with terrestrial habitats, so this is not a relevant route of exposure for 1-BP under the conditions of use of this risk evaluation. Additionally, 1-BP is not expected to bioaccumulate (BAF=12; BCF=11, see Table 2-1); therefore, exposure to terrestrial species through ingestion of prey is negligible. No further analysis of risks to terrestrial receptors was carried out as part of this final risk evaluation as risks from these exposure pathways are not expected.

4.1.1 Aquatic Pathways

The purpose of the environmental risk characterization is to discuss whether there are exceedances of the concentrations of concern for the aquatic environment from levels of 1-BP found in surface water taking into consideration fate properties, relatively high potential for release, and the availability of environmental monitoring data and hazard data. Based on a qualitative assessment of the physical-chemical properties and fate of 1-BP in the environment, EPA did not identify risk concerns for sediment-dwelling aquatic organisms. Using a quantitative comparison of hazards and exposures for aquatic organisms, EPA calculated risks to water-column dwelling aquatic species. The results of both of these analyses are presented below. The environmental risk of 1-bromopropane is characterized by calculating risk quotients or RQs ([U.S. EPA, 1998a](#)) ([Barnhouse et al., 2008](#)); the RQ is defined as:

$RQ = \text{Environmental Concentration/Effect Level}$

To determine the risk of 1-BP to aquatic species using risk quotients (RQs) method., the "environmental concentration" represents the modeled exposure value calculated by E-FAST as described below, while the "effect level" represents the aquatic COCs presented in Table 4-1. 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.

As described in greater detail in Section 3.1, the acute and chronic concentrations of concern (COCs) for aquatic species (shown in Table 4-1) were calculated based on the results of the high

quality study ([Geiger et al., 1988](#)). After selecting the lowest toxicity values, an assessment factor (AF) is applied according to EPA methods ([Suter, 2016](#)) ([U.S. EPA, 2012e](#)) ([U.S. EPA, 2013b](#))³⁷.

Table 4-1. Concentrations of Concern (COCs) for Environmental Toxicity as Described in Section 3.1.5

Environmental Toxicity	Endpoint	Data Source	Concentration of Concern (COC)
Acute Toxicity, aquatic organisms	96-hour Fish LC ₅₀	(Geiger et al., 1988)	13,460 µg/L
	Algae EC ₅₀	ECOSAR (v.2.0)	3,320 µg/L
Chronic Toxicity, aquatic organisms	Fish Chronic Value*	(Geiger et al., 1988)	673 µg/L
	Daphnia ChV	ECOSAR (v.2.0)	426 µg/L

* = The fish chronic toxicity value is calculated by dividing the 96-hour fish LC₅₀ by an acute to chronic ratio (ACR) of 10; due to lack of chronic-duration test data for fish.

As described in Appendix H, EPA used the reported releases to water from EPA’s Toxics Release Inventory (TRI) to predict surface water concentrations near reported facilities for this Risk Evaluation. To examine whether near-facility surface water concentrations could approach 1-BP’s aquatic concentrations of concern, EPA employed a first-tier screening-level approach, using reasonably-available modeling tools and data, as well as conservative assumptions. EPA’s Exposure and Fate Assessment Screening Tool ([U.S. EPA, 2007](#)) was used to estimate site-specific surface water concentrations based on estimated loadings of 1-BP into receiving water bodies as reported to TRI. E-FAST 2014 incorporates stream dilution using stream flow information contained within the model. E-FAST also incorporates wastewater treatment removal efficiencies. Wastewater treatment removal was assumed to be 0% for this exercise, as reported loadings/releases are assumed to account for any treatment. As days of release and operation are not reported, EPA assumed a range of possible release days (*i.e.*, 1, 20, and 100 days/year). Refer to the E-FAST 2014 Documentation Manual for equations used in the model to estimate surface water concentrations ([U.S. EPA, 2007](#)). These estimated exposure concentrations were compared with the reasonably available information for aquatic organisms to identify potential risks.

Table 4-2 summarizes the risk quotients (RQs) associated with acute and chronic exposures of 1-BP, using the best available environmental hazard and release information, as well as using the lowest available endpoint as predicted by ECOSAR modeling. As previously stated, an RQ below 1, indicates that the exposure concentrations of 1-BP is less than the concentrations that would cause an effect to organisms in the aquatic pathways. The RQ values for risks from acute and chronic exposure are <0.01 and 0.12, respectively based on the best available information, while the RQs for acute and chronic exposure predicted with the lowest toxicity values predicted by

³⁷ For fish and aquatic invertebrates (*e.g.*, daphnia), the acute COC values are calculated by dividing the selected environmental hazard endpoint by an AF of 5. For chronic COCs, and to calculate COCs for algae, an AF of 10 is used.

ECOSAR are 0.02 and 0.18, respectively. These values indicate that risks are not identified for aquatic receptors based on the conditions of use in this final risk evaluation.

Table 4-2. Calculated Risk Quotients (RQs) for 1-BP

	Data Source	Concentrations of Concern (CoC)	Maximum Concentration	RQ
Acute Scenario	(Geiger et al., 1988)	13,460 µg/L	78 µg/L	<0.01
	ECOSAR (v2.0)	3,320 µg/L		0.02
Chronic Scenario	(Geiger et al., 1988)	673 µg/L		0.12
	ECOSAR (v2.0)	426 µg/L		0.18

For environmental release pathways, EPA quantitatively evaluated surface water exposure to aquatic species. As explained in Section 2.1, 1-BP is not expected to sorb strongly to sediment or soil. If present in biosolids, 1-BP would be expected to associate with the aqueous component and/or volatilize to air as biosolids are applied to soil and allowed to dry. 1-BP is expected to volatilize readily from dry soil and surfaces due to its vapor pressure (high volatility (vapor pressure= 110 mm Hg at 20°C; Henry’s law constant of 7.3×10^{-3} atm-m³/mole, see Table 1-1). 1-BP has demonstrated moderate toxicity to aquatic organisms, and overall the exposures to surface water from biosolids are estimated to be below concentrations of concern for these taxa. Therefore, no quantitative analysis for risks to aquatic organisms from biosolids is necessary as exposures from this pathway are expected to be negligible.

No sediment monitoring data for 1-BP are reasonably available, but physical-chemical characteristics such as a high vapor pressure = 110 mm Hg at 20°C and Henry’s law constant of 7.3×10^{-3} atm-m³/mole (see Table 1-1) suggest that 1-BP is expected to quickly volatilize from water and resultingly be present in very limited amounts in aquatic environments. Physical-chemical properties input to EPISuite indicate that 1-BP will volatilize from a model river with a half-life on the order of an hour and from a model lake on the order four days. Although volatilization is expected to be rapid, a Level III Fugacity model predicts that when 1-BP is continuously released to water, 80% of the mass will be in water 19% in air due in part to its water solubility, while only <1% is predicted to transition to aquatic sediment. Intermittent releases of 1-BP are not expected to result in long-term presence in the aquatic compartment. Chronic exposure is only a likely scenario for environments near continuous direct release sites. 1-BP in sediment is expected to be in the pore water rather than sorbed to the sediment solids based on a high water solubility (2.4 g/L) and low log Koc (1.6). Overall, because 1-BP is expected to be present in higher concentrations in pore water than sediments, sediment-dwelling organisms are not expected to be exposed to a greater concentration of 1-BP than aquatic organisms. Furthermore, sediment is not expected to be a source of 1-BP to overlying surface water, so additional risk concerns to these sediment-dwelling organisms are not expected.

4.2 Human Health Risk

1-BP exposure is associated with a variety of cancer and non-cancer effects deemed relevant to humans for risk estimations for the acute and chronic scenarios and populations addressed in this risk evaluation. Based on a weight of the scientific evidence analysis of the reasonably available toxicity studies from rats and humans, these effects include liver toxicity, kidney toxicity, reproductive toxicity, developmental toxicity and neurotoxicity. The rationale for using the range of toxic effects for chronic exposures is based on the fact that relatively low dose, short term/sub-chronic exposures can result in long-term adverse consequences. The adverse developmental effects are also deemed important for risk estimation for the acute exposure scenarios and populations addressed in this risk evaluation. The rationale for using 1-BP associated developmental effects for evaluating risks associated with acute exposures is based on the understanding that a single exposure during a critical window of vulnerability can adversely impact the conceptus. 1-BP is carcinogenic in animals. EPA derived an IUR and dermal slope factor based on lung tumors in female mice to evaluate cancer risk.

4.2.1 Risk Characterization Approach

Table 4-3, Table 4-4, and Table 4-5 show the use scenarios, populations of interest and toxicological endpoints used for acute and chronic exposures, respectively.

Table 4-3. Use Scenarios, Populations of Interest and Toxicological Endpoints for Assessing Occupational Risks Following Acute Exposures to 1-BP

Populations And Toxicological Approach	Occupational Use Scenarios of 1-BP
Population of Interest and Exposure Scenario	<p>Workers: Adult male and female¹ (>16 years old) who directly handle 1-BP as part of their job function (typically 8-hr work day).</p> <p>Occupational Non-user: Adult male and female¹ (>16 years old) who do not directly handle 1-BP, but who are potentially exposed by being present in the surrounding work area of building (typically 8-hr work day).</p>
Health Effects of Concern, Concentration and Time Duration	<p><u>Non-Cancer Health Effects:</u> Decreased live litter size (F₁) using BMD modeling; Post-implantation loss in F₀ females using NLogistic modeling (WIL Research, 2001)²</p> <ol style="list-style-type: none"> 1. Non-cancer hazard values or Point of Departures (PODs; BMD): 8-hr HEC: 31 ppm; 24-hr dermal HED: 19 mg/kg-day 2. Non-cancer hazard values or Point of Departures (PODs; NLogistic): 8-hr HEC: 17 ppm; 24-hr dermal HED: 11 mg/kg-day <p><u>Cancer Health Effects:</u> Cancer risks following acute exposures were not estimated. Relationship is not known between a single short-term exposure to 1-BP and the induction of cancer in humans.</p>

Uncertainty Factors (UF) used in Non-Cancer Margin of Exposure (MOE) calculations	$(UFS=1) \times (UFA=10) \times (UFH=10) \times (UFL=1)^3 = 100$ Total UF=Benchmark MOE=100
Notes:	
¹ Includes pregnant women and adults of reproductive age.	
² The risk assessment for acute exposures focused on the most sensitive life stage in humans, which is women and adults of reproductive age and fetus (<i>i.e.</i> , pregnant user) due to concerns for developmental effects. Developmental toxicity effects were considered as the most sensitive health effect when compared to other potential acute effects (<i>i.e.</i> , neurotoxicity).	
³ UFS=subchronic to chronic UF; UFA=interspecies UF; UFH=intraspecies UF; UFL=LOAEL to NOAEL UF	

Table 4-4. Use Scenarios, Populations of Interest and Toxicological Endpoints for Assessing Consumer Risks Following Acute/Chronic Exposures to 1-BP

Population and Toxicological Approach	Consumer Use Scenarios of 1-BP (9 Scenarios)
Population of Interest	Women and adults of reproductive age ¹ Users (Youth 11-15, Youth 16-20, Adult 21 years and greater) Bystander (Any age group (infant to elderly))
Exposure Scenario ² : Users, High-intensity use	95 th percentile duration of use 95 th percentile mass of product used High weight fraction (amount of chemical in product)
Exposure Scenario ² : Users, moderate intensity use	50 th percentile duration of use 50 th percentile mass of product used Mean/median weight fraction (amount of chemical in product)
Exposure Scenario ² : Users, low intensity use	10 th percentile duration of use 10 th percentile mass of product used Low weight fraction (amount of chemical in product)
Population of Interest and Exposure Scenario: Bystander	Women and adults of reproductive age non-users ⁴ and individuals of multiple age groups that are exposed to indirect 1-BP exposures by being in the rest of the house.
Acute Health Effects of Concern, Concentration and Time Duration	<u>Non-Cancer Health Effects:</u> Decreased live litter size (F ₁) using BMD modeling; Post-implantation loss in F ₀ females using NLogistic modeling (WIL Research, 2001) ⁵ <ol style="list-style-type: none"> 1. Non-cancer hazard values or Point of Departures (PODs; BMD): 24-hr HEC: 10 ppm; 24-hr HED: 19 mg/kg-day 2. Non-cancer hazard values or Point of Departures (PODs; NLogistic): 24-hr HEC: 6 ppm; 24-hr HED: 11 mg/kg-day <u>Cancer Health Effects:</u> Cancer risks following acute exposures were not estimated. Relationship is not known between a single short-term exposure to 1-BP and the induction of cancer in humans.

Population and Toxicological Approach	Consumer Use Scenarios of 1-BP (9 Scenarios)
Chronic Non-Cancer Health Effects of Concern, Concentration and Time Duration	<p><u>Non-Cancer Health Effects:</u></p> <p>1. Non-cancer health effects for inhalation and dermal exposures: A range of possible chronic non-cancer adverse effects in liver, kidney, nervous system, reproductive system and developmental effects (including 2 modeling approaches for developmental effects)</p> <p>2. Non-cancer hazard values or Point of Departures (PODs): The most robust and sensitive POD (<i>i.e.</i>, 24-hr HEC expressed in ppm; 24-hr dermal HED expressed as mg/kg-day) within each health endpoint domain. See Table 3-2.</p>
Cancer Health Effects of Concern, Concentration and Time Duration	<p><u>Cancer Health Effects:</u></p> <p>1. Cancer health effects for inhalation exposures: Data for lung tumors (NTP, 2011a) in female mice was selected as the POD considered protective for the other tumor types.</p> <p>2. Cancer Inhalation Unit Risk (IUR): See Table 3-6 for IUR values using model averaging and multistage modeling approaches; the IUR (24 hrs/day) using the multistage modeling are used in the cancer risk estimate calculations.</p>
Uncertainty Factors (UF) used in Non-Cancer Margin of Exposure (MOE) calculations	<p>$(UFS=1) \times (UFA=10) \times (UFH=10) \times (UFL=1)^6 = 100$ Total UF=Benchmark MOE=100</p>
<p>Notes:</p> <p>¹The risk assessment for acute exposures focused on the most sensitive life stage in humans, which is women and adults of reproductive age and fetus (<i>i.e.</i>, pregnant user) due to concerns for developmental effects.</p> <p>²E-FAST/CEM provided the 24-hr acute exposure estimate and the HECs were adjusted to 24-hrs.</p> <p>³It is assumed no substantial buildup of 1-BP in the body between exposure events due to 1-BP's short biological half-life (<2 hours).</p> <p>⁴EPA believes that the users of these products are generally adults or youth (11-20 yrs of age), but any age group may be a bystander living in the house where product was used.</p> <p>⁵The risk assessment for acute exposures focused on developmental toxicity effects as the most sensitive health effect when compared to other potential acute effects (<i>i.e.</i>, neurotoxicity).</p> <p>⁶UFS=subchronic to chronic UF; UFA=interspecies UF; UFH=intraspecies UF; UFL=LOAEL to NOAEL UF</p>	

Table 4-5. Use Scenarios, Populations of Interest and Toxicological Endpoints for Assessing Occupational Risks Following Chronic Exposures to 1-BP

Populations and Toxicological Approach	Occupational Use Scenarios of 1-BP
Population of Interest and Exposure Scenario	<p>Workers: Adult male and female^{1,2} (>16 years old) who directly handle 1-BP as part of their job function (typically 260 days per year over 31 working years, see the <i>1-BP Supplemental File: Supplemental Information on Occupational Exposure Assessment (EPA, 2019f)</i>).</p> <p>Occupational Non-user: Adult male and female^{1,2} (>16 years old) who do not directly handle 1-BP, but who are potentially exposed by being present in the surrounding work area of building (typically 260 days per year over lifetime working years, see the <i>1-BP Supplemental File: Supplemental Information on Occupational Exposure Assessment (EPA, 2019f)</i>).</p>
Health Effects of Concern, Concentration and Time Duration	<p>Non-Cancer Health Effects:</p> <ol style="list-style-type: none"> 1. Non-cancer health effects for inhalation and dermal exposures: A range of possible chronic non-cancer adverse effects in liver, kidney, nervous system, reproductive system and developmental effects (including 2 modeling approaches for developmental effects) 2. Non-cancer hazard values or Point of Departures (PODs): The most robust and sensitive POD (<i>i.e.</i>, 8-hr and 24-hr HEC expressed in ppm; 24-hr dermal HED expressed as mg/kg-day) within each health endpoint domain. See Table 3-2. <p>Cancer Health Effects:</p> <ol style="list-style-type: none"> 1. Cancer health effects for inhalation and dermal exposures: Data for lung tumors (NTP, 2011a) in female mice was selected as the POD considered protective for the other tumor types. 2. Cancer Inhalation Unit Risk (IUR): See Table 3-6 and Table 3-7 for IUR values and dermal slope factors using model averaging and multistage modeling approaches; the IUR (40 hrs/wk and 24 hrs/day) and dermal cancer slope factor using the multistage modeling are used in the cancer risk estimate calculations.
Uncertainty Factors (UF) Used in Non-Cancer Margin of Exposure (MOE) calculations	Study- and endpoint-specific UFs. See Table 3-2.
<p>Notes:</p> <p>¹Includes pregnant women and adults of reproductive age.</p> <p>²The risk assessment for chronic exposures for developmental effects focused on the most sensitive life stage in humans, which are women and adults of reproductive age and fetus (<i>i.e.</i>, pregnant worker). For other health effects (<i>e.g.</i>, liver, kidney, etc.), healthy female or male workers were assumed to be the population of interest.</p>	

EPA applied a composite UF of 100 for the acute and chronic inhalation benchmark MOE, based on the following considerations (see Section 3.2.8.1.3 for full details):

- An interspecies uncertainty/variability factor of 10 (UF_A) was applied for animal-to-human extrapolation. 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, a portion of the toxicokinetic uncertainty may be accounted for by the calculation of an HEC and application of a dosimetric adjustment factor as outlined in the RfC methodology ([U.S. EPA, 1994](#)); however, an UF_A of 10 is retained to account for additional toxicokinetic differences that remain unaccounted; 1-BP is irritating to the respiratory tract and rodents exhibit physiological responses (such as reflex bradypnea) that differ from humans and may alter uptake due to hyper- or hypoventilation, resulting in decreased internal dose relative to the applied concentration. Therefore, an UF_A of 10 is retained to account for toxicokinetic differences ([OECD 39](#));
- A default intraspecies uncertainty/variability factor (UF_H) of 10 was applied to account for variation in sensitivity within human populations due to limited information regarding the degree to which human variability (*i.e.*, gender, age, health status, or genetic makeup) may impact the disposition of or response to, 1-BP;
- Interindividual variability in the expression and functional capacity of CYP2E1 has been observed ([Neafsey et al., 2009](#)) and genetic polymorphisms in CYP2E1 expression have been linked to altered disease susceptibility ([Trafalis et al., 2010](#)); and,
- A LOAEL-to-NOAEL uncertainty factor (UF_L) of 1 was applied because BMD modeling was used to derive the HEC.
- A subchronic-to-chronic uncertainty factor (UF_S) of 1 was applied because the studies used for risk estimation either were of chronic duration or the database did not suggest increased toxicity at longer durations (neurotoxicity).

Acute and chronic MOEs (MOE_{acute} or MOE_{chronic}) were used in this evaluation to estimate non-cancer risks using Equation 4-1.

Equation 4-1. Equation to Calculate Non-Cancer Risks Following Acute or Chronic Exposures Using Margin of Exposures

$$MOE_{acute\ or\ chronic} = \frac{Non - cancer\ Hazard\ value\ (POD)}{Human\ Exposure}$$

Where:

MOE = Margin of exposure (unitless)

Hazard value (POD) = HEC (ppm)

Human Exposure = Exposure estimate (in ppm) from occupational or consumer exposure assessment. ADCs were used for non-cancer chronic scenarios and acute concentrations were used for acute scenarios (see Section 2.3).

EPA used margin of exposures (MOEs)³⁸ to estimate risks associated with acute or chronic non-cancer scenarios based on the following:

- The highest quality HECs/dermal HEDs within each health effects domain reported in the literature;
- The endpoint/study-specific UFs applied to the HECs/dermal HEDs per EPA Guidance ([U.S. EPA, 2002](#)); and
- The exposure estimates calculated for 1-BP uses examined in this risk evaluation.

MOE estimates allow for the presentation of a range of risk estimates. The occupational exposure scenarios considered both acute and chronic inhalation and dermal exposures. All consumer uses considered only acute inhalation and dermal exposure scenarios. Different adverse endpoints were used based on the expected exposure durations. For non-cancer effects, risks for developmental effects were evaluated for acute (short-term) exposures, whereas risks for other adverse effects (toxicity to the liver, kidney, nervous system, developmental effects, and the reproductive system) were evaluated for repeated (chronic) exposures to 1-BP.

For occupational exposure calculations, the 8 hr TWA was used to calculate MOE estimates for acute and chronic exposures.

The total UF for each non-cancer POD was the benchmark MOE used to interpret the MOE risk estimates for each use scenario. The MOE estimate was interpreted as a potential human health concern 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 exceeded the benchmark MOE. Typically, the larger the MOE, the more unlikely it is that a non-cancer adverse effect would occur.

MOE estimates were calculated for all of the studies per health effects domain that EPA considered suitable for the risk evaluation of acute and chronic exposure scenarios in the work plan risk assessment for 1-BP.

Extra cancer risks for repeated exposures to 1-BP were estimated using Equation 4-2. Estimates of extra cancer risks should be interpreted as the incremental probability of an individual developing cancer over a lifetime as a result of exposure to the potential carcinogen (*i.e.*, incremental or extra individual lifetime cancer risk).

Equation 4-2. Equation to Calculate Extra Cancer Risks

$$\mathbf{Risk = Human\ Exposure \times IUR}$$

³⁸ Margin of Exposure (MOE) = (Non-cancer hazard value, POD) ÷ (Human Exposure). Equation 4-1 The benchmark MOE is used to interpret the MOEs and consists of the total UF shown in Table 3-2. See 3.2.8.1 for an explanation of the benchmark MOE.

Where:

Risk = Extra cancer risk (unitless)

Human exposure = Exposure estimate (LADC in ppm) from occupational exposure assessment

IUR = Inhalation unit risk (3×10^{-3} per ppm)

4.2.2 Occupational Inhalation Exposure Summary and PPE Use Determination by OES

EPA considered the reasonably available data for estimating exposures for each OES. EPA also determined whether air-supplied respirator use up to APF = 50 was plausible for those OES based on expert judgement and reasonably available information. Table 4-6 presents this information below, which is considered in the risk characterization for each OES in the following sections.

EPA did not evaluate respirator use for the following occupational scenarios:

- **Dry Cleaning; Spot Cleaner, Stain Remover:** Many dry cleaning shops are small, family - owned businesses and are unlikely to have a respiratory protection program.
- **Aerosol Spray Degreaser/Cleaner:** EPA believes many aerosol degreasing activities occur in commercial settings. For example, the aerosol degreasing model estimates worker exposure at automotive brake servicing shops. Based on reasonably available information, EPA believes workers at brake servicing shops are unlikely to wear respirators.

Table 4-6. Inhalation Exposure Data Summary and Respirator Use Determination

Occupational Exposure Scenario	Inhalation Exposure Approach	Number of Data Points	Model Used	Approach for ONUs	Respirator Use	Industrial or Commercial OES
Manufacture	Monitoring data	3 (8-hr TWA)	N/A – monitoring data only	N/A (expected to be negligible)	Assumed respirator use	Industrial
Import	Modeling	N/A – model only	Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model	N/A (expected to be negligible)	Assumed respirator use	Industrial
Processing as a Reactant	Modeling	N/A – model only			Assumed respirator use	Industrial
Processing – Incorporation into Formulation, Mixture, or Reaction Product	Monitoring data	11 (8-hr TWA)	N/A – monitoring data only	Monitoring data	Assumed respirator use	Industrial
Processing – Incorporation into articles	Modeling	N/A – model only	Tank Truck and Railcar Loading and Unloading	N/A (expected to be negligible)	Assumed respirator use	Industrial

Occupational Exposure Scenario	Inhalation Exposure Approach	Number of Data Points	Model Used	Approach for ONUs	Respirator Use	Industrial or Commercial OES
Repackaging	Modeling	N/A – model only	Release and Inhalation Exposure Model		Assumed respirator use	Industrial
Disposal, Recycling	Modeling	N/A – model only			Assumed respirator use	Industrial
Batch Vapor Degreaser (Open-Top)	Monitoring data and modeling	230 (8-hr TWA)	Open-Top Vapor Degreasing Near-Field/Far-Field Inhalation Exposure Model	Monitoring data and far-field model results	Assumed respirator use	Industrial
Batch Vapor Degreaser (Closed-Loop)	Modeling	N/A – model only		Far-field model results	Assumed respirator use	Industrial
In-line Vapor Degreaser	See Batch Vapor Degreaser (Open-Top)				Assumed respirator use	Industrial
Cold Cleaner	Monitoring data and modeling	6 (8-hr TWA)	Cold Cleaning Near-Field/Far-Field Inhalation Exposure Model	Monitoring data and far-field model results	Assumed respirator use	Industrial
Aerosol Spray Degreaser / Cleaner	Monitoring data and modeling	7 (8-hr TWA)	Brake Servicing Near-Field/Far-Field Inhalation Exposure Model	Far-field model results	Not expected	Commercial
Adhesive Chemicals (Spray Adhesives)	Monitoring data	228 (8-hr TWA)	N/A – monitoring data only	Monitoring data	Assumed respirator use	Commercial
Dry Cleaning	Monitoring data and modeling	14 (8-hr TWA)	Dry Cleaning Multi-Zone Inhalation Exposure Model	Monitoring data and far-field model results	Not expected	Commercial
Spot Cleaner, Stain Remover	Monitoring data and modeling	6 (8-hr TWA)	Spot Cleaning Near-Field/Far-Field Inhalation Exposure Model	Far-field model results	Not expected	Commercial
THERMAX™ Installation	Modeling	N/A – model only	IECCU	Screening-level model analysis	Assumed respirator use	Commercial
Other Uses	Not quantified					Industrial / Commercial

4.2.3 Risk Characterization For Acute, Non-Cancer Inhalation Exposures

Non-cancer MOE estimates for acute inhalation and dermal exposures to 1-BP were derived for both occupational scenarios and consumer scenarios. Cancer risk estimates for acute inhalation exposures to 1-BP were not derived for occupational or consumer scenarios because the published

methodology for extrapolating cancer risks from chronic to short-term exposures includes the caveat that extrapolation of lifetime theoretical extra cancer risks to single exposures has great uncertainty ([NRC, 2001](#)).

The risk assessment for acute inhalation and dermal exposures used developmental toxicity data to evaluate the risks following acute exposures with the TSCA condition of use scenarios identified for 1-BP under the scope of this risk evaluation. EPA based its risk evaluation for the acute exposure scenario on developmental toxicity (*i.e.*, decreased live litter size, and increases in post-implantation loss), the most robust and sensitive HEC/dermal HED identified for an acute exposure duration ([WIL Research, 2001](#)), which is representative of potentially exposed or susceptible subpopulation (*i.e.*, adults of reproductive age and their offspring). For acute occupational exposure scenarios, EPA did not assess risks to children who may be present in the workplace (*e.g.*, dry cleaners). Risk estimates were based on the most robust and sensitive endpoint, which is applicable to pregnant women. EPA expected that risk estimates based on this endpoint are protective of any other acute hazard that could be applicable to children lifestages. See Section 3.2.8.5 and 4.2.1 for additional discussion.

The risk assessment for acute exposures used the hazard value from the ([WIL Research, 2001](#)) two-generation reproductive toxicity study to evaluate risks for each occupational and consumer exposure scenario.

4.2.3.1 Acute Occupational Exposures

Non-cancer MOE estimates for acute occupational exposure scenarios are presented in Table 4-7 through Table 4-26. MOE estimates (HEC in ppm/exposure estimate in ppm; dermal HED exposure estimate in mg/kg-day) that are below the Benchmark MOE (Total UF) are highlighted in red. Where the sample size of the underlying exposure data is sufficiently large to calculate statistics, the central tendency estimate is based on the 50th percentile exposure level of the dataset, while the high-end estimate is based on the 95th percentile exposure. See Section 2.3.1.2 for detailed descriptions of central tendency and high-end estimates.

MOE estimates for worker respirator scenarios presented below are based on the level of APF required to mitigate risk for all health domains (APF of 10, 25, or 50). For some occupational conditions of use, respirators with an APF of 50 do not reduce worker exposure to levels where the calculated MOE is greater than the benchmark MOE. The MOE estimates for these respirator scenarios assume workers are properly trained and fitted on respirator use, and that they wear respirators for the entire duration of the work activity where there is potential exposure to 1-BP. As explained in Section 4.2.2, APFs were not applied to the dry cleaning, spot cleaning, and aerosol degreasing scenarios because EPA assumes respirator use is unlikely for these conditions of use. In addition, EPA does not evaluate respirator use for occupational non-users because they do not directly handle 1-BP and are unlikely to wear respirators.

Table 4-7. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Manufacture Based on Monitoring Data (U.S.)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=10	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	344	N/A	3,444	100
		High-end	115	N/A	1,148	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	189	N/A	1,889	100
		High-end	63	N/A	630	

Note: Exposure monitoring was not performed for ONUs at this manufacturing facility. Based on the process and work activity description, exposure to ONU is expected to be negligible.

Table 4-8. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Import, Repackaging, Processing as a Reactant, and Processing – Incorporation into Articles Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	8,099	N/A	100
		High-end	546	N/A	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	4,441	N/A	100
		High-end	300	N/A	

N/A – Not applicable. Because the model assumes tank truck and railcar loading/unloading occurs outdoors, EPA expects ONU exposure to be negligible due to airborne concentration dilution in ambient air.

Table 4-9. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Processing – Incorporation into Formulation Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	4	200	215	100
		High-end		113		
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	2	110	118	100
		High-end		62		

Table 4-10. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	5	310	231	100
		High-end	1	67	31	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	3	170	127	100
		High-end	0.34	37	17	

Table 4-11. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) Based on Modeling (Pre-EC^a)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	16	31	820	100
		High-end	1	2	65	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	9	17	450	100
		High-end	1	1	36	

^a EC = Engineering Controls. Pre-EC = Modeling where no reduction due to engineering controls was assumed
Post-EC = Engineering controls such as LEV with 90% efficiency.

Table 4-12. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) Based on Modeling (Post-EC^a)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=25	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	164	312	4,099	100
		High-end	13	23	324	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	90	171	2,248	100
		High-end	7	13	178	

^a EC = Engineering Controls. Pre-EC = Modeling where no reduction due to engineering controls was assumed
 Post-EC = Engineering controls such as LEV with 90% efficiency.

Table 4-13. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Closed-Loop) Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=10	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	820	1,561	8,199	100
		High-end	65	115	648	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	450	856	4,496	100
		High-end	36	63	355	

Table 4-14. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Cold Cleaner Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	7	12	360	100
		High-end	4	12	209	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	4	7	198	100
		High-end	2	7	115	

Table 4-15. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Cold Cleaner Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	56	107	2,822	100
		High-end	3	5	130	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	31	59	1,548	100
		High-end	1	2	71	

Table 4-16. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser Based on Monitoring Data (Pre-EC^a)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	2	No data	100
		High-end	1	No data	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	1	No data	100
		High-end	1	No data	

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

^a EC = Engineering Controls.

Table 4-17. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser Based on Monitoring Data (Post-EC^a)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	N/A (Single data point)	6	No data	100
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17		3	No data	100

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

^a EC = Engineering Controls. Post-EC = The vented booth scenario from Tech Spray study.

Table 4-18. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	5	282	100
		High-end	1	33	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	3	155	100
		High-end	1	18	

Table 4-19. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	1	3	100
		High-end	1	2	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001) ; NLogistic Model	17	Central tendency	1	1	100
		High-end	0.34	0.82	

For the dry cleaning condition of use, the MOE estimates for ONUs are expected to be protective of children potentially present at dry cleaners because the modeled exposure concentrations for children (as shown in Table 2-22) are lower than those for adult ONUs. In addition, the use of the developmental toxicity endpoint for risk estimation is protective of any other acute hazards these children may experience.

Table 4-20. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Modeling (3rd Generation Machine)

Health Effect, Endpoint and Study	Exposure Level	Acute MOE			Benchmark MOE
		Spot Cleaner	Machine & Finish	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	7	1	11	100
	High-end	3	0.33	3	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	Central tendency	4	1	6	100
	High-end	1	0.19	2	

Study: ([WIL Research, 2001](#)). Note: Based on acute HEC of 10 ppm and 5.7 ppm.

Table 4-21. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Modeling (4th Generation Machine)

Health Effect, Endpoint and Study	Exposure Level	Acute MOE			Benchmark MOE
		Spot Cleaner	Machine & Finish	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	8	8	15	100
	High-end	4	3	5	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	Central tendency	5	5	9	100
	High-end	2	2	3	

Study: ([WIL Research, 2001](#)). Note: Based on acute HEC of 10 ppm and 5.7 ppm.

Table 4-22. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Spot Cleaner Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	34	No data	100
		High-end	7	No data	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	19	No data	100
		High-end	4	No data	

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

Table 4-23. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Spot Cleaner Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	10	19	100
		High-end	4	7	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	5	10	100
		High-end	2	4	

Table 4-24. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Adhesive Chemicals (Spray Adhesive^a) Based on Monitoring Data (Pre-EC)

Health Effect, Endpoint and Study	Exposure Level	Acute MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	0.23	0.24	10	12	12	100
	High-end	0.12	0.15	0.24	6	7	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	Central tendency	0.13	0.13	6	6	7	100
	High-end	0.07	0.08	0.13	3	4	

Note: Based on acute HEC of 31 ppm and 17 ppm.

^a EC = Engineering Controls. Pre-EC = Initial NIOSH visit; Post EC = Follow-up NIOSH visit engineering controls implemented: Enclosing spray tables to create “spray booths” and/or improve ventilation.

Table 4-25. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Adhesive Chemicals (Spray Adhesive) Based on Monitoring Data (Post-EC^a)

Health Effect, Endpoint and Study	Exposure Level	Acute MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	2	2	16	87	86	100
	High-end	1	1	6	37	54	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	Central tendency	1	1	9	48	47	100
	High-end	0.41	1	3	20	29	

Note: Based on acute HEC of 31 ppm and 17 ppm.

^a EC = Engineering Controls. Pre-EC = Initial NIOSH visit; Post EC = Follow-up NIOSH visit engineering controls implemented: Enclosing spray tables to create “spray booths” and/or improve ventilation.

Table 4-26. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Disposal Based on Modeling

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	8,099	N/A	100
		High-end	546	N/A	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	4,441	N/A	100
		High-end	300	N/A	

N/A – not applicable. Because the model assumes tank truck and railcar loading/unloading occurs outdoors, EPA expects ONU exposure to be negligible due to airborne concentration dilution in ambient air.

4.2.3.2 Acute Consumer Exposures

MOE estimates for acute non-cancer consumer inhalation exposure were determined for nine consumer conditions of use based on modeling (high, moderate, and low intensity use scenarios) and are included in the 1-BP_Supplemental File_Consumer Exposure Risk Calculations ([EPA, 2019c](#)). These MOE estimates are presented in Table 4-27. MOE estimates that are lower than the Benchmark MOE (Total UF) are highlighted in red.

Table 4-27. Non-Cancer Risk Estimates for Acute 24-hr Inhalation Exposure Following Consumer Uses of 1-BP (Benchmark MOE = 100) Based on Modeling

Condition of Use	Scenario Description	Acute Non-Cancer MOE (24-Hour TWA)			
		Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)		Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001)	
		User	Bystander	User	Bystander
Aerosol spray degreaser/cleaner-general	High Intensity Use	7.1E-02	0.24	4.3E-02	0.15
	Moderate Intensity Use	0.53	2.0	0.316	1.2
	Low Intensity Use	10	40	6.0	24
Aerosol spray degreaser/cleaner-electronics	High Intensity Use	0.33	1.2	0.20	0.69
	Moderate Intensity Use	7.1	29	4.3	17
	Low Intensity Use	149	526	90	316
Spot cleaner and stain remover	High Intensity Use	0.21	1.4	0.13	0.83
	Moderate Intensity Use	2.9	19	1.8	11
	Low Intensity Use	38	208	23	125
Coin and scissors cleaner	High Intensity Use	5.0	10	3.0	6.0
	Moderate Intensity Use	6.7	21	4.0	13
	Low Intensity Use	8.3	45	5.0	27
Spray cleaner-general	High Intensity Use	7.5E-02	0.30	4.5E-02	0.18
	Moderate Intensity Use	0.71	3.7	0.43	2.2
	Low Intensity Use	4.3	23	2.6	14
Adhesive accelerant	High Intensity Use	0.56	2.2	0.33	1.3
	Moderate Intensity Use	9.1	50	5.5	30
	Low Intensity Use	83	400	50	240
Automobile AC flush	High Intensity Use	13	20	7.5	12
	Moderate Intensity Use	19	42	11	25
	Low Intensity Use	27	133	16	80
Mold cleaning and release product	High Intensity Use	0.48	2.4	0.29	1.4
	Moderate Intensity Use	7.1	37	4.3	22
	Low Intensity Use	83	385	50	231
Insulation (off-gassing) [A/LS/C]*	Attic	N/A	5,050	N/A	3,030
	Living Space	N/A	11,104	N/A	6,663
	Crawlspace	N/A	4,666	N/A	2,800
Insulation (off-gassing) [A/LS/B]*	Attic	N/A	5,128	N/A	3,077
	Living Space	N/A	31,439	N/A	18,863
	Full Basement	N/A	4,782	N/A	2,869

Note: Acute HEC = 6 ppm (decreased live litter size) and 10 ppm (post-implantation loss).

N/A – Not applicable because EPA assumes consumer exposure from off-gassing will occur after installation.

* Insulation (off-gassing) was evaluated for two building configurations. Attic/Living Space/Crawlspace [A/LS/C] and Attic/Living Space/Basement [A/LS/B]

MOE estimates were generally below the benchmark MOE of 100 by 1-2 orders of magnitude for both the user and bystander for all consumer conditions of use evaluated except for the insulation (off-gassing) condition of use and some low intensity use scenarios for the bystander.

4.2.4 Risk Characterization for Chronic Exposure Scenarios

4.2.4.1 Non-Cancer MOEs for Chronic, Non-Cancer Occupational Inhalation Exposures and Consumer Insulation (Off-Gassing) Condition of Use

EPA estimated the non-cancer MOEs associated with chronic exposures following 1-BP conditions of use in the workplace as well as the insulation (off-gassing) condition of use for the consumer bystander. Since 1-BP exposure may be associated with a variety of non-cancer health effects, this assessment estimated MOEs for liver toxicity, kidney toxicity, reproductive toxicity, developmental toxicity and neurotoxicity following chronic inhalation exposures. EPA used the HEC specific to each health effect domain for calculating MOE estimates. MOE estimates that are lower than the Benchmark MOE are highlighted in red.

Table 4-28 through Table 4-47 present the non-cancer risks for chronic occupational scenarios. MOE estimates for a range of health effects were calculated (See the Supplemental File: Occupational Risk Calculator ([EPA, 2019g](#))). Where the sample size of the underlying exposure data is sufficiently large to calculate statistics, the central tendency estimate is based on the 50th percentile exposure level of the dataset, while the high-end estimate is based on the 95th percentile exposure. See Section 2.3.1.2 for detailed descriptions of central tendency and high-end estimates. These tables also evaluate the impact of potential respirator use and present the respirator that would be needed (based on respirator APF of 10, 25, and 50) to mitigate risk for all health domain. The MOE estimates for these respirator scenarios assume workers wear respirators for the entire duration of the work activity throughout their career (*e.g.*, typically 260 days per year and over 31 years per lifetime for many occupational scenarios). Because respirators are uncomfortable, interfere with communication, limit vision, and make it hard to breathe, and the onus is on the worker to don and doff them correctly, the use of respirators on a continuous, long-term basis may not be practical. As explained in Section 4.2.2, APFs were not applied to the dry cleaning, spot cleaning, and aerosol degreasing scenarios because EPA assumes respirator use is unlikely for these conditions of use. In addition, EPA does not evaluate respirator use for occupational non-users because they do not directly handle 1-BP and are unlikely to wear respirators. For chronic occupational exposure scenarios, EPA did not assess risks to children who may be present in the workplace (*e.g.*, dry cleaners) because their presence in the workplace is likely intermittent and overall exposure is not expected to be chronic in nature.

Table 4-28. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Manufacture (U.S.) Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=10	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	1,667	N/A	16,667	100
		High-end	556	N/A	5,556	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	2,000	N/A	20,000	100
		High-end	667	N/A	6,667	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	589	N/A	5,889	100
		High-end	196	N/A	1,963	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	484	N/A	4,835	100
		High-end	161	N/A	1,612	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	265	N/A	2,652	100
		High-end	88	N/A	884	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	278	N/A	2,778	100
		High-end	93	N/A	926	

Notes: ¹MOEs (HEC in ppm/exposure estimate in ppm) lower than the Benchmark MOE (Total UF) indicate potential health risks and are denoted in bold. Exposure monitoring was not performed for ONUs at this manufacturing facility. Based on the process and work activity description, exposure to ONU is expected to be negligible.

Table 4-29. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Import, Processing as a Reactant, and Processing – Incorporation into Articles Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	39,188	N/A	100
		High-end	2,644	N/A	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	47,026	N/A	100
		High-end	3,173	N/A	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	13,846	N/A	100
		High-end	934	N/A	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	11,370	N/A	100
		High-end	767	N/A	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	6,235	N/A	100
		High-end	421	N/A	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	6,531	N/A	100
		High-end	441	N/A	

N/A – Not applicable. Because the model assumes tank truck and railcar loading/unloading occurs outdoors, EPA expects ONU exposure to be negligible due to airborne concentration dilution in ambient air.

Table 4-30. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Processing – Incorporation into Formulation Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	21	968	1,042	100
		High-end		544		

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	25	1,161	1,250	100
		High-end		653		
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	7	342	368	100
		High-end		192		
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	6	281	302	100
		High-end		158		
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	3	154	166	100
		High-end		87		
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	3	161	174	100
		High-end		91		

Table 4-31. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	22	1,500	1,119	100
		High-end	3	326	152	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	27	1,800	1,343	100
		High-end	4	391	183	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	8	530	396	100
		High-end	1	115	54	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	6	435	325	100
		High-end	1	95	44	

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Post-Implantation Loss (F0) (WIL Research, 2001); NLogistic Model	17	Central tendency	4	239	178	100
		High-end	0.48	52	24	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	4	250	187	100
		High-end	0.51	54	25	

Table 4-32. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) (Pre-EC) Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	79	151	3,967	100
		High-end	6	11	314	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	95	181	4,760	100
		High-end	8	13	376	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	28	53	1,402	100
		High-end	2	4	111	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	23	44	1,151	100
		High-end	2	3	91	
Developmental Effects Post-Implantation Loss (F0) (WIL Research, 2001); NLogistic Model	17	Central tendency	13	24	631	100
		High-end	1	2	50	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	13	25	661	100
		High-end	1	2	52	

Table 4-33. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) (Post-EC) Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=25	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	793	1,510	19,835	100
		High-end	63	111	1,568	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	952	1,812	23,802	100
		High-end	75	133	1,881	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	280	534	7,009	100
		High-end	22	39	554	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	230	438	5,755	100
		High-end	18	32	455	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	126	240	3,156	100
		High-end	10	18	249	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	132	252	3,306	100
		High-end	10	19	261	

Table 4-34. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Closed-Loop) Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=10	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	3,967	7,551	39,671	100
		High-end	314	555	3,135	
Kidney Increased pelvic	180	Central tendency	4,760	9,062	47,605	100

mineralization (WIL Research, 2001)		High-end	376	666	3,763	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	1,402	2,668	14,017	100
		High-end	111	196	1,108	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	1,151	2,191	11,510	100
		High-end	91	161	910	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	631	1,201	6,312	100
		High-end	50	88	499	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	661	1,259	6,612	100
		High-end	52	93	523	

Table 4-35. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Cold Cleaner Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	35	58	1,744	100
		High-end	20	58	1,014	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	42	69	2,093	100
		High-end	24	69	1,216	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	12	20	616	100
		High-end	7	20	358	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	10	17	506	100
		High-end	6	17	294	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	6	9	278	100
		High-end	3	9	161	

Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	6	10	291	100
		High-end	3	10	169	

Table 4-36. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Cold Cleaner Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	273	519	13,657	100
		High-end	13	22	630	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	328	623	16,388	100
		High-end	15	26	756	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	97	183	4,825	100
		High-end	4	8	223	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	79	151	3,962	100
		High-end	4	6	183	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	43	83	2,173	100
		High-end	2	3	100	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	46	86	2,276	100
		High-end	2	4	105	

Table 4-37. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser/Cleaner (Pre-EC^a) Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular	150	Central tendency	9	No data	100

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
vacuolization (WIL Research, 2001)		High-end	5	No data	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	11	No data	100
		High-end	6	No data	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	3	No data	100
		High-end	2	No data	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	3	No data	100
		High-end	1	No data	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	1	No data	100
		High-end	1	No data	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	2	No data	100
		High-end	1	No data	

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling. ^a EC = Engineering Controls.

Table 4-38. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser/Cleaner (Post-EC^a) Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	N/A (single data point)	27	No data	100
				No data	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180		33	No data	100
				No data	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53		10	No data	100
				No data	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31		8	No data	100
		No data			
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	4	No data	100	
			No data		
Nervous System Decreased traction time (Honma et al., 2003)	25	5	No data	100	
			No data		

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

^a EC = Engineering Controls. Post-EC = The vented booth scenario from Tech Spray study.

Table 4-39. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser/Cleaner Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	24	1,364	100
		High-end	7	161	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	28	1,636	100
		High-end	8	194	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	8	482	100
		High-end	2	57	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	7	396	100
		High-end	2	47	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	4	217	100
		High-end	1	26	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	4	227	100
		High-end	1	27	

Table 4-40. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Adhesive Chemicals (Spray Adhesives) (Pre-EC^a) Based on Monitoring Data

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	Central tendency	1	1	50	56	59	100
	High-end	0.59	0.71	1.2	30	36	
Kidney Increased pelvic mineralization (WIL Research, 2001)	Central tendency	1	1	60	68	71	100
	High-end	0.71	0.85	1	35	43	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	Central tendency	0.40	0.42	18	20	21	100
	High-end	0.21	0.25	0.41	10	13	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	0.3	0.34	14.5	16	17	100
	High-end	0.2	0.21	0.34	9	10	
Developmental Effects Post-Implantation Loss (WIL Research, 2001); NLogistic Model	Central tendency	0.3	0.26	11.2	13	13	100
	High-end	0.13	0.16	0.26	7	8	
Nervous System Decreased traction time (Honma et al., 2003)	Central tendency	0.19	0.20	8	9	10	100
	High-end	0.099	0.12	0.19	5	6	

Note: Based on HEC values of 150 ppm, 140 ppm, 53 ppm, 43 ppm, 24 ppm, and 25 ppm.

^a EC = Engineering Controls. Pre-EC = Initial NIOSH visit; Post EC = Follow-up NIOSH visit engineering controls implemented: Enclosing spray tables to create “spray booths” and/or improve ventilation.

Table 4-41. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Adhesive Chemicals (Spray Adhesives) (Post-EC^a) Based on Monitoring Data

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	Central tendency	8	8	75	421	417	100
	High-end	4	5	27	179	260	
Kidney Increased pelvic mineralization (WIL Research, 2001)	Central tendency	10	10	90	505	500	100
	High-end	4	6	33	215	312	

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	Central tendency	3	3	27	149	147	100
	High-end	1	2	10	63	92	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	2	2	22	122	121	100
	High-end	1	2	8	52	75	
Developmental Effects Post-Implantation Loss (WIL Research, 2001); NLogistic Model	Central tendency	2	2	17	95	94	100
	High-end	1	1	6	40	58	
Nervous System Decreased traction time (Honma et al., 2003)	Central tendency	1	1	13	70	69	100
	High-end	1	1	5	30	43	

Note: Based on HEC values of 150 ppm, 140 ppm, 53 ppm, 43 ppm, 24 ppm, and 25 ppm.

^a EC = Engineering Controls. Pre-EC = Initial NIOSH visit; Post EC = Follow-up NIOSH visit engineering controls implemented: Enclosing spray tables to create “spray booths” and/or improve ventilation.

Table 4-42. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	5	12	100
		High-end	3	7	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	6	15	100
		High-end	4	9	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	2	4	100
		High-end	1	3	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	1	4	100
		High-end	1	2	
Developmental Effects Post-Implantation Loss (F ₀)	17	Central tendency	1	2	100

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
(WIL Research, 2001); NLogistic Model		High-end	0.42	1	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	0.85	2	100
		High-end	0.50	1	

Table 4-43. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Modeling (3rd Generation)

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			Benchmark MOE
		Spot Cleaner	Machine & Finish	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	Central tendency	35	7	56	100
	High-end	13	2	15	
Kidney Increased pelvic mineralization (WIL Research, 2001)	Central tendency	43	9	69	100
	High-end	16	2	19	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	Central tendency	13	3	20	100
	High-end	5	1	5	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	10	2	16	100
	High-end	4	0.46	4	
Developmental Effects Post-Implantation Loss (WIL Research, 2001); NLogistic Model	Central tendency	5	1	9	100
	High-end	2	0.26	2	
Nervous System Decreased traction time (Honma et al., 2003)	Central tendency	6	1	10	100
	High-end	2	0.28	3	

Table 4-44. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Modeling (4th Generation)

Health Effect, Endpoint and Study	Exposure Level	Chronic MOE			Benchmark MOE
		Spot Cleaner	Machine & Finish	ONU	
Liver Increased hepatocellular	Central tendency	42	43	78	100
	High-end	18	16	24	

vacuolization (WIL Research, 2001)					
Kidney Increased pelvic mineralization (WIL Research, 2001)	Central tendency	52	53	96	100
	High-end	22	19	30	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	Central tendency	15	16	28	100
	High-end	6	6	9	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	Central tendency	12	12	22	100
	High-end	5	4.4	7	
Developmental Effects Post-Implantation Loss (WIL Research, 2001); NLogistic Model	Central tendency	7	7	12	100
	High-end	3	3	4	
Nervous System Decreased traction time (Honma et al., 2003)	Central tendency	7	7	13	100
	High-end	3	3	4	

Table 4-45. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Spot Cleaner Based on Monitoring Data

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	167	No data	100
		High-end	32	No data	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	200	No data	100
		High-end	38	No data	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	59	No data	100
		High-end	11	No data	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	48	No data	100
		High-end	9	No data	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	27	No data	100
		High-end	5	No data	
	25	Central tendency	28	No data	100

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Nervous System Decreased traction time (Honma et al., 2003)		High-end	5	No data	

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

Table 4-46. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Spot Cleaner Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	197	390	100
		High-end	90	136	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	236	468	100
		High-end	108	163	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	70	138	100
		High-end	32	48	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	57	113	100
		High-end	26	39	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	31	62	100
		High-end	14	22	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	33	65	100
		High-end	15	23	

Table 4-47. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Occupational Use of 1-BP in Disposal Based on Modeling

Health Effect, Endpoint and Study	Chronic HEC (ppm)	Exposure Level	Chronic MOE		Benchmark MOE
			Worker	ONU	
Liver Increased hepatocellular vacuolization (WIL Research, 2001)	150	Central tendency	39,188	N/A	100
		High-end	2,644	N/A	
Kidney Increased pelvic mineralization (WIL Research, 2001)	180	Central tendency	47,026	N/A	100
		High-end	3,173	N/A	
Reproductive System Decreased seminal vesicle weight (Ichihara et al., 2000b)	53	Central tendency	13,846	N/A	100
		High-end	934	N/A	
Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001)	31	Central tendency	11,370	N/A	100
		High-end	767	N/A	
Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001); NLogistic Model	17	Central tendency	6,235	N/A	100
		High-end	421	N/A	
Nervous System Decreased traction time (Honma et al., 2003)	25	Central tendency	6,531	N/A	100
		High-end	441	N/A	

N/A – Not applicable. Because the model assumes tank truck and railcar loading/unloading occurs outdoors, EPA expects ONU exposure to be negligible due to airborne concentration dilution in ambient air.

Consumer MOE Estimates for Non-Cancer Chronic Exposure

MOE estimates for chronic consumer exposures were only derived for the insulation (off-gassing) condition of use. The remaining conditions of use were not evaluated for chronic consumer exposures because they were not considered chronic in nature. Table 4-48 provides a summary of the MOE estimates for non-cancer chronic inhalation exposures under the insulation (off-gassing) condition of use. The supporting calculations are included in the 1-BP_Supplemental File_Consumer Exposure Risk Calculations ([EPA, 2019c](#))

Table 4-48. Non-Cancer Risk Estimates for Chronic Inhalation Exposures Following Installation of THERMAX™ Rigid Insulation Board Within a Residence Based on Modeling

Condition of Use	Scenario Description	Chronic Non-Cancer MOE (7-Year Average TWA)				
		Liver	Kidney	Reproductive	Developmental 1	Developmental 2
Insulation (off-gassing) [A/LS/C]	Attic	7.4E+05	9.0E+05	2.7E+05	2.0E+05	1.2E+05
	Living Space	1.8E+06	2.3E+06	6.7E+05	5.1E+05	3.1E+05
	Crawlspace	8.1E+05	9.9E+05	2.9E+05	2.3E+05	1.4E+05

Insulation (off-gassing) [A/LS/B]	Attic	7.5E+05	9.1E+05	2.7E+05	2.1E+05	1.2E+05
	Living Space	4.6E+06	5.6E+06	1.7E+06	1.3E+06	7.6E+05
	Basement	7.8E+05	9.5E+05	2.8E+05	2.2E+05	1.3E+05

MOE estimates were all at least three orders of magnitude above the benchmark MOE of 100 for non-cancer chronic inhalation exposures.

4.2.4.2 Cancer Evaluation for Occupational Scenarios

EPA estimated the excess cancers associated with chronic inhalation and dermal exposures following 1-BP conditions of use in the workplace, based on monitoring data and modeling (probabilistic vs deterministic). The excess cancer estimation for 1-BP consisted of multiplying the occupational scenario-specific estimates (*i.e.*, LADC) for both workers and occupational non-users by EPA’s inhalation unit risk (IUR) to estimate the excess cancers. Excess cancer risks were expressed as number of cancer cases per million. For chronic occupational exposure scenarios, EPA did not assess risks to children who may be present in the workplace (*e.g.*, dry cleaners) because their presence in the workplace is likely intermittent and overall exposure is not expected to be chronic in nature.

Table 4-49 presents the inhalation cancer risk estimates for all occupational 1-BP conditions of use. The table also presents the impact of potential respirator use based on respirator APF of 10, 25, and 50. Figure 4-1 and Figure 4-2 present the incremental individual lifetime cancer risks for the 50th and 95th percentile for exposures to 1-BP during these same occupational conditions of use.

The exposure frequency (*i.e.*, the amount of days per year for workers or occupational non-users exposed to 1-BP) was assumed to be 260 days per year for all conditions of use except for dry cleaning, where employees at small, family-owned businesses were assumed to work up to six days per week over 52 weeks per year. The number of working years was assumed to be 31 years as central tendency, and 40 years as high-end over a 78-year lifespan.

EPA, consistent with OSHA (878 F.2d 389 (D.C. Cir. 1989)) and 2016 NIOSH guidance, used 1×10^{-4} as the benchmark for determining cancer risk to individuals in industrial and commercial work environments subject to OSHA requirements. EPA has consistently applied a cancer risk benchmark of 1×10^{-4} for assessment of occupational scenarios under TSCA. This is in contrast with cancer risk assessments for consumers or the general population, for which 1×10^{-6} is applied as a benchmark (Section 4.2.4.3). The 1×10^{-4} value is not a bright line and EPA has discretion to find unreasonable risk based on other benchmarks as appropriate. Cancer risk estimates that exceed the benchmark are highlighted in red below.

Table 4-49. Inhalation Cancer Risk Estimates for Occupational Use of 1-BP (Benchmark = 1×10^{-4})

Condition of Use	Category		IUR (ppm ⁻¹)	Cancer Risk		Respirator APF	Cancer Risk with Respirator		Exposure Data Type
				Central tendency	High-end		Central tendency	High-end	
Manufacturing (US)	-	Worker	0.004	1.4E-04	5.5E-04	10	1.4E-05	5.5E-05	Monitoring Data
Import, Repackaging, Processing -- Incorporation into Article	-	Worker	0.004	6.1E-06	1.2E-04	10	6.1E-07	1.2E-05	Model (Deterministic)
Processing - Incorporation into Formulation	-	Worker	0.004	1.1E-02		50	2.3E-04		Monitoring Data
	-	ONU	0.004	2.5E-04	5.7E-04	N/A	N/A	N/A	
Vapor Degreasing, Open-Top	-	Worker	0.004	1.1E-02	1.0E-01	50	2.1E-04	2.0E-03	Monitoring Data
	-	ONU	0.004	1.6E-04	9.4E-04	N/A	N/A	N/A	
	Pre-EC	Worker	0.004	2.8E-03	3.7E-02	50	5.6E-05	7.4E-04	Model (Probabilistic)
	Post-EC	Worker	0.004	2.8E-04	3.7E-03	50	5.6E-06	7.4E-05	
	Pre-EC	ONU	0.004	1.5E-03	2.1E-02	N/A	N/A	N/A	
	Post-EC	ONU	0.004	1.5E-04	2.1E-03				
Vapor Degreasing, closed-loop	-	Worker	0.004	5.6E-05	7.4E-04	10	5.6E-06	7.4E-05	Model (Probabilistic)
	-	ONU	0.004	3.0E-05	4.2E-04	N/A	N/A	N/A	
Cold Cleaning	-	Worker	0.004	6.8E-03	1.5E-02	50	1.4E-04	3.0E-04	Monitoring Data
	-	ONU	0.004	4.1E-03	5.3E-03	N/A	N/A	N/A	
	-	Worker	0.004	8.2E-04	1.8E-02	50	1.6E-05	3.7E-04	Model (Probabilistic)
	-	ONU	0.004	4.3E-04	1.1E-02	N/A	N/A	N/A	
Aerosol Degreasing	Pre-EC	Worker	0.004	2.6E-02	6.5E-02	N/A	N/A	N/A	Monitoring Data
	Post-EC	Worker	0.004	8.7E-03	1.1E-02	N/A	N/A	N/A	
	-	Worker	0.004	9.5E-03	3.6E-02	N/A	N/A	N/A	Model (Probabilistic)
	-	ONU	0.004	1.6E-04	1.4E-03	N/A	N/A	N/A	

Condition of Use	Category		IUR (ppm ⁻¹)	Cancer Risk		Respirator APF	Cancer Risk with Respirator		Exposure Data Type
				Central tendency	High-end		Central tendency	High-end	
Spray Adhesive	Pre-EC	Sprayer	0.004	2.1E-01	5.2E-01	50	4.2E-03	1.0E-02	Monitoring Data
	Post-EC	Sprayer	0.004	2.8E-02	8.6E-02	50	5.7E-04	1.7E-03	
	Pre-EC	Non-Sprayer	0.004	2.0E-01	4.3E-01	50	4.0E-03	8.7E-03	
	Post-EC	Non-Sprayer	0.004	2.9E-02	5.9E-02	50	5.7E-04	1.2E-03	
	Pre-EC	ONU	0.004	4.8E-03	2.6E-01	N/A	N/A	N/A	
	Post-EC	ONU	0.004	3.2E-03	1.1E-02	N/A	N/A	N/A	
Dry Cleaning	-	Worker	0.004	4.7E-02	1.0E-01	N/A	N/A	N/A	Monitoring Data
	-	ONU	0.004	1.9E-02	4.2E-02				
	3rd Gen	Spot Cleaner	0.004	1.6E-03	4.6E-03				Model (Probabilistic)
	3rd Gen	Machine & Finish	0.004	7.5E-03	3.4E-02				
	3rd Gen	ONU	0.004	9.7E-04	3.8E-03				
	4th Gen	Spot Cleaner	0.004	1.3E-03	3.3E-03				
	4th Gen	Machine & Finish	0.004	1.3E-03	3.7E-03				
	4th Gen	ONU	0.004	6.9E-04	2.4E-03				
Spot Cleaning	-	Worker	0.004	1.4E-03	9.7E-03	N/A	N/A	N/A	Monitoring Data
	-	Worker	0.004	1.2E-03	2.7E-03				Model (Probabilistic)
	-	ONU	0.004	5.8E-04	1.8E-03				
Disposal, Recycling	-	Worker	0.004	6.1E-06	1.2E-04	10	6.1E-07	1.2E-05	Model (Deterministic)

N/A – Not applicable. EPA believes respirator use is unlikely for workers at small commercial facilities (dry cleaners, spot cleaners) and for occupational non-users.

The range of extra cancer risks calculated for workers in each use category are described in Table 4-49, Figure 4-1 and Figure 4-2. Risk estimates are based on occupational exposure values derived from monitoring and modeling data (with and without engineering controls). The benchmark cancer risk estimate of 1×10^{-4} was exceeded for all of the uses in workers and occupational non-users for both central tendency and high-end exposure estimates for both monitoring and modeling data with or without the use an APF in most cases, with few exceptions. These exceptions included cancer risk estimates when respirators were assumed to be used for: manufacturing, import, repacking, processing – incorporation into article for the worker; vapor degreasing open-top for the occupational workers; vapor degreasing closed-loop for workplace exposures; cold cleaning for workers, and disposal, recycling for the worker. In most cases, benchmark cancer risk estimates were similar between monitoring and modeling within each use.

Figure 4-1. Central Tendency Inhalation Cancer Risk Estimates for Occupational Use of 1-BP

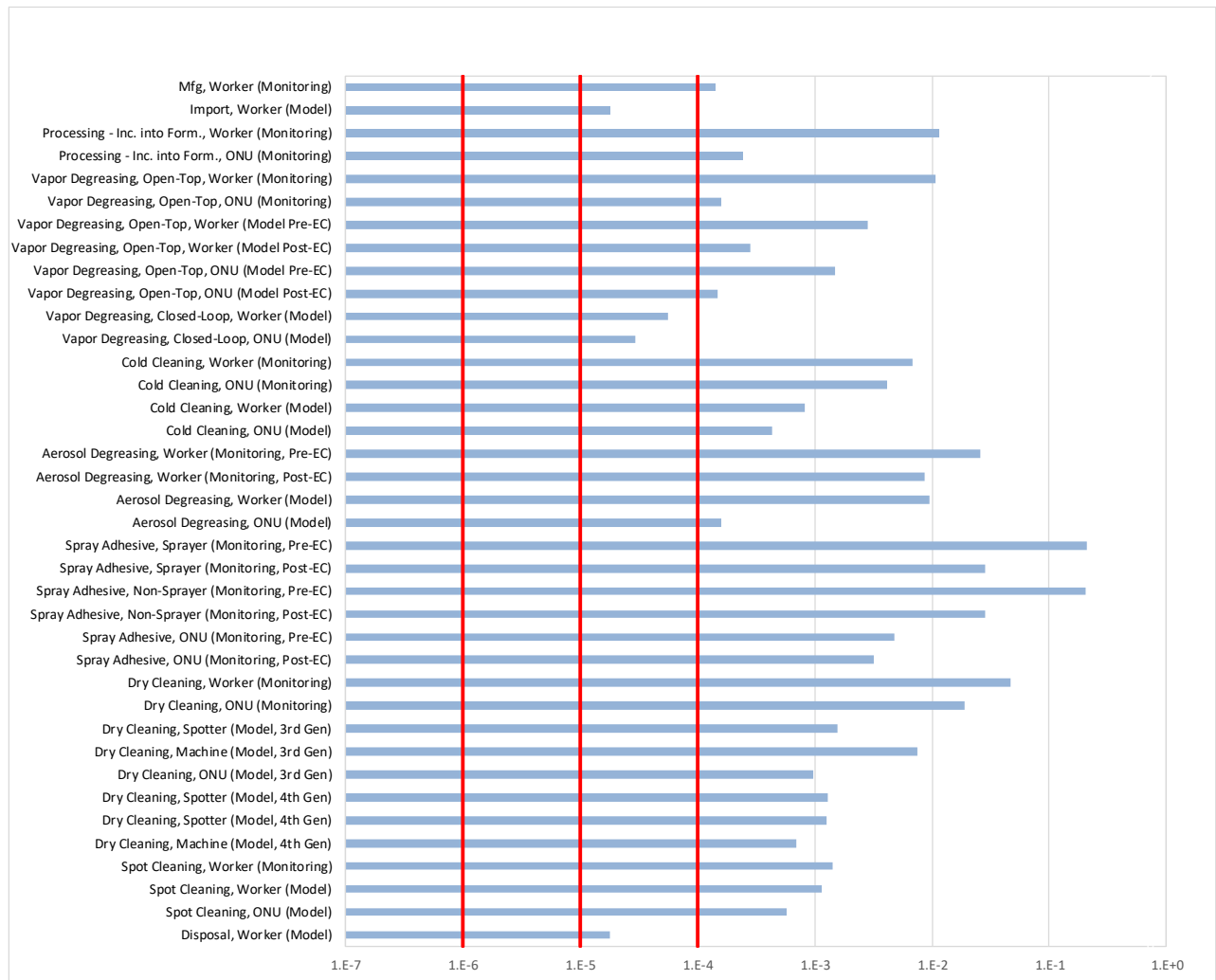
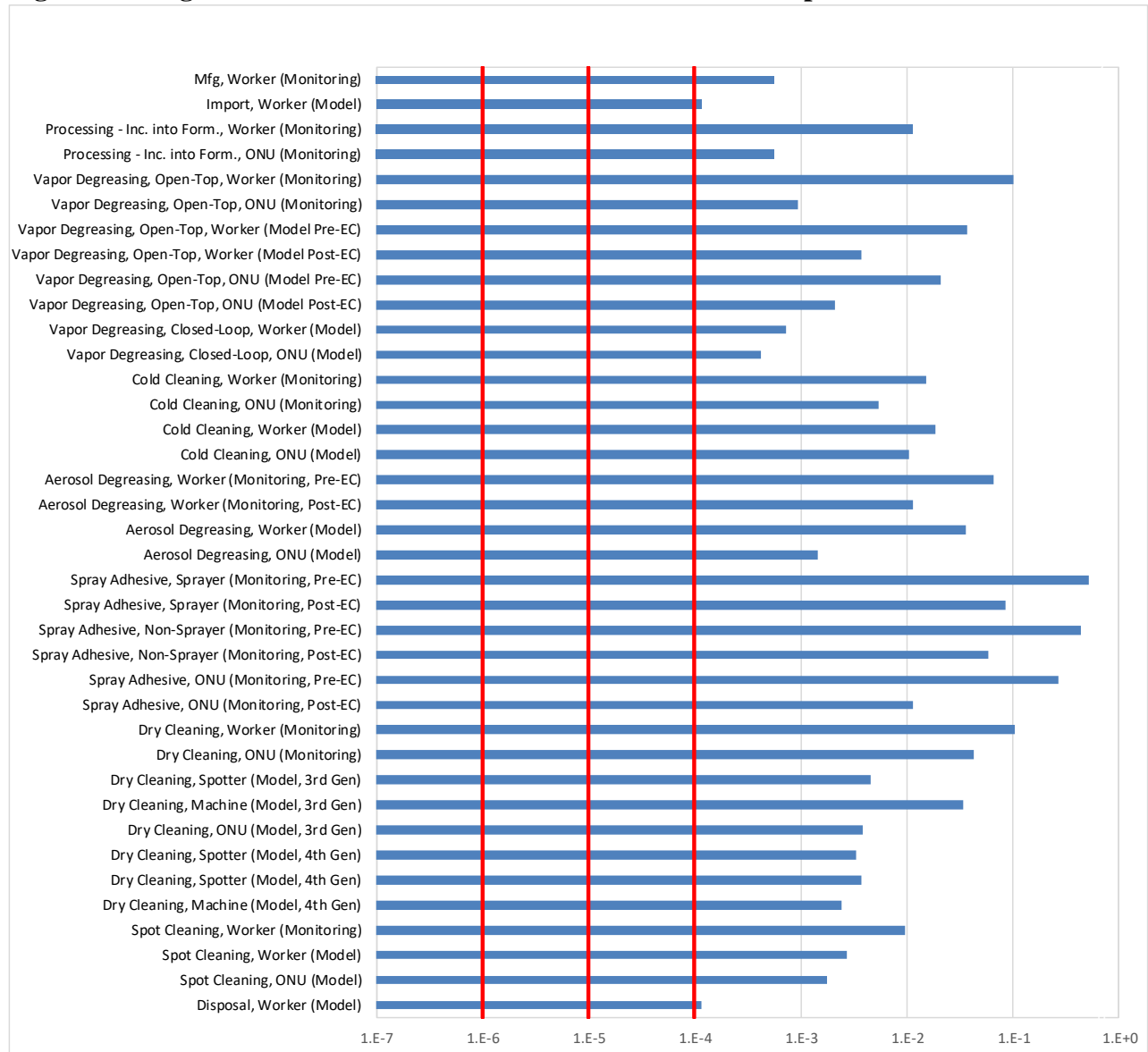


Figure 4-2. High-End Inhalation Cancer Risk Estimates for Occupational Use of 1-BP



4.2.4.3 Cancer Evaluation for Consumer Scenario (Insulation Off-Gassing)

EPA also estimated the excess cancers associated with chronic inhalation exposures under the insulation (off-gassing) condition of use for the consumer bystander. The excess cancer estimation for the insulation (off-gassing) condition of use was determined by multiplying the 7-year average TWA concentration by EPA's inhalation unit risk (IUR) identified in Table 3-6 for human exposure: 24 hours/day (5.00 E-03, 6.00 E-03, and 9.00 E-03). The supporting calculations are included in the 1-BP_Supplemental File_Consumer Exposure Risk Calculations ([EPA, 2019c](#)). ADAFs were not used for younger lifestages due to an inconclusive MMOA (Appendix K).

For consumer bystander exposure, EPA used the following benchmark for determining the acceptability of the cancer risk:

1×10^{-6} : the probability of 1 chance in 1 million of an individual developing cancer

Table 4-50 provides a summary of the excess cancer estimates for the Insulation (off-gassing) condition of use for the consumer bystander. Estimates are provided for all three locations within each building configuration evaluated for each of the three IURs.

Table 4-50. Inhalation Cancer Risk Estimates Under the Insulation (Off-Gassing) Condition of Use for the Consumer Bystander

Condition of Use	Scenario Description	Cancer MOE (7-Year Average TWA)		
		IUR (5.00E-03)	IUR (6.00E-03)	IUR (9.00E-03)
Insulation (off-gassing) A/LS/C	Attic	2.4E-07	2.9E-07	4.4E-07
	Living Space	9.8E-08	1.2E-07	1.8E-07
	Crawlspace	2.2E-07	2.7E-07	4.0E-07
Insulation (off-gassing) A/LS/B	Attic	2.4E-07	2.9E-07	4.3E-07
	Living Space	3.9E-08	4.7E-08	7.1E-08
	Basement	2.3E-07	2.8E-07	4.2E-07

MOE estimates were one to two orders of magnitude smaller than the benchmark MOEs for each location within each building configuration.

4.2.5 Risk Characterization For Acute and Chronic, Non-Cancer and Cancer Dermal Exposures

For dermal exposure, conditions of use with similar exposure concentration, exposure level, and potential for occlusion are “binned” as described in Section 2.3.1.23 for occupational exposures. MOE estimates for occupational conditions of use (Bins 1-5) following acute and chronic dermal exposures based on modeling and what-if glove protection factors are presented in Table 4-51, Table 4-52, Table 4-53, Table 4-54 and Table 4-55. Cancer risk estimates for these same conditions of use following chronic dermal exposures are presented in Table 4-56.

Use: Manufacture, Import, Processing, and Disposal (Bin 1)

MOE estimates for manufacture, import, processing, and disposal activities for both acute and chronic dermal exposure scenarios are presented in Table 4-51.

Table 4-51. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Manufacture, Import, Processing, and Disposal (Bin 1, Benchmark = 100)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	Exposure Level	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)
Acute, Non-Cancer	Develop. (litter size)	19	Central tendency	700	3,499	6,998	13,996
			High-end	233	1,166	2,333	4,665
	Develop. (post-impl. loss)	11	Central tendency	405	2,026	4,051	8,103
			High-end	135	675	1,350	2,701
Chronic, Non-Cancer	Liver	95	Central tendency	3,499	17,495	34,989	69,978
			High-end	1,166	5,832	11,663	23,326
	Kidney	115	Central tendency	4,236	21,178	42,355	84,711
			High-end	1,412	7,059	14,118	28,237
	Reproductive System	33	Central tendency	1,215	6,077	12,154	24,308
			High-end	405	2,026	4,051	8,103
	Develop. (litter size)	19	Central tendency	982	4,912	9,824	19,648
			High-end	327	1,637	3,275	6,549
	Develop. (post-impl. loss)	11	Central tendency	569	2,844	5,688	11,375
			High-end	190	948	1,896	3,792
	Nervous System	16	Central tendency	589	2,946	5,893	11,786
			High-end	196	982	1,964	3,929

MOE estimates for Manufacture, Import, Processing, and Disposal (Bin 1) were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to increase above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Vapor Degreaser and Cold Cleaner (Bin 2)

MOE estimates for vapor degreaser and cold cleaner conditions of use for both acute and chronic exposure scenarios are presented in Table 4-52.

Table 4-52. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Vapor Degreaser and Cold Cleaner (Bin 2, Benchmark = 100)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	Exposure Level	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)
Acute, Non-Cancer	Develop. (litter size)	19	Central tendency	721	3,607	7,214	14,429
			High-end	240	1,202	2,405	4,810
	Develop. (post-impl. loss)	11	Central tendency	418	2,088	4,177	8,353
			High-end	139	696	1,392	2,784
Chronic, Non-Cancer	Liver	95	Central tendency	3,607	18,036	36,071	72,143
			High-end	1,202	6,012	12,024	24,048
	Kidney	115	Central tendency	4,367	21,833	43,665	87,331
			High-end	1,456	7,278	14,555	29,110
	Reproductive System	33	Central tendency	1,253	6,265	12,530	25,060
			High-end	418	2,088	4,177	8,353
	Develop. (litter size)	19	Central tendency	1,013	5,064	10,128	20,255
			High-end	338	1,688	3,376	6,752
	Develop. (post-impl. loss)	11	Central tendency	586	2,932	5,863	11,727
			High-end	195	977	1,954	3,909
	Nervous System	16	Central tendency	608	3,038	6,075	12,150
			High-end	203	1,013	2,025	4,050

MOE estimates for vapor degreaser and cold cleaner conditions of use were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to increase above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Spray Adhesive (Bin 3)

MOE estimates for spray adhesive conditions of use for both acute and chronic exposure scenarios are presented in Table 4-53.

Table 4-53. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Spray Adhesive (Bin 3, Benchmark = 100)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	Exposure Level	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)
Acute, Non-Cancer	Develop. (litter size)	19	Central tendency	875	4,374	8,747	N/A
			High-end	292	1,458	2,916	
	Develop. (post-impl. loss)	11	Central tendency	506	2,532	5,064	
			High-end	169	844	1,688	
Chronic, Non-Cancer	Liver	95	Central tendency	4,374	21,868	43,736	
			High-end	1,458	7,289	14,579	
	Kidney	115	Central tendency	5,294	26,472	52,944	
			High-end	1,765	8,824	17,648	
	Reproductive System	33	Central tendency	1,519	7,596	15,193	
			High-end	506	2,532	5,064	
	Develop. (litter size)	19	Central tendency	1,228	6,140	12,280	
			High-end	409	2,047	4,093	
	Develop. (post-impl. loss)	11	Central tendency	711	3,555	7,109	
			High-end	237	1,185	2,370	
	Nervous System	16	Central tendency	737	3,683	7,366	
			High-end	246	1,228	2,455	

MOE estimates for spray adhesive conditions of use were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to increase above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Dry Cleaning and Spot Cleaner (Bin 4)

MOE estimates for dry cleaning and spot cleaner conditions of use for both acute and chronic exposure scenarios are presented in Table 4-54.

Table 4-54. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Dry Cleaning and Spot Cleaner (Bin 4, Benchmark = 100)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	Exposure Level	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)
Acute, Non-Cancer	Develop. (litter size)	19	Central tendency	744	3,722	7,445	N/A
			High-end	248	1,241	2,482	
	Develop. (post-impl. loss)	11	Central tendency	431	2,155	4,310	
			High-end	144	718	1,437	
Chronic, Non-Cancer	Liver	95	Central tendency	3,722	18,611	37,223	
			High-end	1,241	6,204	12,408	
	Kidney	115	Central tendency	4,236	21,178	42,355	
			High-end	1,412	7,059	14,118	
	Reproductive System	33	Central tendency	1,293	6,465	12,930	
			High-end	431	2,155	4,310	
	Develop. (litter size)	19	Central tendency	1,045	5,225	10,451	
			High-end	348	1,742	3,484	
	Develop. (post-impl. loss)	11	Central tendency	605	3,025	6,051	
			High-end	202	1,008	2,017	
	Nervous System	16	Central tendency	627	3,135	6,269	
			High-end	209	1,045	2,090	

MOE estimates for dry cleaning and spot cleaner conditions of use were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to increase above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Aerosol Spray Degreaser/Cleaner, Other Aerosol and Non-aerosol Uses (Bin 5)

MOE estimates for aerosol spray degreaser/cleaner, and other aerosol and non-aerosol conditions of use for both acute and chronic exposure scenarios are presented in Table 4-55.

Table 4-55. Non-Cancer Risk Estimates for Acute and Chronic Dermal Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser/Cleaner, Other Aerosol and Non-aerosol Uses (Bin 5, Benchmark = 100)

Exposure Duration for Risk Analysis	Target Organ/System	HED (mg/kg-day)	Exposure Level	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)
Acute, Non-Cancer	Develop. (litter size)	19	Central tendency	700	3,499	6,998	N/A
			High-end	233	1,166	2,333	
	Develop. (post-impl. loss)	11	Central tendency	405	2,026	4,051	
			High-end	135	675	1,350	
Chronic, Non-Cancer	Liver	95	Central tendency	3,499	17,495	34,989	
			High-end	1,166	5,832	11,663	
	Kidney	115	Central tendency	4,236	21,178	42,355	
			High-end	1,412	7,059	14,118	
	Reproductive System	33	Central tendency	1,215	6,077	12,154	
			High-end	405	2,026	4,051	
	Develop. (litter size)	19	Central tendency	982	4,912	9,824	
			High-end	327	1,637	3,275	
	Develop. (post-impl. loss)	11	Central tendency	569	2,844	5,688	
			High-end	190	948	1,896	
	Nervous System	16	Central tendency	589	2,946	5,893	
			High-end	196	982	1,964	

MOE estimates aerosol spray degreaser/cleaner, and other aerosol and non-aerosol conditions of use were above the benchmark MOE by 1-2 orders of magnitude in all acute and chronic exposure scenarios for all health effect endpoints when no gloves were used (PF=1). As the PF increased, MOE estimates continued to increase above the benchmark MOE in both acute and chronic exposure scenarios for all health effect endpoints.

Use: Bins 1-5

Cancer risk estimates for occupational conditions of use (category Bins 1-5) are presented in Table 4-56.

Table 4-56. Cancer Risk Estimates for Dermal Exposure Following Occupational Use of 1-BP

Category	Dermal Slope Factor (mg/kg-day) ⁻¹	Exposure Level	No Gloves (PF = 1)	Protective Gloves (PF = 5)	Protective Gloves (PF = 10)	Protective Gloves (PF = 20)	Benchmark
Bin 1: Manufacture, Import, Proc	0.006	Central tendency	6.47E-05	1.29E-05	6.47E-06	3.24E-06	1E-04
		High-end	2.51E-04	5.01E-05	2.51E-05	1.25E-05	
Bin 2: Degreasing and cold cleaning		Central tendency	6.28E-05	1.26E-05	6.28E-06	3.14E-06	1E-04
		High-end	2.43E-04	4.86E-05	2.43E-05	1.22E-05	
Bin 3: Spray adhesives		Central tendency	5.18E-05	1.04E-05	5.18E-06	N/A	1E-04
		High-end	2.01E-04	4.01E-05	2.01E-05	N/A	
Bin 4: Dry cleaning, spot cleaning		Central tendency	6.09E-05	1.22E-05	6.09E-06	N/A	1E-04
		High-end	2.36E-04	4.71E-05	2.36E-05	N/A	
Bin 5: Aerosol spray degreaser, Other aerosol and non-aerosol uses		Central tendency	6.47E-05	1.29E-05	6.47E-06	N/A	1E-04
		High-end	2.51E-04	5.01E-05	2.51E-05	N/A	

The benchmark cancer risk estimate (1x10⁻⁴) was exceeded for all conditions of use in the high-end scenario (Bins 1-5) when no gloves were used (PF=1); however, as the PF increased between 5 and 20, the benchmark cancer risk estimate (1x10⁻⁴) was not exceeded.

Consumer MOE Estimates for Acute, Non-Cancer Dermal Exposure

MOE estimates for acute, non-cancer consumer dermal exposures were derived for all conditions of use except the insulation (off-gassing) condition of use. Table 4-57 provides a summary of acute, non-cancer consumer dermal exposure for the eight conditions of use evaluated

for dermal exposure. The supporting calculations are included in the 1-BP_Supplemental File_Consumer Exposure Risk Calculations ([EPA, 2019c](#))

Table 4-57. Non-Cancer Risk Estimates for Acute 24-hr Dermal Exposure Following Consumer Uses of 1-BP

Condition of Use	Scenario Description	Developmental Effects Decreased live litter size (F ₁) (WIL Research, 2001) HED = 19 mg/kg-day			Developmental Effects Post-Implantation Loss (F ₀) (WIL Research, 2001) HED = 11 mg/kg-day		
		Adult	Youth A	Youth B	Adult	Youth A	Youth B
		Aerosol spray degreaser/cleaner-general	High Intensity Use	5.4	5.8	5.3	3.1
	Moderate Intensity Use	83	86	79	48	50	46
	Low Intensity Use	1118	1188	1118	647	688	647
Aerosol spray degreaser/cleaner-electronic	High Intensity Use	413	442	404	239	256	234
	Moderate Intensity Use	559	594	543	324	344	314
	Low Intensity Use	792	864	792	458	500	458
Spot cleaner and stain remover	High Intensity Use	22	23	21	13	14	12
	Moderate Intensity Use	209	224	204	121	129	118
	Low Intensity Use	4419	4634	4318	2558	2683	2500
Coin and scissors cleaner	High Intensity Use	250	268	247	145	155	143
	Moderate Intensity Use	500	543	487	289	314	282
	Low Intensity Use	1462	1583	1462	846	917	846
Spray cleaner-general	High Intensity Use	5.3	5.8	5.3	3.1	3.3	3.1
	Moderate Intensity Use	43	45	42	25	26	24
	Low Intensity Use	322	345	311	186	200	180
Adhesive accelerant	High Intensity Use	396	422	388	229	244	224
	Moderate Intensity Use	396	422	388	229	244	224
	Low Intensity Use	396	422	388	229	244	224
Automobile AC flush	High Intensity Use	38	40	37	22	23	21
	Moderate Intensity Use	38	40	37	22	23	21
	Low Intensity Use	38	40	37	22	23	21
Mold cleaning and release products	High Intensity Use	442	475	432	256	275	250
	Moderate Intensity Use	679	731	655	393	423	379
	Low Intensity Use	1267	1357	1267	733	786	733

MOE estimates were below the benchmark MOE of 100 for four of the eight conditions of use evaluated. Generally, MOE estimates were one to two orders of magnitude lower than the benchmark MOE.

4.3 Assumptions and Key Sources of Uncertainty

The characterization of variability and uncertainty is fundamental to any risk evaluation. Variability refers to “the true heterogeneity or diversity in characteristics among members of a population (*i.e.*, inter-individual variability) or for one individual over time (intra-individual variability)” ([U.S. EPA, 2001](#)). The risk evaluation was designed to reflect critical sources of variability to the extent allowed by available methods and data and given the resources and time available.

On the other hand, uncertainty is “the lack of knowledge about specific variables, parameters, models, or other factors” ([U.S. EPA, 2001](#)) and can be described qualitatively or quantitatively. Uncertainties in the risk evaluation can raise or lower the confidence of the risk estimates. In this assessment, the uncertainty analysis also included a discussion of data gaps/limitations. The next sections describe the uncertainties and data gaps in the exposure, hazard/dose-response and risk characterization.

One key uncertainty is whether the human populations that are at the greatest risk, based on the integration of information regarding highly exposed groups (or “potentially exposed”) and biologically susceptible subpopulations, have been adequately defined and characterized. Workers and ONUs who are also biologically susceptible individuals (*e.g.*, reproductive age men and women, pregnant women and their fetus, and adolescent workers) would represent the most susceptible population. Consumers (product users) and bystanders who are biologically susceptible individuals would also represent the most susceptible populations. Analyses have been performed to understand the risk for the identified potentially susceptible populations.

4.3.1 Uncertainties of the Occupational Exposure Assessment

EPA addressed variability in the exposure models by identifying key model parameters to apply a statistical distribution that mathematically defines the parameter’s variability. EPA defined statistical distributions for parameters using documented statistical variations where available. Where the statistical variation is not known, assumptions are made to estimate the parameter distribution using available literature data. See the *Supplemental Information on Occupational Exposure Assessment* ([EPA, 2019f](#)) for statistical distribution for each model input parameter. The following sections discuss uncertainties in the occupational exposure assessment.

One overarching uncertainty is that exposures to 1-BP from outside the workplaces are not included in the occupational assessment, which may lead to an underestimate of occupational exposure. Another overarching uncertainty is that inhalation and dermal exposures were assessed separately, which may also lead to an underestimation of occupational exposure.

4.3.1.1 Number of Workers

There are a number of uncertainties surrounding the estimated number of workers potentially exposed to 1-BP, as outlined below. Most are unlikely to result in a systematic underestimate or overestimate, but could result in an inaccurate estimate.

CDR data are used to estimate the number of workers associated with the following conditions of use: Manufacturing, Import, Processing as a Reactant, and Incorporation into Formulation, Mixture, or Reaction Product. There are inherent limitations to the use of CDR data. First, manufacturers and importers are only required to report if they manufactured or imported 1-BP in excess of 25,000 pounds at a single site during any calendar from 2012 to 2015; as such, CDR may not capture all sites and workers associated with any given chemical. Second, the estimate is based on information that is known or reasonably ascertainable to the submitter. CDR submitters (chemical manufacturers and importers) do not always have accurate information on the number of potentially exposed workers at downstream processing sites.

There are also uncertainties associated with BLS data, which are used to estimate the number of workers for the remaining conditions of use. First, BLS' OES employment data for each industry/occupation combination are only available at the 3-, 4-, or 5-digit NAICS level, rather than the full 6-digit NAICS level. This lack of granularity could result in an overestimate of the number of exposed workers if some 6-digit NAICS are included in the less granular BLS estimates but are not, in reality, likely to use 1-BP for the assessed condition of use. EPA addressed this issue by refining the OES estimates using total employment data from the U.S. Census' SUBS. However, this approach assumes that the distribution of occupation types (SOC codes) in each 6-digit NAICS is equal to the distribution of occupation types at the parent 5-digit NAICS level. If the distribution of workers in occupations with 1-BP exposure differs from the overall distribution of workers in each NAICS, then this approach will result in inaccuracy.

Second, EPA's judgments about which industries (represented by NAICS codes) and occupations (represented by SOC codes) are associated with the uses assessed in this report are based on EPA's understanding of how 1-BP is used in each industry. Designations of which industries and occupations have potential exposures is nevertheless subjective, and some industries/occupations with few exposures might erroneously be included, or some industries/occupations with exposures might erroneously be excluded. This would result in inaccuracy but would be unlikely to systematically either overestimate or underestimate the count of exposed workers.

4.3.1.2 Analysis of Occupational Exposure Monitoring Data

To analyze exposure monitoring data, EPA categorized individual PBZ data point as either "worker" or "occupational non-user." Exposures for occupational non-users can vary substantially. Most data sources do not sufficiently describe the proximity of these employees to the 1-BP exposure source. As such, exposure levels for the "occupational non-user" category will have high variability depending on the specific work activity performed. It is possible that some employees

categorized as “occupational non-user” have exposures similar to those in the “worker” category depending on their specific work activity pattern.

Some data sources may provide exposure estimates that are higher than typical across the distribution of facilities for that condition of use. For example, NIOSH HHEs for the spray adhesive use were conducted to address concerns regarding adverse human health effects reported following 1-BP exposure with spray adhesive use in furniture manufacturing. Two HHEs were requested by the North Carolina Department of Labor; one was conducted in response to a confidential request submitted by the facility’s employees.

There are limited exposure monitoring data in literature for certain conditions of use or job categories. For example, very few data points are available for cold cleaning and for spot-cleaning. Where few data are available, the assessed exposure levels are unlikely to be representative of worker exposure across the entire job category or industry. In addition, exposure data for compliance safety and health officers may not be representative of typical exposure levels for occupational non-users.

For vapor degreasing and cold cleaning, several sources do not contain detailed information describing the type of degreaser or cleaner present at the facility. The lack of such information results in uncertainty in the assessed exposure levels associated with specific subcategories of such equipment. For example, the data presented for batch open-top vapor degreasers may actually include data associated with other types of degreaser.

Where the sample data set contains six or more data points, the 50th and 95th percentile exposure concentrations were calculated from the sample to represent central tendency and high-end exposure levels. The underlying distribution of the data, and the representativeness of the available data, are not known.

4.3.1.3 Near-Field / Far-Field Model Framework

The near-field / far-field approach is used as a framework to model inhalation exposure for many conditions of use. The following describe uncertainties and simplifying assumptions generally associated with this modeling approach:

- There is uncertainty associated with each model input parameter. In general, the model inputs were determined based on review of 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 each well mixed, such that each of these zones can be approximated by a single, average concentration.

- All of the emissions from the facility are assumed to enter the near-field zone. This assumption will overestimate exposures and risks in facilities where some of the emissions do not enter the airspaces relevant to the 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). Since vapor degreasing and cold cleaning involve automated processes, a worker may actually walk away from the near-field during part of the process and return when it is time to unload the degreaser. As such, assuming the worker is exposed at the near-field concentration for the entire activity duration may overestimate exposure. Conversely, assuming the occupational non-user is exposed at the far-field concentration for the entire work day may underestimate exposure as they may not remain exclusively in the far-field.
- For certain 1-BP applications (*e.g.*, vapor degreasing and cold cleaning), 1-BP vapor is assumed to emit continuously while the equipment operates (*i.e.*, constant vapor generation rate). Actual vapor generation rate may vary with time. However, small time variability in vapor generation is unlikely to have a large impact in the exposure estimates as exposures are calculated as a time-weighted average.
- The exposure models represent model workplace settings for each 1-BP condition of use. The models have not been regressed or fitted with monitoring data.
- The models represent a baseline scenario that do not have LEV. EPA does not have adequate data to construct LEV systems into the exposure models. Additionally, there is no data on the fraction of U.S. facilities that use LEV. Where available, “what-if” values on engineering control effectiveness are applied to the model baseline to provide post-EC scenarios. These values were obtained by reviewing statements made in published literature regarding potential emission or exposure reductions after implementation of engineering control or equipment substitution.

Each subsequent section below discuss uncertainties associated with the individual models.

4.3.1.4 Vapor Degreasing and Cold Cleaning Model

The vapor degreasing and cold cleaning assessments use a near-field / far-field approach to model worker exposure. In addition to the uncertainties described above, the vapor degreasing and cold cleaning models have the following uncertainties:

- To estimate vapor generation rate for vapor degreasing, EPA references a 1-BP emission factor developed by CARB for the California Solvent Cleaning Emissions Inventories ([CARB, 2011](#)). The emission factor is an average emission for the “vapor degreasing” category for the California facilities surveyed by CARB. The category includes batch-loaded vapor degreaser, aerosol surface preparation process, and aerosol cleaning process. For the purpose of modeling, EPA assumes the 1-BP emission factor is entirely attributed to vapor degreasing applications. The representativeness of the emission factor for vapor degreasing emissions in other geographic locations within the U.S. is uncertain.

- The CARB emission factor covers batch degreasing units. However, CARB does not further specify whether these are open-top vapor degreasers, enclosed, or other types of batch degreasers. EPA assumes the emission factor is representative of open-top vapor degreaser, as it is the most common design for batch units using 1-BP. In addition, EPA assumes that the surveyed facilities likely switched to using 1-BP, an alternative, non-HAP solvent, as a way of complying with Federal and State regulations for HAP halogenated solvents (*i.e.*, chemical substitution, rather than equipment changes).
- The CARB emission factor, in the unit of pound per employee-year, was developed for the purpose of estimating annual emissions. These types of emission factor typically reflect the amount of solvent lost / emitted, some of which may not be relevant to worker exposure. For example, 1-BP emitted and captured through a stack may not result in worker exposure. Therefore, assuming all of the 1-BP is emitted into the workplace air may result in overestimating of exposure. In addition, the use of an annual emission factor does not capture time variability of emissions. The approach assumes a constant emission rate over a set number of operating hours, while actual emissions and worker exposures will vary as a function of time and worker activity.
- EPA combines the CARB emission factor with nationwide Economic Census employment data across 78 NAICS industry sector codes. It should be noted that vapor degreasing is not an industry-specific operation. Only a subset of facilities within the 78 selected industry sectors are expected to operate vapor degreasers. Therefore, the industry-average employment data may not be representative of the actual number of employees at vapor degreasing facilities.
- To estimate worker exposure during cold cleaning, EPA applied an emission reduction factor to the vapor degreasing model by comparing the AP-42 emission factors for the two applications. The AP-42 emission factors are dated. Furthermore, the cold cleaning model results have not been validated with actual monitoring data.
- EPA assumes workers and occupational non-users remove themselves from the contaminated near- and far-field zones at the conclusion of the task, such that they are no longer exposed to any residual 1-BP in air.
- The model assumes an exposure reduction of 90 percent with engineering controls. In reality, engineering controls and their effectiveness are site-specific. Additionally, the 90 percent reduction is a value based on TCE, and may not be applicable to a more volatile chemical such as 1-BP.

4.3.1.5 Aerosol Degreasing Model

The aerosol degreasing assessment also uses a near-field/far-field approach to model worker exposure. Specific uncertainties associated with the aerosol degreasing scenario are presented below:

- The model references a CARB ([2000](#)) study 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 1-BP.

- The Use Dossier ([U.S. EPA, 2017c](#)) identifies 25 different aerosol degreasing formulations containing 1-BP. For each *Monte Carlo* iteration, the model determines the 1-BP concentration in product by selecting one of 25 possible formulations, assuming equal probability of each formulation being used. In reality, some formulations are likely more prevalent than others.

4.3.1.6 Dry Cleaning Model

The multi-zone dry cleaning model also uses a near-field/far-field approach. Specific uncertainties associated with the dry cleaning scenario are presented below:

- The model assumes each facility only has one dry cleaning machine, cleaning one to fourteen loads of garments per day. While the dry cleaning facilities in Blando et al. ([2010](#)) and NIOSH ([2010](#)) appear to only have one machine, the representativeness of these two studies is not known. Larger facilities are likely to have more machines, which could result in additional 1-BP exposures.
- The model conservatively uses a hemispherical volume based on the dry cleaning machine door diameter as the near-field for machine unloading. The small near-field volume results in a large spike in concentration when the machine door is opened, where any residual 1-BP solvent is assumed to be instantaneously released into the near-field. In reality, the residual solvent will likely be released continuously over a period of time. In addition, the worker may move around while unloading the garments, such that the worker's breathing zone will not always be next to the machine door throughout the duration of this activity. Therefore, these assumptions may result in an overestimate of worker exposure during machine unloading.
- Many of the model input parameters were obtained from ([Von Grote et al., 2003](#)), which is a German study. Aspects of the U.S. dry cleaning facilities may differ from German facilities. However, it is not known whether the use of German data will under- or over-estimate exposure.
- The model does not cover all potential worker activities at dry cleaners. For example, workers could be exposed to 1-BP emitted due to equipment leaks, when re-filling 1-BP solvent into dry cleaning machines, when interrupting a dry cleaning cycle, or when performing maintenance activities (*e.g.*, cleaning lint and button traps, raking out the still, changing solvent filter, and handling solvent waste) ([OSHA, 2005](#)). However, there is a lack of information on these activities in the literature, and the frequency of these activities is not well understood. The likelihood of equipment leaks is dependent on whether the machines are properly converted and maintained. The frequency of solvent re-filling depends on a specific dry cleaner's workload and solvent consumption rate, which is also affected by the presence of leaks. Based on observations reported by ([NIOSH, 2010](#)) and ([Blando et al., 2010](#)), solvent charging is not performed every day. EPA was unable to develop a modeling approach for these exposure activities due to the lack of available information.

4.3.1.7 Spot Cleaning Model

The spot cleaning assessment also uses a near-field/far-field approach to model worker exposure. The model estimates a use rate of 16 gallons per year spot cleaner. This value was derived using a MassDEP case study for one specific dry cleaner in Massachusetts, handling 100 pieces of garments per day. MassDEP noted that the size of each dry cleaner can vary substantially. As such, the spot cleaner use rate will also vary by the individual facility work load. The representativeness of the spot cleaner use rate from this case study is not known.

4.3.1.8 Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model

For Import/repackaging, Processing as a reactant, and Processing – Incorporation into articles, the *Tank Truck and Railcar Loading and Unloading Release and Inhalation Exposure Model* is 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 1-BP 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 judgment. These dimensions may not be representative of the whole range of loading equipment used at industrial facilities handling 1-BP.
- The model estimates fugitive emissions from equipment leaks using total organic compound emission factors from EPA's Protocol for Equipment Leak Emission Estimates (1995), and engineering judgement on the likely equipment type used for transfer (*e.g.*, number of valves, seals, lines, and connections). The applicability of these emission factors to 1-BP, and the accuracy of EPA's assumption on equipment type are not known.
- The model assumes the use a vapor balance system to minimize fugitive emissions. Although most industrial facilities are likely to use a vapor balance system when loading/unloading volatile chemicals, EPA does not know whether these systems are used by all facilities that potentially handle 1-BP.

4.3.1.9 Modeling Dermal Exposures

The Dermal Exposure to Volatile Liquids Model is used to estimate dermal exposure to 1-BP in occupational settings. The model assumes a fixed fractional absorption of the applied dose; however, fractional absorption may be dependent on skin loading conditions. The model also assumes a single exposure event per day based on existing framework of the EPA/OPPT 2-Hand Dermal Exposure to Liquids Model and does not address variability in exposure duration and frequency.

The model accounts for potential glove use by presenting the dermal dose estimates using several what-if values for glove protection factor (PF). These PF values depend on whether the glove is chemically resistant, and whether the employee has received training on glove use. It should be

noted that PF values are not chemical-specific, and using PF values to adjust the dermal dose may either under- or over-estimate actual exposure. For example, assumption of certain glove PF value may underestimate exposure as 1-BP easily penetrates most common glove materials. In addition, incorrect glove use may lead to glove contamination or occluded exposure, resulting in higher exposure than when gloves are not used. In this case, actual PF value may be less than one.

4.3.2 Uncertainties of the Consumer Exposure Assessment

Modeling was used to evaluate consumer exposure concentrations resulting from the use of the following consumer products containing 1-BP: aerosol spray degreaser/cleaner-general; aerosol spray degreaser/cleaner-electronics, spot cleaner and stain remover, coin and scissors cleaner, spray cleaner-general, adhesive accelerant, automobile AC flush, mold cleaning and release product, and insulation (off-gassing). Inputs for this modeling approach relied on default values (based on experimental data) within the models used, survey information, and various assumptions. As with any approach to risk evaluations, there are uncertainties associated with the assumptions, data used, and approaches used. These are discussed in detail within Section 2.3.2.

4.3.2.1 Consumer Use Information

The consumer use dossier and market profile documents ([U.S. EPA, 2017c](#)) were developed in 2016 and 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 occurring after the documents were compiled. While there may be some uncertainty associated with products identified in 2016 and 2017 remaining readily available, EPA believes the information utilized to identify the consumer uses is the best available information.

EPA found national survey information related to use of household products containing solvents ([EPA, 1987](#)) that was compiled in 1987. While this survey is an older survey, many of the product categories within the survey align well with the consumer conditions of use identified for this evaluation. Additionally, the consumer use profiles and patterns evaluated by the survey remain strong when compared to modern day consumer use patterns even though some aspects of the use may have changed. Regardless of these similarities and strengths, EPA realizes there is still some level of uncertainty associated with the survey data and its application to modern day consumer use patterns, amount used, or duration of use. While some level of uncertainty remains, the approach taken for this evaluation to vary key inputs across the spectrum of use patterns captured by the survey should reduce the uncertainties.

The frequency of use values extracted from the Westat Survey ([EPA, 1987](#)) and utilized for consumer modeling were assumed to be infrequent, non-consecutive time periods and therefore not expected to create risk concerns for chronic exposure scenarios (with the exception of insulation in residential homes). However, it is unknown whether frequency of use patterns are expected to be clustered or intermittent and how this type of exposure would compare to continuous-exposure toxicity studies. Therefore, while EPA cannot fully rule out the possibility that consumers at the high-end frequencies of use could be at risk for chronic hazard effects, it is expected to be unlikely.

4.3.2.2 Model Assumptions and Input Parameters

Inhalation Models and Results

There is a high confidence in the three models used to evaluate inhalation exposure and the inhalation results found for the conditions of use identified in Table 2-31. This confidence derives from a review of the strengths of the models used, sensitivity of the models, data and inputs utilized for modeling, and approaches taken for this evaluation to capture a range of consumer use patterns.

Dermal Models and Results

There is a low confidence in the two models used to evaluate dermal exposure and the dermal results found for the conditions of use identified in Table 2-31. This confidence derives from the limitations and uncertainties inherent within the two dermal models selected and associated assumptions necessary to correctly apply the two models to the conditions of use evaluated and the consumer use patterns considered for consumer exposure. The switch from an aqueous based K_p value to a neat K_p value, along with use of a neat permeability coefficient and experimental absorption coefficient increases the confidence in the dermal results presented. Additional discussion on limitations and uncertainties along with a sensitivity analysis comparing the two methods selected and a third method published by Frasch ([Frasch and Bunge, 2015](#)) is provided in Appendix F.

There is a high degree of confidence in the consumer product weight fractions identified for the consumer products evaluated in this assessment. Product weight fractions were obtained from product specific SDS and when a range of weight fractions exists across several products within a single condition of use evaluated, modeling was conducted across the range of weight fractions capturing a low, moderate, and high weight fraction value.

There is a high degree of confidence in inputs to the various models used, including vapor pressure, molecular weight, room volumes, whole house volume, and air exchange rate. The physical-chemical properties of 1-BP are well documented and therefore have a high degree of confidence. The room and house volumes as well as air exchange rates are based on values from U.S. EPA's Exposure Factors Handbook ([U.S. EPA, 2011](#)) and therefore also have a high degree of confidence.

4.3.3 Uncertainties in the Hazard and Dose-Response Assessments

EPA's risk assessment relied on the hazard values (*i.e.*, HECs/HEDs/ADAFs) derived in this evaluation. These hazard values were used to estimate risks to various health effects following 1-BP exposure related to specific 1-BP uses.

There are several uncertainties inherent to the data and the assumptions used to support the derivation of the acute and chronic non-cancer PODs for different health effects domains. Below is a summary of the major uncertainties affecting the non-cancer hazard/dose response approach used for this assessment.

The uncertainties in hazard and dose response assessment are predicated on the health protective assumptions of relevancy of cancer and non-cancer findings in rodents being relevant to humans.

Decreased live litter size was selected as an endpoint to evaluate risks associated with acute exposures to 1-BP. Although the developmental toxicity studies included repeated exposures, EPA considered evidence that a single exposure to a toxic substance can result in adverse developmental effects, described by ([Van Raaij et al., 2003](#)), as relevant to 1-BP. The selection of an endpoint from a short-term developmental exposure study is a health protective assumption stated in the EPA Guidelines for Developmental Toxicity Risk Assessment (<https://www.epa.gov/risk/guidelines-developmental-toxicity-risk-assessment>).

Although there is evidence of biological effects in both the fetus and neonate, there are uncertainties in extrapolating doses for these lifestages. It is not known if 1-BP or its metabolites are transferred to the pups via lactation. It is possible that the doses reaching the fetus and the neonate are similar and that these lifestages are equally sensitive; however, it is also possible that one lifestage is more sensitive than the other or that internal doses are different. Additional data would be needed to refine dose estimates for the fetus and pups in order to identify the specific windows of sensitivity. EPA assumes that a single exposure at any point during pregnancy can have a detrimental impact (leading to fetal mortality). This health protective approach will overestimate risks to the workers and consumers following acute exposures, especially for those lifestages below reproductive age.

Neurotoxicity produced by 1-BP are based on rodent and human literature, with considerable similarities in both qualitative and quantitative outcomes (Appendix J.2 and J.3). In the human and rodent literature, the most consistent responses are symptoms of frank neurotoxicity occurring at high exposures, with effects that are progressive at repeated exposures to low concentrations. In humans, the reports of effects in factory workers with lower exposures are limited by questions regarding exposure characterization, measurement techniques, and sensitivity. For these reasons, the data are not sufficiently robust for quantitative dose-response analysis. On the other hand, the findings of decreased peripheral nerve function are supported by parallel measures in several rodent studies.

Uncertainties in the acute and chronic hazard values stem from the following sources:

Non-cancer hazard values (e.g., NOAELs, LOAELs, BMD): PODs were identified from the animal studies that were suitable for dose-response analysis. The process of identifying PODs for various health effects domains involved the evaluation of the strengths and limitations of the data and the weight of the scientific evidence for a particular health effects domain before supporting an association between 1-BP exposure and various human health effects. The selected PODs values (e.g., NOAEL, LOAEL or BMD) depend on the current available data and could change as additional studies are published.

Also, when selecting a BMD as a POD, the selection of the benchmark dose response (BMR) (e.g., 1%, 5% or 10% level) directly affects the calculation of the BMD. There are uncertainties related to

the BMRs since their selection depends on scientific judgments on the statistical and biological characteristics of the dataset and how the BMDs will be finally used.

In addition, there are uncertainties about the appropriate dose-response model used to generate the BMDs. However, these uncertainties should be minimal if the chosen model fits well the observable range of the data, as discussed in EPA [Benchmark Dose Technical Guidance](#).

- **Duration adjustment to continuous exposure:** Most of the PODs used to derive HECs came from studies that did not expose animals or humans to 1-BP on a continuous basis. These PODs were then mathematically adjusted to reflect equivalent continuous exposures (daily doses) over the study exposure period under the assumption that the effects are related to concentration \times time ($C \times t$), independent of the daily (or weekly) exposure regimen ([U.S. EPA, 2011](#)). However, the validity of this assumption is generally unknown, and, if there are dose-rate effects, the assumption of $C \times t$ equivalence would tend to bias the POD downwards ([U.S. EPA, 2011](#)). A single exposure to 1-BP at a critical window of fetal development was assumed to produce adverse developmental effects. This is a health protective approach and no duration adjustment was performed for adverse developmental outcomes.
- **Extrapolation of repeated dose developmental effects to acute scenarios:** EPA considers developmental toxicity endpoints to be applicable to acute exposures. While there is some uncertainty surrounding this consideration because the precise critical exposure window is unknown, multiple publications suggest that developmental effects (*e.g.*, decreased live litter size and increased post-implantation loss) may result from a single exposure during a critical window of development. There are uncertainties related to whether developmental effects observed in developmental toxicity studies may result from a single exposure to 1-BP. In this evaluation, the risk assessment associated with acute exposure used the hazard value for decreases in litter size and increases in post-implantation loss from the ([WIL Research, 2001](#)) two-generation reproductive toxicity study. This is considered a health protective approach.

For cancer hazard assessment, the major uncertainty is whether the mechanism/mode of action of 1-BP carcinogenesis should be considered mutagenic. The uncertainty arises because the results of genotoxicity testing have been mixed, as described in detail in Section 3.2.5.6 above. While a MMOA may be operative at least in part for the carcinogenicity of 1-BP, the default linear extrapolation method for dose-response is used. For the cancer dose-response assessment, uncertainties exist arising from the animal to human extrapolation in the derivation of the IUR. A source of uncertainty is the cancer model used to estimate the POD for the IUR derivation. The POD was based on a model averaging approach to fit the bioassay data for lung tumors. Although the model average fit the data, alternate model selections can also fit the data. A sensitivity analysis comparing reasonable alternate model choices found similar PODs therefore, the impact of selecting between alternative models results in similar IURs.

Data gaps include conclusive information on the mutagenic properties of 1-BP and its metabolites in vitro and in vivo, data on the nature and frequencies of mutations in workers exposed to 1-BP over time, information on variations in susceptibility of the human population to cancer (*e.g.*, related to CYP2E1 polymorphisms or other differences), and associations between developmental life stage exposure and cancer in childhood and adulthood. The available data are not sufficient to establish the molecular initiating and/or key events in the adverse outcome pathway from 1-BP exposure to development of cancer.

4.3.4 Uncertainties in the Risk Assessment

4.3.4.1 Environmental Risk Characterization

While EPA has determined that sufficient data are available to characterize the overall environmental hazards of 1-BP under the conditions of use of this evaluation, there are uncertainties regarding the available environmental hazard data for 1-BP. As discussed in Section 3.1.2, the single acute study identified for 1-BP was part of a larger EPA-funded effort to generate an acute toxicity database for a variety of organic chemicals ([Geiger et al., 1988](#)). As such, this study was subject to the editing, quality assurance, and peer review procedures set forth by the EPA for grant-funded projects. This study was reviewed by EPA for data quality, where it was found to be of high quality. The systematic review of this study is available in the Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Studies. ([EPA, 2019k](#)). Many of the data quality evaluation metrics used in this evaluation are similar to the peer review procedures used to understand the quality of published scientific articles. The confidence in the available data to characterize the environmental hazards of 1-BP is bolstered by the use of the QSAR modeling program ECOSAR (v2.0) ([EPA, 2017](#)) lending greater confidence to the risk estimates. The strength of the evidence for the multiple lines of evidence is medium based on high quality empirical data for fish and modeling data from analogues that provide support for multiple taxa including fish.

The ECOSAR modeling program used the most robust and data rich chemical class, neutral organics, to predict the environmental hazards to fish, aquatic invertebrates, and algae from acute and chronic exposure to 1-BP. This substantially broadens the available data that can be used to validate the use of the single acute fish toxicity study to characterize the environmental hazards and risks of 1-BP. As explained in Section 3.1.4, the extensive dataset used to populate the neutral organics chemical class includes several chemicals that are similar to 1-BP in terms of molecular weight and logK_{ow}. In addition, much of the data used to populate the ECOSAR training set was comprised of data generated as part of the same research effort as the single acute fish toxicity study ([Geiger et al., 1988](#)). The acute fish toxicity data and the predicted toxicity values from ECOSAR are consistent in that both indicate that 1-BP presents a moderate environmental hazard (see section 3.1.6 for a comparison of the available ecotoxicity data with ECOSAR modeling outputs).

No chronic toxicity studies were identified that directly assess the chronic duration effects of 1-BP to the environment. As a result, hazard to aquatic species resulting from chronic exposure was

estimated by applying an acute-to-chronic ratio to acute hazard data as well as ECOSAR modeling. As these values are estimates of chronic hazard, there are uncertainties regarding the use of these values to estimate the environmental risks from chronic exposure to 1-BP. Both the use of an acute to chronic ratio and ECOSAR modeling are commonly utilized techniques to estimate potential hazards to environmental receptors from chronic exposures and represent the best available data for 1-BP. Frequency and duration of exposure also affects potential for adverse effects in aquatic organisms, especially for chronic exposures. In the case of 1-BP, the number of days that a COC was exceeded was not calculated using E-FAST, but instead the maximum expected surface water concentration from an acute exposure, representing a high-end estimate of exposure interval or pulse exposure, was compared to the estimated chronic concentrations of concern. This conservative screening-level approach is expected to be protective of longer-term chronic exposures which are generally lower than acute-duration exposures. As described in Section 4.1, this assessment presents a screening-level assessment of relevant routes of exposure, which in the case of 1-BP are the aquatic exposure pathways, evaluate ecological exposures in the US that may be associated with releases of 1-BP to surface waters. This assessment was intended as a first-tier, or screening-level, evaluation. Discharging or releasing facilities were chosen from EPA's TRI.

EPA did not quantitatively assess potential risks to terrestrial receptors and sediment-dwelling organisms. Instead, a considerations of the physical-chemical and environmental fate characteristics of the chemical led EPA to determine that the potential exposures to organisms in these compartments are expected to be low and risks are not expected. As discussed above in Section 3.1, as well as in the Problem Formulation ([U.S. EPA, 2018c](#)), this assumption was based on the high volatility (Henry's Law constant of 7.3×10^{-3} atm-m³/mole), high water solubility (2.4 g/L), and low log K_{oc} (1.6) which suggests that 1-BP will only be present at low concentrations in the sediment and terrestrial environmental compartments. Although the conclusion of a low potential for exposure to sediment-dwelling organisms is not verified with monitoring data or hazard data specifically conducted with sediment-dwelling organisms, the available physical chemical property data for 1-BP provide sufficient evidence to determine that these exposures are not significant enough to be biologically relevant.

The foundation of the ecological risk assessment process is the relationship between the amount of a substance a receptor is exposed to and the potential for adverse effects resulting from the exposure. This established dose-response relationship provides the ability to quantitatively evaluate the potential environmental impacts that may result from a given exposure scenario. Because of uncertainties inherent in deriving RQs, values are protective so that the risk estimate can state with a high degree of confidence that RQ values < 1 are not an ecological risk and can be screened out from further analysis. The environmental risk evaluation used reasonably available environmental hazard, exposure, fate, and chemistry data, but was still a screening-level evaluation due to the limited amount of hazard and exposure information.

The environmental risk assessment for 1-BP applied two assessment factors to the reasonably available environmental hazard data for aquatic species in order to perform a screening-level analysis of potential environmental risks under the conditions of use within the scope of this risk

evaluation. Assessment factors (AFs) were used to calculate the acute and chronic COCs for 1-BP. As described in Section 3.1.1, 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). Some uncertainty may be associated with the use of the specific AFs used in the hazard assessment.

The first AF, an acute-to-chronic ratio (ACR) extrapolation, is utilized to estimate the hazards of chronic exposure to 1-BP in the absence of empirical data. As data characterizing the environmental hazards of chronic exposure to 1-BP are not available, an ACR value of 10 is used to extrapolate these hazard values from acute toxicity endpoints for aquatic species. Utilizing 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 utilized by EPA to assess the hazard of new industrial chemicals, there is uncertainty with regard to using a single ACR value to estimate chronic hazards across species and chemicals. Available information in the literature that indicates the use of an ACR value between 10 may not be protective across all chemicals, species, trophic levels, and modes of action. For example, Kenaga ([1982](#)) indicates that acute to chronic ratios can vary by as much as 1-18,000. Using an ACR of 10 is representative of the median ACR for chemicals that exhibit non-polar narcosis³⁹ ([Ahlers et al., 2006](#); [Chapman et al., 1998](#); [Kenaga, 1982](#); [Giesy and Graney, 1989](#)). For example, Ahlers et al., ([2006](#)) analyzed available ecotoxicity data for 240 chemicals and determined that the median (50th percentile) ACR is 10.5 for fish, 7.0 for *Daphnia magna*, and 5.4 for green algae. While the authors concluded that an ACR of 10 is not protective across all chemicals and trophic levels, these findings add a line of evidence in support of utilizing an ACR of 10 to estimate chronic hazard from exposure of 1-BP ([Ahlers et al., 2006](#)).

Elsewhere, a median ACR of 12 was determined for fish and 8.8 for *Daphnia magna*, resulting in a median ACR for both species of 9.9 ([May et al., 2016](#)). Additionally, variation in ACR is reported based on the mode of action of the chemical. A comparison of 240 chemicals found that >50% of non-polar narcotic chemicals exhibit an ACR below 10 for aquatic species ([Kienzler et al., 2017](#)). Additionally, May et al., ([2016](#)) reported a median ACR of 7.6 for non-polar narcotic chemicals, with a 90th percentile ACR value of 24.1. While there is uncertainty about the degree of protection afforded by the use of an ACR of 10 for fish and *Daphnia*, the above evidence as well as the ECOSAR-predicted toxicity values for acute and chronic exposure to 1-BP, as shown in Table 3-1, provide lines of evidence to indicate that an ACR of 10 is protective for 1-BP. Furthermore, given the limited potential for chronic-duration aquatic exposures as a result of the high volatility and low persistence of 1-BP in the environment, chronic exposure of 1-BP to aquatic species is expected to be limited. Finally, to account for any additional sources of variability not accounted for in the ACR extrapolation, a second assessment factor of 10 is applied to the estimate hazard value for chronic exposure as discussed below.

³⁹ OECD QSAR Toolbox version 4.3.(Accessed November, 2019; <https://qsartoolbox.org/>)

A second AF is applied to the acute and chronic hazard endpoints for aquatic species to calculate a Concentration of Concern (COC) for use in the screening-level analysis of environmental hazards to account for differences in inter- and intra-species variability, as well as laboratory-to-field variability. For fish and aquatic invertebrates (*e.g.*, *Daphnia*), the acute COC values are calculated by dividing the most sensitive endpoint by an AF of 5. For chronic COCs, and to calculate a COC for algae, where multiple generations can be present over the course of a standard toxicity test, an AF of 10 is used. Similarly to the use of an acute to chronic ratio, the use of this assessment factor is consistent with EPA methodology for the screening and assessment of industrial chemicals ([Suter, 2016](#)) ([U.S. EPA, 2012e](#)) ([U.S. EPA, 2013b](#)).

4.3.4.2 Human Health Characterization

The non-cancer acute or chronic evaluations were expressed in terms of MOEs. MOEs are obtained by comparing the hazard values (*i.e.*, HEC) for various 1-BP-related health effects with the exposure concentrations for the specific use scenarios. Given that the MOE is the ratio of the hazard value divided by the exposure, the confidence in the MOEs is directly dependent on the uncertainties in the hazard/dose-response and exposure assessments that supported the hazard and exposure estimates used in the MOE calculations.

Overall uncertainties in the exposure estimates used in the MOE calculations include uncertainties in the exposure monitoring and modeling. In the occupational exposure monitoring data for workers, the sites used to collect 1-BP were not selected randomly; therefore, the reported data may not be representative of all occupational exposure scenarios. The exposure modeling approaches used for both occupational and consumer scenarios employed knowledge-based assumptions that may not apply to all occupational- and consumer-use scenarios.

The human populations quantitatively evaluated in this risk evaluation include individuals of both sexes (≥ 16 and older, including pregnant females) for occupational and consumer settings. Although exposures to younger non-users may be possible, the margins of exposure calculated for women and men of reproductive age are expected to be protective of this sensitive subpopulation. Currently there are insufficient data regarding specific genetic and/or lifestage differences that could impact 1-BP metabolism and toxicity for further refinement of the risk assessment.

The chronic exposures leading to risk for the occupational scenarios assumed that the non-cancer human health effects are constant for a working lifetime based on the exposure assumptions used in the occupational exposure assessment. However, the risks could be under- or over-estimated depending on the variations to the exposure profile of the workers and occupational non-users using 1-BP-containing adhesives, dry cleaning and spot cleaners, vapor degreasing, cold cleaning, and aerosol degreasers.

Confidence in the PBPK model predictions for 1-BP concentrations in blood and tissues are limited by the lack of comparison of model predictions with measured data. The PBPK model was further extended to simulate human exposures by scaling the physiological parameters to humans,

assuming the partition coefficients are the same in rats and humans and scaling metabolic parameters by $BW^{3/4}$. Cross species and route to route extrapolations with the Garner et al. (2015) model are precluded by the lack of data to inform a model of a species other than rat and a route other than inhalation.

Limited toxicological data is available by the oral route, and no repeated-dose toxicity studies by the dermal route were identified on 1-BP. However, although the toxicological data via the oral route is insufficient for quantitative dose-response assessment, data from these studies were used for qualitative support in the weight of the scientific evidence for nervous system effects (see Section 3.2.5.5 and Appendix J), suggesting that, at least for the nervous system endpoint, the delivery of 1-BP via the inhalation- (*i.e.*, pulmonary/systemic circulation) and oral- (*i.e.*, portal circulation) routes of exposure results in comparable toxic endpoints.

EPA chose to derive dermal HEDs for dermal exposures by extrapolating from other routes for systemic endpoints (*i.e.*, not point of contact effects) and none of the key endpoints for 1-BP (liver, kidney, reproductive, developmental and nervous system effects) were considered point of contact therefore all were used for route-to-route extrapolation. The route-to-route extrapolations enabled EPA to estimate applied dermal PODs. Since physiologically based pharmacokinetic/pharmacodynamic (PBPK/PD) models that would facilitate route-to-route extrapolation have not been identified, there is no relevant kinetic or metabolic information for 1-BP that would facilitate development of dosimetric comparisons. The studies by the oral route were insufficient for quantitative dose-response assessment; therefore, EPA chose to derive dermal HEDs for dermal exposures by extrapolating from the inhalation PODs. However, the inhalation studies were performed by whole body exposure, rather than nose only exposure, which may have led to additional dosing by the oral and dermal routes of exposure, due to deposition on fur and the grooming behavior of rodents, resulting in uncertainty of actual dose received. EPA was unable to conclude with certainty that comparable toxic endpoints would be associated with the dermal route of exposure, considering the expected quantitative ADME differences and the absence of an adequate PBPK model. Notwithstanding these uncertainties, EPA considered this approach appropriate considering the comparable toxic endpoints identified in the available repeated-dose oral/inhalation toxicity studies and the uncertainty with the putative toxicant (*i.e.*, 1-BP or a metabolite(s)).

As discussed previously, the estimates for extra cancer risk were based on the assumption of linearity in the relationship between 1-BP exposure and probability of cancer at low doses, in the absence of sufficient information on mode of action.

4.4 Other Risk Related Considerations

4.4.1 Potentially Exposed or Susceptible Subpopulations

TSCA 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 (PESS) identified as relevant to the risk evaluation by the Administrator, 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 exposure assessment for 1-BP, EPA analyzed reasonably available information to ascertain whether some human receptor groups may have greater exposure or susceptibility than the general population to the hazard posed by 1-BP. Exposures of 1-BP would be expected to be higher amongst groups with 1-BP containing products in their homes, and workers who use 1-BP as part of typical processes.

EPA identified potentially exposed or susceptible subpopulations for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios, and analysis plan. In Section 2.3.1, EPA addressed the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure in occupational settings. In Section 2.3.2, EPA addressed the potentially exposed or susceptible subpopulations for consumer users between the ages of 11-21 as well as adults. EPA also addressed potentially exposed or susceptible subpopulations for bystanders within residences where a consumer product containing 1-BP may be used. Bystanders, for purposes of this risk evaluation, can be any age group (infant to elderly).

Of the human receptors identified in the previous sections, EPA identifies the following as potentially exposed or susceptible subpopulations due to their greater exposure and considered them in the risk evaluation:

- Workers and occupational non-users. EPA assessed exposure to these subpopulations using a combination of personal exposure monitoring data (measured data) and modeling approaches. The exposure estimates were applicable to both male and female workers of reproductive age, including adolescents. Section 2.4 provides more details on these subpopulations across various industry sectors that are likely to use 1-BP.
- Consumer users and bystanders associated with consumer use. 1-BP has been identified as being present in products available to consumers for purchase and use; however, only some individuals within the general population are expected to use these products. Therefore, those who do use these products are a potentially exposed or susceptible subpopulation due to greater exposure. Consumer bystanders, although they do not use a product containing 1-BP, are also a potentially exposed or susceptible subpopulation due to the possibility that bystanders can be any age group (including infants, toddlers, children, and elderly) with greater exposure when in a residence where products containing 1-BP are used. A description of the exposure assessment for consumers is available in Section 2.3.2.

There are some exposure scenarios where greater exposure from multiple sources may occur and individuals who may have greater potential for exposure to 1-BP. For example, some workers and occupational non-users may also use consumer products containing 1-BP, and have additional exposure outside of the workplace. EPA also investigated the effects of 1-BP on susceptible lifestages and subpopulations. Consideration of other lifestages, such as male and non-pregnant female workers in the occupational environment, children in the home environment would require using an alternative POD based on systemic toxicity, instead of using the POD based on developmental toxicity. Other endpoints associated with systemic toxicity generally had higher human equivalent concentrations than those associated with developmental toxicity. Therefore EPA assumed that margins of exposure for pregnant women would also be protective of other lifestages.

While it is anticipated that there may be differential 1-BP metabolism based on lifestage; currently there are no data available, therefore the impact of this cannot be quantified. Similarly, while it is known that there may be genetic differences that influence CYP2E1 metabolic capacity, there may also be other metabolizing enzymes that are functional and impact vulnerability. There is insufficient data to quantify these differences for risk assessment purposes.

Heterogeneity among humans is an uncertainty associated with extrapolating the derived PODs to a diverse human population. One component of human variability is toxicokinetic, such as variations in CYP2E1 and glutathione transferase activity in humans ([Arakawa et al., 2012](#); [Trafalis et al., 2010](#)) which are involved in 1-BP metabolism in humans. EPA did not have chemical-specific information on susceptible subpopulations, or the distribution of susceptibility in the general population that could be used to decrease or increase the default intraspecies UF_H for toxicodynamic variability of 3. As such, EPA used an intraspecies UF_H of 10 for the risk assessment.

EPA was unable to directly account for all possible PESS considerations and subpopulations in the risk estimates. It is unknown whether the 10x UF to account for human variability will cover the full breadth of human responses, and subpopulations with particular disease states or genetic predispositions may fall outside of the range covered by this UF. As previously discussed, EPA also only considered acute effects for all consumer COUs evaluated except for the insulation (off-gassing) COU as described in Section 2.3.2.1. While typical use patterns are unlikely to result in any chronic effects for the vast majority of consumers, EPA cannot rule out that consumers at very high frequencies of use may be at risk for chronic hazards, especially if those consumers also exhibit biological susceptibilities. EPA can also not rule out that certain subpopulations, whether due to very elevated exposure or biological susceptibility, may be at risk for hazards that were not fully supported by the weight of the scientific evidence or could not be quantified (*e.g.*, immune and blood effects). However, in these circumstances EPA assumes that these effects are likely to occur at a higher dose than more sensitive endpoints that were accounted for by risk estimates.

4.4.2 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 § 702.33). In this risk evaluation, EPA determined that aggregating dermal and inhalation exposure for risk characterization was not appropriate due to uncertainties in quantifying the relative contribution of dermal vs inhalation exposure, since dermally applied dose could evaporate and then be inhaled. Aggregating exposures from multiple routes could therefore inappropriately overestimate total exposure, as simply adding exposures from different routes without an available PBPK model for those routes would compound uncertainties. Without a PBPK model to account for toxicokinetic processes, the true internal dose for any given exposure cannot be determined. Conversely, not aggregating exposures may underestimate total exposure for a given individual. EPA also did not consider aggregate exposure among individuals who may be exposed both in an occupational and consumer context because there is insufficient information reasonably available as to the likelihood of this scenario or the relative distribution of exposures from each pathway.

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.” In terms of this risk evaluation, EPA considered sentinel exposures by considering exposures to populations who may have upper bound exposures – for example, workers who perform activities with higher exposure potential, or consumers who have higher exposure potential (*e.g.*, those involved with do-it-yourself projects) or certain physical factors like body weight or skin surface area exposed. EPA characterized high-end exposures in evaluating exposure using both monitoring data and modeling approaches. Where statistical data are available, EPA typically uses the 95th percentile value of the available dataset to characterize high-end exposure for a given condition of use. For consumer and bystander exposures, EPA characterized sentinel exposure through a “high-intensity use” category based on both product and user-specific factors.

4.5 Risk Conclusions

4.5.1 Environmental Risk Conclusions

Based on a consideration of the physical chemical properties and uses of 1-BP, exposure to aquatic species is the only route of exposure to the environment that was quantitatively assessed in this risk evaluation. Risks to terrestrial and sediment-dwelling aquatic species were qualitatively evaluated by considering physical-chemical and environmental fate properties, which indicate that there is a low potential for exposure to terrestrial and sediment-dwelling aquatic species. The conclusions for these pathways were not updated since the preliminary assessment presented in the Problem Formulation and Draft Risk Evaluation. The quantitative assessment of water column-dwelling aquatic species was updated in this final risk evaluation to incorporate ECOSAR modeling results for environmental hazards to reduce uncertainty about the limited environmental hazard data

available for 1-BP. EPA conducted a screening-level assessment of the available environmental hazards and release information to calculate RQs to quantify potential risks to the environment from 1-BP. As previously stated, an RQ below 1 indicates that the exposure concentrations of 1-BP is less than the concentrations that would cause an effect to organisms in the aquatic pathways. The RQ values for risks from acute and chronic exposure to 1-BP are <1, based on a comparison of all available data characterizing exposure and hazard to aquatic species. These values indicate that risks to the environment are not identified based on the conditions of use within the scope of this risk evaluation.

4.5.2 Human Health Risk Conclusions

4.5.2.1 Summary of Risk Estimates for Workers and ONUs

Table 4-58 summarizes the risk estimates for inhalation and dermal exposures for all occupational exposure scenarios. Risk estimates that exceed the benchmark (*i.e.*, MOE less than the benchmark MOE or cancer risks greater than the benchmark cancer risk) are highlighted by shading the cell. When both monitoring and modeling inhalation exposures are available, EPA presented the more conservative estimate in the table. The occupational exposure assessment and risk characterization are described in more detail in Sections 2.3.1 and 4.2.3, respectively.

The risk summary below is based on the POD selected from among the most sensitive acute and chronic non-cancer endpoints, as well as cancer. EPA selected developmental effects based on NLogistic modeling as the most sensitive acute and chronic non-cancer endpoints. Risk estimates are also presented considering PPE up to respirator APF 50 and glove PF 10 or 20. For each exposure scenario, the lowest protection factor that results in no indication of risks is shown (*i.e.*, if estimated risks do not exceed the benchmark for APF 10 and above, the risk estimate for APF 10 only is shown).

Inhalation Exposure

For acute and chronic exposures via inhalation without PPE (*i.e.*, no respirators), there are non-cancer and cancer risks for workers relative to the benchmark for most conditions of use at the high-end exposure level. For batch vapor degreasing (open-top), cold cleaning, and spray adhesive conditions of use, risks were present at the high-end exposure level even when respirators (up to APF 50) are worn.

While ONUs are assumed to have lower exposure levels than workers, there are also non-cancer and cancer risks following acute and chronic exposures at the high-end exposure level for many conditions of use. ONUs are assumed to not wear respirators.

Dermal Exposure

For acute and chronic exposures via dermal contact without PPE (*i.e.*, no gloves), risks are not indicated for workers for non-cancer effects at both central tendency and high-end exposure levels across all conditions of use (ONUs are assumed to not have direct dermal contact with 1-BP).

Risks are indicated for cancer effects at the high-end exposure level across all conditions of use, except when gloves with a protection factor of at least 5 are worn.

Table 4-58. Occupational Risk Summary Table

Life Cycle Stage / Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Route and Duration	Exposure Est. Method	Exposure Level	Risk Estimates for No PPE			Risk Estimates with PPE		
							Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)	Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)
Manufacture - Domestic manufacture	Domestic manufacture	Manufacture (see Section 2.3.1.5) ¹	Worker	Inhalation	Monitoring data	Central Tendency	189	265	1.4E-04	1,889 (APF 10)	2,652 (APF 10)	1.4E-05 (APF 10)
						High-end	63	88	5.5E-04	630 (APF 10)	884 (APF 10)	5.5E-05 (APF 10)
				Dermal	Model	Central Tendency	405	569	6.5E-05	-	-	-
						High-end	135	190	2.5E-04	-	-	5.0E-05 (PF 5)
Manufacture - Import	Import	Import (see Section 2.3.1.6) ²	Worker	Inhalation	Model	Central Tendency	4,441	6,235	6.1E-06	-	-	-
						High-end	300	421	1.2E-04	-	-	1.2E-05 (APF 10)
				Dermal	Model	Central Tendency	405	569	6.5E-05	-	-	-
						High-end	135	190	2.5E-04	-	-	5.0E-05 (PF 5)
Processing - Processing as a reactant	Intermediate in various chem and pdt mfg,	Processing as a Reactant (see Section 2.3.1.7) ²	Worker	Inhalation	Model	Central Tendency	4,441	6,235	6.1E-06	-	-	-
						High-end	300	421	1.2E-04	-	-	1.2E-05 (APF 10)
				Dermal	Model	Central Tendency	405	569	6.5E-05	-	-	-
						High-end	135	190	2.5E-04	-	-	5.0E-05 (PF 5)

Life Cycle Stage / Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Route and Duration	Exposure Est. Method	Exposure Level	Risk Estimates for No PPE			Risk Estimates with PPE		
							Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)	Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)
Processing – Incorp. into formulation, mixture or reaction product	Solvents for cleaning or degreasing	Processing - Incorporating into formulation, mixture or reaction product (see Section 2.3.1.8)	Worker	Inhalation	Monitoring Data	Central Tendency	2	3	1.1E-02	118 (APF 50)	166 (APF 50)	2.3E-04 (APF 50)
						High-end						
				Dermal	Model	Central Tendency	405	569	6.5E-05	-	-	-
			High-end			135	190	2.5E-04	-	-	5.0E-05 (PF 5)	
			ONU	Inhalation	Monitoring Data	Central Tendency	110	154	2.5E-04	N/A	N/A	N/A
						High-end	62	87	5.7E-04	N/A	N/A	N/A
Processing – Incorp. into articles	Solvents (which become part of product formulation or mixture) in construction	Processing – Incorporation into Articles (see Section 2.3.1.9) ²	Worker	Inhalation	Model	Central Tendency	4,441	6,235	6.1E-06	-	-	-
						High-end	300	421	1.2E-04	-	-	1.2E-05 (APF 10)
			Dermal	Model	Central Tendency	405	569	6.5E-05	-	-	-	
					High-end	135	190	2.5E-04	-	-	5.0E-05 (PF 5)	
Processing - Repackaging	Solvent for cleaning or degreasing in all other basic organic chemical manufacturing	Repackaging (see Section 2.3.1.10) ²	Worker	Inhalation	Model	Central Tendency	4,441	6,235	6.1E-06	-	-	-
						High-end	300	421	1.2E-04	-	-	1.2E-05 (APF 10)
			Dermal	Model	Central Tendency	405	569	6.5E-05	-	-	-	
					High-end	135	190	2.5E-04	-	-	5.0E-05 (PF 5)	

Life Cycle Stage / Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Route and Duration	Exposure Est. Method	Exposure Level	Risk Estimates for No PPE			Risk Estimates with PPE		
							Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)	Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)
Processing - Recycling	Recycling	Disposal, Recycling (see Section 2.3.1.21) ²	Worker	Inhalation	Model	Central Tendency	4,441	6,235	6.1E-06	-	-	-
						High-end	300	421	1.2E-04	-	-	1.2E-05 (APF 10)
				Dermal	Model	Central Tendency	405	569	6.5E-05	-	-	
						High-end	135	190	2.5E-04	-	-	5.0E-05 (PF 5)
Distribution in commerce	Distribution	Not assessed as a separate operation; exposures/releases from distribution are considered within each condition of use.										
Industrial / commercial use - Solvent (for cleaning or degreasing)	Batch vapor degreaser (e.g., open-top, closed-loop)	Batch Vapor Degreaser (Open-Top) (see Section 2.3.1.11)	Worker	Inhalation	Monitoring Data	Central Tendency	3	4	1.1E-02	127 (APF 50)	178 (APF 50)	2.1E-04 (APF 50)
						High-end	0.34	0.48	1.0E-01	17 (APF 50)	24 (APF 50)	2.0E-03 (APF 50)
				Dermal	Model	Central Tendency	418	586	6.3E-05	-	-	-
			High-end			139	195	2.4E-04	-	-	4.9E-05 (PF 5)	
			ONU	Inhalation	Monitoring Data	Central Tendency	170	239	1.6E-04	N/A	N/A	N/A
						High-end	37	52	9.4E-04	N/A	N/A	N/A
		Batch Vapor Degreaser (Closed-Loop) (see Section 2.3.1.12)	Worker	Inhalation	Model	Central Tendency	450	631	5.6E-05	4,496 (APF 10)	6,312 (APF 10)	5.6E-06 (APF 10)
						High-end	36	50	7.4E-04	355 (APF 10)	499 (APF 10)	7.4E-05 (APF 10)
				Dermal	Model	Central Tendency	418	586	6.3E-05	-	-	-
			High-end			139	195	2.4E-04	-	-	4.9E-05 (PF 5)	
			ONU	Inhalation	Model	Central Tendency	856	1,201	3.0E-05	N/A	N/A	N/A

Life Cycle Stage / Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Route and Duration	Exposure Est. Method	Exposure Level	Risk Estimates for No PPE			Risk Estimates with PPE			
							Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)	Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)	
						High-end	63	88	4.2E-04	N/A	N/A	N/A	
	In-line vapor degreaser (e.g., conveyORIZED, web cleaner)	In-line Vapor Degreaser (see Section 2.3.1.13)	See exposure estimates for Batch Vapor Degreaser (Open-Top)										
Cold Cleaner	Cold Cleaner (see Section 2.3.1.14)	Worker	Inhalation	Monitoring Data	Central Tendency	4	6	6.8E-03	198 (APF 50)	278 (APF 50)	1.4E-04 (APF 50)		
					High-end	2	3	1.5E-02	115 (APF 50)	161 (APF 50)	3.0E-04 (APF 50)		
			Dermal	Model	Central Tendency	418	586	6.3E-05	-	-	-		
					High-end	139	195	2.4E-04	-	-	4.9E-05 (PF 5)		
		ONU	Inhalation	Monitoring Data	Central Tendency	7	9	4.1E-03	N/A	N/A	N/A		
					High-end				N/A	N/A	N/A		
		Aerosol spray degreaser/cleaner	Aerosol Spray Degreaser/Cleaner (see Section 2.3.1.15)	Worker	Inhalation	Model	Central Tendency	3	4	9.5E-03	N/A	N/A	N/A
							High-end	1	1	3.6E-02	N/A	N/A	N/A
Dermal	Model				Central Tendency	405	569	6.5E-05	-	-	-		
					High-end	135	190	2.5E-04	-	-	5.0E-05 (PF 5)		
ONU	Inhalation			Model	Central Tendency	155	217	1.6E-04	N/A	N/A	N/A		
					High-end	18	26	1.4E-03	N/A	N/A	N/A		

Life Cycle Stage / Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Route and Duration	Exposure Est. Method	Exposure Level	Risk Estimates for No PPE			Risk Estimates with PPE					
							Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)	Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)			
Industrial / commercial use - Adhesives and sealants	Adhesive chemicals - spray adhesive for foam cushion manufacturing and other uses	Adhesive Chemicals (Spray Adhesives) (see Section 2.3.1.18)	Sprayer	Inhalation	Monitoring Data (Post-EC)	Central Tendency	1	1	2.8E-02	48 (APF 50)	67 (APF 50)	5.7E-04 (APF 50)			
						High-end	0.41	1	8.6E-02	20 (APF 50)	28 (APF 50)	1.7E-03 (APF 50)			
				Dermal	Model	Central Tendency	506	711	5.2E-05	-	-	-			
						High-end	169	237	2.0E-04	-	-	4.0E-05 (PF 5)			
			Non-Sprayer	Inhalation	Monitoring Data (Post-EC)	Central Tendency	0.94	1	2.9E-02	47 (APF 50)	66 (APF 50)	5.7E-04 (APF 50)			
						High-end	0.59	1	5.9E-02	29 (APF 50)	41 (APF 50)	1.2E-03 (APF 50)			
			ONU	Inhalation	Monitoring Data (Post-EC)	Central Tendency	9	12	3.2E-03	N/A	N/A	N/A			
						High-end	3	4	1.1E-02	N/A	N/A	N/A			
			Industrial / commercial use - Cleaning and furniture care products	Dry cleaning solvent	Dry Cleaning (see Section 2.3.1.16)	Worker	Inhalation	Monitoring Data	Central Tendency	0.58	0.82	4.7E-02	N/A	N/A	N/A
									High-end	0.34	0.42	1.0E-01	N/A	N/A	N/A
							Dermal	Model	Central Tendency	431	605	6.1E-05	N/A	N/A	N/A
						High-end			144	202	2.4E-04	N/A	N/A	N/A	
ONU	Inhalation	Monitoring Data				Central Tendency	1	2	1.9E-02	N/A	N/A	N/A			
						High-end	1	1	4.2E-02	N/A	N/A	N/A			
Spot cleaner, stain remover	Spot Cleaner, Stain Remover (see Section 2.3.1.17)	Worker		Inhalation	Model	Central Tendency	5	31	1.2E-03	N/A	N/A	N/A			
						High-end	2	14	2.7E-03	N/A	N/A	N/A			
				Dermal	Model	Central Tendency	431	605	6.1E-05	N/A	N/A	N/A			
						High-end	144	202	2.4E-04	N/A	N/A	N/A			

Life Cycle Stage / Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Route and Duration	Exposure Est. Method	Exposure Level	Risk Estimates for No PPE			Risk Estimates with PPE		
							Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)	Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)
			ONU	Inhalation	Model	Central Tendency	10	62	5.8E-04	N/A	N/A	N/A
						High-end	4	22	1.8E-03	N/A	N/A	N/A
	Liquid cleaner (e.g., coin and scissor cleaner)	Other Uses (see Section 2.3.1.20)	See Section 2.3.1.20									
	Liquid spray/aerosol cleaner											
Industrial / commercial use - Other uses	Automotive care products – engine degreaser, brake cleaner	Aerosol Spray Degreaser/Cleaner	See Aerosol Spray Degreaser/Cleaner									
	Building/construction materials not covered elsewhere - insulation	THERMAX™ Installation (see Section 2.3.1.19)	See Section 2.3.1.19									
	Other uses (e.g., Arts, crafts and hobby materials, anti-adhesive agents, functional fluids, etc.)	Other uses (see Section 2.3.1.20)	See Section 2.3.1.20									
Disposal	Municipal waste incinerator Off-site waste transfer	Disposal, Recycling (see Section 2.3.1.21) ²	Worker	Inhalation	Model	Central Tendency	4,441	6,235	6.1E-06	-	-	-
						High-end	300	421	1.2E-04	-	-	1.2E-05 (APF 10)
				Dermal	Model	Central Tendency	405	569	6.5E-05	-	-	-

Life Cycle Stage / Category	Subcategory	Occupational Exposure Scenario	Population	Exposure Route and Duration	Exposure Est. Method	Exposure Level	Risk Estimates for No PPE			Risk Estimates with PPE		
							Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)	Acute Non-cancer (benchmark MOE =100)	Chronic Non-cancer (benchmark MOE =100)	Cancer (benchmark = 10 ⁻⁴)
						High-end	135	190	2.5E-04	-	-	5.0E-05 (PF 5)

¹ Based on the process and work activity description, exposure to ONUs at the manufacturing facility is expected to be negligible.

² Because the model assumes tank truck and railcar loading/unloading occurs outdoors, EPA expects ONU exposure to be negligible due to airborne concentration dilution in ambient air.

4.5.2.2 Summary of Risk Estimates for Consumer Users and Bystanders

Table 4-59 summarizes the risk estimates for consumer inhalation and dermal exposure scenarios evaluated for 1-BP. Risk estimates showing increased risk or excess cancer risks are presented in shaded cells. The consumer exposure assessment and risk characterization are described in more detail in Sections 2.3.2, 4.2.3, and 4.2.5.

The risk summary below is based on the POD selected from among the most sensitive acute and chronic non-cancer endpoints, and three cancer endpoints. EPA selected developmental effects (Post Implantation Loss) based on NLogistic modeling as the most sensitive acute and chronic non-cancer endpoints as well as cancer endpoint (IUR of 6.00E-03). EPA presents only the comparison to the 1.00E-06 cancer benchmark in Table 4-59.

Inhalation Exposure

Non-cancer effects following acute inhalation exposure were evaluated for all nine consumer conditions of use identified in Table 2-31. Non-cancer and cancer effects following chronic inhalation exposures were only evaluated for the insulation (off-gassing) condition of use. Inhalation exposures are based on multi-zone modeling approaches for air concentrations (rather than dose) and therefore independent of any age-specific exposure factors. As a result, the risk estimates associated with inhalation exposure are applicable to all age groups (infant to elderly) and PESS.

Risks for non-cancer effects following acute inhalation exposure were identified for all conditions of use evaluated for the consumer user. Risks for non-cancer effects following acute inhalation exposure were identified for most conditions of use evaluated for the bystander except several low intensity use scenarios (aerosol spray degreaser/cleaner-electronics, spot cleaner and stain remover, adhesive accelerant, and mold cleaning and release products) and all locations evaluated for the insulation (off-gassing) condition of use for both building configurations evaluated. Risks for non-cancer or cancer effects following chronic inhalation exposure were not identified for any of the locations evaluated for the insulation (off-gassing) condition of use in either building configuration evaluated.

Dermal Exposure

Risks for non-cancer effects following acute dermal exposure were identified for four of the eight conditions of use evaluated for dermal exposure (aerosol spray degreaser/cleaner-general, spot cleaner and stain remover, spray cleaner-general, and automobile AC flush). Dermal exposure was evaluated for three consumer user age groups Bystanders were not evaluated for dermal exposure as they are not expected to receive a dermal exposure.

Table 4-59. Consumer Risk Summary Table

Life Cycle Stage	Category/ (Subcategory)	Assessed Condition of Use	Scenario Description <i>Intensity of Use/ Location</i>	Risk Estimates (Inhalation)				Risk Estimates (Dermal)		
				Acute Non-Cancer <i>Benchmark=100</i>		Chronic Non-Cancer <i>Benchmark =100</i>	Chronic Cancer <i>Benchmark =1E-06</i>	Acute Non-Cancer <i>Benchmark=100</i>		
				User	Bystander	Bystander	Bystander	Adult	Youth A	Youth B
Consumer Use	Solvent (for cleaning or degreasing)/ (Aerosol spray degreaser/cleaner)	Aerosol Spray Degreaser/Cleaner-General	High	4.3E-02	0.15	N/A	N/A	3.1	3.3	3.1
			Moderate	0.32	1.2	N/A	N/A	48	50	46
			Low	6.0	24	N/A	N/A	647	688	647
		Aerosol Spray Degreaser/Cleaner-Electronics	High	0.20	0.69	N/A	N/A	239	256	234
			Moderate	4.3	17	N/A	N/A	324	344	314
			Low	90	316	N/A	N/A	458	500	458
	Cleaning and Furniture Care Products/ (Spot cleaner and stain remover)	Spot Cleaner and Stain Remover	High	0.13	0.83	N/A	N/A	13	14	12
			Moderate	1.8	11	N/A	N/A	121	129	118
			Low	23	125	N/A	N/A	2558	2683	2500
	Cleaning and Furniture Care Products/ (Liquid cleaner- <i>e.g.</i> , coin and scissors cleaner)	Coin and Scissors Cleaner	High	3.0	6.0	N/A	N/A	145	155	143
			Moderate	4.0	13	N/A	N/A	289	314	282
			Low	5.0	27	N/A	N/A	846	917	846
	Cleaning and Furniture Care Products/ (Liquid spray/aerosol cleaner)	Spray Cleaner-General	High	4.5E-02	0.18	N/A	N/A	3.1	3.3	3.1
			Moderate	0.43	2.2	N/A	N/A	25	26	24
			Low	2.6	14	N/A	N/A	186	200	180
	Other Uses/ (Arts, crafts, and hobby materials-adhesive accelerant)	Adhesive Accelerant	High	0.33	1.3	N/A	N/A	229	244	224
			Moderate	5.5	30	N/A	N/A	229	244	224
			Low	50	240	N/A	N/A	229	244	224
	Other Uses/ (Automotive care products-refrigerant flush)	Automobile AC Flush	High	7.5	12	N/A	N/A	22	23	21
			Moderate	11	25	N/A	N/A	22	23	21
			Low	16	80	N/A	N/A	22	23	21
Other Uses/ Mold Cleaning and Release Product	Mold Cleaning and Release Product	High	0.29	1.4	N/A	N/A	256	275	250	
		Moderate	4.3	22	N/A	N/A	393	423	379	

Life Cycle Stage	Category/ (Subcategory)	Assessed Condition of Use	Scenario Description <i>Intensity of Use/ Location</i>	Risk Estimates (Inhalation)				Risk Estimates (Dermal)		
				Acute Non-Cancer <i>Benchmark=100</i>		Chronic Non-Cancer <i>Benchmark =100</i>	Chronic Cancer <i>Benchmark =1E-06</i>	Acute Non-Cancer <i>Benchmark=100</i>		
				User	Bystander	Bystander	Bystander	Adult	Youth A	Youth B
	(Anti-adhesive agent-mold cleaning and release product)		Low	50	231	N/A	N/A	733	786	733
	Other Uses/ (Building construction materials not covered elsewhere-insulation)	Insulation (off-gassing) Attic/Living Space/Crawlspace	Attic	N/A	3,030	1.2E+05	2.9E-07	N/A	N/A	N/A
Living Space			N/A	6,663	3.1E+05	1.2E-07	N/A	N/A	N/A	
Crawlspace			N/A	2,800	1.4E+05	2.7E-07	N/A	N/A	N/A	
Insulation (off-gassing) Attic/Living Space/Basement		Attic	N/A	3,077	1.2E+05	2.9E-07	N/A	N/A	N/A	
		Living Space	N/A	18,863	7.6E+05	4.7E-08	N/A	N/A	N/A	
		Basement	N/A	2,869	1.3E+05	2.8E-07	N/A	N/A	N/A	

4.5.2.3 Summary of Risk for General Population

EPA considered reasonably available information to characterize general population exposure and risk. As described in the Problem Formulation and in Section 1.4.2, there are no data of 1-BP found in U.S. drinking water. TRI reporting from 2016 indicates zero pounds released to POTWs and five pounds released directly to water from one facility. TRI reporting from 2017 and 2018 indicate only one pound per year released to water. 1-BP is slightly soluble in water, is somewhat biodegradable, volatilizes rapidly from water, and has a relatively high Henry's law constant. As such, 1-BP is not expected to be present in drinking water supplied from public water systems or sorb to solids in wastewater.

Additionally, 1-BP is not expected to adsorb strongly to sediment or soil based on its log K_{oc} of 1.6. If present in biosolids, 1-BP would be expected to associate with the aqueous component and volatilize to air as the biosolids are applied to soil and allowed to dry. Due to its water solubility and low sorption, some 1-BP associated with land applied sludge could migrate with water towards groundwater; however, volatilization and biodegradation may attenuate migration.

Based on this information and environmental fate properties, EPA does not expect general population exposure from contaminated drinking water, surface water, or sediment via the oral and dermal routes. Therefore, EPA did not identify risk for the general population for these pathways.

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 potentially exposed or susceptible subpopulations (PESS)); 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. This approach is in keeping with the Agency's final rule, [*Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* \(82 FR 33726\)](#).⁴⁰

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 in the final risk evaluation, which may differ from the risk estimates in the draft risk evaluation due to peer review and public comments. 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 and chronic inhalation and dermal exposures to 1-BP, and cancer from chronic inhalation and dermal exposures to 1-BP. The health risk estimates for all conditions of use in Section 4.5 (Table 4-58 and Table 4-59).

For the 1-BP risk evaluation, EPA identified as Potentially Exposed or Susceptible Subpopulations: workers and ONUs, including men, women of reproductive age, and adolescents; and consumer uses and bystanders (of any age group, including infants, toddlers, children, and elderly).

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 1-BP; therefore, non-cancer effects and cancer from dermal exposures to 1-BP were not evaluated. The description of the data used for human health exposure is in Section 2.3. Uncertainties in the analysis are discussed in Section 4.3 and considered

⁴⁰ 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.

in the unreasonable risk determination for each condition of use presented below, including the fact that the dermal model used does not address variability in exposure duration and frequency.

EPA considered reasonably available information and environmental fate properties to characterize general population exposure from contaminated drinking water, surface water, or sediment via the oral and dermal routes. EPA does not expect general population exposure from contaminated drinking water, surface water, or sediment via the oral and dermal routes. EPA has made no unreasonable risk determinations to the general population from all conditions of use from drinking water, surface water, and sediment pathways (Section 5.2.1.26). EPA did not evaluate risk to the general population from ambient air and disposal pathways for any conditions of use, and the no unreasonable risk determinations do not account for any risk to the general population from ambient air and disposal pathways. Additional details regarding the general population are in Sections 1.4.2. and 4.5.2.3.

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 point of departure (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 3.2.8 presents the PODs for non-cancer effects for 1-BP 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 lowest observed adverse effect level (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 1-BP is 100 (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 (ELCR)) 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.*, 1×10^{-6} to 1×10^{-4})

depending on the subpopulation exposed.⁴¹ For this risk evaluation, EPA used 1×10^{-6} as the benchmark for the cancer risk to consumers and bystanders from consumer use of insulation.

EPA, consistent with 2017 NIOSH guidance,⁴² used 1×10^{-4} as the benchmark for the purposes of this unreasonable risk determination for individuals in industrial and commercial work environments. The 1×10^{-4} value is not a bright line and EPA has discretion to make unreasonable risk determinations based on other benchmarks as appropriate.

5.1.1.3 Determining Unreasonable Risk of Injury to Health

Calculated risk estimates (MOEs or cancer risk estimates) 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 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, administrative controls, or use of personal protective equipment (PPE) are implemented in the workplace. While OSHA has not issued a specific PEL for 1-BP, some level of PPE is assumed to be used due to the hazard alert for occupational exposure to 1-BP jointly issued by OSHA and NIOSH in 2013, and the Threshold Limit Value™ (TLV™) adopted in 2014 by the American Conference of Governmental Industrial Hygienists (ACGIH™). 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

⁴¹ 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 Clean Air Act 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).

⁴² NIOSH Current intelligence bulletin 68: NIOSH chemical carcinogen policy ([Whittaker et al., 2016](#)).

uncertainties related to whether or not workers are using PPE. However, EPA does not assume that ONUs use PPE. For each condition of use, depending on the reasonably available information and professional judgement, EPA assumes the use of respirators with APFs ranging from 10 to 50, and gloves with a PF of 5. However, EPA assumes that for some conditions of use, the use of respirators is not a standard industry practice, based on professional judgement given the burden associated with the use of respirators, including the expense of the equipment and the necessity of fit-testing and training for proper use. Similarly, EPA does not assume that as a standard industry practice that workers in dry cleaning facilities use gloves. 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 1-BP risk characterization, developmental toxicity (*i.e.*, post-implantation loss) was identified as the most sensitive endpoint for non-cancer adverse effect from acute and chronic inhalation and dermal exposures for all conditions of use. However, additional risks associated with other adverse effects (*e.g.*, additional developmental toxicity, reproductive toxicity, liver toxicity, kidney toxicity, neurotoxicity) were identified for acute and chronic inhalation and dermal exposures. Determining unreasonable risk by using developmental toxicity will also include the unreasonable risk from other endpoints resulting from acute or chronic inhalation or dermal exposures.

The 1-BP risk determination considers the uncertainties associated with the reasonably available information to justify the linear cancer dose-response model when compared to other available models. The cancer analysis is described in Section 3.2.2. EPA considered cancer risks estimates from chronic dermal or inhalation exposures in the unreasonable risk determination.

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 risk quotient (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 concentrations of concern that represent hazard data for aquatic, sediment-dwelling, and terrestrial organisms. Section 4.1 provides more detail regarding the risk quotient for 1-BP.

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 the aquatic, sediment dwelling and terrestrial organisms. EPA provides estimates for environmental risk in Section 4.1 and Table 4-2.

5.2 Detailed Unreasonable Risk Determinations by Condition 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
Manufacture	Domestic manufacture	Domestic manufacture	No	Sections 5.2.1.1, 5.2.1.26, and 5.2.2
	Import	Import	No	Sections 5.2.1.2, 5.2.1.26, and 5.2.2

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
Processing	Processing as a reactant	Intermediate in all other basic inorganic chemical manufacturing, all other basic organic chemical manufacturing, and pesticide, fertilizer and other agricultural chemical manufacturing	No	Sections 5.2.1.3, 5.2.1.26, and 5.2.2.
Processing	Processing - incorporation into formulation, mixture or reaction products	Solvents for cleaning or degreasing in manufacturing of: <ul style="list-style-type: none"> - all other chemical product and preparation - computer and electronic product - electrical equipment, appliance and component - soap, cleaning compound and toilet preparation - services 	Yes	Sections 5.2.1.4, 5.2.1.26, and 5.2.2
Processing	Processing - incorporation into articles	Solvents (becomes part of product formulation or mixture) in construction	No	Sections 5.2.1.5, 5.2.1.26, and 5.2.2
Processing	Repackaging	Solvents (cleaning or degreasing in all other basic organic chemical manufacturing)	No	Sections 5.2.1.6, 5.2.1.26, and 5.2.2
Processing	Recycling	Recycling	No	Sections 5.2.1.7, 5.2.1.26, and 5.2.2
Distribution in commerce	Distribution	Distribution	No	Sections 5.2.1.8, 5.2.1.26, and 5.2.2

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
Industrial/ commercial use	Solvent (for cleaning or degreasing)	Batch vapor degreaser (<i>e.g.</i> , open-top, closed-loop)	Yes	Batch vapor degreaser (open-top) - Sections 5.2.1.9, 5.2.1.26, and 5.2.2. Batch vapor degreaser (closed-loop) – Sections 5.2.1.10, 5.2.1.26, and 5.2.2
		In-line vapor degreaser (<i>e.g.</i> , conveyORIZED, web cleaner)	Yes	Sections 5.2.1.9, 5.2.1.26, and 5.2.2.
		Cold cleaner	Yes	Sections 5.2.1.11, 5.2.1.26, and 5.2.2
		Aerosol spray degreaser/cleaner	Yes	Sections 5.2.1.12, 5.2.1.26, and 5.2.2
	Adhesives and sealants	Adhesive chemicals - spray adhesive for foam cushion manufacturing and other uses	Yes	Sections 5.2.1.13, 5.2.1.26, and 5.2.2
	Cleaning and furniture care products	Dry cleaning solvent	Yes	Sections 5.2.1.14, 5.2.1.26, and 5.2.2.
		Spot cleaner, stain remover	Yes	Sections 5.2.1.14, 5.2.1.26, and 5.2.2
		Liquid cleaner (<i>e.g.</i> , coin and scissor cleaner)	Yes	Sections 5.2.1.15, 5.2.1.26, and 5.2.2
		Liquid spray/aerosol cleaner	Yes	Sections 5.2.1.15, 5.2.1.26, and 5.2.2
	Other uses	Arts, crafts and hobby materials - adhesive accelerant	Yes	Sections 5.2.1.16, 5.2.1.26, and 5.2.2
		Automotive care products - engine degreaser, brake cleaner	Yes	Sections 5.2.1.16, 5.2.1.26, and 5.2.2
		Anti-adhesive agents - mold cleaning and release product	Yes	Sections 5.2.1.16, 5.2.1.26, and 5.2.2

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	
		Building/construction materials not covered elsewhere - insulation	No	Sections 5.2.1.24, 5.2.1.26, and 5.2.2	
		Electronic and electronic products and metal products	Yes	Sections 5.2.1.16, 5.2.1.26, and 5.2.2	
		Functional fluids (closed systems) - refrigerant	Yes	Sections 5.2.1.16, 5.2.1.26, and 5.2.2	
		Functional fluids (open system) - cutting oils	Yes	Sections 5.2.1.16, 5.2.1.26, and 5.2.2	
		Other - asphalt extraction	Yes	Sections 5.2.1.16, 5.2.1.26, and 5.2.2	
		Other - Laboratory chemicals ^c	Yes	Sections 5.2.1.16, 5.2.1.26, and 5.2.2	
		Temperature Indicator – Coatings	Yes	Sections 5.2.1.16, 5.2.1.26, and 5.2.2	
Consumer uses	Solvent (cleaning or degreasing)	Aerosol spray degreaser/cleaner	Yes	Sections 5.2.1.17, 5.2.1.26, and 5.2.2	
		Cleaning and furniture care products	Spot cleaner, stain remover	Yes	Sections 5.2.1.18, 5.2.1.26, and 5.2.2
			Liquid cleaner (e.g., coin and scissor cleaner)	Yes	Sections 5.2.1.19, 5.2.1.26, and 5.2.2
			Liquid spray/aerosol cleaner	Yes	Sections 5.2.1.20, 5.2.1.26, and 5.2.2
	Other uses	Arts, crafts and hobby materials - adhesive accelerant	Yes	Sections 5.2.1.21, 5.2.1.26, and 5.2.2	
		Automotive care products – refrigerant flush	Yes	Sections 5.2.1.22, 5.2.1.26, and 5.2.2	
		Anti-adhesive agents - mold cleaning and release product	Yes	Section 5.2.1.23, 5.2.1.26, and 5.2.2	

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
		Building/construction materials not covered elsewhere - insulation	No	Sections 5.2.1.24, 5.2.1.26, and 5.2.2
Disposal (Manufacturing, Processing, Use)	Disposal	Municipal waste incinerator	No	Sections 5.2.1.25, 5.2.1.26, and 5.2.2
		Off-site waste transfer		

^a These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent additional information regarding all conditions of use of 1-BP.
^b These subcategories reflect more specific information regarding the conditions of use of 1-BP.
^c “Other – Laboratory Chemicals” was changed from “Temperature Indicator – Laboratory Chemicals” since the problem form because other uses of 1-BP as a laboratory chemical were identified.

Although EPA has identified both industrial and commercial uses here for purposes of distinguishing scenarios in this document, the Agency interprets the authority over “any manner or method of commercial use” under TSCA section 6(a)(5) to reach both.

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 1-BP: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation and dermal exposures at the central tendency and high-end, when assuming use of PPE. In addition, for workers, EPA found that there was no unreasonable risk of cancer from chronic inhalation or dermal exposures at the central tendency and high-end, when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures or of cancer from chronic inhalation exposures.

EPA’s determination that the domestic manufacturing of 1-BP does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, 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 exposures at the high-end,

risk estimates of cancer from inhalation exposures at the high-end, and risk estimates of cancer from dermal exposures at the high-end do not support an unreasonable risk determination. Respirators with APF of 10 and gloves with PF of 5 are the assumed personal protective equipment for workers at manufacturing facilities, based on process and work activity descriptions at a manufacturing facility.

- Inhalation exposures were assessed using personal breathing zone monitoring data reflective of current operations at one manufacturing facility and may not represent activities at other manufacturing facilities.
- Though inhalation exposures monitoring was not performed for occupational non-users at the manufacturing facility, based on the process and work activity description, inhalation exposures to ONUs are assumed to be negligible.
- Dermal exposures were assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (workers and ONUs) from domestic manufacturing of 1-BP.

5.2.1.2 Manufacture – Import (Import)

Section 6(b)(4)(A) unreasonable risk determination for import of 1-BP: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation and dermal exposures at the central tendency and high-end, even when PPE is not used. In addition, for workers, EPA found that there was no unreasonable risk of cancer from chronic inhalation and dermal exposures at the central tendency and high-end, when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures and of cancer from chronic inhalation exposures.

EPA's determination that the import of 1-BP does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects (developmental) and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, 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 cancer from chronic inhalation and dermal exposures at the high-end do not support an unreasonable risk determination. Respirators with APF of 10 and gloves with PF of 5 are the assumed personal protective equipment for workers at importing facilities, based on professional judgement regarding practices at an importing facility.
- Inhalation exposures were assessed using modeled data. The model is representative of exposures associated with bulk container loading; however, the model does not account for other potential sources of exposure at industrial facilities, such as sampling or equipment cleaning.

- The uncertainties include the inhalation exposures for ONUs, which are assumed to be negligible due to the dilution of 1-BP into the ambient air in the model used.
- Dermal exposures were assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (workers and ONUs) from import of 1-BP.

5.2.1.3 Processing – Processing as a reactant – Intermediate in all other basic inorganic chemical manufacturing, all other basic organic chemical manufacturing, and pesticide, fertilizer, and other agricultural chemical manufacturing (Processing as reactant)

Section 6(b)(4)(A) unreasonable risk determination for the processing of 1-BP as a reactant: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation or dermal exposures at the central tendency and high-end, even when PPE is not used. In addition, for workers, EPA found that there was no unreasonable risk of cancer from chronic inhalation or dermal exposures at the central tendency and high-end, when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures and of cancer from chronic inhalation exposures.

EPA's determination that processing of 1-BP as a reactant does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, 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 cancer from chronic inhalation and dermal exposures at the high-end do not support an unreasonable risk determination. Respirators with APF of 10 and gloves with PF of 5 are the assumed personal protective equipment for workers at processing facilities, based on professional judgement regarding practices at processing facilities.
- Inhalation exposures were assessed using modeled data. The model is representative of exposures associated with bulk container loading; however, the model does not account for other potential sources of exposure at processing facilities, such as sampling or equipment cleaning.
- Inhalation exposures for ONUs are assumed to be negligible due to the dilution of 1-BP into the ambient air in the model used.
- Dermal exposures were also assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (workers and ONUs) from processing of 1-BP as a reactant.

5.2.1.4 Processing – Incorporation into formulation, mixture, or reaction products – Solvents for cleaning or degreasing in manufacturing of: all other chemical product and preparation; computer and electronic product; electrical equipment, appliance and component; soap, cleaning compound and toilet preparation; and services (Processing into a formulation, mixture, or reaction product)

Section 6(b)(4)(A) unreasonable risk determination for processing of 1-BP into a formulation, mixture, or reaction product: Presents an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found that there was unreasonable risk of cancer from chronic inhalation exposures, even when assuming use of PPE. For ONUs, EPA found that there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the high-end and of cancer from chronic inhalation exposures at the central tendency and high-end.

EPA's determination that the processing of 1-BP into a formulation, mixture, or reaction product presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- For workers, when assuming the use of respirators with APF of 50, the risk estimates of cancer from chronic inhalation exposures support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 50, the risk estimates of non-cancer effects from acute and chronic inhalation exposures do not support an unreasonable risk determination. Similarly, when assuming the use of gloves with PF of 5, the risk estimates of cancer from dermal exposures at the high-end do not support an unreasonable risk determination. Respirators with APF of 50 and gloves with PF of 5 are the maximum assumed personal protective equipment for workers at processing facilities, based on professional judgement regarding practices at processing facilities.
- For workers, the risk estimates of non-cancer effects from dermal exposures do not support an unreasonable risk determination.
- Inhalation exposures for workers and ONUs were assessed using personal breathing zone monitoring data collected at one formulation facility. The data have a high confidence rating and are directly applicable to this condition of use; however, the data may not be representative of exposures across the range of facilities that formulate products containing 1-BP. Based on EPA's analysis of the data for workers' inhalation exposures, central tendency or high-end exposures could not be distinguished.
- Dermal exposures were assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers and ONUs) from processing of 1-BP into a formulation, mixture, or reaction product.

5.2.1.5 Processing – Incorporation into articles – Solvents (becomes part of product formulation or mixture) in construction (Processing into articles)

Section 6(b)(4)(A) unreasonable risk determination for the processing of 1-BP into articles: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation or dermal exposures at the central tendency and high-end, even when PPE is not used. In addition, for workers, EPA found that there was no unreasonable risk of cancer from chronic inhalation or dermal exposures at the central tendency and high-end, when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures and of cancer from chronic inhalation exposures.

EPA's determination that the processing of 1-BP into articles does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, the exposures for 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 cancer from chronic inhalation and dermal exposures at the high-end do not support an unreasonable risk determination. Respirators with APF of 10 and gloves with PF of 5 are the assumed personal protective equipment for workers at processing facilities, based on professional judgement regarding practices at processing facilities.
- Inhalation exposures were assessed using modeled data. The model is representative of exposures associated with bulk container loading; however, the model does not account for other potential sources of exposure at processing facilities, such as sampling or equipment cleaning.
- Inhalation exposures for ONUs are assumed to be negligible due to the dilution of 1-BP into the ambient air in the model used.
- Dermal exposures were also assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, 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 incorporation of 1-BP into articles.

5.2.1.6 Processing – Repackaging – Solvents (cleaning or degreasing in all other basic organic chemical manufacturing) (Processing in repackaging as solvent)

Section 6(b)(4)(A) unreasonable risk determination for processing in repackaging of 1-BP as solvent: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation or dermal exposures at the central tendency and high-end, even when PPE is not used. In addition, for workers, EPA found that there was no unreasonable risk of cancer from chronic inhalation or dermal exposures at the central tendency and high-end, when assuming use of PPE. For

ONUs, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures and of cancer from chronic inhalation exposures.

EPA's determination that the processing of 1-BP in repackaging does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, the exposures for 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 cancer from chronic inhalation and dermal exposures at the high-end do not support an unreasonable risk determination. Respirators with APF of 10 and gloves with PF of 5 are the assumed personal protective equipment for workers at processing facilities, based on professional judgement regarding practices at processing facilities.
- Inhalation exposures were assessed using modeled data. The model is representative of exposures associated with bulk container loading; however, the model does not account for other potential sources of exposure at repackaging facilities, such as sampling or equipment cleaning.
- Inhalation exposures for ONUs are assumed to be negligible due to the dilution of 1-BP into the ambient air in the model used.
- Dermal exposures were also assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, 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 repackaging of 1-BP.

5.2.1.7 Processing – Recycling – Recycling (Processing as recycling)

Section 6(b)(4)(A) unreasonable risk determination for recycling of 1-BP: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation or dermal exposures at the central tendency and high-end, even when PPE is not used. In addition, for workers, EPA found that there was no unreasonable risk of cancer from chronic inhalation or dermal exposures at the central tendency and high-end, when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures and of cancer from chronic inhalation exposures.

EPA's determination that the processing of 1-BP in recycling does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, the exposures for 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 cancer from chronic inhalation and dermal exposures at the high-end do not

support an unreasonable risk determination. Respirators with APF of 10 and gloves with PF of 5 are the assumed personal protective equipment for workers at processing facilities, based on professional judgement regarding practices at recycling facilities.

- Inhalation exposures were assessed using modeled data. The model is representative of exposures associated with bulk container loading; however, the model does not account for other potential sources of exposure at recycling facilities, such as sampling or equipment cleaning.
- Inhalation exposures for ONUs are assumed to be negligible due to the dilution of 1-BP into the ambient air in the model used.
- Dermal exposures were also assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, 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 recycling of 1-BP.

5.2.1.8 Distribution in Commerce

Section 6(b)(4)(A) unreasonable risk determination for distribution in commerce of 1-BP: 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 1-BP is the transportation associated with the moving of 1-BP in commerce. The loading and unloading activities are associated with other conditions of use. EPA assumes transportation of 1-BP is in compliance with existing regulations for the transportation of hazardous materials, and emissions are therefore minimal (with the exception of spills and leaks, which are outside the scope of the risk evaluation). Based on the limited emissions from the transportation of chemicals, EPA determines there is no unreasonable risk of injury to health (workers and ONUs) from the distribution in commerce of 1-BP.

5.2.1.9 Industrial/Commercial Use – Solvent (for cleaning or degreasing) – Batch vapor degreaser (open-top) and in-line vapor degreaser (conveyorized, web cleaner)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of 1-BP as solvent in batch vapor degreaser (open-top) and in-line vapor degreaser (conveyorized, web cleaner): **Presents an unreasonable risk of injury to health (workers and ONUs).**

For workers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the high-end, and of cancer from chronic inhalation exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end, and of cancer from chronic inhalation exposures at the central tendency and high-end.

EPA's determination that the industrial and commercial use of 1-BP as solvent for cleaning or degreasing in open-top batch vapor degreasers and in-line vapor degreasers presents an unreasonable risk is based on

the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- For workers, when assuming the use of respirators with APF of 50, the risk estimates of non-cancer and cancer from inhalation exposures at the high-end support an unreasonable risk determination.
- For workers, when assuming the use of gloves with PF of 5, the risk estimates of cancer from dermal exposures at the high-end do not support an unreasonable risk determination. Gloves with PF of 5 are the assumed worker protection at facilities with open-top batch vapor degreasers and in-line vapor degreasers, based on professional judgement regarding practices at such facilities.
- Inhalation exposures for workers and ONUs from open-top batch vapor degreasers were assessed using personal breathing zone monitoring data collected from several different sources; however, some of the data do not clearly specify the type of vapor degreaser. Since open-top vapor degreasers typically have the highest emissions, based on EPA's analysis the data may underestimate exposures from batch vapor degreasers. The exposures data from open-top vapor degreasers was supplemented with a peer reviewed model using emission factors developed by the California Air Resources Board. The model results are in general agreement with monitoring data.
- There are no monitoring data specific to in-line vapor degreasers using 1-BP or data specific enough to develop a model; however, based on National Emission Inventory data, emissions from in-line vapor degreasers are generally similar to emissions from batch vapor degreasers.
- Dermal exposures were assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers and ONUs) from the industrial and commercial use of 1-BP as solvent for cleaning or degreasing in open-top batch vapor degreasers and in-line vapor degreasers.

5.2.1.10 Industrial/Commercial Use – Solvent (for cleaning or degreasing) – Batch vapor degreaser (closed-loop)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of 1-BP as solvent for batch vapor degreaser (closed-loop): Presents an unreasonable risk of injury to health (ONUs); does not present an unreasonable risk of injury to health (workers).

For ONUs, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the high-end and of cancer from chronic inhalation exposures at the high-end. For workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation at central tendency and at high-end and of cancer from chronic inhalation at central tendency and high-end, when assuming use of PPE. In addition, for workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from dermal exposure, and of cancer from dermal exposure, when assuming use of PPE.

EPA's determination that the industrial and commercial use of 1-BP as solvent for cleaning or degreasing in closed-loop batch vapor degreasers presents an unreasonable risk is based on the comparison of the risk

estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- For workers, when assuming the use of respirators with APF of 10, the risk estimates of non-cancer effects from acute and chronic inhalation exposures at the high-end, and the risk estimates of cancer from chronic inhalation exposures at the high-end do not support an unreasonable risk determination. Similarly, when assuming the use of gloves with PF of 5, the risk estimates of cancer from dermal exposures at the high-end do not support an unreasonable risk determination. Respirators with APF of 10 and gloves with PF of 5 are the assumed worker protection at facilities using 1-BP in closed-loop vapor degreasers, based on professional judgement regarding practices at such facilities.
- Inhalation exposures for workers and ONUs were assessed using a model with information from the open-top vapor degreaser and assuming 98 percent exposure reduction when switching from open-top to closed-loop.
- Dermal exposures were assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (ONUs) from industrial and commercial use of 1-BP as solvent for cleaning or degreasing in closed-loop batch vapor degreasers.

5.2.1.11 Industrial/Commercial Use – Solvent (for cleaning or degreasing) – Cold cleaners

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of 1-BP as solvent in cold cleaners: **Presents an unreasonable risk of injury to health (workers and ONUs).**

For workers, EPA found there was unreasonable risk of cancer from chronic inhalation exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures, and of cancer from chronic inhalation exposures.

EPA's determination that the industrial and commercial use of 1-BP as solvent in cold cleaners presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1., EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- For workers, when assuming the use of respirators with APF of 50, the risk estimates of cancer from inhalation exposures support an unreasonable risk determination.
- For workers, when assuming the use of respirators with APF of 50, the risk estimates of non-cancer effects from inhalation exposures do not support an unreasonable risk determination. Similarly, when assuming the use of gloves with PF of 5, the risk estimates of cancer from dermal exposures at the high-end do not support an unreasonable risk determination. Respirators with APF of 50 and

gloves with PF of 5 are the assumed maximum worker protection at facilities with cold cleaners, based on professional judgement regarding practices at a such facilities.

- Inhalation exposures for workers and ONUs from cold cleaners were assessed using personal breathing zone monitoring data from OSHA inspections, which are not intended to represent typical exposure levels at the workplace. In addition, the monitoring data may not be representative of the exposure level for the typical ONU (resulting in similar risk estimates for inhalation exposures at central tendency and high-end). The exposures monitoring data for cold cleaners was supplemented with modeling using emission factors for generic non-methane VOC. Exposures results are in good agreement with the exposure monitoring data for cold cleaners.
- Dermal exposures were assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers and ONUs) from the industrial and commercial use of 1-BP as solvent in cold cleaners.

5.2.1.12 Industrial/Commercial Use – Solvent (for cleaning or degreasing) – Aerosol spray degreaser/cleaner

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of 1-BP as solvent in aerosol spray degreasers/cleaners: Presents an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end, and of cancer from chronic inhalation exposures at the central tendency and high-end, without assuming use of respirators. For ONUs, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end, and of cancer from chronic inhalation exposures at the central tendency and high-end.

EPA's determination that the industrial and commercial use of 1-BP as solvent for cleaning or degreasing in aerosol spray degreasers/cleaners presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- EPA does not assume workers to use any type of respirator during industrial and commercial use of 1-BP as solvent for cleaning or degreasing in aerosol spray degreasers/cleaners.
- For workers, the risk estimates of non-cancer effects from dermal exposures do not support an unreasonable risk determination. When assuming the use of gloves with PF of 5, the risk estimates of cancer from dermal exposures at the high-end do not support an unreasonable risk determination. Gloves with PF of 5 are the assumed worker protection at facilities using 1-BP in aerosol degreasing based on professional judgement regarding practices at such facilities.

- Inhalation exposures for workers and ONUs from aerosol degreasing were assessed using a model which provides exposure estimates for a brake cleaning scenario. Although the model scenario is specific to brake cleaning and may not encompass the full range of aerosol degreasing uses, the model results are in good agreement with monitoring data. EPA also considered monitoring data from personal breathing zone collected from two studies, which indicated similar risks.
- Dermal exposures were also assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers and ONUs) from industrial and commercial use of 1-BP as solvent for cleaning or degreasing in aerosol spray degreasers/cleaners.

5.2.1.13 Industrial/Commercial Use – Adhesives and sealants – Adhesive chemicals (spray adhesive for foam cushion manufacturing and other uses)

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of 1-BP in adhesives and sealants: Presents an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end and of cancer from chronic inhalation exposures at the central tendency and high-end, even when assuming use of PPE. For ONUs, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end, and of cancer from chronic inhalation exposures at the central tendency and high-end.

EPA's determination that the industrial and commercial use of 1-BP in adhesives and sealants presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- The workers considered included the "sprayers" of the 1-BP adhesive and "non-sprayers" that handle the 1-BP adhesive or spend the majority of their shift working in an area where spraying occurs.
- For workers (sprayers and non-sprayers), when assuming the use of respirators with APF of 50, the risk estimates of non-cancer effects from acute and chronic inhalation exposures, and the risk estimates of cancer from chronic inhalation exposures support an unreasonable risk determination.
- For workers (sprayers and non-sprayers), the risk estimates of non-cancer effects from dermal exposures do not support an unreasonable risk determination. When assuming the use of gloves with PF of 5, the risk estimates of cancer from dermal exposures at the high-end do not support an unreasonable risk determination. Gloves with PF of 5 are the assumed worker protection at facilities using 1-BP in adhesives and sealants, based on professional judgement regarding practices at such facilities.

- Inhalation exposures for workers (sprayers and non-sprayers) and ONUs were assessed using personal breathing zone monitoring data collected from several studies, and EPA also considered model data which indicated similar risks.
- Dermal exposures were assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers and ONUs) from industrial and commercial use of 1-BP in adhesives and sealants.

5.2.1.14 Industrial/Commercial Use – Cleaning and furniture care products – Dry cleaning solvent, spot cleaner and stain remover

Section 6(b)(4)(A) unreasonable risk determination for the industrial and commercial use of 1-BP in cleaning and furniture care products in dry cleaning solvents, spot cleaners and stain removers: Presents an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end and of cancer from chronic inhalation exposures at the central tendency and high-end, without assuming use of respirators. In addition, for workers, EPA found there was unreasonable risk of cancer from chronic dermal exposures at the high-end, without assuming use of gloves. For ONUs, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end and cancer from chronic inhalation exposures at the central tendency and high-end.

EPA's determination that the industrial and commercial use of 1-BP in dry cleaning solvents, spot cleaners and stain removers presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- EPA does not assume workers to use any type of respirator or gloves during industrial and commercial use of 1-BP at dry cleaning facilities.
- The workers considered included those operating the dry-cleaning machines (adding make-up solvent, opening the machine door during the wash cycle, and removing loads from the machines) and workers doing spot cleaning of garments.
- For workers, the risk estimates of non-cancer effects from dermal exposures do not support an unreasonable risk determination.
- Inhalation exposures from dry cleaning solvent were assessed using personal breathing zone monitoring data from three different studies of facilities using converted third generation machines. A model was also used to represent exposures for larger facilities that may have multiple machines and machine types, that indicated similar risks.
- Inhalation exposures for workers and ONUs for spot cleaners and stain removers were assessed using personal breathing zone monitoring from OSHA inspections, which are not intended to

represent typical exposure levels at the workplace. The monitoring data was supplemented with a model, and while there is uncertainty in the representativeness of the spot cleaner use rate, the model results are in good agreement with the monitoring data.

- The modeled exposure concentrations for children (as shown in Table 2-22) are lower than those for adult ONUs. Chronic scenarios were not calculated due to uncertainty in the exposure frequency and number of years of exposure for children. In addition, it is unclear whether children are present at any of the remaining eight dry cleaners.
- Dermal exposures were assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers and ONUs) from industrial and commercial use of 1-BP in dry cleaning solvents, spot cleaners and stain removers.

5.2.1.15 Industrial/Commercial Use – Cleaning and furniture care products – Liquid cleaner (e.g., coin and scissor cleaner); liquid spray/aerosol cleaner

Section 6(b)(4)(A) unreasonable risk determination for industrial and commercial use of 1-BP in cleaning and furniture care products in liquid cleaners (e.g., coin and scissor cleaner) and liquid spray/aerosol cleaners: Presents an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end, and of cancer from chronic inhalation exposures at the central tendency and high-end, without assuming use of respirators. For ONUs, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end, and of cancer from chronic inhalation exposures at the central tendency and high-end.

EPA's determination that the industrial and commercial use of 1-BP in liquid cleaners (e.g., coin and scissor cleaner) and liquid spray/aerosol cleaners presents an unreasonable risk is based on comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- EPA does not assume workers to use any type of respirator during industrial and commercial use of 1-BP in liquid cleaners (e.g., coin and scissor cleaner) and liquid spray/aerosol cleaners.
- For workers, the risk estimates of non-cancer effects from dermal exposures do not support an unreasonable risk determination. When assuming the use of gloves with PF of 5, the risk estimates of cancer from dermal exposures at the high-end do not support an unreasonable risk determination. Gloves with PF of 5 are the assumed worker protection at facilities using 1-BP in liquid cleaners and liquid spray/aerosol cleaners, based on professional judgement regarding practices at such facilities.
- Inhalation and dermal exposures from industrial and commercial use of 1-BP in liquid cleaners (e.g., coin and scissor cleaner) and liquid spray/aerosol cleaners were considered similar to the

exposures from the use of 1-BP in aerosol degreasing and the same risk estimates were considered for this risk determination.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers and ONUs) from other industrial and commercial use of 1-BP in liquid cleaners (*e.g.*, coin and scissor cleaner) and liquid spray/aerosol cleaners.

5.2.1.16 Other Industrial/Commercial Use – Arts, crafts, and hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner); anti-adhesive agents (mold cleaning and release product); electronic and electronic products and metal products; functional fluids – closed systems (refrigerant) and open-systems (cutting oils); asphalt extraction; laboratory chemicals; and temperature indicator (coatings)

Section 6(b)(4)(A) unreasonable risk determination for other industrial and commercial use of 1-BP in arts, crafts, hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner); anti-adhesive agents (mold cleaning and release product); electronic and electronic products and metal products; functional fluids – closed systems (refrigerant) and open-systems (cutting oils); asphalt extraction; laboratory chemicals; and temperature indicator (coatings): Presents an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end, and of cancer from chronic inhalation exposures at the central tendency and high-end, without assuming use of respirators. For ONUs, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency and high-end, and of cancer from chronic inhalation exposures at the central tendency and high-end.

EPA's determination that the industrial and commercial use of 1-BP in other industrial and commercial uses presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- EPA does not assume workers to use any type of respirator during other industrial and commercial uses of 1-BP.
- For workers, the risk estimates of non-cancer effects from dermal exposures do not support an unreasonable risk determination. When assuming the use of gloves with PF of 5, the risk estimates of cancer from dermal exposures at the high-end do not support an unreasonable risk determination. Gloves with PF of 5 are the assumed worker protection at facilities using 1-BP in other industrial and commercial uses, based on professional judgement regarding practices at such facilities.

- Inhalation and dermal exposures from other industrial and commercial uses for 1-BP were considered similar to the exposures from the use of 1-BP in aerosol degreasing and the same risk estimates were considered for this risk determination.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (workers and ONUs) from other industrial and commercial use of 1-BP in arts, crafts, hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner); anti-adhesive agents (mold cleaning and release product); electronic and electronic products and metal products; functional fluids – closed systems (refrigerant) and open-systems (cutting oils); asphalt extraction; laboratory chemicals; and temperature indicator (coatings).

5.2.1.17 Consumer Use – Solvent (cleaning or degreasing) – Aerosol spray degreasers/cleaners

Section 6(b)(4)(A) unreasonable risk determination for the consumer use of 1-BP as solvent in aerosol spray degreasers/cleaners: Presents an unreasonable risk of injury to health (consumers and bystanders).

For consumers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate, and high intensity use. In addition, for consumers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute dermal exposures at the moderate and high intensity use. For bystanders, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate and high intensity use.

EPA's determination that the consumer use of 1-BP as solvent in aerosol spray degreasers/cleaners presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-59) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- Risk estimates for the consumer use of 1-BP as solvent in aerosol spray degreasers/cleaners was based on modeled risk estimates of two products: aerosol spray degreaser/cleaner-general, aerosol spray degreaser/cleaner-electronics.
- Inhalation exposures to consumers and bystanders were evaluated with the Consumer Exposure Model (CEM). The magnitude of inhalation exposures to consumers and bystanders depends on several factors, including the concentration of 1-BP in products used, use patterns (including frequency, duration, amount of product used, room of use, and local ventilation), and application methods.
- Dermal exposures to consumers were evaluated for one product with the CEM (Permeability) and for the other product with the CEM (Fraction Absorbed). Dermal exposures to consumers result from direct contact with the product or from vapor or mist deposition onto the skin while using the product (dermal permeation). The magnitude of dermal exposures depends on several factors, including skin surface area, product volume, concentration of 1-BP in product used, and dermal

exposure duration. The potential for dermal exposures to 1-BP is limited by several factors including physical-chemical properties of 1-BP, high vapor pressure, and quick volatilization of product containing 1-BP from surfaces.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (consumers and bystanders) from the consumer use of 1-BP as solvent in aerosol spray degreasers/cleaners.

5.2.1.18 Consumer Use – Cleaning and furniture care products – Spot cleaner and stain remover (Spot cleaners and stain removers)

Section 6(b)(4)(A) unreasonable risk determination for the consumer use of 1-BP in spot cleaners and stain removers: Presents an unreasonable risk of injury to health (consumers and bystanders).

For consumers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate, and high intensity use. In addition, for consumers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute dermal exposures at the high intensity use. For bystanders, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the moderate and high intensity use.

EPA's determination that the consumer uses of 1-BP in spot cleaners and stain removers presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-59) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- Inhalation exposures to consumers and bystanders were evaluated with the Consumer Exposure Model (CEM). The magnitude of inhalation exposures to consumers and bystanders depends on several factors, including the concentration of 1-BP in products used, use patterns (including frequency, duration, amount of product used, room of use, and local ventilation), and application methods.
- Dermal exposures to consumers were evaluated with the CEM (Permeability). Dermal exposures to consumers result from direct contact with the product or from vapor or mist deposition onto the skin while using the product (dermal permeation). The magnitude of dermal exposures depends on several factors, including skin surface area, product volume, concentration of 1-BP in product used, and dermal exposure duration. The potential for dermal exposures to 1-BP is limited by several factors including physical-chemical properties of 1-BP, high vapor pressure, and quick volatilization of product containing 1-BP from surfaces.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (consumers and bystanders) from the consumer use of 1-BP in spot cleaners and stain removers.

5.2.1.19 Consumer Use – Cleaning and furniture care products – Liquid cleaner (e.g., coin and scissor cleaner)

Section 6(b)(4)(A) unreasonable risk determination for the consumer use of 1-BP in liquid cleaner (e.g., coin and scissor cleaner): **Presents an unreasonable risk of injury to health (consumers and bystanders).**

For consumers and bystanders, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate and high intensity use.

EPA's determination that the consumer uses of 1-BP in liquid cleaner (e.g., coin and scissor cleaner) presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-59) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- For consumers, the risk estimates of non-cancer effects from acute dermal exposures do not support an unreasonable risk determination.
- Inhalation exposures to consumers and bystanders were evaluated with the Multi-Chamber Concentration and Exposure Model (MCCEM). The magnitude of inhalation exposures to consumers and bystanders depends on several factors, including the concentration of 1-BP in products used, use patterns (including frequency, duration, amount of product used, room of use, and local ventilation), and application methods.
- Dermal exposures to consumers were evaluated with the CEM (Permeability). Dermal exposures to consumers result from direct contact with the product or from vapor or mist deposition onto the skin while using the product (dermal permeation). The magnitude of dermal exposures depends on several factors, including skin surface area, product volume, concentration of 1-BP in product used, and dermal exposure duration. The potential for dermal exposures to 1-BP is limited by several factors including physical-chemical properties of 1-BP, high vapor pressure, and quick volatilization of product containing 1-BP from surfaces.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (consumers and bystanders) from the consumer use of 1-BP in liquid cleaner (e.g., coin and scissor cleaner).

5.2.1.20 Consumer Use – Cleaning and furniture care products – Liquid spray/aerosol cleaner

Section 6(b)(4)(A) unreasonable risk determination for the consumer use of 1-BP in liquid spray/aerosol cleaners: **Presents an unreasonable risk of injury to health (consumers and bystanders).**

For consumers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate, and high intensity use. In addition, for consumers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute dermal exposures at the moderate and high intensity use. For bystanders, EPA found there was

unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate and high intensity use.

EPA's determination that the consumer uses of 1-BP in liquid spray/aerosol cleaners presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-59) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- Risk estimates for the consumer use of 1-BP in liquid spray/aerosol cleaners were based on modeled risk estimates of one product: spray cleaner-general.
- Inhalation exposures to consumers and bystanders were evaluated with the Consumer Exposure Model (CEM). The magnitude of inhalation exposures to consumers and bystanders depends on several factors, including the concentration of 1-BP in products used, use patterns (including frequency, duration, amount of product used, room of use, and local ventilation), and application methods.
- Dermal exposures to consumers were evaluated with the CEM (Permeability). Dermal exposures to consumers result from direct contact with the product or from vapor or mist deposition onto the skin while using the product (dermal permeation). The magnitude of dermal exposures depends on several factors, including skin surface area, product volume, concentration of 1-BP in product used, and dermal exposure duration. The potential for dermal exposures to 1-BP is limited by several factors including physical-chemical properties of 1-BP, high vapor pressure, and quick volatilization of product containing 1-BP from surfaces.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (consumers and bystanders) from the consumer use of 1-BP in liquid spray/aerosol cleaners.

5.2.1.21 Consumer Use – Other uses – Arts, crafts and hobby materials (adhesive accelerant)

Section 6(b)(4)(A) unreasonable risk determination for the consumer use of 1-BP in arts, crafts, hobby materials (adhesive accelerant): Presents an unreasonable risk of injury to health (consumers and bystanders).

For consumers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate, and high intensity use. For bystanders, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the moderate and high intensity use.

EPA's determination that the consumer uses of 1-BP in arts, crafts, hobby materials (adhesive accelerant) presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-59) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- Inhalation exposures to consumers and bystanders were evaluated with the Consumer Exposure Model (CEM). The magnitude of inhalation exposures to consumers and bystanders depends on several factors, including the concentration of 1-BP in products used, use patterns (including frequency, duration, amount of product used, room of use, and local ventilation), and application methods.
- Dermal exposures to consumers were evaluated with the CEM (Fraction Absorbed). Dermal exposures to consumers result from direct contact with the product or from vapor or mist deposition onto the skin while using the product (dermal permeation). The magnitude of dermal exposures depends on several factors, including skin surface area, product volume, concentration of 1-BP in product used, and dermal exposure duration. The potential for dermal exposures to 1-BP is limited by several factors including physical-chemical properties of 1-BP, high vapor pressure, and quick volatilization of product containing 1-BP from surfaces.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (consumers and bystanders) from the consumer use of 1-BP in arts, crafts, hobby materials (adhesive accelerant).

5.2.1.22 Consumer Use – Other uses – Automotive care products (refrigerant flush)

Section 6(b)(4)(A) unreasonable risk determination for the consumer use of 1-BP in automotive care products (refrigerant flush): **Presents an unreasonable risk of injury to health (consumers and bystanders).**

For consumers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation and dermal exposures at the low, moderate, and high intensity use. For bystanders, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate and high intensity use.

EPA's determination that the consumer uses of 1-BP in automotive care products (refrigerant flush) presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-59) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- Inhalation exposures to consumers and bystanders were evaluated with the Multi-Chamber Concentration and Exposure Model (MCCEM). The magnitude of inhalation exposures to consumers and bystanders depends on several factors, including the concentration of 1-BP in products used, use patterns (including frequency, duration, amount of product used, room of use, and local ventilation), and application methods.
- Dermal exposures to consumers were evaluated with the CEM (Fraction Absorbed). Dermal exposures to consumers result from direct contact with the product or from vapor or mist deposition onto the skin while using the product (dermal permeation). The magnitude of dermal exposures depends on several factors, including skin surface area, product volume, concentration of 1-BP in product used, and dermal exposure duration. The potential for dermal exposures to 1-BP

is limited by several factors including physical-chemical properties of 1-BP, high vapor pressure, and quick volatilization of product containing 1-BP from surfaces.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (consumers and bystanders) from the consumer use of 1-BP in automotive care products (refrigerant flush).

5.2.1.23 Consumer Use – Other uses – Anti-adhesive agents (mold cleaning and release product)

Section 6(b)(4)(A) unreasonable risk determination for the consumer use of 1-BP in anti-adhesive agents (mold cleaning and release product): **Presents an unreasonable risk of injury to health (consumers and bystanders).**

For consumers, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate and high intensity use. For bystanders, EPA found there was unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the moderate and high intensity use.

EPA's determination that the consumer uses of 1-BP in anti-adhesive agents (mold cleaning and release product) presents an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects to the benchmarks (Table 4-59) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for the condition of use, and the uncertainties in the analysis (Section 4.3):

- Inhalation exposures to consumers and bystanders were evaluated with the Consumer Exposure Model (CEM). The magnitude of inhalation exposures to consumers and bystanders depends on several factors, including the concentration of 1-BP in products used, use patterns (including frequency, duration, amount of product used, room of use, and local ventilation), and application methods.
- Dermal exposures to consumers were evaluated with the CEM (Fraction Absorbed). Dermal exposures to consumers result from direct contact with the product or from vapor or mist deposition onto the skin while using the product (dermal permeation). The magnitude of dermal exposures depends on several factors, including skin surface area, product volume, concentration of 1-BP in product used, and dermal exposure duration. The potential for dermal exposures to 1-BP is limited by several factors including physical-chemical properties of 1-BP, high vapor pressure, and quick volatilization of product containing 1-BP from surfaces.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is unreasonable risk of injury to health (consumers and bystanders) from the consumer use of 1-BP in anti-adhesive agents (mold cleaning and release product).

5.2.1.24 Commercial and Consumer Use – Insulation (building/construction materials not covered elsewhere)

Section 6(b)(4)(A) unreasonable risk determination for the use of 1-BP in insulation: Does not present an unreasonable risk of injury to health (workers, ONUs, consumers, and bystanders).

For workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation and dermal exposures at the central tendency and high-end, and of cancer from chronic inhalation and dermal exposures at the central tendency and high-end, without assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures at the central tendency or high-end, and of cancer from chronic inhalation exposures at the central tendency or high-end. For consumers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation and dermal exposures at the low, moderate or high intensity use. For bystanders EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute inhalation exposures at the low, moderate or high intensity use. For consumers and bystanders, EPA found that there was no an unreasonable risk of non-cancer effects (developmental) and cancer from chronic inhalation exposures.

EPA's determination that the use of 1-BP in insulation does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58 and Table 4-59) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures from the condition of use, and the uncertainties in the analysis (Section 4.3):

- EPA conducted a screening-level analysis using EPA's Indoor Environment Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU) model to estimate the potential 1-BP concentration from off-gassing of insulation.
- For workers and ONUs, exposures to 1-BP during installation is negligible since 1-BP concentrations are below 0.01 ppm 8-hr TWA inside a residential home for the initial work day, and less on subsequent days after installation.
- For consumers and bystanders, two building configurations were evaluated encompassing attic, living space, crawlspace and basement. Also, the evaluation encompassed both acute and chronic exposures to account for the off-gassing of the installed board that may be ongoing for months.

In summary, the risk estimates, the health effects of 1-BP, the exposures, and consideration of uncertainties support EPA's determination that there is no unreasonable risk of injury to health (workers, ONUs, consumers and bystanders) from the use of 1-BP in insulation.

5.2.1.25 Disposal – Disposal – municipal waste incinerator, off-site waste transfer (Disposal)

Section 6(b)(4)(A) unreasonable risk determination for the disposal of 1-BP: Does not present an unreasonable risk of injury to health (workers and ONUs).

For workers, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation or dermal exposures at the central tendency and high-end, even when PPE is

not used. In addition, for workers, EPA found that there was no unreasonable risk of cancer from chronic inhalation or dermal exposures at the central tendency or high-end, when assuming use of PPE. For ONUs, EPA found that there was no unreasonable risk of non-cancer effects (developmental) from acute and chronic inhalation exposures or of cancer from chronic inhalation exposures.

EPA's determination that the disposal of 1-BP does not present an unreasonable risk is based on the comparison of the risk estimates for non-cancer effects and cancer to the benchmarks (Table 4-58) and other considerations. As explained in Section 5.1, EPA considered the health effects of 1-BP, the exposures for 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 cancer from chronic inhalation and dermal exposures at the high-end do not support an unreasonable risk determination. Respirators with APF of 10 and gloves with PF of 5 are the assumed personal protective equipment for workers at disposal facilities, based on professional judgement regarding likely practices at a processing facility.
- Inhalation exposures were assessed using modeled data. The model is representative of exposure associated with bulk container loading; however, the model does not account for other potential sources of exposure at disposal facilities, such as equipment cleaning.
- The uncertainties also include the inhalation exposures for ONUs, which are assumed to be negligible due to the dilution of 1-BP into the ambient air in the model used.
- Dermal exposures were also assessed using modeled data.

In summary, the risk estimates, the health effects of 1-BP, 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 disposal of 1-BP.

5.2.1.26 General Population

Section 6(b)(4)(A) unreasonable risk determination for **all conditions** of use of 1-BP: Does not present an unreasonable risk of injury to health (general population). For all conditions of use, EPA found that there were no exposures from drinking water, surface water and sediment. EPA considered reasonably available information and environmental fate properties to characterize general population exposure. EPA does not expect general population exposure from the ingestion of contaminated drinking water. EPA did not evaluate risks to the general population from ambient air and disposal pathways for any conditions of use, and the unreasonable risk determinations do not account for exposures to the general population from ambient air and disposal pathways.

5.2.2 Environment

Section 6(b)(4)(A) unreasonable risk determination for **all conditions** of use of 1-BP: Does not present an unreasonable risk of injury **to the environment** (aquatic, sediment dwelling and terrestrial organisms).

For all conditions of use, EPA found that there were no exceedances of benchmarks to aquatic organisms from exposures to 1-BP. The RQ values associated with acute and chronic exposures are <0.01 and 0.12, respectively, based on the best available science (Table 4-2). While one single study was used to characterize the environmental hazards, it was of high quality, based on EPA's systematic review, and the analysis was complemented with modeling. The experimental procedures used in this effort represent the best practices for conducting acute toxicity testing with fathead minnows and are consistent with the test guidelines currently recommended by EPA and international regulatory partner organizations for conducting ecological risk assessment purposes for fish. The confidence in the available data to characterize the environmental hazards of 1-BP is bolstered by the use of the QSAR modeling program ECOSAR (v2.0) ([EPA, 2017](#)) lending greater confidence to the risk estimates.

The high volatility, high water solubility and low Log K_{oc} of 1-BP suggest that 1-BP will only be present at low concentrations in the sediment and terrestrial environmental compartments.

In summary, the risk estimates, the environmental effects of 1-BP, the exposures, physical-chemical properties of 1-BP and consideration of uncertainties support EPA's determination that there is no unreasonable risk to the environment from all conditions of use of 1-BP.

5.3 Changes to the Unreasonable Risk Determination from Draft Risk Evaluation to Final Risk Evaluation

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 sometimes unreasonable risk determinations are based on multiple exposure scenarios. EPA makes an unreasonable risk determination for each condition of use within the scope of the risk evaluation. In the draft risk evaluation, EPA evaluated the commercial uses of 1-BP in insulation as part of the other industrial and commercial uses of 1-BP; however, the Occupational Exposure Scenario used for the other industrial and commercial uses of 1-BP was not adequate to evaluate the installation of insulation containing 1-BP. EPA has developed an occupational scenario for the commercial use of 1-BP in insulation and therefore such use has a different unreasonable risk determination in this final risk evaluation. In addition, for further clarity, EPA is now issuing a single unreasonable risk determination for dry cleaning solvent and spot cleaner, stain remover. EPA is also issuing an unreasonable risk determination for the liquid cleaner and liquid spray/aerosol cleaner that is separate from the unreasonable risk determination for other industrial and commercial uses.

Table 5-2. 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 (emphasis added)
<ul style="list-style-type: none"> Industrial and commercial use in cleaning and furniture care products in liquid cleaners (e.g., coin and scissor cleaner) and liquid spray/aerosol cleaners 	<ul style="list-style-type: none"> Industrial and commercial use as a cleaning and furniture care product in the form of liquid cleaner (e.g., coin and scissor cleaner) and liquid spray or aerosol cleaner as well as other industrial and commercial uses: arts, crafts, hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner, refrigerant flush); anti-adhesive agents (mold cleaning and release product); building/construction materials not covered elsewhere (insulation); electronic and electronic products and metal products; functional fluids (close/open-systems) – refrigerant/cutting oils; asphalt extraction; laboratory chemicals; and temperature indicator – coatings
<ul style="list-style-type: none"> Commercial and consumer uses of building/construction materials (insulation) 	
<ul style="list-style-type: none"> Other industrial and commercial use in arts, crafts, hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner); anti-adhesive agents (mold cleaning and release product); electronic and electronic products and metal products; functional fluids – closed systems (refrigerant) and open-systems (cutting oils); asphalt extraction; laboratory chemicals; and temperature indicator (coatings) 	
<ul style="list-style-type: none"> Industrial and commercial use as cleaning and furniture care products in dry cleaning solvents, spot cleaners and stain removers 	<ul style="list-style-type: none"> Industrial and commercial use as cleaning and furniture care products in dry cleaning solvents
	<ul style="list-style-type: none"> Industrial and commercial use as cleaning and furniture care products in the form of spot cleaner and stain remover

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 1-BP do not present an unreasonable risk of injury to health or the environment:

- Manufacturing: domestic manufacturing (Section 5.2.1.1, Section 5.2.1.26, Section 5.2.2, Section 4, Section 3, and Section 2.3.1.5)
- Manufacturing: import (Section 5.2.1.2, Section 5.2.1.26, Section 5.2.2, Section 4, Section 3, and Section 2.3.1.6)
- Processing: as a reactant (Section 5.2.1.3, Section 5.2.1.26, Section 5.2.2, Section 4, Section 3, and Section 2.3.1.7)
- Processing: incorporation into articles (Section 5.2.1.5, Section 5.2.1.26, Section 5.2.2, Section 4, Section 3, and Section 2.3.1.9)
- Processing: repackaging (Section 5.2.1.6, Section 5.2.1.26, Section 5.2.2, Section 4, Section 3, and Section 2.3.1.10)
- Processing: recycling (Section 5.2.1.7, Section 5.2.1.26, Section 5.2.2, Section 4, Section 3, and Section 2.3.1.21)
- Distribution in commerce (Section 5.2.1.8, Section 5.2.1.26, Section 5.2.2, Section 4, and Section 3)
- Commercial and consumer uses of building/construction materials (insulation) (Section 5.2.1.24, Section 5.2.1.26, Section 5.2.2, Section 4, Section 3, and Section 2.3.1.19)
- Disposal (Section 5.2.1.25, Section 5.2.1.26, Section 5.2.2, Section 4, Section 3, and Section 2.3.1.21)

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 1-BP present an unreasonable risk of injury:

- Processing: incorporation into formulation, mixture, or reaction products
- Industrial and commercial use as solvent for cleaning and degreasing in vapor degreaser (batch vapor degreaser – open-top, inline vapor degreaser)
- Industrial and commercial use as solvent for cleaning and degreasing in vapor degreaser (batch vapor degreaser – closed-loop)
- Industrial and commercial use as solvent for cleaning and degreasing in cold cleaners
- Industrial and commercial use as solvent in aerosol spray degreaser/cleaner
- Industrial and commercial use in adhesives and sealants
- Industrial and commercial use in dry cleaning solvents, spot cleaners and stain removers
- Industrial and commercial use in liquid cleaners (*e.g.*, coin and scissor cleaner) and liquid spray/aerosol cleaners
- Other industrial and commercial uses: arts, crafts, hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner, refrigerant flush); anti-adhesive agents (mold cleaning and release product); electronic and electronic products and metal products; functional fluids (close/open-systems) – refrigerant/cutting oils; asphalt extraction; laboratory chemicals; and temperature indicator – coatings
- Consumer use as solvent in aerosol spray degreasers/cleaners
- Consumer use in spot cleaners and stain removers
- Consumer use in liquid cleaner (*e.g.*, coin and scissor cleaner)
- Consumer use in liquid spray/aerosol cleaners
- Consumer use in arts, crafts, hobby materials (adhesive accelerant)
- Consumer use in automotive care products (refrigerant flush)
- Consumer use in anti-adhesive agents (mold cleaning and release product)

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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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
US EPA Regulations		
Toxic Substances Control Act (TSCA) – Section 6(b)	EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments.	1-BP is on the initial list of chemicals to be evaluated for unreasonable risk under TSCA (81 FR 91927, December 19, 2016)
Toxic Substances Control Act (TSCA) – Section 8(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.	1-BP manufacturing, importing, processing, and use information is reported under the Chemical Data Reporting (CDR) rule (76 FR 50816, August 16, 2011).
Toxic Substances Control Act (TSCA) – Section 8(b)	EPA must compile, keep current, and publish a list (the TSCA Inventory) of each chemical substance manufactured, processed, or imported in the United States.	1-BP was on the initial TSCA Inventory and therefore was not subject to EPA’s new chemicals 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.	Eleven notifications of substantial risk (Section 8(e)) received before 2001 (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.	One submission from a test rule (Section 4) received in 1981 (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 Toxics Release Inventory (TRI)-listed chemical in quantities above threshold levels.	1-BP is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 1, 2016, with reporting due July 1, 2017 (80 FR 72906, November 23, 2015).
Clean Air Act (CAA) – Section 112(b)	The Clean Air Act (CAA) contains a list of hazardous air pollutants (HAP) and provides EPA with the authority to add to that list pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. For all major source categories emitting HAP, the CAA requires issuance of technology-based standards and, 8 years later, if necessary, additions or revisions to address developments in practices, processes, and control technologies, and to ensure the standards adequately protect public health and the environment. The CAA thereby provides	EPA received petitions from the Halogenated Solvent Industry Alliance and the New York State Department of Environmental Conservation to list 1-BP as a <i>hazardous air pollutant</i> (HAP) under section 112(b)(1) of the Clean Air Act (80 FR 6676, February 6, 2015). On January 9, 2017, EPA published a draft notice on the rationale for granting the petitions to add 1-BP to the list of HAP. The public comment period closed on June 8, 2017 (82 FR 2354, January 9, 2017). On June 18, 2020, EPA granted the petition to add 1-BP to the list of HAP (85 FR 36851) and will

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
	EPA with comprehensive authority to regulate emissions to ambient air of any hazardous air pollutant.	take a separate regulatory action to add 1-BP to the list of HAP under CAA section 112(b)(1). Since 1-BP is not a HAP, currently, there are no National Emissions Standards for Hazardous Air Pollutants (NESHAPs).
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 (NAAQS) 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.	1-BP is listed under the National Volatile Organic Compound Emission Standards for Aerosol Coatings (40 CFR part 59, subpart E). 1-BP has a reactivity factor of 0.35 g O3/g VOC.
Clean Air Act (CAA) – Section 612	Under Section 612 of the Clean Air Act (CAA), EPA’s Significant New Alternatives Policy (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.	Under EPA’s SNAP program, EPA evaluated 1-BP as an acceptable substitute for ozone-depleting substances. In 2007, EPA listed 1-BP as an acceptable substitute for chlorofluorocarbon (CFC)-113 and methyl chloroform in the solvent and cleaning sector for metals cleaning, electronics cleaning, and precision cleaning. EPA recommended the use of personal protective equipment, including chemical goggles, flexible laminate protective gloves and chemical-resistant clothing (72 FR 30142, May 30, 2007). In 2007, the Agency also proposed to list 1-BP as an unacceptable substitute for CFC-113, hydrochlorofluorocarbon (HCFC)- 114b and methyl chloroform when used in adhesives or in aerosol solvents; and in the coatings end use (subject to use conditions) (72 FR 30168, May 30, 2007). The proposed rule has not been finalized by the Agency. The rule identifies 1-BP as acceptable and unacceptable substitute for ozone-depleting substances in several sectors.
Other Federal 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 issued a PEL for 1-BP. OSHA and the National Institute for Occupational Safety and Health (NIOSH) issued a Hazard Alert regarding 1-BP (OSHA-NIOSH, 2013) providing information regarding health effects, how workers are exposed, how to control the exposures and how OSHA and NIOSH can help. The Hazard Alert states that: "ACGIH currently recommends a 10 ppm time-weighted average threshold limit value but has proposed lowering the value to 0.1 ppm [ACGIH

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
		2013]." OSHA also released an Enforcement Policy for Respiratory Hazards Not Covered by OSHA Permissible Exposure Limits that explain OSHA requirements and the applicability of this policy pertaining to 1-BP exposure limits under certain conditions.
Department of Energy (DOE)	The Atomic Energy Act authorizes DOE to regulate the health and safety of its contractor employees.	10 CFR 851.23, Worker Safety and Health Program, requires the use of the 2005 ACGIH TLVs if they are more protective than the OSHA PEL. The 2005 TLV for 1-BP is 10 ppm (8hr Time Weighted Average).

A.2 State Laws and Regulations

Table_Apx A-2. State Laws and Regulations

State Actions	Description of Action
State Air Regulations	Allowable Ambient Levels Rhode Island (Air Pollution Regulation No. 22) New Hampshire (Env-A 1400: Regulated Toxic Air Pollutants) New York has a de facto ban on the use of 1-BP in dry cleaning. New York will not issue an Air Facility Registration to any facility proposing to use that chemical as an alternative dry cleaning solvent as it is not an approved alternative solvent.
Chemicals of High Concern	Massachusetts designated 1-BP as a higher hazard substance requiring reporting starting in 2016 (301 CMR 41.00). Minnesota listed 1-BP as chemical of high concern to children (Minnesota Statutes 116.9401 to 116.9407).
State Permissible Exposure Limits	California PEL: 5 ppm as an 8-hr-time-weighted average (TWA) (California Code of Regulations, title 8, section 5155).
State Right-to-Know Acts	New Jersey (42 N.J.R. 1709(a)), Pennsylvania (Chapter 323. Hazardous Substance List).
Other	In California, 1-BP was added to proposition 65 list in December 2004 due to developmental, female and male, toxicity; and in 2016 due to cancer. (Cal. Code Regs. title 27, section 27001). 1-BP is listed as a Candidate Chemical under California's Safer Consumer Products Program (Health and Safety Code sections 25252 and 25253). California also selected 1-BP as the first chemical for early warning and prevention activities under SB 193 Early Warning Authority and issued a Health Hazard Alert for 1-BP (Hazard Evaluation System and Information Service, 2016). Oregon has adopted, and is considering, several state-specific statutes and regulations to manage the impacts of toxic and hazardous pollutants, including air toxics permits and benchmarks for industrial facilities, and the Toxics Use and Hazardous Waste Reduction planning requirements, which apply to large and small quantity generators of hazardous waste and Toxic Release Inventory reporters. The District of Columbia's Hazardous Waste Management Act includes provisions for toxic chemical source reporting and reduction. Businesses identified by the Standard Industrial Classification (SIC) as the largest generators or within the top 25% of all hazardous waste generators within the District, or that release a toxic chemical subject to

State Actions	Description of Action
	regulation are required to file an annual Toxic Release Inventory (TRI) Form R for each TRI-listed chemical it manufactures, processes or otherwise uses in quantities above the threshold reporting quantity. In addition, reporting facilities must prepare and submit a toxic chemical source reduction plan which must be updated every four years.

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 2012, 1-BP was listed on the Candidate list as a Substance of Very High Concern (SVHC) under regulation (EC) No 1907/2006 - REACH (Registration, Evaluation, Authorization and Restriction of Chemicals due to its reproductive toxicity (category 1B). In June 2017, 1-BP was added to Annex XIV of REACH (Authorisation List) with a sunset date of July 4, 2020 (European Chemicals Agency (ECHA) database. Accessed December 6, 2017).
Australia	1-BP was assessed under Environment Tier II of the Inventory Multi-tiered Assessment and Prioritisation (IMAP) (National Industrial Chemicals Notification and Assessment Scheme (NICNAS), 2017, <i>Human Health Tier II Assessment for Propane, 1-bromo-</i> . Accessed April, 18 2017).
Japan	1-BP 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; CSCL) Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof Industrial Safety and Health Act (ISHA) Air Pollution Control Law (National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP). Accessed April 13, 2017).
Belgium, Canada, Finland, Japan, Poland, South Korea and Spain	Occupational exposure limits for 1-BP. (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017).
Basel Convention	Halogenated organic solvents (Y41) are listed as a category of waste under the Basel Convention – Annex I. Although the United States is not currently a party to the Basel Convention, this treaty still affects U.S. importers and exporters.
OECD Control of Transboundary Movements of Wastes Destined for Recovery Operations	Halogenated organic solvents (A3150) are listed as a category of waste subject to The Amber Control Procedure under Council Decision C (2001) 107/Final.

Appendix B LIST OF SUPPLEMENTAL DOCUMENTS

List of supplemental documents:

Associated Systematic Review Data Quality Evaluation Documents – Provides additional detail and information on individual study evaluations including criteria and scoring results.

1. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Updates to Data Quality Criteria for Epidemiological Studies. ([EPA, 2019q](#)).
2. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies. ([EPA, 2019l](#)).
3. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation for Consumer Exposure. ([EPA, 2019j](#)).
4. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation for Release and Occupational Exposure. ([EPA, 2019m](#)).
5. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation for Release and Occupational Exposure - Common Sources. ([EPA, 2019n](#)).
6. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Study. ([EPA, 2019k](#)).
7. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies - Epidemiologic Studies. ([EPA, 2019p](#)).
8. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies - Animal and In Vitro Studies. EPA-HQ-OPPT-2019-0235 ([EPA, 2019o](#)).
9. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction Tables for Environmental Fate and Transport Studies. ([EPA, 2019i](#)).
10. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction for Consumer Exposure. ([EPA, 2019h](#)).
11. Final Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Physical-Chemical Property Studies. ([U.S. EPA, 2019](#))

Associated Supplemental Information Documents – Provides additional details and information on engineering and exposure assessments.

1. Final Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Information on Consumer Exposure Assessment Model Input Parameters. ([EPA, 2019a](#)).
2. Final Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Information on Consumer Exposure Assessment Model Outputs. ([EPA, 2019b](#)).
3. Final Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Consumer Exposure Risk Calculations. ([EPA, 2019c](#)).

4. Final Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Information on Occupational Exposure Assessment ([EPA, 2019f](#)). This document provides additional details and information on the occupational exposure assessment, including estimates of number of sites and workers, summary of monitoring data, and exposure modeling equations, inputs and outputs.
5. Final Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Occupational Risk Calculator. ([EPA, 2019g](#)).
6. Final Risk Evaluation for 1-Bromopropane (1-BP), Supplemental File: Human Health Benchmark Dose Modeling. ([EPA, 2019d](#)).

Appendix C FATE AND TRANSPORT

C.1 Fate in Air

If released to the atmosphere, 1-BP is expected to exist solely in the vapor-phase based on its vapor pressure. In the vapor phase, it is degraded by reaction with photochemically produced hydroxyl radicals. The half-life of this reaction is approximately 9 - 12 days assuming a hydroxyl radical concentration over a 12 hour day of 1.5×10^6 hydroxyl radicals per cubic centimeter of air (Version 4.10 EPISuite). Its atmospheric degradation and its photooxidation products were investigated for their ozone depletion potential ([Burkholder et al., 2002](#)). It was shown that the hydroxyl radical initiated degradation does not lead to long-lived bromine containing species that can migrate to the stratosphere. The major photodegradation products were bromoacetone, propanal and 3-bromopropanal. Bromoacetone was rapidly photolyzed releasing bromine which was removed from the atmosphere by wet deposition. 1-BP does not absorb light greater than 290 nm; therefore, degradation of this substance by direct photolysis is not expected to be an important fate process. The bromoacetone and propanal constitute about 90% of 1-BP that is degraded in the atmosphere, and they, as well as 3-bromopropanal, are expected to be rapidly degraded. Apparently, the major atmospheric degradative fate of 1-BP is the rapid and irreversible release of Br atoms. Based on the 1-BP estimated half-life of 9-12 days in air, it is possible that it can undergo long range transport via the atmosphere.

C.2 Fate in Water

When released to water, 1-BP is not expected to sorb to suspended solids and sediment in the water column based upon its estimated Koc value of about 40 ([U.S. EPA, 2013b](#)). The rate of volatilization is expected to be rapid based on a Henry's Law constant of 7.3×10^{-3} atm-m³/mole. 1-BP was reported to achieve 70% of its theoretical biochemical oxygen demand (BOD) in the MITI (OECD 301C) test ([Sakuratani et al., 2005](#)) which is considered readily biodegradable. Bacterial strains isolated from organobromide-rich industrial wastewater were shown to degrade 1-BP ([Shochat et al., 1993](#)). *Arthrobacter* HA1 debrominated 1-BP under aerobic conditions yielding 1-propanol as a degradation product ([Belkin, 1992](#)) and *Acinetobacter* strain GJ70, isolated from activated sludge was able to utilize it as a carbon source ([Janssen et al., 1987](#)). These results suggest that 1-BP will undergo biodegradation in the environment under aerobic conditions. Hydrolysis of 1-BP is expected based on studies of ([Mabey and Mill, 1978](#)). A hydrolysis half-life of about 26 days was calculated at pH 7 and 25 degrees Celsius from its first-order neutral rate constant of 3.01×10^{-7} sec⁻¹. The expected hydrolysis product is propanol and the hydrodebromination product propene is also possible. Photooxidation in water has not been reported to be an important environmental fate process. 1-BP is not expected to be persistent in water.

C.3 Fate in Sediment and Soil

1-BP is expected to have high mobility in soil based on an estimated log K_{oc} of 1.6. Volatilization is expected to be an important fate process given its relatively high Henry's law constant of 7.3×10^{-3} atm m³/mole. Its biodegradation is considered to be moderate in sediment and soil. 1-BP is not persistent in sediment or soil.

Appendix D CHEMICAL DATA REPORTING RULE DATA FOR 1-BP

EPA's [2012 Chemical Data Reporting \(CDR\)](#) reported a 1-BP production volume of 15.4 million pounds. Albemarle Corporation and a CBI company reported domestic manufacturing of 1-BP ([U.S. EPA, 2012d](#)). Dow Chemical Company, Special Materials Company, and ICL reported imports of 1-BP ([U.S. EPA, 2012d](#)). Data in Table_Apx D-1 through Table_Apx D-3 were extracted from the 2012 CDR records ([U.S. EPA, 2012d](#)).

Table_Apx D-1. National Chemical Information for 1-BP from 2012 CDR

Production Volume (aggregate)	15.4 million pounds
Maximum Concentration (at manufacture or import site)	>90%
Physical form(s)	Liquid
Number of reasonably likely to be exposed industrial manufacturing, processing, and use workers (aggregated)	>1,000
Was industrial processing or use information reported?	Yes
Was commercial or consumer use information reported?	Yes

Table_Apx D-2. Summary of Industrial 1-BP Uses from 2012 CDR

Industrial Sector (Based on NAICS)	Industrial Function	Type of Processing
Soap, Cleaning Compound, and Toilet Preparation Manufacturing	Solvents (for cleaning or degreasing)	Processing-repackaging
Soap, Cleaning Compound, and Toilet Preparation Manufacturing	Solvents (for cleaning or degreasing)	Processing-incorporation
Abbreviations: NAICS=North American Industry Classification System		

Table_Apx D-3. Commercial/Consumer Use Category Summary of 1-BP

Commercial/Consumer Product Category	Intended for Commercial and/or Consumer Uses or Both	Intended for Use in Children's Products in Related Product Category
Cleaning and Furnishing Care Products	Commercial	No
Electrical and Electronic Products	Commercial	No

Appendix E EXPERIMENTAL MEASUREMENT OF FRACTION ABSORBED FOR DERMAL EXPOSURE MODELING

Section 2.3.1.23 presents EPA’s modeling approach to estimate dermal exposure in occupational scenarios. The *Dermal Exposure to Volatile Liquids Model* (Equation 2-2) calculates the dermal retained dose by incorporating a “fraction absorbed (f_{abs})” parameter to account for the evaporation of volatile chemicals. This parameter can either be estimated (using steady-state approximation) or measured. This appendix discusses measured experimental value of f_{abs} used in the 1-BP Risk Evaluation.

In a 2011 study, Frasch et al. tested dermal absorption characteristics of 1-BP. For the finite dose scenario, Frasch et al. (2011) determined that unoccluded exposure resulted in a fractional absorption of 0.16 percent of applied 1-BP. The measurement was performed in an open fume hood with an average air speed of 0.3 m/s (30 cm/s) – a value likely higher than typical air velocity that workers would experience indoors. Because higher air velocity increases the rate of chemical evaporation, the experimental value likely underestimates fractional absorption. As such, this measured value should be adjusted to account for typical environmental conditions relevant to worker exposures.

E.1 f_{abs}

Fraction absorbed ($0 \leq f_{abs} \leq 1$) refers to the fraction of chemical that is absorbed through the stratum corneum (upper layer) of the skin. It is a function of the dimensionless χ , which is defined as the ratio of evaporative flux to absorption flux (Kissel et al., 2018):

Equation_Apx E-1. Ratio of Evaporative Flux to Absorption Flux (χ)

$$\chi = \frac{J_{evap}}{J_{max,SS}} = \frac{k_{evap} \times \rho}{J_{max,SS}}$$

Where:

J_{evap} is the evaporative flux (mg/cm²-h)

$J_{max,SS}$ is the maximum steady-state absorption flux (mg/cm²-h)

k_{evap} is the liquid-phase evaporation mass transfer coefficient (cm/h)

ρ is density (mg/cm³)

The liquid-phase evaporation mass transfer coefficient (k_{evap}) is a function of the gas-phase mass transfer coefficient, which is dependent on the wind speed, u (Kissel et al., 2018):

Equation_Apx E-2. Liquid-Phase Evaporation Mass Transfer Coefficient

$$k_{evap} = k_g \frac{P_{vap} MW}{RT}$$

Equation_Apx E-3. Gas-Phase Mass Transfer Coefficient

$$k_g = \frac{6320 \cdot u^{0.78}}{MW^{1/3}}$$

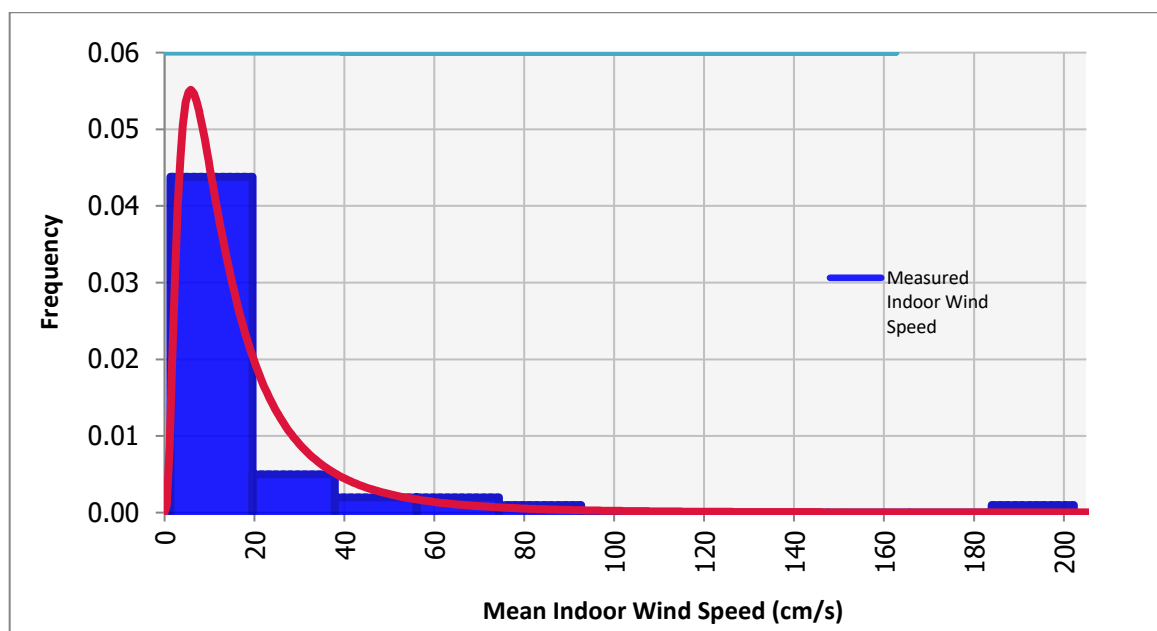
Where:

- k_g is the gas-phase mass transfer coefficient
- P_{vap} is the vapor pressure at the temperature of the liquid
- R is the gas constant
- T is temperature
- u is wind speed
- MW is molecular weight

Equation_Apx E-1 through Equation_Apx E-3 demonstrate that the evaporative flux J_{evap} is a function of wind speed (u) to the 0.78 power.

E.2 Experimental Wind Speed Measurements

Baldwin and Maynard ([1998](#)) measured indoor air speeds across 55 workplaces in the United Kingdom. These workplaces cover both industrial and commercial facilities. The authors suggest indoor wind speed data could be approximated by a lognormal distribution. Figure_Apx E-1 fits the wind speed measurements to a lognormal distribution. The fitted distribution has a mean of 17.6 cm/s and a standard deviation of 18.4 cm/s. The lower bound of the distribution is set to zero. The 50th percentile wind speed within this distribution is 12.2 cm/s. Approximately 85 percent of the distribution are below 30 cm/s (0.3 m/s), the wind speed noted by Frasch et al. ([2011](#)) during the 1-BP evaporative flux measurement.



Figure_Apx E-1. Distribution of Mean Indoor Wind Speed as Measured by Baldwin and Maynard (1998)

E.3 Adjusting χ and f_{abs} for Wind Speed

In the 1-BP *in vitro* dermal penetration study, Frasch et al. (2011) measured an evaporative flux (J_{evap}) of 470 mg/cm²-h. The experimentally measured steady-state absorption flux ($J_{max,ss}$) ranges from 625 to 960 µg/cm²-h (infinite-dose, neat 1-BP). The evaporative flux was measured at 23°C, whereas the absorption flux was measured near the typical skin surface temperature of 32°C.

From the relationship given in Equation_Apx E-1 through Equation_Apx E-3, the adjusted evaporative flux (J'_{evap}) can be calculated as:

Equation_Apx E-4. Adjusted Dermal Evaporative Flux

$$J'_{evap} = J_{evap} \left(\frac{u'}{u} \right)^{0.78} \left(\frac{P_{vap}'}{P_{vap}} \cdot \frac{T}{T'} \right)$$

1-BP has a vapor pressure of 110.8 mmHg at 20°C (293K). At the skin surface temperature of 32°C ($T' = 305K$), the adjusted vapor pressure can be calculated using the Clausius-Clapeyron equation:

Equation_Apx E-5. Adjusted Vapor Pressure

$$\ln \left(\frac{P_{vap}'}{P_{vap}} \right) = \frac{\Delta H_{vap}}{R} \left(\frac{1}{T} - \frac{1}{T'} \right)$$

$$\ln\left(\frac{P_{vap}'}{110.8 \text{ mmHg}}\right) = \frac{32,130 \text{ J/mol}}{8.314 \text{ J/mol-K}} \left(\frac{1}{20 + 273} - \frac{1}{T' + 273}\right)$$

$$\text{If } T' = 23^\circ\text{C (296K)}, P_{vap}' = 126.6 \text{ mmHg}$$

$$\text{If } T' = 32^\circ\text{C (305K)}, P_{vap}' = 186.2 \text{ mmHg}$$

At the 50th percentile wind speed measured by Baldwin and Maynard (1998) ($u' = 12.2 \text{ cm/s}$), the adjusted evaporative flux is:

$$J'_{evap} = 470 \frac{\text{mg}}{\text{cm}^2\text{-h}} \cdot \left(\frac{12.2 \text{ cm/s}}{30 \text{ cm/s}}\right)^{0.78} \left(\frac{186.2 \text{ mmHg}}{126.6 \text{ mmHg}} \cdot \frac{296\text{K}}{305\text{K}}\right) = 332 \frac{\text{mg}}{\text{cm}^2\text{-h}}$$

From Equation_Apx E-1 and the steady-state approximation for fraction absorbed (f_{abs}):

$$f_{abs}(\infty) = \frac{1}{\chi + 1}$$

$$c = \frac{J_{evap}}{J_{max,SS}} = \frac{332}{0.96} = 346$$

$$f_{abs} \sim \frac{1}{346 + 1} \sim 0.0029 \text{ (0.29\%)}$$

As such, the adjusted fraction absorbed is 0.29%, approximately an 80 percent increase from the measured 0.16% value.

Appendix F CONSUMER EXPOSURE ASSESSMENT

F.1 Consumer Exposure

Consumer exposure was evaluated utilizing a modeling approach because emissions and chemical specific personal monitoring data associated with consumer use of products containing 1-BP were not identified during data gathering and literature searches performed as part of EPA’s Systematic Review process. A detailed discussion of the approaches taken to evaluate consumer inhalation exposure is provided in Section 2.3.2.

F.2 Consumer Inhalation Exposure

Three models were used to evaluate consumer inhalation exposures, EPA’s Consumer Exposure Model (CEM), EPA’s Multi-Chamber Concentration and Exposure Model (MCCEM), and EPA’s Indoor Environment Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU) model. EPA varied three key parameters when modeling consumer inhalation exposure to capture a range of potential exposure scenarios. The key parameters varied were duration of use per event (minutes/use), amount of chemical in the product (weight fraction), and mass of product used per event (gram(s)/use). These key parameters were varied because CEM is sensitive to all three parameters and they are representative of expected consumer behavior patterns for product use (based on survey data). Modeling was conducted for all possible combinations of the three varied parameters. This results in a maximum of 27 different iterations for each consumer use as summarized in Table_Apx F-1.

Table_Apx F-1. Example Structure of CEM Cases Modeled for Each consumer Product/Article Use Scenario.

CEM Set	Scenario Characterization (Duration-Weight Fraction-Product Mass)	Duration of Product Use Per Event (min/use) [not scalable]	Weight Fraction of Chemical in Product (unitless) [scalable]	Mass of Product Used (g/use) [scalable]	
Set 1 (Low Intensity Use)	Case 1: Low-Low-Low	Low	Low	Low	
	Case 2: Low-Low-Mid			Mid	
	Case 3: Low-Low-High			High	
	Case 4: Low-Mid-Low		Mid	Mid	Low
	Case 5: Low-Mid-Mid				Mid
	Case 6: Low-Mid-High				High
	Case 7: Low-High-Low		High	High	Low
	Case 8: Low-High-Mid				Mid
	Case 9: Low-High-High				High
Set 2 (Moderate Intensity Use)	Case 10: Mid-Low-Low	Mid	Low	Low	
	Case 11: Mid-Low-Mid			Mid	
	Case 12: Mid-Low-High			High	
	Case 13: Mid-Mid-Low		Mid	Low	

	Case 14: Mid-Mid-Mid		High	Mid
	Case 15: Mid-Mid-High			High
	Case 16: Mid-High-Low			Low
	Case 17: Mid-High-Mid			Mid
	Case 18: Mid-High-High			High
Set 3 (High Intensity Use)	Case 19: High-Low-Low	High	Low	Low
	Case 20: High-Low-Mid			Mid
	Case 21: High-Low-High			High
	Case 22: High-Mid-Low		Mid	Low
	Case 23: High-Mid-Mid			Mid
	Case 24: High-Mid-High			High
	Case 25: High-High-Low		High	Low
	Case 26: High-High-Mid			Mid
	Case 27: High-High-High			High

F.3 Consumer Dermal Exposure

Two models were used to evaluate consumer dermal exposures, the CEM (Fraction Absorbed) model and the CEM (Permeability) model. A third dermal model from a paper published by Frasch ([Frasch and Bunge, 2015](#)) was considered but not selected for use in this evaluation. A brief comparison of these three dermal models through the calculation of acute dose rate (ADR) is provided below. This is followed by comparison of results from all three models for all eight conditions of use evaluated for dermal exposure for the adult age group. Finally, a brief discussion on a sensitivity analysis of the three models is provided along with explanations related to why the two CEM models were selected and utilized to evaluate dermal exposure for this risk evaluation.

F.3.1 Comparison of Three Dermal Model Methodologies to Calculate Acute Dose Rate (ADR)

CEM (Permeability) Model: The CEM (Permeability) model estimates acute dose rates based primarily on the permeability coefficient of the chemical of concern and duration of use. The CEM (Permeability) model assumes a constant supply of product on the skin throughout the exposure duration and does not consider evaporation from the skin. The CEM (Permeability) model estimates the acute dose rate (ADR) using the following equation:

Equation_Apx F-1. CEM Permeability Model, Acute Dose Rate

$$ADR = \frac{K_p \times D_{ac} \times Dil \times \rho \times \frac{SA}{BW} \times FQ_{ac} \times WF \times ED_{ac} \times CF_1}{AT_{ac} \times CF_2}$$

The key inputs driving this calculation are the permeability coefficient (K_p), duration of use, product density (ρ), and weight fraction (WF). The K_p is particularly important in this calculation because its values can vary widely for a single chemical depending on the literature or estimation

source. The CEM (Permeability) model the permeability coefficient is estimated as a function of the permeation coefficients of the lipid medium, protein fraction of the stratum corneum, and the water epidermal layer utilizing the following equation:

Equation_Apx F-2. CEM Permeability Model, Permeability Coefficient K_p

$$K_p = \frac{1}{\left(\frac{1}{K_{lip} + K_{pol}}\right) + \left(\frac{1}{K_{aq}}\right)}$$

CEM (Fraction Absorbed) Model: The CEM (Fraction Absorbed) model estimates dermal exposure for products that are applied on the skin in a thin film and partially absorbed. This partial absorption is modeled by an absorption fraction which accounts for the amount of substance that penetrates across the absorption barriers of an organism. The CEM (Fraction Absorbed) model requires an assumption that the entire mass of the chemical of concern within the thin film enters the skin surface (stratum corneum) to correctly apply the absorption fraction. Utilizing this assumption, the CEM (Fraction Absorbed) model estimates the (ADR) using the following equation:

Equation_Apx F-3. CEM Absorption Fraction Model, Acute Dose Rate

$$ADR = \frac{AR \times \frac{SA}{BW} \times FQ_{ac} \times FR_{abs} \times Dil \times WF \times ED_{ac} \times CF_1}{AT_{ac}}$$

All terms listed in the above equation are singular inputs except AR, the amount retained on skin, and FR_{abs} , the absorption fraction (or fraction absorbed). The amount retained on skin (AR) represents the amount of product remaining on the skin after use, and is in the units of grams of product per square centimeter of skin area. Equation_Apx F-4 shows the AR variable can be calculated as a product of the film thickness of the liquid on the skin’s surface and the density of the product, subtracting any removal that may occur through washing or other removal methods.

Equation_Apx F-4. CEM Absorption Fraction Model, Amount Retained on Skin

$$AR = FT \times \rho \times (1 - \text{FracRemove})$$

The absorption fraction (FR_{abs}) represents how much of the available material can be absorbed into the skin and can be estimated through an exponential function defined primarily by D, the duration of use, and χ , the ratio of the evaporation rate from the stratum corneum surface to the dermal absorption rate through the stratum corneum. The equation for FR_{abs} , Equation_Apx F-5, is a simplification of the equation used by Frasch ([Frasch and Bunge, 2015](#)).

Equation_Apx F-5. CEM Absorption Fraction Model, Fraction Absorbed

$$FR_{abs} = \frac{3 + \chi \left[1 - \exp\left(-a_{\frac{D_{cr}}{t_{lag} \times CF_1}}\right)\right]}{3(1 + \chi)}$$

The equation for χ , Equation_Apx F-6, relies on chemical properties like molecular weight and vapor pressure, making χ values chemical-specific.

Equation_Apx F-6. CEM Absorption Fraction Model, χ

$$\chi = \frac{h \times P_{vap} \times MW \times CF_1}{K_p \times S_W \times R \times T}$$

After simplifying the acute dose rate equation and substituting in for constants, the CEM Absorption Fraction acute dose rate becomes a function of the product density, film thickness, fraction absorbed, and weight fraction. Though the duration of use does impact the FR_{abs} term, its influence only extends to the limit of the FR_{abs} equation. As the duration of use and χ value approach infinity the FR_{abs} will plateau at 3.33E-01.

The relationship between duration and FR_{abs} will be explained in greater detail in the sensitivity analysis section and will highlight the relationship between CEM FR_{abs} values and Frasch F_{abs} values.

Frasch Model (Frasch and Bunge, 2015): The absorption fraction methodology presented by Frasch (Frasch and Bunge, 2015) provides a dose calculation for a fully transient exposure. A fully transient exposure is one in which dermal exposure occurs from an unlimited supply of chemical against the skin for a finite duration. The chemical is then fully removed from the skin surface at the end of the exposure with the assumption that no residue remains on the exposed section of skin, although a portion of chemical remains within the skin surface (stratum corneum). This fully transient exposure framework then considers a fraction of the chemical within the skin, not residue at the surface, at the end of the exposure period (or duration of product use), can still enter the systemic circulation. If the chemical has some volatility, a portion of the chemical within the skin will evaporate before it has a chance to be absorbed by the body. The Frasch equation for calculating the ADR is as follows:

Equation_Apx F-7. Frasch, Acute Dose Rate

$$ADR = \frac{m_T \times CF \times FQ \times ED}{BW \times AT}$$

Similar to the CEM (Fraction Absorbed) model, all terms listed in the above equation are singular inputs except m_T , the total mass absorbed, which represents the mass of the chemical that has been absorbed into the body at the end of the exposure time or duration of product use and the fraction absorbed following the exposure time. The total mass absorbed is therefore calculated by the following equation:

Equation_Apx F-8. Frasch. Total Mass Absorbed m_T

$$m_T = m_{abs}(t_{exp}) + F_{abs}m_0$$

The first term in the total mass calculation represents the mass absorbed at the end of the exposure time or duration of product use. This mass term, $m_{abs}(t_{exp})$, includes absorption throughout the use of the product. The second mass term, m_0 , in the total mass calculation represents the mass of the

product left at the end of the exposure duration. This ending mass is then multiplied by the absorption fraction, F_{abs} , to find the mass absorbed after the exposure duration or the duration of product use has ended (the Frasch methodology uses F_{abs} to denote the fraction absorbed, as opposed to FR_{abs} used in the CEM (Fraction Absorbed) model). Each of the mass terms is given per unit area within the stratum corneum and considers the permeability coefficient, exposure duration, lag time, and the differential solution of the concentration distribution. A more in-depth explanation of each mass term will be provided in the sensitivity analysis section.

Equation_Apx F-9. Frasch, Mass Absorbed at End of Exposure Time $m_{abs}(t_{exp})$

$$m_{abs}(t_{exp}) = k_p C_V t_{lag} \left[\frac{t_{exp}}{t_{lag}} - 1 - \frac{12}{\pi^2} \sum_{n=1}^{\infty} \frac{(-1)^n}{n^2} \exp\left(-\frac{n^2 \pi^2 t_{exp}}{6 t_{lag}}\right) \right]$$

Equation_Apx F-10. Frasch, Mass at the End of Exposure Time m_0

$$m_0 = k_p C_V t_{lag} \left[1 - \frac{8}{\pi^2} \sum_{n=0}^{\infty} \frac{1}{(2n+1)^2} \exp\left(\frac{-(2n+1)^2 \pi^2 t_{exp}}{6 t_{lag}}\right) \right]$$

The fraction absorbed, F_{abs} , is calculated based on the concentration distributions as well, using the following equation:

Equation_Apx F-11. Frasch, Fraction Absorbed F_{abs}

$$F_{abs} = \frac{m_{abs}(\infty)}{m_0} \frac{3 + \chi \left[\frac{1 + \frac{12}{\pi^2} \sum_{n=1}^{\infty} \frac{(-1)^n}{n^2} \exp\left(\frac{-n^2 \pi^2 t_{exp}}{6 t_{lag}}\right)}{1 - \frac{8}{\pi^2} \sum_{n=0}^{\infty} \frac{1}{(2n+1)^2} \exp\left(\frac{-(2n+1)^2 \pi^2 t_{exp}}{6 t_{lag}}\right)} \right]}{3(1 + \chi)}$$

This fraction absorbed equation can be simplified into the one used in the CEM (Fraction Absorbed) model, described in the previous section.

F.3.2 Comparison of Estimated ADRs Across Three Dermal Models

The three dermal models described in Section F.3.1 were each run for all eight conditions of use for which consumer dermal exposure was evaluated. The purpose was to allow a comparison between the three results while recognizing each model is unique in its approach to estimating dermal exposure and may not be directly comparable. Keeping these limitations in mind, Table_Apx F-2 shows the results from all three dermal models for each condition of use evaluated for dermal exposure.

Table_Apx F-2. Comparison of Adult Acute Dermal Exposure Estimates from Three Dermal Models

Assessed Condition of Use	Scenario Description	Adult Acute Dermal Exposure (by method)
---------------------------	----------------------	---

		Average Daily Dose/Rate (mg/kg/day)		
		Permeability	Fraction Absorbed	Frasch
Aerosol spray degreaser/cleaner-general	High intensity use	3.54E+00	1.11E-01	2.98E-01
	Moderate intensity use	2.35E-01	5.90E-02	3.73E-02
	Low intensity use	1.69E-02	1.27E-02	1.24E-02
Aerosol spray degreaser/cleaner-electronics	High intensity use	3.68E-01	4.61E-02	2.98E-02
	Moderate intensity use	1.81E-02	3.42E-02	1.99E-03
	Low intensity use	3.13E-03	2.35E-02	5.00E-04
Spot cleaner and stain remover	High intensity use	8.71E-01	1.09E-01	7.45E-02
	Moderate intensity use	9.13E-02	6.88E-02	1.24E-02
	Low intensity use	4.34E-03	3.27E-02	1.25E-03
Coin and scissors cleaner	High intensity use	7.56E-02	9.49E-02	5.97E-03
	Moderate intensity use	3.78E-02	7.12E-02	3.99E-03
	Low intensity use	1.26E-02	4.75E-02	2.00E-03
Spray cleaner-general	High intensity use	3.55E+00	1.11E-01	2.98E-01
	Moderate intensity use	4.44E-01	1.11E-01	3.73E-02
	Low intensity use	5.92E-02	1.11E-01	4.98E-03
Adhesive accelerant	High intensity use	7.65E-01	4.80E-02	5.96E-02
	Moderate intensity use	5.42E-02	4.80E-02	4.23E-03
	Low intensity use	6.37E-03	4.80E-02	4.99E-04
Automobile AC flush	High intensity use	3.96E+00	4.97E-01	3.79E-01
	Moderate intensity use	1.98E+00	4.97E-01	1.89E-01
	Low intensity use	6.60E-01	4.97E-01	6.32E-02
Mold cleaning and release products	High intensity use	2.23E-01	4.27E-02	2.98E-02
	Moderate intensity use	1.49E-02	2.80E-02	1.99E-03
	Low intensity use	1.98E-03	1.49E-02	4.99E-04

Generally, the estimated exposure concentrations for 1-BP are highest utilizing the CEM (Permeability) model for high intensity use scenarios under all but one condition of use (coin and scissors cleaner). Additionally, estimates from the CEM (Permeability) model for those high intensity use scenarios is approximately one order of magnitude higher than CEM (Fraction absorbed) model estimates and Frascch model estimates.

Estimated exposure concentrations for 1-BP at moderate intensity uses are highest utilizing CEM (Permeability) model for five of the eight conditions of use evaluated. The remaining three conditions of use have higher estimated exposure concentrations utilizing the CEM (Fraction Absorbed) model.

Estimated exposure concentrations for 1-BP at low intensity uses are higher utilizing the CEM (Fraction Absorbed) model for all but one condition of use (aerosol spray degreaser/cleaner-general). The majority of the estimates tend to be within an order of magnitude compared to the CEM (Permeability) method.

The Frasch model estimates are consistently lower than the CEM (Permeability) model estimates. They are also lower than the CEM (Fraction Absorbed) model estimates in all but three high intensity use scenarios within the Aerosol spray degreaser/cleaner-general, spray cleaner-general, and adhesive accelerant conditions of use. For these three specific scenarios the Frasch model is higher than the CEM (Fraction Absorbed) model but still lower than the CEM (Permeability) model.

It is possible that the Frasch model tends to be lower due to its consideration of lag time in both mass components as well as the use of a C_v term, identified in equations Apx F-9 and Apx F-10, which is based on solubility rather than density. Since density can be orders of magnitude higher than solubility, adjusting the C_v for density could result in considerable increases within the mass term utilized in the ADR equation. This may drive the Frasch model estimates closer to the CEM (Permeability) model estimates but would require a change to the published Frasch model.

F.3.3 Sensitivity Analysis of Three Dermal Models

Selection of the models used to evaluate dermal exposure considered the sensitivity of the three models as well as the representativeness of the model estimates to the expected consumer exposure scenarios for each condition of use. The sensitivity and impacts of several parameters within the three dermal models considered are discussed below followed by a broad consolidation of considerations which led to EPA's selection of the CEM (Permeability) model and the CEM (Fraction Absorbed) model to estimate dermal exposures for this evaluation.

F.3.3.1 Duration of Use

The duration of use for this evaluation was assumed equal to the exposure time for all three models. The basic relationship between the duration of use or exposure time to the acute dose rate is quite distinct for each of the three models. The CEM (Permeability) model and the Frasch model maintain a strong positive correlation between duration of use and ADR, with ADR increasing by the same factor of the duration of use. The exact slopes of these lines are influenced differently by other factors, such as weight fraction, which will be discussed later. The CEM (Fraction Absorbed) model maintains a logarithmic relationship between duration of use and ADR, hitting a horizontal asymptote limit of 3.33E-01 after a certain duration (that duration varies by chemical). This limit will be discussed in the next section as it relates to the fraction absorbed term.

F.3.3.2 Fraction Absorbed

The fraction absorbed is essentially the factor that determines what mass of chemical is absorbed into the body. It is intended to be the mass absorbed from the stratum corneum as presented by Frasch ([Frasch and Bunge, 2015](#)), but the CEM (Fraction Absorbed) model and Frasch model calculate and utilize this factor differently. In terms of the equations within the two models utilizing fraction absorbed, the CEM (Fraction Absorbed) model identifies this factor as FR_{abs} while Frasch identifies this factor as F_{abs} .

For both the CEM (Fraction Absorbed) model and the Frasch model, the fraction absorbed factor relies on χ (the ratio of evaporation rate to steady-state dermal permeation rate), the exposure time, and certain physical-chemical properties (*e.g.*, molecular weight, vapor pressure). As the χ value

increases, at least $\frac{2}{3}$ of the chemical in the skin will evaporate at the end of the exposure. Therefore, for highly volatile chemicals with large χ values (e.g., 1-BP) the fraction absorbed factor will quickly reach a maximum ($\frac{1}{3}$) with increasing duration (represented by taking the limit at infinity of the absorption fraction equations). After a certain duration, the fraction that will evaporate, and the fraction that will be absorbed remains constant.

The lag time (calculated based on the chemical molecular weight) used in the two fraction absorbed equations influences how quickly the fraction absorbed limit of $3.33\text{E-}01$ is reached. Chemicals with shorter lag times will reach the limit of FR_{abs} at shorter durations of use. For 1-BP, the calculated lag time is about 0.77 with an estimated χ value of about 4218. This results in the FR_{abs} for 1-BP reaching the limit of $3.33\text{E-}01$ at an exposure time of about 90 minutes (based on an estimated K_p of 0.0196). Linking this to the calculation of the ADR in the CEM (Fraction Absorbed) model, while duration of use influences the fraction absorbed term, and the fraction absorbed term influences the ADR, the influence of the fraction absorbed on the ADR calculation peaks as the fraction absorbed approaches the $3.33\text{E-}01$ limit. Therefore, for 1-BP, while the fraction absorbed term increases quickly as exposure time increases, after about 90 minutes, the exposure time has little influence on the fraction absorbed or the ADR.

Unlike the CEM (Fraction Absorbed) model, the Frasch model is not limited by the fraction absorbed term in the same way. This is the case because the Frasch method considers both the mass absorbed into the skin after the exposure time ends and the absorption during the use of the product or chemical.

However, the weight fraction and amount retained on skin terms used in CEM ultimately control the ADR value and will be discussed in the next sections.

F.3.3.3 Mass Terms

Ultimately, the ADRs for the three models are driven by how much product is available and absorbed into the skin. However, all three models calculate those mass terms quite differently. To help distinguish the three models apart, the mass terms were investigated primarily as they relate to the exposure time (assumed to be the duration of product use obtained from survey data in this evaluation).

The CEM (Permeability) model calculates the mass absorbed term within the ADR equation (equation Apx_F-1) based on the permeability coefficient, dilution factor, duration of exposure, density, surface area of skin, and weight fraction. The dilution factor is assumed to be 1 in all modeling scenarios (no dilution). The product of these terms gives the mass of the chemical of concern absorbed by the body from exposure to the modeled product(s). The CEM (Permeability) model assumes an unlimited supply of the product is present against the skin for the entire duration period and does not consider losses due to evaporation or rinsing.

The CEM (Fraction Absorbed) model calculates the mass available for absorption within the ADR equation (equation Apx_F-3) utilizing the following terms: amount retained on skin (the mathematical product of film thickness and product density), the surface area of skin, and weight fraction. The product of these terms multiplied by the absorption fraction gives the total absorbed mass. This assumes that the product or chemical is applied once to the skin's surface in a thin film

and then absorbed based on the absorption fraction. What this model doesn't consider is the mass of the product or chemical that may enter the skin continuously during the use of the product or chemical.

The Frasch ([Frasch and Bunge, 2015](#)) model calculates the total mass of the chemical of concern taken into the body, for the ADR equation (Equation_Apx F-7), in two parts: (1) mass taken in during the duration of exposure and (2) mass absorbed into the body from the product that remains within the skin (in the stratum corneum) after the duration of exposure. These mass values are found through the solutions to differential functions based on permeation and diffusion characteristics. The mass taken in during the period of use is calculated based on the assumptions that the skin does not initially contain any of the chemical before the specified exposure duration, the skin is exposed to a constant concentration for that specified exposure duration, and that the chemical does not bind to the skin while the skin acts as a perfect sink at the bottom of the tissue. This mass term creates the potential for overestimation of exposure based on the assumption that the exposure is constant throughout the use of the product. The other mass term considers the absorption of the chemical after the exposure duration ends. This absorption occurs from any chemical remaining within the skin (in the stratum corneum) that does not evaporate.

Because neither the CEM (Permeability) model nor the CEM (Fraction Absorbed) model considers the mass of chemical in the ADR equations, both models have the potential to overestimate the dermal absorption by modeling a mass which is larger than the mass used in a scenario. Therefore, when utilizing either of the CEM models for dermal exposure estimations, a mass check is necessary outside of the CEM model to make sure the mass absorbed does not exceed the mass used in a given scenario. Unlike the two CEM models, the Frasch model has built in mass checks such that the mass calculated by the model is not larger than the mass being applied in a scenario.

F.3.3.4 Weight Fraction

Both the CEM (Permeability) model and the CEM (Fraction Absorbed) model calculate mass values considering a weight fraction multiplier. This gives the weight fraction a potential to have considerable influence over the final ADR. The Frasch model does not consider a weight fraction in its calculations, although it is referenced in the mass checks mentioned above. As a result, weight fraction does not change the calculated ADR in the Frasch model, although it can impact the scale at which the Frasch estimates compare to the CEM ADR values.

The weight fraction term in both the CEM (Permeability) model and the CEM (Fraction Absorbed) model influences the mass over time component of the models. A higher weight fraction results in a higher mass term within the models. In contrast, the mass components of the Frasch model are not affected by weight fraction and therefore do not increase with increased weight fractions.

The influence of weight fraction on the relationship between duration of use and acute dose rate (ADR) is similar to that between duration of use and the modeled mass terms for the two CEM models. As noted in Section F.3.3.1, the weight fraction influences the slope of the curves associated with the duration of use and ADR. Although not the only factor, since both CEM models are affected by weight fraction and the Frasch model is not, the relative ADR estimates from the three models can vary considerably under scenarios with different weight fractions. At

lower weight fractions, the Frasch estimates are more likely to be greater than estimates from either of the CEM model estimates. However, at higher weight fractions, the CEM (Permeability) model estimates will begin to be greatest, in particular over increasingly high durations of use.

F.3.3.5 Permeability Coefficients

The permeability coefficient (K_p) is a term used in all three of the dermal models considered for this evaluation. This value represents the rate of transfer of a compound across a membrane (cm/hr). The K_p value is used directly in the ADR calculation within the CEM (Permeability) model and therefore has a direct influence on the ADR estimates. The K_p value indirectly influences the ADR estimates within the CEM (Fraction Absorbed) model through the fraction absorbed term (via χ). The K_p value also indirectly influences the ADR calculation within the Frasch model through the fraction absorbed term (via χ), but also in its use within both mass term calculations (therefore influencing total mass absorbed).

Experimental K_p values may be found in the literature or can be estimated utilizing various methods. Experimental K_p values can be directly entered into both CEM dermal models or can be estimated within CEM as described in the CEM Users Guide ([U.S. EPA, 2019a](#)) and associated User Guide Appendices ([U.S. EPA, 2019b](#)). The Frasch model also provides a method to estimate K_p in ([Frasch and Bunge, 2015](#)).

The sensitivity of the three models to changing K_p values on the ADR estimates shows the CEM (Permeability) model has a very strong response to changing K_p values in relation to the slope of the curve. Larger K_p values increase the slope of the curve showing the ADR estimates resulting in a much more rapid increase in ADR estimates over a shorter duration of use. A similar influence of changing K_p values can be seen with the Frasch model, although to a lesser degree than seen with the CEM (Permeability) model. The CEM (Fraction Absorbed) model is only very slightly influenced by changing K_p values.

F.3.3.6 Other Parameters

While the parameters discussed in previous sections have the potential to significantly impact ADR estimates from the three models, other parameters can still influence the model outputs or provide insight into differences between model outputs.

Product Density: Product density is a factor in both the CEM (Permeability) model and the CEM (Fraction Absorbed) models but not within the Frasch model. Product density is directly utilized within the CEM (Permeability) model ADR calculation and indirectly utilized within the CEM (Fraction Absorbed) model ADR calculation (through amount retained on skin). While not directly used within the Frasch model, it is utilized in the mass checks described previously.

Both of the CEM model ADR estimates change proportionately to changes in the product density, while the Frasch ADR does not respond. While the general behavior and curve shapes for the ADR do not appear to change much for either of the CEM models in response to product density, the ADR estimates decrease with lower densities. Though the influence of product density does not explain or describe much difference between the CEM (Permeability) model and the CEM

(Fraction Absorbed) model ADR estimates the absence of product density from the Frasch model is a consideration when comparing the CEM model outputs to Frasch model outputs.

Film Thickness on Skin: Film thickness is only an input to the CEM (Fraction Absorbed) model ADR calculations (as an input to the amount retained on skin term). Similar to the product density influence, the ADR estimates from the CEM (Fraction Absorbed) model change proportionately to changes in the film thickness. A larger film thickness results in a larger ADR estimate with the CEM (Fraction Absorbed) model.

F.3.3.7 Selection of Dermal Models

Three dermal models were evaluated, outputs compared, and a sensitivity analysis conducted on all three models to help identify fit-for-purpose models which would be representative of expected consumer exposure scenarios for eight conditions of use involving 1-BP containing products. Two general exposure scenarios were applied to select conditions of use.

- 1) Evaporation is inhibited/prohibited or full immersion of a body part occurs during product use.
- 2) Evaporation is uninhibited and full immersion of a body part does not occur during product use.

When applying the general constructs outlined above, both the CEM (Permeability) model and Frasch model have a component which is applicable to conditions of use where evaporation is inhibited/prohibited or full immersion of a body part occurs during use. However, only the CEM (Permeability) model directly considers product density (rather than solubility) within components of the ADR equation. Since most of the products utilized for these conditions of use are solvent based (rather than aqueous), utilization of the CEM (Permeability) model along with a neat permeability coefficient (K_p) is expected to provide a more representative ADR estimate for this evaluation.

When applying the general constructs outlined above, both the CEM (Fraction Absorbed) model and the Frasch model have a component which is applicable to conditions of use where evaporation is uninhibited and full immersion of a body part does not occur during use. Similar to the discussion above, the products utilized for these conditions of use are solvent based (rather than aqueous) based. Since the CEM (Fraction Absorbed) model considers product density (indirectly through the amount retained on skin), utilization of the CEM (Fraction Absorbed) model is expected to provide a more representative ADR estimate for this evaluation. Further, while the Frasch model has a fraction absorbed component, it also has the transient exposure with an unlimited supply of product against the skin during the exposure period which may not be directly applicable to the conditions of use where evaporation is assumed to be uninhibited for the entire duration of product use.

Appendix G ECOSAR Modeling Outputs

The Ecological Structure Activity Relationships (ECOSAR) Class Program (v2.0) ([EPA, 2017](https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model)) is a computerized predictive system that estimates aquatic toxicity. The program estimates a chemical's acute (short-term) toxicity and chronic (long-term or delayed) toxicity to aquatic organisms, such as fish, aquatic invertebrates, and aquatic plants, by using computerized Structure Activity Relationships (SARs). More information on the program can be found at: <https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model>

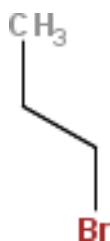
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Organic Module Report

Results of Organic Module Evaluation

CAS	Name	SMILES
106945	Propane, 1-bromo-	BrCCC

Structure



Details	
Mol Wt	122.99
Selected LogKow	2.16
Selected Water Solubility (mg/L)	2450
Selected Melting Point (°C)	-110
Estimated LogKow	2.16
Estimated Water Solubility (mg/L)	2402.61
Measured LogKow	2.1
Measured Water Solubility (mg/L)	2450

Measured Melting Point (°C)	-110
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Neutral Organics

Organism	Duration	End Point	Concentration (mg/L)	Max Log Kow	Flags
Fish	96h	LC50	72.85	5	
Daphnid	48h	LC50	41.97	5	
Green Algae	96h	EC50	33.21	6.4	
Fish		ChV	7.24	8	
Daphnid		ChV	4.26	8	
Green Algae		ChV	8.98	8	
Fish (SW)	96h	LC50	91.79	5	
Mysid	96h	LC50	61.29	5	

Organism	Duration	End Point	Concentration (mg/L)	Max Log Kow	Flags
Fish (SW)		ChV	10.97	8	
Mysid (SW)		ChV	5.05	8	
Earthworm	14d	LC50	205.91	6	

Appendix H ESTIMATES OF SURFACE WATER CONCENTRATION

SCENARIO 1. REPORTED RELEASES TO TRI

Estimating Surface Water Concentrations

Surface water concentrations were estimated for multiple scenarios using E-FAST which can be used to estimate site-specific surface water concentrations based on estimated loadings of 1-bromopropane into receiving water bodies. For TRI, the reported releases are based on monitoring, emission factors, mass balance and/or other engineering calculations. These reported annual loading amounts (lbs/year) were first converted to release inputs required by E-FAST (kg/day) by converting from lbs to kgs and dividing by the number of release days for a given scenario.

E-FAST incorporates stream dilution at the point of release using stream flow distribution data contained within the model. The stream flow data have not been updated recently and may differ from current values obtained from NHD or USGS gages. 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 (*i.e.*, Industrial POTW).

E-FAST 2014 can incorporate wastewater treatment removal efficiencies. Wastewater treatment removal is assumed to be 0% for this exercise, as reported direct loadings/releases are assumed to account for any pre-release treatment. Because the days of release and/or operation are not reported in these sources, E-FAST is run assuming hypothetical release-day scenarios. Refer to the E-FAST 2014 Documentation Manual for equations used in the model to estimate surface water concentrations ([U.S. EPA, 2014b](#)).

The modeled surface water concentrations presented below in Table_Apx H-1 are associated with a low flow – 7Q10, which is an annual minimum seven-day average stream flow over a ten-year recurrence interval. The 10th percentile 7Q10 stream flow is used to derive the presented surface water concentrations. 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.

Modeled Surface Water Concentrations

It is assumed that these modeled surface water concentrations are higher than those that would be present from non-point sources based on the conservative nature of the estimation approaches including the following: surface water concentrations would be expected to decrease downstream and this modeling analysis does not account for downstream transport and fate processes; non-zero wastewater removal rates would be applied for any indirect releases that pass through a treatment facility before release; and assuming a low-end number of release days (*i.e.*, 1 day per year) assumes the total annual loading estimate occurs over 1 day.

For 1-BP, there is one facility reporting non-zero water releases from the 2016 TRI reporting period, the Flint Hills Resources facility. This facility, located in Corpus Christi, TX, has reported 1 lb of 1-BP released to the Neuces River with 100% from stormwater on an annual basis. They also reported 4 lbs of 1-BP released to an unnamed water body with 83% from stormwater on an annual basis. These are direct releases to water and thus are presumed to be untreated at a POTW. A quick calculation of site-specific surface water concentration was performed using E-FAST assuming that the total release occurs over 1 day, 20 days or 100 days. Two receiving waters were used:

- a. Neuces River – the NPDES permit for Corpus Christ City POTW TX0047082 was used as a surrogate for this direct release. 0% removal was assumed since this is listed as a direct release.
- b. Unnamed Waterbody – the NPDES permit for the reporting facility was available in EFAST with the receiving water body listed as the Corpus Christi Bay. Acute dilution factors were used to estimate the surface water concentration, again with 0% removal.

The resulting estimated surface water concentrations presented below in Table_Apx H-1 are based on the reported releases and locations and are well below the acute and chronic concentrations of concern even if the annual release amount occurs over 1 day. The maximum estimated surface water concentration is 78 µg/L for this scenario. The acute concentrations of concern are 13,460 µg/L (96-hour fish LC50) and 3640 µg/L (algae EC50) and the chronic concentrations of concern are 673 µg/L (fish chronic value) and 470 µg/L (daphnia ChV).

Table_Apx H-1. Estimated Surface Concentrations from Water Releases Reported to TRI

SCENARIO 1: REPORTED RELEASES TO TRI						
Acute COC = 13460 µg/L (96-hour fish LC ₅₀) and 3640 µg/L (algae EC ₅₀)						
Chronic COC = 673 µg/L (fish chronic value) and 470 µg/L (daphnia ChV)						
From TRI reporting: 1 reporting facility: Flint Hills Resources Corpus Christi LLC – West Plant						
1 lb to Neuces River (100% from stormwater);						
4 lbs to ‘unnamed water body’ (83% from stormwater)						
Wastewater Treatment Removal= 0%; direct release						
(Note: NPDES for Corpus Christi City POTW used as surrogate for Neuces River. Flint Hills Resources facility modeled directly)						
	Neuces River (Corpus Christi City - TX0047082)			Flint Hills Resources - Corpus Christi Bay, (TX0006289)		
	7Q10 SWC µg/L			SWC* µg/L		
Annual Release Amount lb (kg)	1 day/yr	20 days/yr	100 days/yr	1 day/yr	20 days/yr	100 days/yr
1 (0.45)	7.86	0.39	0.08	19.4	0.97	0.19
4 (1.81)	31.60	1.58	0.31	77.90	3.90	0.77
	*Acute dilution factor for bay					

Appendix I TOXICOKINETICS

The studies summarized in this section were identified for consideration in the human health hazard assessment, as described in Section 3.2.3.

Empirical evidence from rodent toxicity studies and from occupational exposure studies indicate that 1-BP is absorbed by both inhalation and dermal routes. Additional evidence of the systemic uptake of 1-BP via the oral route has been reported ([Lee et al., 2007](#)). Absorption is rapid by all routes, and a significant portion of the absorbed dose (39% to 48% in mice and 40% to 70% in rats) is eliminated in exhaled breath as unspecified volatile organic compounds ([Garner et al., 2006](#); [Jones and Walsh, 1979](#)). Garner and Yu ([2014](#)) provided supplemental evidence on the toxicokinetics of BP in rodents. Rodents exposed to 1-BP via intravenous injection or inhalation exhibited rapid systemic clearance and elimination that decreased as the dose increased. Previous studies showed that the remaining absorbed dose is eliminated, unchanged, in urine (humans) or as metabolites in the urine and exhaled breath of all species studied ([Garner et al., 2006](#); [Kawai et al., 2001](#)). Available toxicokinetic data indicate that glutathione (GSH) conjugation and oxidation via cytochrome P450 (CYP450) significantly contribute to the metabolism of 1-BP ([Garner and Yu, 2014](#); [Garner et al., 2006](#)).

I.1 Absorption

The detection of carbon-containing metabolites and elevated bromide ion concentrations in urine samples of workers exposed to 1-BP by inhalation and dermal contact provides qualitative evidence that 1-BP is absorbed by the respiratory tract and the skin in humans ([Hanley et al., 2010, 2009](#); [Valentine et al., 2007](#); [Hanley et al., 2006b](#)). In addition, reports of neurological and other effects in occupationally exposed subjects provide indirect evidence of absorption of 1-BP ([Samukawa et al., 2012](#); [CDC, 2008](#); [Majersik et al., 2007](#); [Raymond and Ford, 2007](#); [NIOSH, 2003a](#); [Ichihara et al., 2002](#); [Sclar, 1999](#)).

Dermal absorption characteristics estimated in human epidermal membranes mounted on static diffusion cells included steady-state fluxes averaging 625–960 $\mu\text{g cm}^{-2}\text{ hour}^{-1}$ with pure 1-BP and 441–722 $\mu\text{g cm}^{-2}\text{ hour}^{-1}$ with a commercial dry cleaning solvent, an average dermal penetration of about 2% from an applied dose of 13.5 mg/cm^2 under non-occluded conditions, and a dermal permeability coefficient for 1-BP in water of 0.257 cm/hour ([Frasch et al., 2011](#)).

Animal studies provide qualitative evidence of absorption by the gastrointestinal and respiratory tracts ([Garner et al., 2006](#); [Jones and Walsh, 1979](#)). ^{13}C -labeled metabolites were detected in urine collected from rats and mice exposed by inhalation to 800 ppm [1,2,3- ^{13}C]-1-BP for 6 hours ([Garner et al., 2006](#)). A number of mercapturic acid derivative metabolites were detected in pooled urine samples collected from rats given oral doses of 200 mg 1-BP/kg/day in arachis oil for five days ([Jones and Walsh, 1979](#)).

No other human or animal studies were located that determined the rate or extent of 1-BP absorption following inhalation, oral, or dermal exposure.

I.2 Distribution

Metabolic disposition studies in rats and mice given single intravenous injections of [1,2,3-¹³C]-1-BP indicate that 1-BP is not expected to accumulate in tissues ([Garner et al., 2006](#)). Following intravenous injection of [1-¹⁴C]-1-BP at nominal doses of 5, 20, or 100 mg/kg, radioactivity remaining in the carcass 48 hours after dose administration accounted for about 6, 6, and 2% of the administered dose in rats, and 4, 2, and 4% in mice ([Garner et al., 2006](#)). In these studies, most of the administered radioactivity was exhaled (as the parent material or CO₂) or excreted as metabolites in urine.

I.3 Metabolism

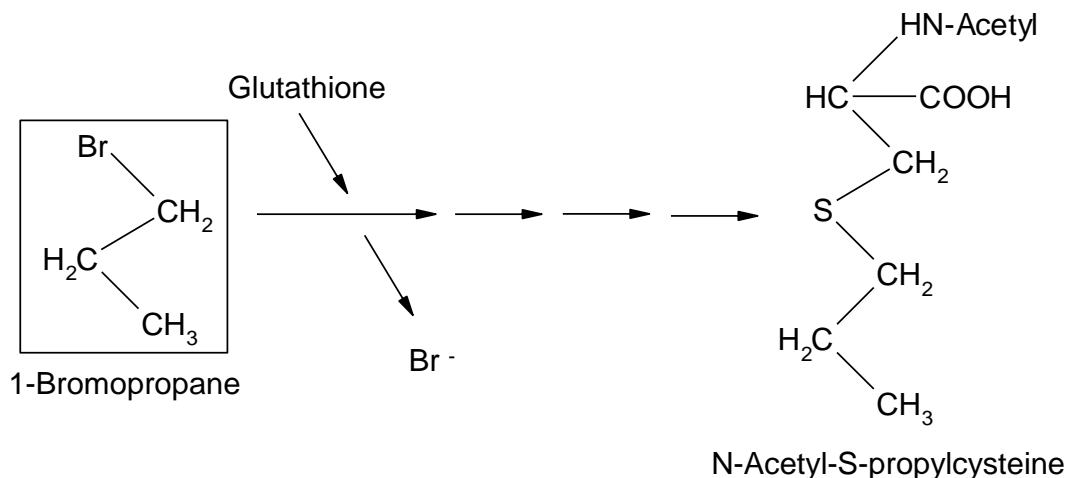
The metabolism of 1-BP in mammals involves: (1) conjugation, principally with glutathione, leading to the release of bromide ions and formation of mercapturic acid derivatives and (2) cytochrome P-450 mediated oxidation leading to formation of metabolites with hydroxyl, carbonyl, and sulfoxide groups, as well as CO₂. These concepts are based on studies of urinary metabolites in workers exposed to 1-BP ([Hanley et al., 2010, 2009](#); [Valentine et al., 2007](#); [Hanley et al., 2006b](#)), *in vivo* metabolic disposition studies in rats and mice ([Garner et al., 2007](#); [Garner et al., 2006](#); [Ishidao et al., 2002](#); [Jones and Walsh, 1979](#); [Barnsley et al., 1966](#)), and *in vitro* metabolism studies with rat liver preparations ([Kaneko et al., 1997](#); [Tachizawa et al., 1982](#); [Jones and Walsh, 1979](#)).

N-Acetyl-S-propylcysteine has been identified in urine samples from workers in a 1-BP manufacturing plant ([Valentine et al., 2007](#)), in foam fabricating plants using spray adhesives containing 1-BP ([Hanley et al., 2010, 2009](#); [Hanley et al., 2006b](#)), and in degreasing operations in plants using 1-BP as a cleaning solvent in the manufacture of aerospace components, hydraulic equipment, optical glass, and printed electronic circuit assemblies ([Hanley et al., 2009](#)). Other urinary metabolites identified in 1-BP workers are the bromide ion ([Hanley et al., 2010](#)) and three oxygenated metabolites present at lower urinary concentrations than N-acetyl-S-propylcysteine: N-acetyl-S-propylcysteine-S-oxide (also known as N-acetyl-3-(propylsulfinyl) alanine), N-acetyl-S-(2-carboxyethyl) cysteine, and N-acetyl-S-(3-hydroxy-propyl) cysteine ([Cheever et al., 2009](#); [Hanley et al., 2009](#)). The correlations between time weighted average workplace air concentrations of 1-BP and urinary levels of bromide and N-acetyl-S-propylcysteine ([Hanley et al., 2010, 2009](#); [Valentine et al., 2007](#); [Hanley et al., 2006b](#)) support the hypothesis that conjugation with glutathione is an important pathway in humans (see Figure 3-3). The detection of oxygenated metabolites in urine samples indicates that oxidation pathways also exist in humans (see Figure 3-3 for structures of identified oxygenated metabolites).

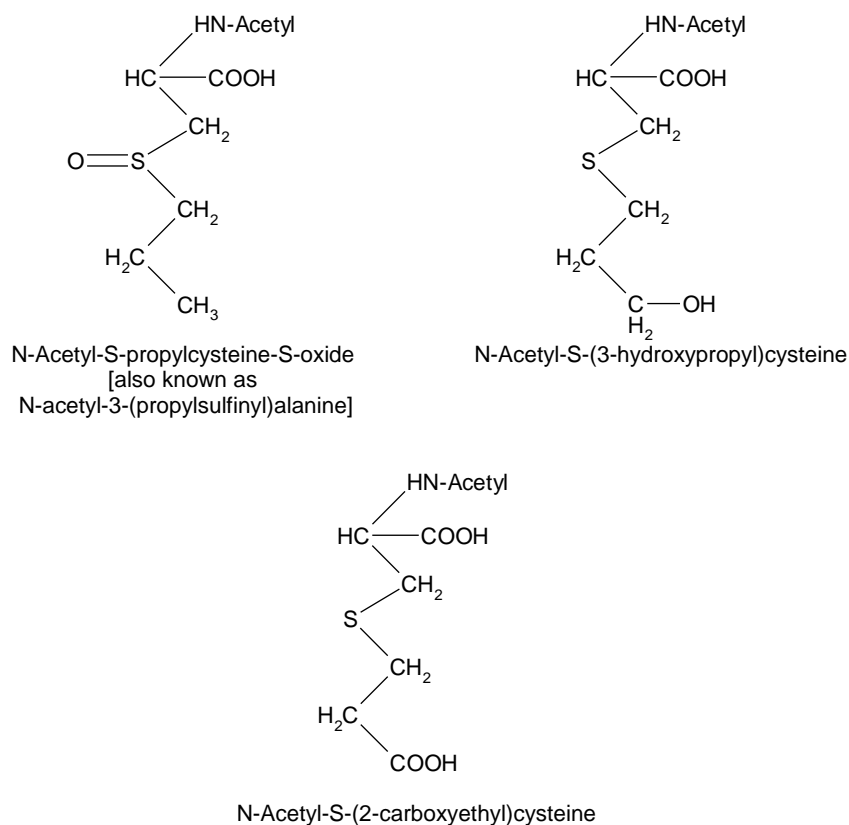
Results from metabolic disposition studies in rats and mice illustrate that the metabolism of 1-BP in mammals is complex, involving initial competing conjugation or oxidation steps, followed by subsequent conjugation, oxidation, or rearrangement steps. Figure 3-3 presents proposed metabolic pathways based on results from studies of F-344 rats and B6C3F1 mice exposed to [1-¹⁴C]-1-BP by intravenous injection or [1,2,3-¹³C]-1-BP by inhalation or intravenous injection ([Garner et al., 2006](#)).

The metabolic scheme shows an oxidation path to CO₂ formation which involves cytochrome P450 (CYP) oxidation steps to 1-bromo-2-propanol and bromoacetone. This path is proposed based on several findings:

1. Following intravenous injection of ¹⁴C-1-BP at nominal doses of 5, 20, or 100 mg/kg, radioactivity in CO₂ exhaled within 48 hours accounted for approximately 28, 31, and 10% of the administered dose in rats, and 22, 26, and 19% in mice ([Garner et al., 2006](#)). (These data also indicate that oxidative metabolism of 1-BP in rats is more dependent on dose than oxidative metabolism in mice; the decrease in percentage dose exhaled as CO₂ at the highest dose is greater in rats than mice.)
2. Pretreatment of rats with 1-aminobenzotriazole (ABT) before administration of a single intravenous dose of ~20 mg/kg ¹⁴C-1-BP or inhalation exposure to 800 ppm ¹³C-1-BP for 6 hours caused decreased exhalation of radioactivity as CO₂ and decreased formation of oxidative urinary metabolites ([Garner et al., 2006](#)). ABT is an inhibitor of a number of CYP enzymes ([Emoto et al., 2003](#)).
3. Urinary metabolites derived from 1-bromo-2-propanol accounted for over half of all carbon-containing urinary metabolites identified in rats and mice exposed by inhalation or intravenous injection of ¹³C-1-BP, and no 1-bromo-2-propanol-derived metabolites were found in urine of ABT-pretreated rats exposed to ¹³C-1-BP ([Garner et al., 2006](#)). 1-Bromo-2-propanol and bromoacetone themselves were not detected in urine of 1-BP-exposed rodents.



Figure_Apx I-1. Formation of N-Acetyl-S-Propylcysteine from 1-Bromopropane Via Conjugation with Reduced Glutathione (GSH)



Figure_Apx I-2. Mercapturic Acid Metabolites with a Sulfoxide Group or a Hydroxyl or Carbonyl Group on the Propyl Residue Identified in Urine Samples of 1-Bromopropane-Exposed Workers

Sources: ([Cheever et al., 2009](#); [Hanley et al., 2009](#))

Results from metabolic disposition studies indicate that 1-BP is eliminated from the body by exhalation of the parent material and metabolically derived CO₂ and by urinary excretion of metabolites ([Garner et al., 2006](#); [Jones and Walsh, 1979](#)). Following intraperitoneal injection of 200 mg/kg of [1-¹⁴C]-1-BP in rats, about 60 and 1.4% of the administered dose was recovered as the parent material and CO₂ respectively, in air expired within 6 hours; about 15% of the administered dose was recovered in urine collected over a 48- hour period ([Jones and Walsh, 1979](#)). Following intravenous injection of [1-¹⁴C]-1-BP at nominal doses of 5, 20, or 100 mg/kg, the radioactivity in CO₂ exhaled within 48 hours accounted for approximately 28, 31, and 10% of the administered dose in rats, and 22, 26, and 19% in mice ([Garner et al., 2006](#)). Radioactivity in the exhaled parent material accounted for about 25, 32, and 71% of the administered dose in rats, and 45, 39, and 48% in mice ([Garner et al., 2006](#)). Radioactivity in urine collected for 48 hours accounted for about 17, 19, and 13% of the administered dose in rats, and 23, 19, and 14% in mice ([Garner et al., 2006](#)). Radioactivity in feces accounted for <4% of administered doses, regardless of dose level, in both species ([Garner et al., 2006](#)).

Animal studies also show rapid elimination of 1-BP from the body ([Garner and Yu, 2014](#); [Garner et al., 2006](#); [Ishidao et al., 2002](#)). Following intravenous injection of [$1-^{14}\text{C}$]-1-BP at nominal doses of 5, 20, or 100 mg/kg, radioactivity remaining in the carcass 48 hours after dose administration accounted for about 6, 6, and 2% of the administered dose in rats, and 4, 2, and 4% in mice ([Garner et al., 2006](#)). ([Garner et al., 2006](#)) proposed that radioactivity remaining in the carcass could represent covalently bound residues from interactions with reactive metabolites or incorporation of ^{14}C into cellular macromolecules. Following intravenous injection of 5 or 20 mg 1-BP/kg doses into rats, the mean half-life for 1-BP elimination from blood was 0.39 or 0.85 hours, respectively ([Garner and Yu, 2014](#)). In gas uptake studies with male and female rats, 1-BP elimination was rapid, with a decrease in the elimination half-life observed with increasing air concentrations of 1-BP ([Garner and Yu, 2014](#)). Pretreatment of female rats with ABT, an inhibitor of CYP metabolism (intraperitoneal injection of 50 mg 1-BP/kg 4 hours prior to gas uptake measurements) or buthionine sulfoxime, an inhibitor of glutathione synthesis (1,000 mg 1-BP/kg/day orally for 3 days before gas uptake), resulted in longer elimination half-times: 9.6 hours with ABT and 4.1 hours with D,L-buthionine(S,R)-sulfoximine (BSO), as compared with 2.0 hours in females not pretreated with ABT or BSO prior to 1-BP exposure at 800 ppm in the gas uptake chamber ([Garner and Yu, 2014](#)). These results suggest that oxidative metabolism and glutathione conjugation play an important role in the elimination of 1-BP. Blood levels decreased rapidly (to detection limits) < 1 hour after the cessation of exposure in Wistar rats exposed to 700 or 1,500 ppm 1-BP 6 hours/day for ≥ 3 weeks ([Ishidao et al., 2002](#)). Clearance of bromide ions from blood and urine showed slower elimination kinetics; the elimination half-life for bromide was 4.7-15 days in blood and 5.0-7.5 days in urine ([Ishidao et al., 2002](#)).

Based on urinary metabolites identified with nuclear magnetic resonance spectroscopy, liquid chromatography-tandem mass spectrometry, and high-performance liquid chromatography ([Garner et al., 2006](#)), the scheme in Figure 3-3 also shows an initial conjugation of 1-BP with glutathione leading to N-acetyl-S-propylcysteine, an oxidation step from 1-bromo-2-propanol to alpha-bromohydrin, a glucuronic acid conjugation step from 1-bromo-2-propanol to 1-bromo-2-hydroxypropane-O-glucuronide, and glutathione conjugation of 1-bromo-2-propanol and bromoacetone followed by oxidation steps leading to metabolites with sulfoxide groups (*e.g.*, N-acetyl-3-[(2-hydroxypropyl)sulfinyl] alanine). The steps involving oxidation of sulfur in the glutathione conjugate derivatives were proposed to be catalyzed by CYP oxygenases or flavin-containing monooxygenases (FMO) as suggested by Krause et al. ([2002](#)).

Catalysis of the oxidation steps by a number of CYP enzymes is supported by results from metabolic disposition studies in wild-type and *Cyp2e1*^{-/-} knock-out mice (F1 hybrids of 129/Sv and C57BL/6N strains) exposed by inhalation to 800 ppm ^{13}C -1-BP for 6 hours ([Garner et al., 2007](#)). Three major metabolites were identified in urine collected from wild-type mice during exposure: N-acetyl-S-(2-hydroxypropyl) cysteine (34 μmoles in collected urine), 1-bromo-2-hydroxypropane-O-glucuronide (5 μmoles), and N-acetyl-S-propylcysteine (8 μmoles). In *Cyp2e1*^{-/-} mice, the amounts of these metabolites in collected urine were changed to 21, 2, and 24 μmoles , respectively. The ratio of 2-hydroxylated metabolites to N-acetyl-S-propylcysteine was approximately 5:1 in wild-type and 1:1 *Cyp2e1*^{-/-} mice. The results indicate that the elimination of CYP2E1 increased the relative importance of the glutathione conjugation pathway, but did not

eliminate the formation of oxygenated metabolites, suggesting the involvement of other CYP enzymes, in addition to CYP2E1, in oxidation steps illustrated in Figure 3-5.

Evidence for the initial conjugation of 1-BP with glutathione leading to the formation of N-acetyl-S-propylcysteine comes from a number of studies in rats and mice ([Garner et al., 2007](#); [Garner et al., 2006](#); [Khan and O'Brien, 1991](#); [Jones and Walsh, 1979](#)).

1. N-Acetyl-S-propylcysteine was detected in the urine of wild-type and *Cyp2e1*^{-/-} mice exposed to 800 ppm 1-BP for 6 hours, at molar ratios to hydroxylated metabolites of 5:1 and 1:1 ([Garner et al., 2007](#)).
2. N-Acetyl-S-propylcysteine and N-acetyl-3-(propylsulfinyl) alanine (*i.e.*, N-acetyl-S-propylcysteine-S-oxide) accounted for approximately 39 and 5% of excreted urinary metabolites, respectively, in urine collected for 24 hours after inhalation exposure of rats to 800 ppm 1-BP for 6 hours ([Garner et al., 2006](#)).
3. N-Acetyl-S-propylcysteine was a relatively minor urinary metabolite in rats given single 5-mg 1-BP/kg intravenous doses, but accounted for >80% of urinary metabolites following administration of 100 mg 1-BP/kg ([Garner et al., 2006](#)).
4. N-Acetyl-S-propylcysteine and N-acetyl-S-propylcysteine-S-oxide were among the six mercapturic acid derivatives identified in urine from rats given 200 mg 1-BP/kg by gavage (in arachis oil) for 5 days ([Jones and Walsh, 1979](#)). The structures of the other four mercapturic acid derivatives identified were consistent with glutathione conjugation of oxygenated metabolites of 1-BP, rather than 1-BP itself. These included N-acetyl-S-(2-hydroxypropyl) cysteine, N-acetyl-S-(3-hydroxypropyl) cysteine, and N-acetyl-S-(2-carboxyethyl) cysteine ([Jones and Walsh, 1979](#)). The techniques used in this study did not determine the relative amounts of the urinary mercapturic acid derivatives.
5. Isolated hepatocytes incubated for 60 minutes with 1-BP showed a decrease in glutathione content (from 58.4 to 40.8 nmol/10⁶ cells), consistent with the importance of glutathione conjugation in metabolic disposition of 1-BP in mammals ([Khan and O'Brien, 1991](#)).

Other studies have identified other metabolites, not included in Figure 3-3, in urine from rats and mice exposed to 1-BP ([Ishida et al., 2002](#); [Jones and Walsh, 1979](#)) and in *in vitro* systems ([Kaneko et al., 1997](#); [Tachizawa et al., 1982](#); [Jones and Walsh, 1979](#)). ([Jones and Walsh, 1979](#)) reported detecting metabolites in urine from rats orally exposed to 1-BP that are consistent with the initial oxidation of the 3-C of 1-BP: N-acetyl-S-(3-hydroxypropyl) cysteine, 3-bromopropionic acid, and N-acetyl-S-(2-carboxyethyl) cysteine. ([Garner et al., 2006](#)) were not able to detect these

metabolites in urine following administration of single intravenous doses up to 100 mg 1-BP/kg in rats or exposure to 800 ppm for 6 hours in rats or mice. ([Garner et al., 2006](#)) proposed that the apparent discrepancy may have been due to an amplification of minor metabolites from the pooling, concentration, and acid hydrolysis processes used in the earlier study. Glycidol (1,2-epoxy-3-propanol) was detected in urine of Wistar rats exposed by inhalation 6 hours/day to 700 ppm for 3 or 4 weeks or 1,500 ppm for 4 or 12 weeks; but no determination of the amount of this compound was made, and the report did not mention the detection of any other carbon-containing metabolites ([Ishida et al., 2002](#)). ([Kaneko et al., 1997](#)) monitored the formation of n-propanol during incubation of rat liver microsomes with 1-BP. 3-Bromopropanol and 3-bromopropionic acid were detected when 1-BP was incubated in an *in vitro* oxidizing system, but 1-BP metabolism with rat liver homogenates was not examined due to the water solubility of 1-BP ([Jones and Walsh, 1979](#)). Propene, 1,2-epoxypropane, 1,2-propanediol, and propionic acid were detected when liver microsomes from phenobarbital-treated rats were incubated with 1-BP, and the addition of glutathione to the reaction mixture led to formation of S-(1' propyl)glutathione and S-(2' hydroxyl-1' propyl) glutathione ([Tachizawa et al., 1982](#)). ([Garner et al., 2006](#)) reported that propene, propylene oxide, propanediol, and propionic acid were not detected in liver homogenate incubations with 1-BP; they suggested that the use of phenobarbital as a CYP inducer may have resulted (in the ([Tachizawa et al., 1982](#)) studies) in the formation of metabolites not generated by constitutive CYP enzymes.

1-BP may be converted to either of two epoxide metabolites (see section O-5-7), glycidol (which was found in the urine of 1-BP-exposed rats, see above) and propylene oxide. Metabolic pathways by which propylene oxide may be generated from 1-BP are shown in Jones and Walsh ([Jones and Walsh, 1979](#)), NTP ([2013b](#)), and IARC ([2018](#)) and a pathway by which glycidol may be generated from 1-BP is shown in IARC ([2018](#)).

I.4 Elimination

Results from animal metabolic disposition studies indicate that 1-BP is eliminated from the body by exhalation of the parent material and metabolically derived CO₂ and by urinary excretion of metabolites ([Garner et al., 2006](#); [Jones and Walsh, 1979](#)). Following single intraperitoneal injections of 200 mg/kg doses of [1-¹⁴C]-1-BP in rats, about 60 and 1.4% of the administered dose was in parent material and CO₂ in air expired within 6 hours, respectively, and about 15% of the administered dose was in urine collected for 48 hours ([Jones and Walsh, 1979](#)). Following intravenous injection of [1-¹⁴C] 1 bromopropane at nominal doses of 5, 20, or 100 mg/kg, radioactivity in CO₂ exhaled in 48 hours accounted for about 28, 31, and 10% of the administered dose in rats, and 22, 26, and 19% in mice ([Garner et al., 2006](#)). Radioactivity in exhaled parent material accounted for about 25, 32, and 71% of the administered dose in rats, and 45, 39, and 48% in mice ([Garner et al., 2006](#)). Radioactivity in urine collected for 48 hours accounted for about 17, 19, and 13% of the administered dose in rats, and 23, 19, and 14% in mice ([Garner et al., 2006](#)). Radioactivity in feces accounted for <4% of administered doses, regardless of dose level, in both species ([Garner et al., 2006](#)).

Animal studies also show that the elimination of 1-BP from the body is rapid and accumulation in the body is not expected ([Garner and Yu, 2014](#); [Garner et al., 2006](#); [Ishidao et al., 2002](#)). Following intravenous injection of [1-¹⁴C]-1-BP at nominal doses of 5, 20, or 100 mg/kg, radioactivity remaining in the carcass 48 hours after dose administration accounted for about 6, 6, and 2% of the administered dose in rats, and 4, 2, and 4% in mice ([Garner et al., 2006](#)). ([Garner et al., 2006](#)) proposed that radioactivity remaining in the carcass could represent covalently bound residues from reactive metabolites or incorporation of ¹⁴C into cellular macromolecules from intermediate metabolic pathways. Following intravenous injection of 5 or 20 mg 1-BP/kg doses into rats, the mean half-times of elimination of 1-BP from the blood were 0.39 and 0.85 hours, respectively ([Garner and Yu, 2014](#)). In gas uptake studies with male and female rats, calculated half-times of elimination for 1-BP were rapid and decreased with increasing air concentrations of 1-BP ([Garner and Yu, 2014](#)). Terminal elimination half-times were 0.5, 0.6, 1.1, and 2.4 hours for males, and 1.0, 1.0, 2.0, and 6.1 hours for females, exposed to initial air concentrations of 70, 240, 800, and 2,700 ppm, respectively. Pretreatment of female rats with ABT to inhibit CYP metabolism (intraperitoneal injection of 50 mg 1-BP/kg 4 hours prior to gas uptake measurements) or buthionine sulfoxime, an inhibitor of glutathione synthesis (1,000 mg 1-BP/kg/day orally for 3 days before gas uptake), resulted in longer elimination half-times: 9.6 hours with ABT and 4.1 hours with D,L-buthionine(S,R)-sulfoximine (BSO), compared with 2.0 hours in untreated females at 800 ppm 1 bromopropane in the gas uptake chamber ([Garner and Yu, 2014](#)). The results with the inhibitors show that both CYP mediated oxidative metabolism and glutathione conjugation play important roles in the elimination of 1-BP. Levels of 1-BP in blood decreased rapidly to detection limits within 0.7 hours after exposure stopped in Wistar rats exposed to 700 or 1,500 ppm 1-BP 6 hours/day for ≥3 weeks ([Ishidao et al., 2002](#)). Clearance of the bromide ion from blood and urine, however, showed slower elimination kinetics: elimination half-times for bromide were 4.7–15.0 days in blood and 5.0–7.5 days in urine ([Ishidao et al., 2002](#)).

Appendix J ANIMAL AND HUMAN TOXICITY STUDIES CONSIDERED FOR USE IN RISK ASSESSMENT

The 1-BP hazard information subjected to data quality evaluation consisted primarily of studies designed to examine the effects of repeated inhalation exposure (*e.g.*, liver and kidney toxicity) and specialized repeated-dose studies of reproductive and developmental toxicity, neurotoxicity and carcinogenesis. Most of the available laboratory animal studies were considered useful for characterizing the potential human health hazards of 1-BP exposure; however, limitations were noted in some studies. This hazard information is summarized in the evidence tables shown in Table_Apx J-2. Additional information regarding the data evaluation results for individual studies can be found in the *Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies*. EPA-HQ-OPPT-2019-0235 ([EPA, 2019o](#)). Any study evaluation concerns thought to have influenced the reliability or interpretation of a specific hazard endpoint are discussed in the synthesis of evidence for a given hazard (See section 3.2.5). All endpoints considered for dose-response analysis were obtained from toxicity studies that scored high during data evaluation.

J.1 Reproductive Toxicity

A two-generation reproduction study in rats reported adverse effects on male and female reproductive parameters ([WIL Research, 2001](#)). The majority of these effects exhibited a dose-response beginning at 250 ppm, with statistical significance observed at 500 ppm. The F₀ generation showed significant dose-related decreases in male and female fertility indices at 500 ppm (fertility was 52% and 0% at 500 and 750 ppm, respectively). A significant increase in the number of females that displayed evidence of mating without delivery was also observed at 500 (10 of 25, 40%) and 750 ppm (17 of 25, 68%) in the F₀ generation. In the F₁ generation, the number of females that displayed evidence of mating without delivery was greater than controls, but not statistically significant at 500 ppm (8 of 25, 32% versus 3/25, 12% in treated and control dams, respectively). The number of males in the F₀ generation that did not sire a litter numbered 2, 0, 3, 12 and 25 (8, 0, 12, 48 and 100%) in the control, 100, 250, 500 and 750 ppm groups respectively. In addition, two females treated at 500 ppm showed evidence of mating, and were gravid, but did not deliver litters. The number of implantation sites, the actual number of litters produced, and live litter size were significantly reduced at 500 ppm in the F₀ and F₁ generations.

Significant changes in female reproductive parameters included a decrease in absolute and relative ovary weights at 750 ppm in the F₀ generation and an increase in estrous cycle length in F₀ and F₁ females (500 ppm). Estrous cycling was not observed in two F₀ females in the 500 ppm group, three F₀ females in the 750 ppm group, three F₁ females in the 250 ppm group, and four F₁ females in the 500 ppm group. This finding is supported by an inhalation study which showed significant treatment-related effects on estrous cycling in female rats and mice following three months of 1-BP inhalation exposure at ≥ 250 ppm ([NTP, 2011a](#)).

The toxicological significance of these findings is underscored by related findings at comparable doses in F₀ and F₁ generations:

- Decreased fertility (significant in 500 and 750 ppm groups). Because both males and females were treated, the observed decreases in fertility could be due in part, to dose-related impairment of male reproductive function.
- An increase in the number of primordial follicles at the highest dose evaluated (750 ppm in F₀ and 500 ppm in F₁) and a decrease in the number of corpora lutea in F₀ females at ≥ 500 ppm (significant at 750 ppm; endpoint was not measured at 100 or 250 ppm).
- No difference in the numbers of corpora lutea was observed in F₁ females treated at 500 ppm as compared to control (no other doses were evaluated for this endpoint).
- A significantly decreased number of implantation sites in F₀ and F₁ females at ≥ 500 ppm (no implantations observed at 750 ppm).
- Decreased live litter size (significant at 500 ppm in F₀ and F₁ treatment groups).

Statistically significant changes in male reproductive and spermatogenic endpoints included:

- Decreased sperm motility and morphologically normal sperm in the F₀ (≥ 500 ppm) and F₁ generations (500 ppm)
- Reduced absolute weight of the left and right cauda epididymides at ≥ 500 ppm in F₀/F₁
- Decreased absolute prostate weight in F₀ (≥ 250 ppm) and F₁ males (500 ppm)
- Decreased seminal vesicle weight in F₀ (750 ppm) and F₁ males (250 ppm)
- Decreased mean epididymal sperm numbers in F₀ males at 750 ppm

These findings positively correlate with the negative effects on fertility observed at 500 ppm, and the complete lack of fertility observed in F₀ mating pairs treated at 750 ppm.

([Zong et al., 2016](#)) investigated the potential effects of 1-aminobenzotriazole (1-ABT), a general inhibitor of cytochrome P450s, on the induction of toxicity to the reproductive system of male mice that were exposed by inhalation to vapors of 1-bromopropane (1-BP). Groups of six 10-week-old male C57BL/6J mice were exposed whole-body to 1-BP for 8 hours/day, 7 days/week for 4 weeks at vapor concentrations of 0, 50, or 250 ppm with twice-daily s.c. injections of saline and at 0, 50, 250, or 1200 ppm with twice-daily s.c. injections of 50 mg 1-ABT/kg in saline. Timing of 1-ABT/saline injections was not indicated. The only treatment-related effect on body weight at the end of exposure was significantly lower mean body weight in mice exposed to 1200 ppm 1-BP/1-ABT, compared with the 1-ABT-treated control. Weights of prostate plus seminal vesicle were significantly decreased at 250 ppm 1-BP without 1-ABT treatment and at 250 ppm and 1200 ppm 1-BP with 1-ABT treatment. No other organ weights were affected in mice that were exposed to 1-BP in the absence of 1-ABT treatment. However, in mice treated with 1-ABT, spleen weights were significantly decreased at 50, 250, and 1200 ppm 1-BP and testes and epididymide weights were significantly decreased at 1200 ppm 1-BP. Epididymal sperm count and percent mobile sperm were significantly decreased at 250 ppm 1-BP in the absence of 1-ABT treatment but were not decreased at 250 ppm 1-BP in the 1-ABT-treated mice. In mice exposed to 1200 ppm 1-BP and treated with 1-ABT, epididymal sperm count, percent mobile sperm, and the number of round spermatids per seminiferous tubule were significantly decreased, and percent morphologically

abnormal epididymal sperm was significantly increased. The number of retained elongated spermatids per seminiferous tubule was significantly increased at 50 and 250 ppm 1-BP without 1-ABT treatment, but only at 1200 ppm 1-BP with 1-ABT treatment. The number of periodic acid-Schiff (PAS)-positive round structures per seminiferous tubule was significantly increased at 250 ppm 1-BP in the absence of 1-ABT treatment and at 250 and 1200 ppm 1-BP in mice treated with 1-ABT. In 1-ABT treated mice, the numbers of retained elongated spermatids per tubule at 50 and 250 ppm 1-BP and PAS-positive round structures per tubule at 250 ppm were significantly lower than in the mice not treated with 1-ABT. The study authors concluded that treatment of male mice with 1-ABT, a general inhibitor of cytochrome P450s, inhibited the decreased epididymal sperm count, decreased epididymal sperm motility, increased retained elongated spermatids per seminiferous tubule, and increased PAS-positive round structures per seminiferous tubule that were found in mice exposed to 50 and 250 ppm 1-BP in the absence of 1-ABT treatment.

J.2 Neurotoxicity

A number of laboratory animal studies report that both acute and repeated inhalational exposure to high concentrations of 1-BP produce peripheral neurotoxicity indicated by changes in both function and structure of the peripheral nervous system. The degree or severity of peripheral neurotoxicity produced by 1-BP depends on the concentration as well as duration of exposure. Most studies using concentrations of ≥ 1000 ppm report ataxia progressing to severely altered gait, hindlimb weakness or loss of hindlimb control, convulsions, and death (*e.g.*, ([Banu et al., 2007](#); [Yu et al., 2001](#); [Fueta et al., 2000](#); [Ichihara et al., 2000a](#); [Ohnishi et al., 1999](#); [ClinTrials, 1997a, b](#)). Concentrations of 400-1000 ppm produce neuropathological changes including peripheral nerve degeneration, myelin sheath abnormalities, and spinal cord axonal swelling ([Wang et al., 2002](#); [Yu et al., 2001](#); [Ichihara et al., 2000a](#)).

Physiological and behavioral measures have been used to characterize and develop dose-response data for this peripheral neurotoxicity. Motor nerve conduction velocity and latency measured in the rat tail nerve were altered at ≥ 800 ppm with progressive changes observed from 4 to 12 weeks of exposure ([Yu et al., 2001](#); [Ichihara et al., 2000a](#)). These findings in rats agree with neurological symptoms reported in exposed humans, including peripheral weakness, tingling in extremities, and gait disturbances. The nerve conduction velocity endpoint that was altered in rats ([Yu et al., 2001](#); [Ichihara et al., 2000a](#)) is directly comparable to the increased latencies and lower conduction velocity measured in a population of female factory workers exposed to 1-BP ([Li et al., 2010](#); [Ichihara et al., 2004b](#)).

Behavioral tests such as grip strength, landing foot splay, traction (hang) time, and gait score provide dose-response data and appear somewhat more sensitive than neuropathology or physiological changes. Ichihara et al. ([2000a](#)) reported progressively worsening effects over 12 weeks of exposure at 400 and 800 ppm including decreased hindlimb and forelimb grip strength, and inability to walk on a slightly-sloped plane; exposure at 200 ppm significantly decreased hindlimb grip only at 4 weeks and otherwise was without effect. Hindlimb grip was preferentially decreased compared to forelimb as is often observed with peripheral neuropathy. Similarly decreased hindlimb strength was reported by Banu et al. ([2007](#)) after 6 weeks of 1-BP

exposure at 1000 ppm (but not 400 ppm); these changes had not recovered at 14 weeks post exposure. Honma et al. (2003) measured the time for a rat to hang onto a suspended bar, which they called a traction test. The average time to hang appeared to be decreased following 21 days of exposure to 50 ppm, and was significantly so with 200 and 1000 ppm; these changes were still evident when animals were tested 7 days later. The ability to stay on a rotarod was not altered in these rats, suggesting that the weakness is peripherally mediated.

Results reported following oral dosing with 1-BP are similar to those reported following inhalation exposure. Over 16 weeks of dosing (200-800 mg/kg/d), Wang et al. (2012), reported progressively decreased hindlimb grip strength, wider landing foot splay, and increased gait abnormalities. The high-dose group was too debilitated to test after 14 weeks, but at that time their grip strength was decreased by 42%, somewhat comparable to the 56% decrease reported with 13 weeks of 800 ppm inhalational exposure (Ichihara et al., 2000a). Rats exposed to the lowest concentration of 200 mg/kg/d showed less, but still statistically significant changes in gait and decreased (9%) hindlimb grip strength. Subcutaneous administration of 455 or 1353 mg/kg/d (said to be equal to inhalation of 300 or 1000 ppm) over a 4 week period also produced changes in tail motor nerve function (Zhao et al., 1999) similar to the effects reported by others following inhalation exposure.

Some behavioral assays conducted in rats exposed to 1-BP reflect involvement of central as well as peripheral nervous systems. Increased motor activity levels were measured following inhalation of 50 or 200 ppm for three weeks (Honma et al., 2003). Spatial learning and memory measured in a Morris water maze was severely impaired while rats were receiving oral doses of 200 mg/kg/d and greater (Guo et al., 2015; Zhong et al., 2013). Guo et al. (2015) also reported that these cognitive deficits correlated with lowered levels of neuroglobin and glutathione depletion indicative of oxidative stress in the same rats. During inhalational exposure, water maze performance was impaired at concentrations of 200 ppm and above (Honma et al., 2003). However, these concentrations also produced neuromotor difficulties, which would interfere with performance of the task. There were no changes in water maze performance when training was initiated after exposure ended. Furthermore, there were no differences in memory of a passive avoidance task when the initial learning took place before exposures began (Honma et al., 2003).

A number of features reflecting CNS neurotoxicity have been reported for 1-BP. Brain pathology has been reported in several, but not all, studies, which may be due to experimental differences such as tissue sampling, staining, and measurement. Histological examination of the brain showed widespread pathology at 1000 and 1600 ppm, and mild myelin vacuolization at 400 ppm, following 28 days of exposure (ClinTrials, 1997b); however, the same testing laboratory reported no neuropathology with exposures up to 600 ppm for 13 weeks (ClinTrials, 1997a). In the cerebellum, exposure at 400 ppm and higher produced degeneration of Purkinje cells (Mohideen et al., 2013; Ohnishi et al., 1999) without morphological changes in the hippocampus (Mohideen et al., 2013). Similar exposure levels decreased noradrenergic but not serotonergic axonal density in frontal cortex and amygdala (Guo et al., 2015; Mohideen et al., 2011). In contrast to these reports, no degeneration was observed across several brain sections up to 800 ppm despite marked peripheral and spinal cord changes in the same rats (Wang et al., 2002; Ichihara et al., 2000a). In two other studies conducted in the same laboratory, one reported no histological or morphological changes in

brain following exposures up to 1250 ppm for 13 weeks ([Sohn et al., 2002](#)) and another reported no neuropathology after daily exposures of 1800 ppm for up to eight weeks ([Kim et al., 1999a](#)), even though in the latter study other indicators of neurotoxicity were observed.

Decreased absolute brain weight has been reported in several studies, both in the context of adult exposures and long-term exposures during a 2-generation reproductive study. Studies involving exposures from 4 to 12 weeks reported decreased brain weight at 800 and 1000 ppm ([Subramanian et al., 2012](#); [Wang et al., 2003](#); [Ichihara et al., 2000a](#)). Kim et al. ([1999a](#)) also reported decreased brain weight at 300 ppm for 8 weeks, but only provided relative brain:body weight data. In the parental generation of a 2-generation study, exposure for at least 16 weeks also produced brain weight changes, with males being more sensitive (NOAEL=100 ppm, LOAEL=250 ppm) than females (NOAEL=250 ppm) ([WIL Research, 2001](#)). The F₁ generation, which was exposed during gestation and at least 16 weeks after weaning, had lower brain weight at 100 ppm in males, and again females were less sensitive (NOAEL=250 ppm). Histopathological evaluations in the WIL study revealed no correlative macroscopic or microscopic alterations in unperfused brain tissue. Two studies have measured brain weight and reported no effects: 1) ([Wang et al., 2002](#)), in which exposure was only 7 days and may not have been a sufficient exposure duration, and 2) the 13-wk study of ([ClinTrials, 1997a](#)), even though the same laboratory reported decreased brain weight at the same concentration with only 4 weeks of exposure.

Fueta and colleagues ([Fueta et al., 2007](#); [Ueno et al., 2007](#); [Fueta et al., 2004](#); [Fueta et al., 2002a](#); [Fueta et al., 2002b](#); [Fueta et al., 2000](#)), reported a series of studies using electrophysiological measures of hippocampal slices (dentate gyrus and CA1 regions) from rats exposed to 1-BP for four to 12 weeks. Concentrations of 400 ppm and higher showed disinhibition in paired-pulse population spikes, and the effect was dependent on exposure concentration and duration. This hyperexcitability appeared to be due to a reduction in feedback inhibition rather than a change in excitatory synaptic drive. There was a moderate correlation with the level of bromide ion in the brain. Pharmacological probes, proteins and receptor mRNA levels suggest that these effects are related to actions on the GABA and NMDA neural systems, and/or intracellular signaling cascades ([Ueno et al., 2007](#); [Fueta et al., 2004](#); [Fueta et al., 2002a](#); [Fueta et al., 2002b](#)). A recent Society of Toxicology presentation (abstract only available) reported similar effects in hippocampal slices from 14-day old rat pups whose mothers were exposed to 400 or 700 ppm during gestation ([Fueta et al., 2013](#)).

A number of investigators have probed potential molecular mechanisms for some of these CNS effects. Exposures of 200 ppm and greater produce changes in biomarkers and proteome expressions suggesting alterations in the function and maintenance of neural and astrocytic cell populations. Some of these include indicators of oxidative stress (reactive oxygen species, glutathione depletion), ATP loss, protein damage, altered apoptotic signaling, neurotransmitter dysregulation, decreased hippocampal neurogenesis, and others ([Huang et al., 2015](#); [Mohideen et al., 2013](#); [Zhang et al., 2013](#); [Zhong et al., 2013](#); [Huang et al., 2012](#); [Subramanian et al., 2012](#); [Huang et al., 2011](#); [Yoshida et al., 2007](#); [Wang et al., 2003](#); [Wang et al., 2002](#)). Concentrations as low as 50 ppm for three weeks were reported to decrease levels of the serotonin metabolite 5-HIAA in frontal cortex and taurine in midbrain, while concentrations of 200 ppm and greater

impacted additional markers (protein levels, mRNA) of monoaminergic and amino acid neurotransmitter systems ([Zhang et al., 2013](#); [Mohideen et al., 2009](#); [Suda et al., 2008](#); [Ueno et al., 2007](#)). Overall these data suggest several and perhaps overlapping cellular and molecular mechanisms that could contribute to the functional and structural alterations reported for 1-BP. ([Zong et al., 2016](#)), citing studies from the literature, noted that the potential of 1-bromopropane (1-BP) to induce neurotoxicity in mice had not been studied because 1-BP induced lethal hepatotoxicity in mice before the appearance of potential overt evidence of neurotoxicity. To develop a murine model of neurotoxicity, ([Zong et al., 2016](#)) proposed treatment of mice with 1-aminobenzotriazole (1-ABT), a general inhibitor of cytochrome P450s, to reduce severe hepatotoxicity and allow studies on the effects of 1-BP on the mouse brain. A preliminary experiment showed that subcutaneous (s.c) or intraperitoneal injections of male C57BL/6J mice with 50 mg/kg 1-ABT twice daily for three days inhibited CYP2E1 activity by 62-64% in the brain and by 92-96% in the liver, compared with values in saline-injected control mice. Since the route of injection had no significant effect on the extent of CYP2E1 activity inhibition, the s.c. route of 1-ABT administration was chosen for model development to minimize potential for damage of internal organs. For the main study, groups of six 8-week-old male C57BL/6J mice were exposed whole-body to 1-BP for 8 hours/day for 4 weeks at vapor concentrations of 0, 50, or 250 ppm with s.c. injections of saline before and after each inhalation exposure and at 0, 50, 250, or 1200 ppm with s.c. injections of 50 mg 1-ABT/kg in saline before and after each inhalation exposure (100 mg 1-ABT/kg-day). The only treatment-related effect on body weight was significant loss of body weight on day 28 in mice exposed to 1200 ppm 1-BP/1-ABT. In mice not treated with 1-ABT, mild histological changes in hepatocytes included centrilobular degeneration and nuclear and cytoplasmic changes at 50 ppm 1-BP. Exposure to 250 ppm without 1-ABT produced severe pathological changes in the liver including macroscopic and microscopic liver necrosis, hemorrhage, and foci of hepatocyte degeneration. In contrast, no serious histopathological changes were found in the livers of 1-ABT-treated mice that were exposed to 50, 250, or 1200 ppm 1-BP. Absolute mean liver weights were significantly decreased at 50 ppm 1-BP in the absence of 1-ABT treatment and at 250 and 1200 ppm 1-BP in animals treated with 1-ABT. Absolute mean brain weight was significantly lower than control in the group treated with 1-ABT and exposed to 1200 ppm 1-BP, but brain weights were unaffected in other exposure groups. Cerebral cortex and hippocampal expression of Ran, GRP78, γ -enolase, and c-Fos proteins was determined by western blotting analysis in all treated mouse groups. Studies from the literature showed that expression of these four proteins was altered in brain tissues of rats exposed to 1-BP in the absence of treatment with 1-ABT. In the male C57BL/6J mice treated with 1-ABT, hippocampal Ran expression and cortex GRP78 expression were significantly increased at 1200 ppm 1-BP and hippocampal Ran expression was significantly increased at 250 ppm 1-BP. No changes in Ran or GRP78 expression occurred in other mouse groups, including those treated with 50 or 250 ppm 1-BP in the absence of 1-ABT treatment. No treatment-related changes were found in the expression of γ -enolase or c-Fos in the hippocampus or cerebral cortex. The treatment of mice in this study with 1-ABT, a general inhibitor of cytochrome P450s, reduced the severe hepatotoxicity/lethality of 1-BP to mice, thus allowing mouse survival at 1-BP exposure concentrations as high as 1200 ppm for 8 hours/day for 28 days and the study of the effects of 1-BP on the mouse brain.

J.3 Human Case Reports

Several case studies have reported various neurological effects in workers exposed to 1-BP ([Samukawa et al., 2012](#); [CDC, 2008](#); [Majersik et al., 2007](#); [Raymond and Ford, 2007](#); [Ichihara et al., 2002](#); [Sclar, 1999](#)). Some of the neurological effects experienced by workers included peripheral neuropathy, muscle weakness, pain, headaches, numbness, gait disturbance, confusion, ocular symptoms, slowed mental activity, and dizziness. In some instances, the effects were still observed many months after exposure had ceased or had been reduced.

Workers described in the case reports were exposed to 1-BP in the following activities: metal cleaning, circuit board cleaning, and gluing foam cushions or furniture. In almost all of the cases reported in the table below, personal protective equipment was not used and air concentrations of 1-BP, when available, were greater than 100 ppm. Bromide levels, both serum and in a few cases, urinary, were provided in some of the studies and are included in the table below. Bromide concentrations have been used as a biomarker of exposure to 1-BP. A description of the use of bromide levels and the investigation into using other biomarkers of exposure are included in Section 2.2.

([Raymond and Ford, 2007](#)) reported high levels of urinary arsenic, as well as serum bromide, in the workers described in their case report of four employees who required hospitalization, suggesting arsenic and bromide synergism. All four of the workers had total (organic and inorganic) urinary arsenic levels greater than 200 µg/L, but the source of the arsenic could not be identified. NIOSH reported on these 4 employees in a HHE on a plant where workers applied spray adhesive to cushions, and concluded that the exposure was likely not occupational and could not have been the sole cause of ataxia and paresthesia that the four hospitalized workers experienced

Table_Apx J-1. Case Reports on 1-BP

Reference ¹	# Cases	Primary Symptoms	Activity	Air levels	Serum Bromide levels (mg/dL) ²
(Majersik et al., 2007)	6	Headache, nausea, dizziness, lower extremity numbness, pain, paresthesia, difficulty walking/balance	Foam cushion gluing at furniture plant (glue contained 70% 1-BP)	130 ppm (range, 91-176); TWA 108 ppm (range, 92-127)	Peak range: 44-170
(Sclar, 1999)	1	Peripheral neuropathy, weakness of lower extremities and hand, numbness, dysphagia	Metal stripping (degreasing and cleaning)	Not available	Not available
(CDC, 2008)	2	Confusion, dysarthria, dizziness, paresthesias, ataxia; Headache, nausea, dizziness, malaise	Cleaning circuit boards (spray) Solvent in dry cleaning	178 ppm	48 mg/dL and not available for case #2

Table_Apx J-1. Case Reports on 1-BP

Reference ¹	# Cases	Primary Symptoms	Activity	Air levels	Serum Bromide levels (mg/dL) ²
				75-250x background levels	
(Samukawa et al., 2012)	1	Muscle weakness, pain, numbness in lower extremities, gait disturbance	Metal cleaning	553 ppm, mean TWA (range, 353-663)	58 µg/mL (peak)
(Raymond and Ford, 2007) (4 cases from NIOSH (2003a) HHE report on Marx Industries)	4	Dizziness, anorexia, dysesthesias, nausea, numbness, ocular symptoms, unsteady gait, weakness, weight loss	Gluing in furniture making	Mean 107 ppm (range, 58-254 ppm) collected 9 months after workers became ill	3.0 - 12.5 mEq/L (100 mg/dL) Arsenic levels > 200 µg/L for all 4 employees ³
(NIOSH, 2003a)	16 (incl. 4 from Raymond (2007))	Headache, anxiety, feeling “drunk,” numbness and “pins and needles” sensation in legs and feet	Spray application of glue to polyurethane foam to make cushions	1999 (16 personal breathing zone samples): GM 81.2 ppm (range, 18-254 ppm); 2001 (13 PBZ samples): GM 45.7 ppm (range, 7-281 ppm)	Serum GM: 4.8 mg/dL (2.7-43.5; n=39); Urinary: 46.5 mg/dL (15.4-595.4, n=40) Includes both exposed and unexposed workers
(Ichihara et al., 2002)	3	Staggering gait, paresthesia in lower extremities, numbness in legs, headache, urinary incontinence, decr in vibration sense in legs	Spray application of glue to polyurethane foam to make cushions	Mean 133 ppm, (range, 60-261 ppm daily TWA); avg over 11 days 133 ± 67 ppm--after ventilation improved	Not available
Biomarker Studies also Containing Case Report Data					
(Hanley et al., 2006b)	13	(focused on exposure and urinary Br)	Spray application of glue to polyurethane foam to make cushions	Mean 92 ppm (range, 45-200 ppm)	Urinary: 190 (43-672; composite of 2 days)
(Ichihara et al., 2004b; Ichihara et al., 2004a)	24 female 13 male China	Nose, throat, eye irritation; malaise, headache, dizziness	1-BP production	3.3-90.2 ppm No severe neurological effects	Urinary bromide measured but not reported

Table_Apx J-1. Case Reports on 1-BP

Reference ¹	# Cases	Primary Symptoms	Activity	Air levels	Serum Bromide levels (mg/dL) ²
				< 170 ppm	

¹EPA has not published systematic review criteria for reports/case studies, therefore data quality evaluation for these reports are not available

²Serum bromide unless otherwise indicated; Reference ranges vary by report

³Arsenic Reference range: <0.06

J.4 Human Epidemiology Studies

The 1-BP database includes three epidemiological studies of workers occupationally exposed to 1-BP ([Li et al., 2010](#); [Toraason et al., 2006](#); [Ichihara et al., 2004b](#)); two of the studies report neurologic effects and the third analyzed for DNA damage in workers' leukocytes. The evaluation of 1-BP epidemiology studies by each of the five aspects of study design – study population characteristics and representativeness, exposure measures, outcome measures, confounding, and analysis – is discussed below; additional information regarding the data evaluation results for individual studies can be found in the *Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies*. EPA-HQ-OPPT-2019-0235 ([EPA, 2019o](#)). Twenty-three female workers involved in 1-BP production in China were surveyed in 2001 and compared with age-matched controls from a beer factory located in the same city ([Ichihara et al., 2004b](#)). The study authors did not report the method of recruitment. Neurological tests (vibration sensation, electrophysiologic studies), blood tests, neurobehavioral tests and postural sway tests were administered. Passive sampling indicated individual exposure levels ranging from 0.34 – 49.2 ppm in an 8-hour shift (median 1.61 ppm; geometric mean 2.92 ppm). Some of the employees in this plant were also exposed to 2-BP and were analyzed separately. Although some of the neurologic measures indicated reduced function in exposed workers compared to controls, because of the past exposures to 2-BP and the small number of cases who entered the study after 2-BP was no longer used (n= 12 pairs), it was difficult to interpret the results of this study. In workers who were employed at the plant after 2-BP was no longer used, Benton visual memory test scores, POMS depression, and POMS fatigue were significantly different. It is not clear whether this indicates a lack of power to detect differences in the larger group or whether the exposure to 2-BP affected the results.

As a follow-up to the Ichihara study ([Ichihara et al., 2004b](#)) described above, ([Li et al., 2010](#)) combined data from three 1-BP production facilities in China to analyze a larger sample of workers. Sixty female and 26 male workers and controls from other types of factories matched by age, sex and geographic region were analyzed from four time periods (2001, 2003, 2004, 2005). Data were collected over 3 days between 2001 and 2005. The authors did not describe the recruitment process, and it is not clear whether the same workers included in the Ichihara 2004 study were recruited for this study. The authors reported that none of the workers had a history of diabetes.

Exposures were measured for each plant using passive samplers. Exposure was measured either once or twice over 8 or 12 hour work shifts. TWA exposure concentrations to 1-BP ranged from 0.07-106.4 ppm for female workers and 0.06-114.8 ppm for male workers. It was reported that none of the workers wore gloves or masks in the plant. However, the authors later clarified that some workers wore gloves ([Ichihara et al., 2011](#)). Employees were placed into low-, medium-, and high-exposure groups (for females) to include equal numbers. Median exposures for the three groups (n=20 per group) were 1.28, 6.60 and 22.58 ppm for females and 1.05 (low) and 12.5 (high) ppm for males (n=13 per group). Ambient exposure levels varied by job and by plant and were collected in different years for each plant. For example, the ambient concentrations of “raw product collection” were more than 3 times higher at the Yancheng plant (analyzed in 2003) than at the Yixing plant ([Li et al., 2010](#)).

Clinical chemistries were obtained, and electrophysiological studies and neurological and neurobehavioral tests were conducted for each employee. A single neurologist performed most of the neurological assessments except for those collected in 2004 from one plant, which included 5 female workers. Electrophysiological tests conducted included: motor nerve conduction velocity, distal latency (DL), F-wave conduction velocity in the tibial nerve, sensory nerve conduction velocity in the sural nerve (SNCV), and amplitude of the electromyogram induced by motor nerve stimulation, F-wave, and potential of sensory nerve. Vibration sense, reflex, and muscle strength were measured using a tuning fork on the big toe. Neurobehavioral tests and blood tests were also performed.

In regression analyses, the authors reported a statistically significant increase ($p < 0.05$) in mean tibial motor distal latency and a decrease in mean sural nerve conduction velocity in women in the middle exposure group only (compared to controls). Statistically significant decreased vibration sense in toes (vibration loss) was reported in all exposure groups compared to controls. In addition, thyroid stimulating hormone (TSH) was significantly different in the middle and high exposure groups compared to controls and FSH in low and medium exposure groups in females. Red blood cell count was significantly decreased in all exposure groups compared to controls in females. In males, the only statistically significant difference between the high exposure group and controls was for blood urea nitrogen.

Analyses of cumulative exposure measures (exposure level x duration) indicated statistically significant ($p < 0.05$) increases in vibration sense in toes in females across all exposure levels when compared to controls (5.6 ± 4.3 , 6.4 ± 3.8 , and 6.5 ± 3.4 secs, mean \pm SD for low, medium and high cumulative exposure groups, respectively). In females, only the high cumulative exposure group for tibial motor DL was statistically higher than in controls and only the low cumulative exposure group for sural NCV. Analyses to adjust for other factors that could influence vibration loss (examining neurologist, age, height, body weight, alcohol consumption) were conducted using analysis of covariance in female workers. The effect of 1-BP exposure on vibration loss was significant ($p = 0.0001$ or $p = 0.0002$) based on cumulative exposures as well as exposures not considering duration of exposure, respectively, but the effect of examining neurologist was also significant ($p < 0.0001$).

Both of the neurological studies described above ([Li et al., 2010](#); [Ichihara et al., 2004b](#)) showed neurological effects related to 1-BP exposure. The co-exposures to 2-BP and the small sample size of workers exposed only to 1-BP was a limitation in the Ichihara et al. 2004 study. Li et al. ([2010](#)) selected workers exposed to 1-BP from 3 plants to include more study participants; however, the exposure data reported by plant were limited, the job activities were somewhat different between plants (but for those jobs with similar activities between plants, some exposures were more than 3 times higher at one plant than another), and ambient exposure levels of 1-BP and 2-BP reported by job and by plant were collected in different years for each plant. Several of these issues could lead to exposure misclassification of the workers. TWAs (8- and 12- hour) were used to assign exposure groups, based on either 1 or 2 samples. Using the TWA does not account for the fluctuations or potential peaks that may have occurred during the shift. In addition, the median exposure level of the high exposure group for females was 22.58 ppm but the range was 15.28-106.4 ppm, indicating that some of the workers were exposed to levels much higher than the lowest exposed workers in that group. In addition, the cumulative exposure measures were based on only 1-3- day measurements of individual exposure levels.

Skin temperature is important when conducting electrophysiological studies; however, the only control for temperature in this study was to acclimate study participants to 24° C in a room for 30 minutes. Individual skin temperatures should have been taken at the site of the test (on the foot) because the results are affected by temperature. Vibration sense can be influenced by BMI, but it was not reported or controlled in the study. As acknowledged in the report by the study authors, vibration sense is inherently imprecise (based on the sensitivity of the subject relative to the examiner). Evidence of a high degree of variability was shown in the large standard deviations reported for vibration sense in females (2.9 ± 3.9 , mean \pm SD for controls; 5.6 ± 4.4 , low exposure group). Other than RBC, only vibration sense in females using the cumulative exposure measure was concentration-dependent. RBC in females could have been influenced by other factors (*e.g.*, menstruation, dehydration) that were not examined in the study.

Toraason et al. ([2006](#)) analyzed DNA damage in peripheral leukocytes of workers exposed to 1-BP during spray application of adhesives in the manufacture of foam cushions for upholstered furniture. Sixty-four workers (18 males, 46 females) at two plants were included in the analysis. There were no unexposed groups. Fifty of 64 workers wore personal air monitors for 1-3 days. Workers employed as sprayers had the highest exposures; 1-BP 8-hr TWA concentrations were substantially higher (4 times) for sprayers at one of the plants than the other. TWA exposures ranged from 0.2 to 271 ppm across both plants. DNA damage was assessed using comet assay. DNA damage was measured by tail moment in leukocytes of workers. At both the start and end of the work week, DNA leukocyte damage was higher for sprayers than non-sprayers but the increases were not statistically significant. In addition, the facility with lower exposures had higher measures of DNA damage than the higher exposure facility at the beginning of the week but not the end. Tail moment dispersion coefficients did not indicate an exposure-response relationship. Three different biomarkers of exposure, 1-BP TWA concentrations and serum and urinary bromide levels, were evaluated in multivariate analyses. After controlling for various potential confounders, starting and ending work week comet tail moments in leukocytes were significantly associated

with serum bromide quartiles and ending work week values of 1-BP TWA concentrations. None of the models that examined associations between DNA damage and dispersion coefficients was statistically significant. There was a slight risk for DNA damage in workers' leukocytes in vitro in workers exposed to 1-BP but the results of the in vivo data were not consistent.

Table_Apx J-2. Summary of the Toxicological Database for 1-BP

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Mortality	Acute	Rat, Wistar, M/F (n=10/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	LC ₅₀ = 7000	Mortality (acute inflammatory response and alveolar edema)	(Elf Atochem, 1997)	N/A
Mortality	Acute	Rat, Sprague-Dawley, M/F (n=10/group)	Inhalation, whole body, vapor	0, 511,000, 13,000, 15,000 or 17,000 ppm	4 hours	LC ₅₀ = 14,374	Mortality	(Kim et al., 1999a)	N/A
Mortality	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250 (M)	Decreased survival	(NTP, 2011a)	High
Mortality	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 250	Decreased survival	(NTP, 2011a)	High
Mortality	Short-term	Mouse, C57BL/6J, DBA/2J and BALB/cA, M (n=6/strain/group)	Inhalation, whole body, vapor	0, 50, 110 or 250 ppm	8 hours/day, 7 days/week for 4 weeks	NOAEL= 110	Mortality (two of three strains affected)	(Liu et al., 2009)	High
Mortality	Short-term/ Subchronic	Mouse, B6C3F1, F (n=5-8/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 4 or 10 weeks	NOAEL= 250 (F)	Mortality (first week on study)	(Anderson et al., 2010)	Medium
Mortality	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250	Decreased survival rate	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Mortality	Acute	Rat, Sprague-Dawley, F (n=10/group)	Oral	0 or 2000 mg/kg	Single exposure	LD ₅₀ > 2000 mg/kg (F)	Mortality	(Elf Atochem, 1993a)	N/A
Body weight	Acute	Rat, M (n=10/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	NOAEL= 8500 (M)	No effects on body weight	(Elf Atochem, 1997)	N/A
Body weight	Short-term	Rat, Wistar, M (n=8/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day for 7 days	NOAEL= 400 (M)	Decreased body weight	(Wang et al., 2002)	N/A
Body weight	Short-term	Rat, Wistar, M (n=6/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day for 7 days	NOAEL= 400 (M)	Decreased body weight	(Zhang et al., 2013)	High
Body weight	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	NOAEL= 1000	Decreased body weight	(NTP, 2011a)	High
Body weight	Short-term	Rat, F344, M (n=5/group)	Inhalation, whole body, vapor	0, 10, 50, 200 or 1000 ppm	8 hours/day, 7 days/week for 3 weeks	NOAEL= 50 (M)	Increased body weight	(Honma et al., 2003)	Low
Body weight	Short-term	Rat, F344, F (n=7-8/group)	Inhalation, whole body, vapor	0, 50, 200 or 1000 ppm	8 hours/day, 7 days/week for 3 weeks	NOAEL= 1000 (F)	No effects on body weight	(Sekiguchi et al., 2002)	N/A
Body weight	Short-term	Rat (n=20/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/week for 4 weeks	NOAEL= 398	Decreased weight gain	(ClinTrials, 1997b)	N/A
Body weight	Short-term	Rat, Wistar-ST, M (n=12/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day, 7 days/week for 4 weeks	NOAEL= 800 (M)	Decreased body weight	(Subramanian et al., 2012)	N/A
Body weight	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/week for 5 or 7 weeks	LOAEL= 1000 (M)	Decreased body weight	(Yu et al., 2001)	Medium

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Body weight	Subchronic	Rat, Wistar, M (n=24/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day, 7 days/week for 6 weeks	NOAEL= 400 (M)	Decreased body weight	(Banu et al., 2007)	N/A
Body weight	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/week for 8 weeks	NOAEL= 300	Decreased body weight	(Kim et al., 1999b)	N/A
Body weight	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/week for 12 weeks	NOAEL= 200 (M)	Decreased body weight	(Ichihara et al., 2000a)	High
Body weight	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/week for 12 weeks	NOAEL= 1200 (M)	Decreased body weight	(Wang et al., 2003)	N/A
Body weight	Subchronic	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/week for up to 12 weeks	NOAEL= 400 (F)	Decreased body weight	(Yamada et al., 2003)	High
Body weight	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/week for 13 weeks	NOAEL= 600	No effects on body weight	(ClinTrials, 1997a)	High
Body weight	Chronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 200, 500 or 1250 ppm	6 hours/day, 5 days/week for 13 weeks	NOAEL= 1250	No effects on body weight	(Sohn et al., 2002)	N/A
Body weight	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500 (M)	Decreased body weight	(NTP, 2011a)	High
Body weight	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on body weight	(NTP, 2011a)	High
Body weight	Developmental	Rat, Albino Crl:CD(SD)IGS BR, F (n=10/group)	Inhalation, whole body, vapor	0, 100, 199, 598 or 996 ppm	6 hours/day on GDs 6-19 and lactation days 4-20	NOAEL= 100 (F)	Decreased body weight gain during gestation	(Huntingdon Life Sciences, 1999)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Body weight	Developmental	Rat, F (n=25/group)	Inhalation	0, 103, 503 or 1005 ppm	6 hours/day on GDs 6-19	NOAEL= 103 (F)	Decreased body weight gain during gestation	(Huntingdon Life Sciences, 2001)	N/A
Body weight	Developmental	Rat, Wistar-Imamichi, F (n=10/group)	Inhalation, whole body, vapor	0, 100, 400 or 800 ppm	8 hours/day during gestation (GDs 0-20) and lactation (PNDs 1-20)	NOAEL= 400 (F)	Decreased body weight at PND 21	(Furuhashi et al., 2006)	N/A
Body weight	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50 F0/group, 49-50 F1 adults/group/generation; 30-47 F1 weanlings/group; 30-44 F2 weanlings/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), through mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 250 (F)	Decreased body weight (F ₀ and F ₁ adults)	(WIL Research, 2001)	High
Body weight	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 500 (M)	Decreased body weight gain	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Body weight	Short-term	Mouse, C57BL/6J, DBA/2J and BALB/cA, M (n=6/strain/group)	Inhalation, whole body, vapor	0, 50, 110 or 250 ppm	8 hours/day, 7 days/ week for 4 weeks	NOAEL= 250 (M)	No effects on body weight	(Liu et al., 2009)	High
Body weight	Short-term/ Subchronic	Mouse, B6C3F1, F (n=5-8/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 4 or 10 weeks	LOAEL= 125 (F)	Decreased body weight	(Anderson et al., 2010)	Medium
Body weight	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on body weight	(NTP, 2011a)	High
Body weight	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on body weight	(NTP, 2011a)	High
Body weight	Acute	Rat (n=10/group)	Oral	0 or 2000 mg/kg	Single exposure	NOAEL= 2000 mg/kg	No effects on body weight	(Elf Atochem, 1993a)	
Body weight	Short-term	Rat, Wistar, M (n=10/group)	Oral, gavage (corn oil vehicle)	0, 200, 400 or 800 mg/kg-day	12 days	NOAEL= 400 mg/kg-day (M)	Decreased final body weight; used for weight of evidence; no route-to-route extrapolation	(Zhong et al., 2013)	Low
Body weight	Short-term	Rat, Sprague-Dawley, M (n=7/group)	Intra-peritoneal	0 or 1000 mg/kg-day	14 days	LOAEL= 1000 mg/kg-day (M)	Decreased body weight	(Xin et al., 2010)	N/A
Body weight	Chronic	Rat, M (n=10/group)	Oral	0, 200, 400 or 800 mg/kg-day	16 weeks	NOAEL= 400 mg/kg-day (M)	Decreased body weight	(Wang et al., 2012)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Body weight	Short-term	Rat, Wistar, M (n=14/group)	Oral, gavage	0, 100, 200, 400 or 800 mg/kg-day	12 days	NOAEL= 400 mg/kg-day (M)	Decreased body weight	(Guo et al., 2015)	High
Body weight	Acute	Mouse, BALB/c, F (n=5/group)	Oral, gavage (corn oil vehicle)	0, 200, 500 or 1000 mg/kg	Single exposure; necropsy after 6, 12, 24 or 48 hours	NOAEL= 1000 mg/kg (F)	No effects on body weight	(Lee et al., 2007)	N/A
Cardio-vascular	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on heart weight or histo-pathology	(Ichihara et al., 2000b)	High
Cardio-vascular	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on heart weight or histo-pathology	(Kim et al., 1999a)	N/A
Cardio-vascular	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on heart weight or histo-pathology	(ClinTrials, 1997a)	High
Cardio-vascular	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on heart weight	(NTP, 2011a)	High
Cardio-vascular	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Cardio-vascular	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 2000 (M)	Decreased absolute and relative heart weight	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Cardio-vascular	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on heart weight or histopathology	(NTP, 2011a)	High
Cardio-vascular	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Skin	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on histopathology	(ClinTrials, 1997a)	High
Skin	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology	(NTP, 2011a)	High
Skin	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Skin	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Skin	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Endocrine	Short-term	Rat, Wistar, M (n=6/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day for 7 days	NOAEL= 1000 (M)	No effects on adrenal gland weight or plasma corticosterone	(Zhang et al., 2013)	High
Endocrine	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on organ weights or histopathology	(Kim et al., 1999a)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Endocrine	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on organ weights or histopathology	(Ichihara et al., 2000a ; Ichihara et al., 2000b)	High
Endocrine	Subchronic	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	NOAEL= 800 (F)	No effects on organ weights or histopathology	(Yamada et al., 2003)	High
Endocrine	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on organ weights or histopathology	(ClinTrials, 1997a)	High
Endocrine	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on organ weights	(NTP, 2011a)	High
Endocrine	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Endocrine	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0/group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 500 (M)	Decreased absolute weights of adrenals and pituitary (F ₁)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Endocrine	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250 (F)	Necrosis of adrenal cortex (moderate to marked)	(NTP, 2011a)	High
Endocrine	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Gastro-intestinal	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on histopathology	(ClinTrials, 1997a)	High
Gastro-intestinal	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology	(NTP, 2011a)	High
Gastro-intestinal	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Gastro-intestinal	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Gastro-intestinal	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Hemato-logical	Acute	Rat, M (n=10/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	NOAEL= 8500 (M)	No effects on hematology parameters	(Elf Atochem, 1997)	N/A
Hemato-logical	Short-term	Rat (n=20/group)	Inhalation	0, 398, 984 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	NOAEL= 398	Decreased erythrocyte parameters	(ClinTrials, 1997b)	N/A
Hemato-logical	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/ week for 5 or 7 weeks	LOAEL= 1000 (M)	Decreased mean corpuscular volume	(Yu et al., 2001)	Medium

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Hematological	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 300	Decreased WBCs, RBCs, hematocrit and MCV; increased Hgb and MCH	(Kim et al., 1999a)	N/A
Hematological	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 400 (M)	Decreased MCHC; increased MCV	(Ichihara et al., 2000b)	High
Hematological	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 400 (F)	Decreased WBC and absolute lymphocytes (at 6 weeks)	(ClinTrials, 1997a)	High
Hematological	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on hematology parameters	(NTP, 2011a)	High
Hematological	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on hematology parameters	(NTP, 2011a)	High
Immune	Short-term/ Subchronic	Rat, F344/N, F (n=8/group)	Inhalation, whole body, vapor	0, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 4 or 10 weeks	NOAEL= 500 (F)	Decreased spleen IgM response to SRBC; decreased T cells	(Anderson et al., 2010)	Medium
Immune	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on histopathology (thymus and spleen)	(Kim et al., 1999a)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Immune	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on organ weights or histopathology (spleen and thymus)	(Ichihara et al., 2000b)	High
Immune	Subchronic	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	NOAEL= 800 (F)	No effects or organ weights or histopathology (spleen and thymus)	(Yamada et al., 2003)	High
Immune	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No immune effects	(ClinTrials, 1997a)	High
Immune	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology (lymphoreticular tissues)	(NTP, 2011a)	High
Immune	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology (lymphoreticular tissues)	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Immune	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50 F0/group; 49-50 F1 adults/group; 41-47 F1 weanlings/group; 30-44 F2 weanlings/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 750	Increased brown pigment in the spleen	(WIL Research, 2001)	High
Immune	Short-term/Subchronic	Mouse, B6C3F1, F (n=5-8/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 4 or 10 weeks	LOAEL= 125 (F)	Decreased spleen IgM response to SRBC	(Anderson et al., 2010)	Medium
Immune	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology (lymphoreticular tissues)	(NTP, 2011a)	High
Immune	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology (lymphoreticular tissues)	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Immune	Acute	Mouse, BALB/c, F (n=5/group)	Oral, gavage (corn oil vehicle)	0, 200, 500 or 1000 mg/kg	Single exposure; necropsy after 6, 12, 24 or 48 hours	LOAEL= 200 mg/kg (F)	Reduced antibody response to T-antigen; used for weight of evidence; no route-to-route extrapolation	(Lee et al., 2007)	N/A
Hepatic	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	NOAEL= 125 (M)	Increased absolute and relative liver weights	(NTP, 2011a)	High
Hepatic	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/week for 5 or 7 weeks	LOAEL= 1000 (M)	No effects on histopathology	(Yu et al., 2001)	Medium
Hepatic	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/week for 8 weeks	NOAEL= 50 (M)	Increased relative liver weight	(Kim et al., 1999b)	N/A
Hepatic	Subchronic	Rat, Wistar, M (n=10/group)	Inhalation, whole body, vapor	0, 700 or 1500 ppm	6 hours/day, 5 days/ week for 4 and 12 weeks	LOAEL= 700 (M)	Decreased plasma ALT activity	(Fueta et al., 2002b)	N/A
Hepatic	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 400 (M)	Increased absolute and relative liver weight	(Ichihara et al., 2000b)	High
Hepatic	Subchronic	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	LOAEL= 1016 mg/m3 (F)	Increased absolute and relative liver weight	(Yamada et al., 2003)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Hepatic	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	LOAEL= 100 (M)	Increased incidence of cytoplasmic vacuolization	(ClinTrials, 1997a)	High
Hepatic	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 125 (F)	Increased liver weight; increased incidence of cytoplasmic vacuolization	(NTP, 2011a)	High
Hepatic	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Hepatic	Reproductive/Developmental	Rat, CrI:CD(SD)IG S BR, M/F (n=50 F0/group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice	NOAEL= 100 (M)	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	(WIL Research, 2001)	High
Hepatic	Reproductive/Developmental	Rat, CrI:CD(SD)IG S BR, M/F (n=50 F0/group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	NOAEL= 250 (F)	Increased incidence of vacuolization of centrilobular hepatocytes (F ₀)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Hepatic	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 250 (M)	Centrilobular necrosis (mild to moderate)	(NTP, 2011a)	High
Hepatic	Short-term	Mouse, C57BL/6J, DBA/2J and BALB/cA, M (n=6/strain/group)	Inhalation, whole body, vapor	0, 50, 110 or 250 ppm	8 hours/day, 7 days/ week for 4 weeks	LOAEL= 50 (M)	Hepatocellular degeneration and focal necrosis	(Liu et al., 2009)	High
Hepatic	Short-term	Mouse, C57BL/6J (<i>Nrf2</i> -null and wild-type), M (n=8/genotype/group)	Inhalation, whole body, vapor	0, 100 or 300 ppm	8 hours/day, 7 days/ week for 4 weeks	LOAEL= 100 (M)	Necrosis and hepatocyte degeneration	(Liu et al., 2010)	N/A
Hepatic	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250	Necrosis and hepatocyte degeneration	(NTP, 2011a)	High
Hepatic	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Hepatic	Chronic	Rat, M (n=10/group)	Oral	0, 200, 400 or 800 mg/kg-day	16 weeks	LOAEL= 200 mg/kg-day (M)	Increased relative liver weight; used for weight of evidence; no route-to-route extrapolation	(Wang et al., 2012)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Hepatic	Acute	Mouse, BALB/c, F (n=5/group)	Oral, gavage (corn oil vehicle)	0, 200, 500 or 1000 mg/kg	Single exposure; necropsy after 6, 12, 24 or 48 hours	NOAEL= 200 mg/kg (F)	Centrilobular hepatocyte swelling	(Lee et al., 2007)	N/A
Metabolic	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on electrolyte or glucose levels	(ClinTrials, 1997a)	High
Musculo-skeletal	Subchronic	Rat, Wistar, M (n=2/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 400 (M)	Alteration in soleus muscle myofilaments	(Ichihara et al., 2000a)	High
Musculo-skeletal	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on histopathology	(ClinTrials, 1997a)	High
Musculo-skeletal	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology	(NTP, 2011a)	High
Musculo-skeletal	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Musculo-skeletal	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Musculo-skeletal	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Neurological	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 50 (M)	Decreased relative brain weight	(Kim et al., 1999a)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Acute	Rat, Sprague-Dawley, M/F (n=10/group)	Inhalation, whole body, vapor	0, 11,000, 13,000, 15,000 or 17,000 ppm	4 hours	LOAEL= 11,000	Ataxia, lacrimation, decreased activity	(Kim et al., 1999a)	N/A
Neurological	Short-term	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day for 7 days	LOAEL= 200 (M)	Altered neuron-specific proteins and ROS	(Wang et al., 2002)	N/A
Neurological	Short-term	Rat, Wistar, M (n=12/group)	Inhalation, whole body, vapor	0, 200, 400, 800 or 1000 ppm	8 hours/day for 7 or 28 days	LOAEL= 200 (M)	Decreased hippocampal glucocorticoid receptor expression	(Zhang et al., 2013)	High
Neurological	Short-term	Rat, Wistar, M (n=6-13/exposure group; n=6-10/control group)	Inhalation, whole body, vapor	0 or 1500 ppm	6 hours/day, 5 days/ week for 1, 3 or 4 weeks	LOAEL= 1500 (M)	Paired pulse disinhibition (DG and CA1 pyramidal neuron); neuronal dysfunction in dentate gyrus; convulsive behaviors	(Fueta et al., 2002a ; Fueta et al., 2002b)	N/A
Neurological	Short-term	Rat, F344, M (n=9/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 1 or 4 weeks	LOAEL= 400 (M)	Altered regulation and expression of hippocampal proteins	(Huang et al., 2011)	N/A
Neurological	Short-term	Rat, F344, M (n=9/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 1 or 4 weeks	LOAEL= 400 (M)	Increased hippocampal ROS levels	(Huang et al., 2012)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Short-term	Rat, F344, M (n=9/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 1 or 4 weeks	LOAEL= 400 (M)	Altered regulation and expression of hippocampal proteins	(Huang et al., 2015)	N/A
Neurological	Short-term	Rat, F344, M (n=2/group)	Inhalation, whole body, vapor	0, 10, 50 or 200 ppm	8 hours/day, 7 days/week for 3 weeks	NOAEL= 10 (M)	Increased spontaneous locomotor activity	(Honma et al., 2003)	High
Neurological	Short-term	Rat, F344, M (n=5/group)	Inhalation, whole body, vapor	0, 10, 50, 200 or 1000 ppm	8 hours/day, 7 days/ week for 3 weeks	NOAEL= 50 (M)	Decreased time hanging from a suspended bar	(Honma et al., 2003)	High
Neurological	Short-term	Rat, F344, M (n=4-5/group)	Inhalation, whole body, vapor	0, 50, 200 or 1000 ppm	8 hours/day, 7 days/ week for 3 weeks	LOAEL= 50 (M)	Altered neurotransmitter and metabolites	(Suda et al., 2008)	N/A
Neurological	Short-term	Rat (n=20/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	LOAEL= 398	Histo-pathological abnormalities in the CNS	(ClinTrials, 1997b)	N/A
Neurological	Short-term	Rat, F344, M (n=9/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 4 weeks	NOAEL= 400 (M)	Changes in the mRNA expression of serotonin, dopamine, and GABA receptors	(Mohideen et al., 2009)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Short-term	Rat, F344, M (n=6/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/ week for 4 weeks	NOAEL= 400 (M)	Decreased density of noradrenergic axons in frontal cortex and amygdala	(Mohideen et al., 2011)	N/A
Neurological	Short-term	Rat, F344, M (n=12/group)	Inhalation, whole body, vapor	0, 400 or 1000 ppm	8 hours/day, 7 days/week for 4 weeks	LOAEL= 400 (M)	Increased astrogliosis	(Mohideen et al., 2013)	High
Neurological	Short-term	Rat, Wistar-ST, M (n=12/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day, 7 days/ week for 4 weeks	LOAEL= 400 (M)	Morphological changes in cerebellar microglia and increased ROS	(Subramanian et al., 2012)	N/A
Neurological	Short-term	Rat, M (n=8/group)	Inhalation, whole body	0 or 1500 ppm	6 hours/day, 5 days/ week for 4 weeks	LOAEL= 1500 (M)	Decreased activity, behavioral abnormalities, movement disorders, histopathological changes in Purkinje cells	(Ohnishi et al., 1999)	N/A
Neurological	Short-term/ Subchronic	Rat, Wistar, M (n=7-14/group)	Inhalation, whole body, vapor	0 or 700pm	6 hours/day, 5 days/week for 4, 8 or 12 weeks	LOAEL= 700 (M)	Paired pulse disinhibition in ex vivo hippocampal slices (DG and CA1 pyramidal neuron)	(Fueta et al., 2004)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/ week for 5 or 7 weeks	LOAEL= 1000 (M)	Movement disorder, altered motor nerve conduction velocity and distal nerve latency in tail nerve); histo-pathological changes to CNS and PNS	(Yu et al., 2001)	Medium
Neurological	Subchronic	Rat, Wistar, M (n=24/group)	Inhalation, whole body, vapor	0, 400, 800 or 1000 ppm	8 hours/day, 7 days/ week for 6 weeks	NOAEL= 400 (M)	Movement disorder, decreased hind limb grip strength	(Banu et al., 2007)	N/A
Neurological	Subchronic	Rat, Wistar M (n=12/group)	Inhalation, whole body, vapor	0 or 700 ppm	6 hours/day, 5 days/ week for 8 weeks	LOAEL= 700 (M)	Paired pulse disinhibition in ex vivo hippocampal slices (DG and CA1 pyramidal neuron); increased protein kinase activities	(Fueta et al., 2002a)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Subchronic	Rat, Wistar, M (n=6/group)	Inhalation, whole body, vapor	0, 200 or 400 ppm	6 hours/day, 5 days/ week for 8 or 12 weeks	NOAEL= 200 (M)	Paired pulse disinhibition in ex vivo hippocampal slices (DG and CA1 pyramidal neuron)	(Fueta et al., 2007)	Medium
Neurological	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on brain histopathology	(Kim et al., 1999a)	N/A
Neurological	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	LOAEL= 200 (M)	Decreased hind limb grip strength	(Ichihara et al., 2000a)	High
Neurological	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	LOAEL= 200 (M)	Altered neuron-specific proteins and increased ROS	(Wang et al., 2003)	N/A
Neurological	Subchronic	Rat, Wistar, M (n=6/group)	Inhalation, whole body, vapor	0 or 400 ppm	6 hours/day, 5 days/ week for 12 weeks	LOAEL= 400 (M)	Changes in gene expression of anti-apoptotic proteins in astrocytes	(Yoshida et al., 2007)	N/A
Neurological	Subchronic	Rat, Wistar, M (n=8/group)	Inhalation, whole body, vapor	0 or 400 ppm	6 hours/day, 5 days/ week for 12 weeks	LOAEL= 400 (M)	Decreased paired pulse inhibition in ex vivo hippocampal slices (dentate gyrus)	(Ueno et al., 2007)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No changes based on functional observational battery, motor activity, organ weight, or histopathology	(ClinTrials, 1997a)	High
Neurological	Chronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 200, 500 or 1250 ppm	6 hours/day, 5 days/week for 13 weeks	NOAEL= 1250	No effects histopathology of central or peripheral nervous tissues	(Sohn et al., 2002)	N/A
Neurological	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	NOAEL= 1000	Hindlimb splay	(NTP, 2011a)	High
Neurological	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects	(NTP, 2011a)	High
Neurological	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group; 41-47 F1 weanlings/group; 30-44 F2 weanlings/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 100	Decreased brain weight (F ₀)	(WIL Research, 2001)	High
Neurological	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50/group/generation)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	LOAEL= 100 (M)	Decreased brain weight (weanling and adult F ₁)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Reproductive/Developmental	Rat, Crl:CD(SD)IGS BR, M/F (n=50 F0 /group; 49-50 F1 adults/group; 41-47 F1 weanlings/group; 30-44 F2 weanlings/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 250	Decreased brain weight (weanling F ₂)	(WIL Research, 2001)	High
Neurological	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.1 hours/day, 5 days/week for 17 days	NOAEL= 2000	No effects	(NTP, 2011a)	High
Neurological	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects	(NTP, 2011a)	High
Neurological	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Neurological	Short-term	Rat, Wistar, M (n=14/group)	Oral, gavage	0, 100, 200, 400 or 800 mg/kg-day	12 days	LOAEL= 100 mg/kg-day (M)	Impaired spatial learning and memory; neuron loss in prelimbic cortex; increased ROS in cerebral cortex	(Guo et al., 2015)	High
Neurological	Short-term	Rat, Wistar, M (n=10/group)	Oral, gavage (corn oil vehicle)	0, 200, 400 or 800 mg/kg-day	12 days	LOAEL= 200 mg/kg-day (M)	Impaired spatial learning and memory. Used for weight of evidence	(Zhong et al., 2013)	Low
Neurological	Chronic	Rat, M (n=10/group)	Oral	0, 200, 400 or 800 mg/kg-day	16 weeks	LOAEL= 200 mg/kg-day (M)	Decreased hindlimb grip strength; increased gait score; used for weight of evidence; no route-to-route extrapolation	(Wang et al., 2012)	N/A
Neurological	Short-term	Rat, Wistar, M (n=7-9/group)	Sub-cutaneous	0, 3.7 or 11 mmol/kg-day	4 weeks	LOAEL= 3.7 mmol/kg-day (M)	Increased tail motor nerve latency	(Zhao et al., 1999)	N/A
Ocular	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on histopathology	(ClinTrials, 1997a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Ocular	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on histopathology	(NTP, 2011a)	High
Ocular	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Ocular	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Ocular	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology	(NTP, 2011a)	High
Renal	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	LOAEL= 125 (F)	Increased relative kidney weight	(NTP, 2011a)	High
Renal	Short-term	Rat (n=20/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	NOAEL= 398	Changes in BUN, total bilirubin, and total protein levels	(ClinTrials, 1997b)	N/A
Renal	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/week for 5 or 7 weeks	NOAEL= 1000 (M)	No effects on histopathology	(Yu et al., 2001)	Medium
Renal	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50 to 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 300	Decreased urobilinogen (males); increased bilirubin (females)	(Kim et al., 1999a)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Renal	Reproductive	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on kidney weight or histopathology	(Ichihara et al., 2000b)	High
Renal	Reproductive	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	LOAEL= 200 (F)	Increased absolute and relative kidney weight	(Yamada et al., 2003)	High
Renal	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600 (M)	No effects on urinalysis parameters, or organ weights	(ClinTrials, 1997a)	High
Renal	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 500 (F)	Increased absolute and relative kidney weights	(NTP, 2011a)	High
Renal	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology	(NTP, 2011a)	High
Renal	Reproductive/Developmental	Rat, CrI:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100 to 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice	NOAEL = 100 (M)	Increased incidence of pelvic mineralization (F ₀)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Renal	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	NOAEL = 100 (F)	Increased incidence of pelvic mineralization (F ₀)	(WIL Research, 2001)	High
Renal	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 500 (F)	Increased absolute and relative kidney weights	(NTP, 2011a)	High
Renal	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250 (F)	Increased absolute and relative kidney weights	(NTP, 2011a)	High
Renal	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 350 (F)	No effects on histopathology	(NTP, 2011a)	High
Reproductive	Acute	Rat, M (n=5/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	NOAEL= 8500 (M)	No effects on histopathology of the testes	(Elf Atochem, 1997)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Reproductive	Acute Dominant Lethal Assay	Rats, M (n=15/group)	Oral	0, 400 mg/kg/day	1x daily/for 5 days; followed by mating for 8 consecutive weeks	LOAEL= 400 (M)	Increased implantation loss at week 8; no increase in dominant mutation index	Saito-Suzuki et al., 1982	N/A
Reproductive	Short-term	Rat, F344, F (n=7-8/group)	Inhalation, whole body, vapor	50, 200 or 1000 ppm	8 hours/day, 7 days/ week for 3 weeks	NOAEL= 1000 (F)	No effects on number of days per estrous cycle or ovary and uterus weights	(Sekiguchi et al., 2002)	N/A
Reproductive	Short-term	Rat, M (n=10/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	NOAEL= 1000 (M)	Microscopic lesions in male reproductive system	(ClinTrials, 1997b)	N/A
Reproductive	Subchronic	Rat, Wistar, M (n=24/group)	Inhalation, whole body, vapor	400, 800 or 1000 ppm	8 hours/day, 7 days/ week for 6 weeks	LOAEL= 400 (M)	Decreased epididymal sperm count	(Banu et al., 2007)	N/A
Reproductive	Subchronic	Rat, Wistar, M (n=9/group)	Inhalation, whole body, vapor	0 or 1000 ppm	8 hours/day, 7 days/ week for 5 or 7 weeks	NOAEL= 1000 (M)	No effects on testis histopathology	(Yu et al., 2001)	Medium
Reproductive	Reproductive	Rat, Wistar, F (n=10/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for up to 12 weeks	LOAEL= 200 (F)	Decreased number of antral follicles	(Yamada et al., 2003)	High
Reproductive	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	50-1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 300	Increased relative ovary weight	(Kim et al., 1999a)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Reproductive	Reproductive	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	LOAEL = 200 (M)	Decreased relative seminal vesicle weight	(Ichihara et al., 2000b)	High
Reproductive	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on organ weights	(ClinTrials, 1997a)	High
Reproductive	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	LOAEL= 250 (M)	Decreased sperm motility	(NTP, 2011a)	High
Reproductive	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	LOAEL= 250 (F)	Alterations in estrous cycles	(NTP, 2011a)	High
Reproductive	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 500	No effects on histopathology of reproductive organs	(NTP, 2011a)	High
Reproductive	Reproductive/ Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice	NOAEL= 250 (M)	Decreased percent motile sperm (F ₀)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Reproductive	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice	NOAEL= 250 (M)	Decreased percent normal sperm morphology (F ₀)	(WIL Research, 2001)	High
Reproductive	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice	NOAEL= 100 (M)	Decreased absolute prostate weight (F ₀)	(WIL Research, 2001)	High
Reproductive	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until GD 20; from PND 5 until weaning of offspring (~PND 21)	NOAEL= 250 (F)	Increase in estrous cycle length (F ₀)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Reproductive	Short-term	Mouse, C57BL/6J, DBA/2J and BALB/cA, M (n=6/strain/group)	Inhalation, whole body, vapor	0, 50, 110 or 250 ppm	8 hours/day, 7 days/ week for 4 weeks	LOAEL= 50 (M)	Decreased sperm count and motility and/or increased abnormal sperm	(Liu et al., 2009)	High
Reproductive	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/ week for 14 weeks	NOAEL= 125 (M)	Decreased epididymis weight and sperm motility	(NTP, 2011a)	High
Reproductive	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	LOAEL= 125 (F)	Alterations in estrous cycles	(NTP, 2011a)	High
Reproductive	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	NOAEL= 250	No effects on histopathology of reproductive organs	(NTP, 2011a)	High
Reproductive	Short-term	Rat, Sprague-Dawley, M (n=7/group)	Intra-peritoneal	0 or 1000 mg/kg-day	14 days	LOAEL= 1000 (M)	Decreased epididymal sperm count; decreased epididymis and prostate + seminal vesicle weights	(Xin et al., 2010)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Respiratory	Acute	Rat (n=10/group)	Inhalation	0, 6040, 7000, 7400 or 8500 ppm	4 hours	NOAEL= 6040	Pulmonary edema and emphysema	(Elf Atochem, 1997)	N/A
Respiratory	Short-term	Rat, F344/N, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 100 or 2000 ppm	6.2 hours/day, 5 days/week for 16 days	NOAEL= 250 (M)	Nasal lesions (including suppurative inflammation and respiratory epithelial necrosis)	(NTP, 2011a)	High
Respiratory	Short-term	Rat (n=20/group)	Inhalation	0, 398, 994 or 1590 ppm	6 hours/day, 5 days/ week for 4 weeks	NOAEL= 994	Histo-pathological changes in nasal cavities	(ClinTrials, 1997b)	N/A
Respiratory	Subchronic	Rat, Wistar, M (n=8-9/group)	Inhalation, whole body, vapor	0, 200, 400 or 800 ppm	8 hours/day, 7 days/ week for 12 weeks	NOAEL= 800 (M)	No effects on lung weight or histopathology	(Ichihara et al., 2000b)	High
Respiratory	Subchronic	Rat, Sprague-Dawley, M/F (n=20/group)	Inhalation, whole body, vapor	0, 50, 300 or 1800 ppm	6 hours/day, 5 days/ week for 8 weeks	NOAEL= 1800	No effects on lung weight or histopathology	(Kim et al., 1999a)	N/A
Respiratory	Chronic	Rat, Albino, M/F (n=30/group)	Inhalation, whole body, vapor	0, 100, 200, 400 or 600 ppm	6 hours/day, 5 days/ week for 13 weeks	NOAEL= 600	No effects on lung weight or histopathology	(ClinTrials, 1997a)	High
Respiratory	Chronic	Rat, F344/N, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250, 500 or 1000 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 1000	No effects on lung weight or histopathology	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Respiratory	Chronic	Rat, F344/N, M/F (n=100/group)	Inhalation, whole body, vapor	0, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 105 weeks	LOAEL= 635 mg/m ³	Chronic active nasal inflammation and squamous metaplasia in the larynx	(NTP, 2011a)	High
Respiratory	Reproductive/Developmental	Rat, CrI:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250, 500 or 750 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in F ₀ males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in F ₀ females	NOAEL= 750	No effects on lung weight or histopathology	(WIL Research, 2001)	High
Respiratory	Short-term	Mouse, B6C3F1, M/F (n=10/group)	Inhalation, whole body, vapor	0, 125, 250, 500, 1000 or 2000 ppm	6.2 hours/day, 5 days/week for 17 days	NOAEL= 250	Lesions in the lung and nose	(NTP, 2011a)	High
Respiratory	Chronic	Mouse, B6C3F1, M/F (n=20/group)	Inhalation, whole body, vapor	0, 62.5, 125, 250 or 500 ppm	6.2 hours/day, 5 days/week for 14 weeks	NOAEL= 250	Cytoplasmic vacuolization in the nose, larynx, trachea, and lung	(NTP, 2011a)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Respiratory	Chronic	Mouse, B6C3F1, M/F (n=100/group)	Inhalation, whole body, vapor	0, 62.5, 125 or 250 ppm	6.2 hours/day, 5 days/week for 105 weeks	LOAEL= 62.5	Histo-pathological lesions in the nasal respiratory epithelium, larynx, trachea, and bronchioles	(NTP, 2011a)	High
Developmental Effects	Developmental	Rat, Wistar-Imamichi, F (n=10/group)	Inhalation, whole body, vapor	0, 100, 400 or 800 ppm	8 hours/day during gestation (GDs 0-21) and lactation (PNDs 1-21)	NOAEL= 100	Decreased survival during lactation	(Furuhashi et al., 2006)	N/A
Developmental Effects	Developmental	Rat, Albino Crl:CD(SD)IG S BR, F (n=10/group)	Inhalation, whole body, vapor	0, 100, 199, 598 or 996 ppm	6 hours/day on GDs 6-19; PNDs 4-20	NOAEL= 199	Decreased body weight gain in pups	(Huntingdon Life Sciences, 1999)	N/A
Developmental Effects	Developmental	Rat (n=25/group)	Inhalation	0, 103, 503 or 1005 ppm	6 hours/day on GDs 6-19; PNDs 4-20	LOAEL = 103	Decreased fetal weight	(Huntingdon Life Sciences, 2001)	N/A

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Developmental Effects	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250 or 500 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL= 250	Decreased live litter size (F ₁ females)	(WIL Research, 2001)	High
Developmental Effects	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250 or 500 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL = 100	Decreased pup body weights (F ₁ PND 28 males)	(WIL Research, 2001)	High

Target Organ/System	Study Type	Species/Strain/Sex (Number/group) ¹	Exposure Route	Doses/Concentrations ²	Duration ³	Effect Dose/Concentration (ppm or mg/kg-day) ⁴ (Sex)	Effect ⁵	Reference ⁶	Data Quality Evaluation ^{7,8}
Developmental Effects	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250 or 500 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL = 250	Decreased pup body weights (F ₂ PNDs 14 and 21 males)	(WIL Research, 2001)	High
Developmental Effects	Reproductive/Developmental	Rat, Crl:CD(SD)IG S BR, M/F (n=50 F0 /group; 49-50 F1 adults/group)	Inhalation, whole body, vapor	0, 100, 250 or 500 ppm	6 hours/day during pre-mating (≥70 days), throughout mating, and until sacrifice in males; or until GD 20 and from PND 5 until weaning of offspring (~PND 21) in females	NOAEL = 250	Decreased pup body weights (F ₂ PNDs 14 and 21 females)	(WIL Research, 2001)	High

¹Species/strain, sex of animals included in the study.

²Doses and concentrations – values were reported in [2016 Draft Risk Assessment \(U.S. EPA, 2016c\)](#) for 1-BP.

³Acute exposures defined as those occurring within a single day (<24 hr). Short-term exposures are defined as 1-30 days. Subchronic exposures are defined as 30-90 days. Chronic exposures are defined as >90 days, or 10% or more of a lifetime.

⁴ Units are mg/m³ for inhalation exposure and mg/kg-day for oral exposure; sex is identified if one sex has a lower POD; this includes only the PODs identified by the study authors.

⁵The effect(s) listed were the most sensitive effects observed for that target organ/system in that study (*i.e.*, the effect(s) upon which the POD was based).

⁶This column lists the primary reference for the reported data.

⁷Information included in this column is the result of the data quality evaluation for all acceptable studies (those with an overall rating of high, medium or low). Unacceptable studies are not included in this table.

⁸N/A: Only key and supporting studies carried forward for dose-response analysis in the [2016 Draft Risk Assessment \(U.S. EPA, 2016c\)](#) for 1-BP, in addition to any new studies since that time, went through systematic review.

J.5 Carcinogenicity and Mutagenicity

There are no epidemiological studies on the effects of 1-BP exposure on human cancer.

The carcinogenicity of 1-BP has been studied in rats and mice in a two-year bioassay by the National Toxicology Program ([NTP, 2011a](#)). Groups of 50 male and 50 female rats and mice were exposed to 1-BP vapor at concentrations of 62.5, 125, or 250 ppm (mice) and 125, 250, or 500 ppm (rats), 6 hours per day, 5 days per week for up to 105 weeks. Similar groups of 50 animals were exposed to clean air in the same inhalation chambers as the control groups. All animals were observed twice daily. Clinical findings were recorded for all animals every 4 weeks through week 93, every 2 weeks thereafter, and at the end of the studies. Rats and mice were weighed initially, weekly for the first 13 weeks, then every 4 weeks through week 93, every 2 weeks thereafter, and at the end of the studies. Complete necropsies and microscopic examinations were performed on all rats and mice.

At the end of the two-year bioassay, there were treatment-related skin tumors in male rats and large intestine tumors in female rats. Significantly increased incidence of lung tumors was found in female mice. Based on increased incidences of tumors in rats and mice, at multiple sites and the occurrence of rare tumors, it has been concluded that there is sufficient evidence of carcinogenicity in experimental animals for 1-BP. Each of these tumor types is described below.

J.5.1 Skin Tumors

In male rats, there were exposure concentration treatment-related increased incidences of keratoacanthoma, keratoacanthoma or squamous cell carcinoma (combined); and keratoacanthoma, basal cell adenoma, basal cell carcinoma, or squamous cell carcinoma (combined). The incidences of keratoacanthoma and of keratoacanthoma or squamous cell carcinoma (combined) in 250 ppm (12%) and 500 ppm (12%) males were significantly increased as compared to the controls (0% and 2%), and exceeded the historical control ranges (0-8%) for inhalation studies. The incidences of keratoacanthoma, basal cell adenoma, basal cell carcinoma, or squamous cell carcinoma (combined) were significantly increased in all exposed groups of males (125 ppm: 14%; 250 ppm: 18%; and 500 ppm: 20%) as compared to the controls (2%) and exceeded the historical control range (0-10%) for inhalation studies. In female rats, there were increased incidences of squamous cell papilloma, keratoacanthoma, basal cell adenoma, or basal cell carcinoma (combined) in the 500 ppm group (8%) as compared to the control (2%). Although the increased incidences were not significant, they exceeded the respective historical control ranges for inhalation studies.

J.5.2 Large Intestine Tumors

Large intestine tumors are rare tumors in the rat. The incidence of adenoma of the large intestine (colon or rectum) in 500 ppm females (5/50, 10%) was significantly greater than that in the controls (0%). The incidences in the 250 ppm (2%) and 500 ppm (4%) groups of females exceeded the historical controls in inhalation studies (0.1%). In 250 (4%) and 500 (2%) ppm males, the incidences of adenoma of the large intestine were slightly increased compared to that in the

controls (0%); although the increases were not statistically significant, the incidence in the 250 ppm group (4%) exceeded the historical control ranges (0-2%) for inhalation studies.

J.5.3 Lung Tumors

In the female mice, there were treatment-related increased incidences of alveolar/bronchiolar adenoma, alveolar/bronchiolar carcinoma, and alveolar/bronchiolar adenoma or carcinoma (combined). The incidence of alveolar/bronchiolar adenoma in 250 ppm females (20%) and the incidences of alveolar/bronchiolar carcinoma in 62.5 ppm (14%) and 125 ppm (10%) females were significantly increased as compared to the controls (0-2%). The incidences of alveolar/bronchiolar adenoma or carcinoma (combined) were significantly increased in all exposed groups (18%, 16% and 28% in low-, mid- and high-dosed groups) as compared to the controls (2%).

J.5.4 Pancreatic Tumors

The evidence that 1-BP exposure was associated with an increased incidence of pancreatic islet adenoma in male rats was equivocal. Although the incidences of pancreatic islet adenoma were significantly increased in all exposed groups compared to the chamber controls (0%, 10%, 8%, 10%), the incidences were within the historical control ranges for inhalation studies (0% to 12%). The incidences of pancreatic islet carcinoma in exposed male rats were not significantly different from that in the chamber controls and were not considered treatment related. The incidences of pancreatic islet adenoma or carcinoma (combined) were significantly increased only in the low-dose (20%) and mid-dose groups (18%) as compared with the chamber controls (6%); only the incidence in the low-dose group (20%) exceeded the historical control ranges for inhalation studies (6% to 18%).

J.5.5 Malignant Mesothelioma

There were increased incidences of malignant mesothelioma in male rats exposed to 1-BP as compared to the chamber controls: control, 0%; low-dose, 4%; mid-dose, 4%; and high-dose, 8%. The incidence of malignant mesothelioma in high-dose group (8%) was significantly greater than that of the chamber controls (0%) and exceeded that of the historical controls (0-6%) in inhalation studies. The overall strength of this evidence was considered equivocal because the increased incidence in the high-dose (500 ppm) group was barely outside the historical control range (0% to 6%).

Under the conditions of these 2-year inhalation studies, there was clear evidence of carcinogenic activity of 1-BP in female F344/N rats based on increased incidences of adenoma of the large intestine. Increased incidences of skin neoplasms may also have been related to 1-BP exposure. There was some evidence of carcinogenic activity of 1-BP in male F344/N rats based on the increased incidences of epithelial neoplasms of the skin (keratoacanthoma, squamous cell carcinoma, and basal cell neoplasms). Increased incidences of malignant mesothelioma and pancreatic islet adenoma and carcinoma (combined) may also have been related to 1-BP exposure. There was clear evidence of carcinogenic activity of 1-BP in female B6C3F1 mice based on increased incidences of alveolar/bronchiolar neoplasms. There was no evidence of carcinogenic activity of 1-BP in male B6C3F1 mice exposed to concentrations of 62.5, 125, or 250 ppm 1-BP.

Based on increased incidences of tumors in rats and mice, at multiple sites and the occurrence of rare tumors, it has been concluded that there is sufficient evidence of carcinogenicity in experimental animals for 1-BP. The compound has been considered to be “reasonably to be anticipated as a human carcinogen” and will be listed in the next issue of Report on Carcinogens of the National Toxicology Program ([NTP, 2013a](#)).

The tumor data on the skin, large intestine and lung in male and female rats and female mice (Table_Apx J-3) may be used for quantitative assessment of the potential risk of humans exposed to 1-BP.

Table_Apx J-3. Tumors induced by 1-BP in Rats and Mice

Animal	Tumor	Concentration (ppm)	Incidence
F344/N rats, male	Skin (keratoacanthoma, squamous-cell carcinoma, basal-cell adenoma or carcinoma combined)	0	1/50 (2%)
		125	7/50* (14%)
		250	9/50** (18%)
		500	10/50*** (20%)
		Trend	$p=0.003$
F344/N rats, female	Large intestine (colon or rectum adenoma)	0	0/50 (0%)
		125	1/50 (2%)
		250	2/50 (4%)
		500	5/50* (10%)
		Trend	$p=0.004$
B6C3F1 mice, female	Lung (alveolar /bronchiolar adenoma or carcinoma combined)	0	1/50 (2%)
		62.5	9/50** (18%)
		125	8/50* (16%)
		250	14/50*** (28%)
		Trend	$p<0.001$
* $p\leq 0.05$; ** $p\leq 0.01$; *** $p\leq 0.001$			

J.5.6 Genotoxicity

1-BP has been shown to bind covalently to DNA to form N⁷-propyl guanine adducts in an *in vitro* system using 2’deoxyguanosine and calf thymus DNA, with adduct formation increasing in relation to 1-BP concentration ([Thapa et al., 2016](#)). In another study with calf thymus DNA ([Lee et al., 2007](#)), adduct formation was rapid (peaked within 2 hr) and was not affected by addition of liver homogenates, suggesting that the adducts were formed directly by 1-BP. *In vivo*, 1-BP produced N⁷-propyl guanine adducts in liver > spleen > kidney > lung > testis of treated rats ([Nepal et al., 2019](#)). Adduct levels in all of these tissues increased with dose and number of days of treatment. No adducts were found in the heart with any dosing regimen tested. These studies show that 1-BP can interact with DNA to form N⁷-propyl guanine adducts, but there is no established relationship between N⁷-propyl guanine adducts and mutagenic effects (*e.g.*, see Boysen ([2009](#))).

Mixed results have been reported in genotoxicity tests using bacteria. 1-BP was mutagenic in a dose-dependent manner in *Salmonella typhimurium* (*S. typhimurium*) strains TA100 and TA1535 when the assay was conducted using closed chambers/desiccators specifically designed for testing volatile substances ([Barber et al., 1981](#)). The data suggest that 1-BP may be a direct-acting mutagen since similar responses were observed both with and without metabolic activation. An NTP peer review committee considered Barber ([1981](#)) to be a well conducted study ([NTP, 2013a](#)). A second study using a closed test system found no evidence of mutagenicity ([BioReliance, 2015](#)), but the specific method used to achieve the closed system in this study may have been less efficient. See Appendix J.5.7 below for a detailed comparison of these two studies.

A number of other studies reported negative responses in *S. typhimurium* and *Escherichia coli* (*E. coli*) ([NTP, 2011a](#); [Kim et al., 1998](#); [Elf Atochem, 1993b](#)). While these tests may not have been conducted in closed systems, the occurrence of cytotoxicity at high concentrations in the ([NTP, 2011a](#); [Kim et al., 1998](#)) study suggests that sufficient quantities of 1-BP were present to induce that effect, and therefore, that the lack of observed mutagenicity in the study did not result from lack of 1-BP in the test medium, but rather from lack of mutagenic activity of 1-BP.

1-BP was shown to induce base-pair mutations in the L5178Y mouse lymphoma cell assay, with and without S9 metabolic activation ([Elf Atochem, 1996b](#)). Using the comet assay, ([Toraason et al., 2006](#)) demonstrated DNA damage in human leukocytes exposed to 1 mM 1-BP *in vitro*; there was also equivocal evidence of DNA damage in leukocytes from workers exposed to 1-BP on the job. In contrast to the positive *in vitro* studies, negative results were reported with *in vivo* micronucleus assays in mice exposed to 1-BP via intraperitoneal (ip) injection ([Kim et al., 1998](#)), and in rodents exposed via inhalation ([NTP, 2011a](#); [Elf Atochem, 1995](#)). A compilation of *in vivo* micronucleus data by ([Benigni et al., 2012](#)) showed a low correlation between *in vivo* micronucleus data and carcinogenicity, however, suggesting a potential for “false negative” predictions. 1-BP also produced negative results in dominant lethal mutation assays conducted in ICR mice ([Yu et al., 2008](#)) and Sprague-Dawley rats ([Saito-Suzuki et al., 1982](#)).

Mutation frequencies at the *cII* gene in the liver, lung, and colon were determined in groups of female B6C3F1 heterozygous transgenic Big Blue® mice (mutations were evaluated in 6 mice/group) that were exposed by whole-body inhalation to target 1-BP vapor concentrations of 0 (concurrent control), 62.5, 125, or 250 ppm (mean measured concentrations of 0, 62.8, 125, and 258 ppm, respectively) for 6 hours/day, either 5 or 7 days/week for 4 weeks ([Stelljes et al., 2019](#); [Young, 2016](#)). Liver, lung, and colon tissues were collected for DNA isolation and determination of mutation frequencies on the third day after the final exposure. Compared with controls, groups exposed to 1-BP showed no statistically significant elevations in mutation frequencies at the *cII* gene in liver, lung, or colon and showed no treatment-related effects on clinical observations, body weights, food consumption, or organ weights. Mutation frequencies in the liver, lung, and colon from concurrent negative control mice were comparable to values found in historical negative controls. In a positive control group that received 40 mg/kg of the direct-acting mutagen ethyl nitrosourea by gavage on study days 1, 2, and 3, mutation frequencies on study day 31 were statistically significantly elevated in liver, lung, and colon, thus demonstrating the ability of this test system to detect mutations. Of note, despite the negative results it is unclear whether the

protocol was fully adequate to address the intended outcome. The maximum tolerated dose was not evaluated, and the sensitivity of the test system is dependent on the duration of the post-exposure observation period which may be insufficient for slower-dividing tissues.

Mixed results have been reported in genotoxicity tests using bacteria. 1-BP was mutagenic in a dose-dependent manner in *Salmonella typhimurium* (*S. typhimurium*) strains TA100 and TA1535 when the assay was conducted using closed chambers/desiccators specifically designed for testing volatile substances ([Barber et al., 1981](#)). The data suggest that 1-BP may be a direct-acting mutagen since similar responses were observed both with and without metabolic activation. A number of other studies reported negative responses in *S. typhimurium* and *Escherichia coli* (*E. coli*) but some of these studies were not conducted using the appropriate methodology (*i.e.*, treatment and incubation in a closed chamber) for testing a volatile substance ([NTP, 2011a](#); [Kim et al., 1998](#); [Elf Atochem, 1993b](#)). An NTP peer review committee considered Barber ([1981](#)) to be a well conducted study ([NTP, 2013a](#)).

1-BP was shown to induce base-pair mutations in the L5178Y mouse lymphoma cell assay, with and without S9 metabolic activation ([Elf Atochem, 1996b](#)). Using the comet assay, ([Toraason et al., 2006](#)) demonstrated DNA damage in human leukocytes exposed to 1 mM 1-BP *in vitro*; there was also limited evidence that leukocytes from workers exposed to 1-BP may present risk for increased DNA damage. In contrast to the positive *in vitro* studies, negative results were reported with *in vivo* micronucleus assays in mice exposed to 1-BP via intraperitoneal (ip) injection ([Kim et al., 1998](#)), and in rats exposed via inhalation ([NTP, 2011a](#); [Elf Atochem, 1995](#)). It should be noted, however, that a recent compilation of *in vivo* micronucleus data by ([Benigni et al., 2012](#)) showed a low correlation between *in vivo* micronucleus data and carcinogenicity, suggesting a potential for “false negative” predictions. 1-BP was also produced negative results in dominant lethal mutation assays conducted in ICR mice ([Yu et al., 2008](#)) and Sprague-Dawley rats ([Saito-Suzuki et al., 1982](#)).

Several known or proposed metabolites of 1-BP have been shown to be mutagenic ([NTP, 2014](#); [IARC, 2000, 1994](#)). For example, both glycidol and propylene oxide are mutagenic in bacteria, yeast, *Drosophila*, and mammalian cells. These compounds have also been shown to induce DNA and chromosomal damage in rodent and human cells, and can form DNA adducts *in vitro*. α -Bromohydrin and 3-bromo-1-propanol were mutagenic in the *S. typhimurium* reversion assay, and 3-bromo-1-propanol and 1-bromo-2-propanol induced DNA damage in *E. coli*. The available *in vivo* test results for glycidol indicate that it induces micronucleus formation, but not chromosomal aberrations in mice. Studies of propylene oxide indicated chromosomal damage evidenced by positive responses for micronucleus induction in mouse bone marrow and chromosomal aberration tests; DNA damage was evident in the sister chromatid exchange (SCE) assay.

Table_Apx J-4. Key Genotoxicity Studies on 1-BP

Species (test system) and administration route/ exposure duration (for <i>in vivo</i>)	Endpoint	Results		Reference	Data Quality
		With activation	Without activation		
Cell-free <i>in vitro</i>					
Calf thymus DNA	DNA binding and adduct formation	+	N/A	(Thapa et al., 2016)	High
Prokaryotic organisms:					
<i>S. typhimurium</i> TA98, TA100, TA1535, TA1537, TA1538	Reverse mutation	- (open test system)	- (open test system)	(Barber et al., 1981)	High
<i>S. typhimurium</i> TA100, TA1535	Reverse mutation	+ (closed test system)	+ (closed test system)	(Barber et al., 1981)	High
<i>S. typhimurium</i> TA97, TA98, TA100, TA 1535	Reverse mutation	-	-	(NTP, 2011a)	High
Escherichia coli Wp2 uvrA/pKM101	Reverse mutation	-	-	(NTP, 2011a)	High
<i>S. typhimurium</i> TA98, TA100, TA 1535, and TA 1537	Reverse mutation	-	-	(BioReliance, 2015)	Medium
Escherichia coli Wp2 uvrA/pKM101	Reverse mutation	-	-	(BioReliance, 2015)	Medium
Mammalian cells <i>in vitro</i>:					
Human hepatoma cell-line (HepG2)	DNA damage and repair, single strand breaks	-	N/A	(Hasspieler et al., 2006)	High
Human hepatoma cell-line (HepG2)	DNA damage and repair, repair activity	-	N/A	(Hasspieler et al., 2006)	High
Mouse lymphoma cell-line (L51785Y)	Base-pair mutations	+	+	(Elf Atochem, 1996b)	High
Human leukocyte cells	DNA damage and repair	+	N/A	(Toraason et al., 2006)	High
Mammalian <i>in vivo</i>:					
3-month inhalation study in B6C3F1 mice	Micronucleus assay	-	N/A	(NTP, 2011a)	High
4-week inhalation study in Big Blue® B6C3F1 transgenic mice	Mutation frequencies at <i>cII</i> gene	-	N/A	(Stelljes et al., 2019) (Young, 2016)	Medium
3-day intraperitoneal injection in SD rats	DNA binding and adduct formation	+	N/A	(Nepal et al., 2019)	High
Epidemiological					

Human leukocyte cells	DNA damage and repair	+/-	N/A	(Toraason et al., 2006)	Medium
+ = positive results; - = negative results; +/- = equivocal					

J.5.7 Comparison of Bacterial Reverse Mutation Studies

Two bacterial reverse mutation studies of 1-BP both used test systems characterized as ‘closed’ but yielded different results for mutagenicity. In a study by Barber et al. ([1981](#)), a positive mutagenicity result was observed for 1-BP in *Salmonella typhimurium* strains TA 1535 and TA 100 (but not TA 1537, TA 1538, or TA 98) in the presence and absence of metabolic activation. In contrast, a study by BioReliance ([2015](#)) found no evidence of mutagenicity in *S. typhimurium* strains TA 98, TA 100, TA 1535, and TA 1537 or *Escherichia coli* strain WP2 uvrA (a DNA repair-deficient strain) in the presence or absence of metabolic activation.

In many respects, both studies adhered to OECD TG 471 (Bacterial Reverse Mutation Test ([2019o](#))), although only the BioReliance ([2015](#)) study indicated that it conformed to the test guidelines. However, the procedures outlined in the guideline pertain primarily to standard plate incorporation or preincubation methods; OECD TG 471 ([2019o](#)) notes that certain classes of mutagens (including volatile chemicals, such as 1-BP) are not detected using these methods. In these ‘special cases’, the guideline recommends the use of alternative approaches. The studies by Barber et al. ([1981](#)) and BioReliance ([2015](#)) used different methods in an effort to circumvent issues with respect to the volatility of the test substance.

The primary differences between the two studies were the method of exposure, the duration of exposure of test organisms to 1-BP, methods used to control for the volatility of the test substance, and differences between the studies in maintenance of effective concentrations of 1-BP during test organism exposure. Barber et al. ([1981](#)) indicated that the study followed the standard methods originally described by Ames et al. ([1975](#)); only the method of chemical application was modified. Rather than using a standard plate-incorporation test, Barber designed a chemically inert, closed incubation system to test the mutagenicity of volatile chemicals, applied as a vapor. The test system consisted of several Pyrex containers, each designed to accommodate a metal rack housing up to 12 glass plates. The glass plates were considered chemically inert with respect to adsorption of halogenated hydrocarbons, in contrast to plastic plates. The Pyrex containers were fitted with Teflon tops with valve and septum assemblies. A blank plate, containing only sterile distilled water, was inserted into each test system and was used for measurement of the aqueous 1-BP concentration at the end of exposure. Test plates were prepared by mixing an inoculum of an overnight growth culture (growth phase not reported) with top agar (with or without S9 mix) and pouring the mixture onto a plate containing Vogel-Bonner Medium E and agar. The plates were allowed to solidify at room temperature and then placed onto a stainless-steel rack. The racks filled with plates were placed into the Pyrex containers and the containers were sealed. Under a partial vacuum, the liquid test substance was added through the septum using a syringe and was observed to vaporize, after which time air was reintroduced into each incubation system. The test systems were then incubated at 37°C for 48 hours, with continuous stirring to mix the internal atmosphere.

Samples of the vapor, as well as aqueous samples, were taken from the test systems at the end of the 48-hour incubation period and analyzed by gas-liquid chromatography (GLC). The GLC results for the aqueous samples were used to calculate the amount of chemical dissolved per plate (*i.e.*, 1.1, 2.3, 4.9, 9.0, or 20.3 $\mu\text{moles/plate}$, or about 0, 140, 280, 600, 1100, and 2500 $\mu\text{g/plate}$, based on a molecular weight for 1-BP of 122.9 g/mol). Numbers of revertant colonies were tabulated using a colony counter at the end of the 48-hour incubation period. The study authors indicated that advantages of using this system included: 1) an enhanced ability to detect mutagenicity of volatile chemicals in the closed system compared to the standard plate-incorporation test; 2) decreased exposure of laboratory personnel to volatile chemicals that are potentially mutagenic; 3) better simulation of actual exposure (frequently as a vapor); and 4) the purity of the test substance is obtained as part of the analytical result, minimizing the chance of false positives due to mutagenic impurities.

The BioReliance (2015) study tested the mutagenicity of 1-BP using a preincubation method, as described by Yahagi et al. (1977). After an initial toxicity-mutation assay, two confirmatory mutagenicity assays were conducted. Target concentrations of 1-BP tested were 1.5-5000 $\mu\text{g/plate}$ for the initial toxicity-mutation assay and 50-5000 $\mu\text{g/plate}$ for the confirmatory mutagenicity assays. To prepare the dosing formulations, the test substance was diluted in ethanol; the test substance was determined to be stable in this solvent at room temperature for at least 3.25 hours. Dosing formulations were prepared immediately before use. For the repeat test of the confirmatory assay, dilutions of 1-BP were prepared in screw-capped tubes with minimal headspace; it was unclear whether these measures to reduce volatilization were taken during the first confirmatory assay due to a lack of documentation. To prepare the preincubation solutions, the diluted test substance or vehicle (ethanol), S9, or sham mix (containing phosphate buffer), and the tester strain (late log growth phase) were added to glass culture tubes preheated to $37\pm 2^\circ\text{C}$. Tubes receiving the test substance were capped using screw caps (amount of headspace not reported) during the preincubation period, which lasted for 90 ± 2 minutes at $37\pm 2^\circ\text{C}$. Samples for analysis of test substance concentrations by gas chromatography (GC) were taken from the dosing formulations, as well as from the solutions in preincubation tubes (without metabolic activation) at the beginning and end of the preincubation period, from the vehicle control and lowest and highest exposure concentrations (positive controls not evaluated). Measured concentrations of 1-BP in dosing formulations met acceptability criteria (85% to 115% of target concentrations, with $< 5\%$ relative standard deviation [RSD]), except for the low concentration of the second confirmatory assay ($> 5\%$ RSD). A small peak of test substance was detected in the vehicle control dosing formulation used in the second confirmatory assay. Measured concentrations of 1-BP in preincubation tubes were much lower than target (nominal) concentrations. For the first confirmatory assay, the measured concentrations of 1-BP at the beginning of the preincubation period were 37% and 9% of the target concentrations at the lowest and highest exposure concentrations, respectively; by the end of the preincubation period, the measured concentrations had declined to 3% and 2%, respectively, of the target concentrations. For the second confirmatory assay, the measured concentrations at the beginning of the preincubation period were 7% and 4% of the target concentrations at the lowest and highest exposure concentrations, respectively; the measured concentrations at the end of the preincubation period were 5% and 3%, respectively, of the target concentrations. Following preincubation, top agar was added to the tube and the mixture was

overlaid onto minimal bottom agar (Vogel-Bonner minimal medium E). Once solidified, plates containing the test substance were inverted and placed in desiccators by dose level for 48 to 72 hours at $37\pm 2^{\circ}\text{C}$ prior to scoring. Additional plates were prepared using only test substance, vehicle, S9, or sham mix to confirm the sterility of these solutions. Revertant colonies were counted either entirely by automatic colony counter or entirely by hand unless the plate exhibited toxicity (except for positive controls). Plates not scored immediately following the incubation period were stored at $2-8^{\circ}\text{C}$ until counting occurred. Although it was noted in the study report that the use of screw caps, intended to prevent evaporation of the test substance, was not documented in the initial confirmatory assay (and the assay was repeated), the conclusion of both confirmatory assays was the same; no mutagenicity was detected in any strain in the presence or absence of metabolic activation.

In some regards, there were similarities between the two studies. Both studies tested at least 5 concentrations of the test substance, with negative and standard, non-volatile positive controls used (see below for additional information). However, neither study used volatile positive control substances for explicitly demonstrating that their specific test protocols were optimized for detection of volatile chemical mutagens. The purity of the test substance was $> 99\%$ in both studies. Although both studies used at least 5 strains of bacteria, only the BioReliance study (2015) included a DNA repair-deficient strain of *E. coli*. In both studies, the metabolic activation system used S9 from Aroclor-induced rat livers and plates were incubated for 48 to 72 hours prior to the scoring of revertant colonies. The BioReliance study (2015) used target exposure concentrations up to $5000\ \mu\text{g}/\text{plate}$, as recommended by test guidelines; the highest concentration of $5000\ \mu\text{g}/\text{plate}$ was determined to be cytotoxic to all strains in the second confirmatory mutagenicity test. In contrast, Barber et al. (1981) tested concentrations up to $20.3\ \mu\text{moles}/\text{plate}$ (approximately $2500\ \mu\text{g}/\text{plate}$ based on a molecular weight for 1-BP of $122.9\ \text{g}/\text{mol}$) and detected mutagenicity even in the absence of cytotoxicity. The criteria for a positive or negative result were somewhat different for the two studies. Barber et al. (1981) indicated that a result was determined to be positive based on observed increases in the numbers of revertant colonies per plate in comparison to negative controls (not further specified). Statistical analyses (*i.e.*, Student's t-test tables) were used to determine the minimum significant number of revertants per plate for each strain (data not shown), which was used to calculate the minimum vapor concentration with a positive result (*i.e.*, "minimum detectable vapor concentration," equivalent to 31.2 ppm for TA 1535 and 106.5 ppm for TA 100). The BioReliance study (2015) stated that a result was deemed positive if there was a dose-related increase in the mean number of revertants per plate in at least one strain at two increasing concentrations of the test substance; a three-fold increase in the mean number of revertants was required for *S. typhimurium* strains TA 1535 and TA 1537, while a two-fold change was considered positive for all other strains tested. If the criteria for the BioReliance study (2015) were applied to the data provided by Barber et al. (1981), 1-BP would be deemed mutagenic in strains TA 1535 and TA 100 in the presence and absence of metabolic activation (mean data were shown only for *S. typhimurium* strains TA 1535, TA 98, and TA 100); this is the same conclusion reached by Barber et al. (1981).

The guideline pertaining to this type of assay (OECD 471; (2019o)) indicates that a result can be considered positive for mutagenicity based on observed concentration-related increases in

revertants over the range of concentrations tested, and/or a reproducible increase in the number of revertants/plate at one or more concentrations in at least one strain with or without metabolic activation (OECD, 1997). The OECD 471 (2019o) test guideline recommends that biological relevance be considered first; statistical analyses may also be used, but should not be the sole determinant for identifying a positive response. Therefore, although the two studies differed with respect to the classification of a positive versus a negative response, these differences do not suggest that one study followed guideline recommendations while the other did not. The Barber et al. (1981) study used statistics to determine vapor concentrations corresponding to a significantly increased number of revertants. Although the BioReliance (2015) study did not use statistical methods to evaluate mutagenicity, specific criteria for identifying a positive result were provided in the study report. These criteria closely adhere to those set forth in the guidelines, as described above.

In both studies, standard (non-volatile) chemicals were used as positive controls. Barber et al. (1981) used 2-aminoanthracene as a positive control for all strains when metabolic activation was used. In the absence of activation, positive controls were ICR-191 for *S. typhimurium* TA 98, methyl-N-nitro-N'-nitrosoguanidine for strains TA 100 and TA 1535, 9-aminoacridine for TA 1537, and picrolonic acid for TA 1538. Positive and negative control data were provided by Barber et al. (1981); however, no criteria for establishing the validity of the positive control data were reported. For the BioReliance study (2015), 2-aminoanthracene was also identified as the positive control substance for all strains tested in the presence of metabolic activation. The positive controls used in the absence of metabolic activation included 2-nitrofluorene for *S. typhimurium* TA 98, sodium azide for strains TA 100 and TA 1535, 9-aminoacridine for TA 1537, and methyl methanesulfonate for *E. coli* WP2 uvrA. The study report specified that positive controls were subjected to the preincubation process and plated concurrently with each assay (in duplicate in the initial toxicity-mutagenicity assay and in triplicate for subsequent confirmatory assay). The BioReliance study (2015) indicated that the mean number of revertants/plate for each positive control needed to be at least three times higher than the mean value for the respective vehicle control group for the mutagenicity test to be considered valid. Based on this criteria, positive controls responded appropriately in both the study by Barber et al. (1981) and in all three assays in the BioReliance study (2015). The mean numbers of revertants per plate that were observed for negative and positive controls are provided in Table_Apx J-5.

Table_Apx J-5. Comparison of Mean Numbers of Revertants/Plate for Controls in Reverse Mutation Assays

Mean numbers of revertants/plate for controls in reverse mutation assays								
Species and Strain	Barber et al. (1981)				BioReliance (2015) ^a			
	Negative control		Positive control		Negative control		Positive control	
	- S9	+ S9	- S9	+ S9	- S9	+ S9	- S9	+ S9
<i>S. typhimurium</i> TA 98	38	38	170	415	22	32	768	490
<i>S. typhimurium</i> TA 100	85	96	285	678	106	100	1057	554
<i>S. typhimurium</i> TA 1535	20	19	148	267	15	31	463	105
<i>S. typhimurium</i> TA 1537	6	9	265	402	6	5	115	87

S. typhimurium TA 1538	8	21	72	495	NT	NT	NT	NT
E. coli WP2 uvrA	NT	NT	NT	NT	32	41	614	402

^a Values are provided for the repeat (second) confirmatory assay of BioReliance ([BioReliance, 2015](#)), which was the only assay that documented the use of screw-capped tubes for preparation of dosing formulations.

NT = This strain was not tested for mutagenicity.

In summary, the studies by Barber et al. ([1981](#)) and BioReliance ([2015](#)) conformed to most of the recommendations provided in OECD TG 471 ([2019o](#)). The major differences in experimental design between the two studies are the method of test substance application (vapor exposure of plated bacteria for 48 hours in the Barber et al. study ([1981](#)) versus aqueous preincubation exposure for 90 minutes in the BioReliance study ([2015](#)) study and the methods used to achieve a ‘closed’ system to account for the inherent volatility of 1-BP (fully enclosed test chamber versus preparation of solutions in screw-capped tubes). Although the guideline indicates that volatile chemicals should be considered special cases, the alternative methods that should be used to test these types of test substances are not outlined in OECD TG 471 ([2019o](#)). It is likely that the varied mutagenicity results from the two studies (*i.e.*, positive results in the Barber et al. study ([1981](#)) study and negative results in the BioReliance study ([2015](#)) are due to differences in the methods used for exposure and to compensate for the volatility of 1-BP in the bacterial reverse mutation assay.

Based on the following primary differences in methodology, the preincubation exposure test by BioReliance study ([2015](#)) had inadequate sensitivity to assess the mutagenic potential of volatile chemicals such as 1-BP, in contrast to the closed system plate vapor exposure test by Barber et al. ([1981](#)):

1. The BioReliance study report ([2015](#)) stated that “The test system was exposed to the test article via the preincubation methodology described by Yahagi et al. ([1977](#))” but this method was not designed to retain a volatile test substance such as 1-BP within the test system during preincubation (prior to plating) with the bacterial test strains. In contrast, the Barber et al. ([1981](#)) study was explicitly designed to retain vapors of the volatile 1-BP test substance in contact with the bacterial test strains throughout plate incubation.
2. The BioReliance study ([2015](#)) study attempted to circumvent the volatility of 1-BP by using screw-capped tubes for test substance dilutions (documented in the second confirmatory assay only) and during the 90-minute preincubation period in contact with test strains (prior to plating). While the use of minimal headspace was documented for preparation of dosing formulations, it was unclear whether preincubation tubes contained minimal headspace; in the absence of this precaution, 1-BP would be expected to volatilize into the headspace. In contrast, the closed system used in the Barber et al. ([1981](#)) study generated conditions that permitted the test strains to be exposed to 1-BP as a vapor for the entirety of the 48-hour exposure period (*i.e.*, without loss due to volatility); analyses of 1-BP in aqueous samples from blank incubation plates by GLC were used to calculate the 1-BP concentrations in plates.
3. The results of analytical measurements of 1-BP suggest that bacteria were exposed to much higher concentrations of 1-BP in the study that found evidence of mutagenicity in two of five bacterial strains ([Barber et al., 1981](#)) than in the study that found no evidence of

mutagenicity in five bacterial strains ([BioReliance, 2015](#)). Barber et al. ([1981](#)) tested measured concentrations up to 20.3 $\mu\text{moles/plate}$ (approximately 2500 $\mu\text{g/plate}$ based on a molecular weight for 1-BP of 122.9 g/mol) and detected mutagenicity in two of five bacterial strains in the absence of cytotoxicity. In the BioReliance study ([2015](#)) study, analytical measurements by GC confirmed that concentrations of 1-BP in dosing formulations were within 85-115% of target concentrations. However, despite the use of screw-capped tubes to reduce 1-BP loss via volatilization during preincubation with the bacterial test strains, analytical concentrations of 1-BP in preincubation tubes during the BioReliance study ([2015](#)) confirmatory assays were far below target, with 4-37% of target concentrations at the beginning of the preincubation period and 2-5% of target concentrations by the end of the preincubation period. At the highest target exposure concentration of 5000 $\mu\text{g/plate}$, the measured concentrations during preincubation correspond to approximately 100-450 $\mu\text{g/plate}$ (2-9% of the target concentration) in the BioReliance study ([2015](#)) and no evidence of mutagenicity was seen at this or lower concentrations.

4. The duration of exposure of bacteria to 1-BP was much longer in the study that showed mutagenicity from 1-BP exposure Barber et al. study ([1981](#)) than in the study that found no evidence of mutagenicity from 1-BP exposure ([BioReliance, 2015](#)). The closed system used in the positive Barber et al. ([1981](#)) study generated conditions that permitted the tester strains to be exposed to 1-BP as a vapor for the entirety of the 48-hour exposure period (*i.e.*, without loss due to volatility). In contrast, bacteria were exposed to 1-BP in solution for 90 minutes in the negative BioReliance study ([2015](#)).
5. Neither Barber et al. ([1981](#)) nor BioReliance ([2015](#)) included volatile positive control chemicals in their assays. This does not appear to be an issue for the Barber et al. study ([1981](#)), which demonstrated mutagenicity for the volatile 1-BP test substance and for six other volatile halogenated alkane solvents in the presence and absence of metabolic activation. However, given that the Barber et al. study ([1981](#)) method was sufficient to detect the mutagenicity of 1-BP and related volatile chemicals, but the BioReliance study ([2015](#)) method found no evidence of 1-BP mutagenicity and did not show that their method could detect mutagenicity of volatile positive controls, there is uncertainty that the BioReliance study ([2015](#)) protocols and specific methodology were capable of adequately assessing the mutagenic potential of 1-BP. Thus, in the absence of data for volatile positive control chemicals⁴³ in the BioReliance study ([2015](#)) study, it is possible that the lack of demonstrated 1-BP mutagenicity in this study was a false negative.

The differences in results, including both cytotoxicity and mutagenicity, between these two studies (described above and summarized in Table_Apx J-6) suggest that the design of the experimental

⁴³ For examples of volatile positive control mutagens see Hughes et al. ([1987](#)), which was cited by OECD TG 471 ([2019o](#)) as an appropriate method for testing of gaseous or volatile substances.

system used for exposure and retention of the volatile test substance within the test system significantly influenced the response of the test organisms.

Table_Apx J-6. Comparison of Mutagenicity Studies of 1-BP

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
Doses	<p>Measured 1-BP concentrations were 0, 1.1, 2.3, 4.9, 9.0, and 20.3 μmoles/plate (equivalent to approximately 0, 140, 280, 600, 1100, and 2500 μg/plate).</p> <p>There was no indication of cytotoxicity at the highest tested concentration.</p>	<p>Target 1-BP concentrations were 0, 1.5, 5.0, 15, 50, 150, 500, 1500, and 5000 μg/plate (initial toxicity-mutagenicity assay); 0, 50, 150, 500, 1500, 2000, 3000, and 5000 μg/plate (confirmatory mutagenicity assays). 1-BP concentrations measured in confirmation mutagenicity assay preincubation tubes at the beginning and end of the 90-minute exposure were much lower than target (see row “Compound dose confirmation and purity”) and much lower than the highest test concentration used in the study by Barber et al. (1981). In the initial assay, cytotoxicity was observed at 5000 μg/plate (all strains); cytotoxicity was also observed at 3000 and 5000 μg/plate in the repeat of the confirmatory assay.</p>	<p>At least 5 test concentrations of the test substance should be used. The recommended highest test concentration for non-cytotoxic substances is 5000 μg/plate; or, for non-cytotoxic substances that are insoluble at that concentration, a concentration(s) that is insoluble in final treatment mixture. Cytotoxic substances should be tested up to a cytotoxic concentration.</p>
Negative controls	<p>Plates in a closed system with no added test or positive control chemical</p> <p>With the exception of not adding chemical to the system, untreated controls were treated the same as treatment groups. Negative controls were used for each strain, with and without metabolic activation. Average spontaneous reversion rates from negative control plates were reported.</p>	<p>Exposure to vehicle only (ethanol) in preincubation tubes</p> <p>Negative controls were included for each strain, with and without activation, and were treated the same as treatment groups. Raw data (number of revertant colonies per plate) were provided for negative controls.</p> <p>In the repeat of the confirmatory assay, a small peak of the test substance was detected in the vehicle control sample (~0.03 mg/mL). This was noted as a study deviation.</p>	<p>Concurrent strain-specific negative controls, with and without metabolic activation, should be included in each assay. Negative controls, consisting of solvent or vehicle alone, without test substance, should be included and should otherwise be treated the same as treatment groups.</p>
Positive controls	<p><u>With activation:</u> 2-Aminoanthracene (all strains). No mutagen requiring activation by microsomal enzymes was tested.</p> <p><u>Without activation:</u> ICR-191 for <i>Salmonella typhimurium</i></p>	<p><u>With activation:</u> 2-Aminoanthracene (all strains). No mutagen requiring activation by microsomal enzymes was tested; however, each bulk preparation of S9 was assayed for its ability to metabolize benzo(a)pyrene to forms mutagenic to <i>S. typhimurium</i> TA 100.</p>	<p>Concurrent strain-specific positive controls, with and without metabolic activation, should be included in each assay. Examples of chemicals that can be used as positive controls in the presence and absence of metabolic activation are recommended by guideline</p>

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
	<p>TA 98, methyl-N-nitro-N'-nitrosoguanidine for strains TA 100 and TA 1535, 9-aminoacridine for TA 1537, and picrolonic acid for TA 1538. 9-Aminoacridine and ICR-191 are listed as strain-specific positive controls for TA 1537 and TA 97 (but not TA 98) according to OECD TG 471. The other chemicals are not listed in OECD TG 471.</p> <p>The solvent(s) used for positive control substances were not specified. No criteria were provided for a valid response of positive controls.</p>	<p><u>Without activation:</u> 2-Nitrofluorene for <i>S. typhimurium</i> TA 98, sodium azide for strains TA 100 and TA 1535, 9-aminoacridine for TA 1537, and methyl methanesulfonate for <i>Escherichia coli</i> WP2 <i>uvrA</i>. All except methyl methanesulfonate for <i>E. coli</i> WP2 <i>uvrA</i> were listed as strain-specific positive controls according to OECD TG 471.</p> <p>Positive controls were diluted in DMSO except sodium azide, which was diluted in sterile water. The study indicated that for the test to be valid, positive controls had to show a 3-fold increase in the number of revertants compared to the respective vehicle control; however, there were no vehicle controls for DMSO or water.</p>	<p>(other appropriate reference substances may be used). It is noted that 2-aminoanthracene should not be used as the sole indicator of the efficacy of the S9 mix; each batch should also be characterized using a mutagen that requires metabolic activation by microsomal enzymes (<i>i.e.</i>, benzo(a)pyrene, dimethylbenzanthracene).</p>
Compound dose confirmation & purity	<p>Purity of 1-BP (as per GLC) = 99.85%</p> <p><u>Dose confirmation:</u> Plates containing only sterile distilled water were included in the closed system containers for GLC analysis of aqueous 1-BP concentrations at the end of the 48-hour incubation period. Samples of the vapor were also taken from the closed system containers at the end of the 48-hour incubation period and analyzed by GLC. The GLC results from the aqueous samples were used to calculate the amount of chemical dissolved per plate.</p>	<p>Purity of 1-BP (determined by sponsor) > 99%</p> <p><u>Dose confirmation:</u> Samples of dosing formulations and preincubation solutions (at 0 and 90 minutes) were analyzed by GC (vehicle control, low- and high-dose groups only). 1-BP concentrations in dosing formulations were similar to target concentrations, but 1-BP concentrations measured in preincubation solutions were shown to be far below target concentrations. At 0 minutes in the confirmatory mutagenicity assays, 1-BP concentrations in preincubation tubes at the highest target level (5000 µg/plate) were 4% to 9% of target, which corresponds to 1-BP concentrations of 200-450 µg/plate; by the end of the 90-minute preincubation exposure period, measured 1-BP concentrations at the highest target level (5000 µg/plate) were 2% to 3% of target, which corresponds to 1-BP concentrations of approximately 100-150 µg/plate. No analysis of 1-BP concentrations was conducted at the end of the plate incubation period (after 48-72 hours), but negligible 1-BP concentrations would be expected since</p>	<p>OECD TG 471 indicates that the test report must include specific types of information, including purity of the test substance. Given the volatility of 1-BP, it may be especially important to verify concentrations of the test substance as a 'special case'.</p>

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
		no volatility control was used during the plate incubation period.	
Methods reporting details provided	<p><u>Not provided:</u> Bacterial titers (cells/mL); raw data (<i>i.e.</i>, individual plate counts); revertants/plate data for the two strains in which no mutagenicity was observed (<i>i.e.</i>, <i>S. typhimurium</i> strains TA 1537 and TA 1538); standard deviations for mean numbers of revertants/plate (except positive and negative controls); historical control data.</p> <p>Negative control results were noted to have been in good agreement with those found in an interlaboratory survey (De Serres and Shelby, 1979) and those presented by Ames et al. (1975).</p>	<p><u>Not provided:</u> None (items recommended by OECD TG 471 were reported)</p>	The guideline indicates a number of items that must be included in the test report (with respect to the test substance, solvent/vehicle, strains, test conditions, and results).
Closed-system protocol details	<p><u>System used:</u> Modified plate-incorporation test. Pyrex containers with circular Teflon tops (drilled and threaded to accommodate valve and septum assemblies and containing a sampling port); containers accommodated a metal rack holding up to 12 glass plates. An O-ring was used to ensure a good seal between the container and the top; clamps were used to hold tops in place.</p> <p><u>Addition of 1-BP:</u> Under a hood, prepared plates (with or without activation) were introduced to the Pyrex containers. A plate containing sterile, distilled water (30 mL) was added to each container for GLC analysis of 1-BP</p>	<p><u>System:</u> Preincubation method. Screw-capped tubes during preincubation; minimal head space documented for the second confirmatory mutagenicity assay only.</p> <p><u>Addition of 1-BP:</u> Dosing formulations of 1-BP were prepared in screw-capped tubes with minimal headspace; use of minimal headspace was documented only for the second of two confirmatory assays. To prepare preincubation solutions, 1-BP dosing formulations or vehicle (ethanol), S9 or sham mix, and the tester bacterial strain were added to glass culture tubes preheated to 37±2°C. Tubes containing 1-BP were capped using screw caps (amount of headspace not reported) during the preincubation period (90 minutes at 37°C). Following preincubation, top agar was added, and the mixture was overlaid onto minimal bottom agar. Once solidified, plates were inverted and</p>	OECD TG 471 indicates that certain classes of mutagens (including gases and volatile chemicals) are not always detected using standard procedures such as the plate incorporation or preincubation methods; therefore, these are considered 'special cases' and alternative procedures (scientifically justified) should be used for their detection. Gases or volatile substances should be tested by appropriate methods, such as in sealed vessels.

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
	<p>concentrations at the end of the exposure period. After sealing the containers and drawing a partial vacuum, 1-BP was added through the septum using a syringe. Once the liquid vaporized (ascertained visually), air was added via the valve until the pressure inside the containers was equal to ambient pressure. Containers were removed from the hood and incubated for 48 hours at 37°C (with continuous stirring of the atmosphere in each container).</p>	<p>placed in desiccators by dose level for 48 to 72 hours at 37°C.</p>	
Activation system	<p>Aroclor-induced rat liver S9</p> <p>The concentration of S9 in S9 mix was not reported. For plates with metabolic activation, top agar contained 0.2 mL overnight culture, 2.0 mL agar, and 0.5 mL S9 mix.</p>	<p>Aroclor 1254-induced rat liver S9 (male Sprague-Dawley rats)</p> <p>The S9 mix contained a final S9 concentration of 10% v/v. Preincubation tubes contained 0.5 mL S9 or sham mix, 100 µL tester strain, and 25 µL vehicle or test substance dilution, to which 2.0 mL agar was added after the 90-minute preincubation period.</p>	<p>Bacteria should be exposed to the test substance in the presence and absence of an appropriate metabolic activation system. The most commonly used system is a cofactor-supplemented post-mitochondrial fraction (S9) prepared from the livers of rodents treated with enzyme-inducing agents such as Aroclor 1254 or a combination of phenobarbitone and β-naphthoflavone. The post-mitochondrial fraction is usually used at concentrations in the range from 5 to 30% v/v in the S9 mix. Usually, 0.05 or 0.1 mL of test substance/solution, 0.1 mL bacteria, and 0.5 mL S9 mix or sterile buffer are mixed with 2.0 mL of top agar.</p>
Bacterial strains	<p><i>S. typhimurium</i> strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538</p> <p>This combination of strains conforms to the guideline except that TA 1538 was used in lieu of <i>E. coli</i> WP2 uvrA or <i>E. coli</i> WP2 uvrA (pKM101) or <i>S. typhimurium</i> TA 102. The test plates were prepared</p>	<p><i>S. typhimurium</i> strains TA 98, TA 100, TA 1535, and TA 1537; <i>E. coli</i> strain WP2 uvrA</p> <p>This combination of strains conforms to the guideline. To assure that cultures were harvested in the late log phase, the length of incubation was controlled and monitored. Each culture was monitored spectrophotometrically for turbidity and harvested at a percent transmittance yielding a titer $\geq 0.3 \times 10^9$ cells/mL.</p>	<p>Fresh cultures grown up to the late exponential or early stationary phases of growth should be used (approximately 10^9 cells/mL; not late stationary). At least 5 strains of bacteria should be used. These should include 4 strains of <i>S. typhimurium</i> (TA 1535, TA 1537 or TA 97a or TA 97, TA 98, and TA 100). These strains have GC base pairs at the</p>

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
	from overnight growth cultures (phase of growth not reported); the number of cells/mL was not specified.	Actual titers were determined by viable counts assays (actual counts were 1.3 to 5.7×10^9 cells/mL).	primary reversion site and may not detect certain oxidizing mutagens, cross-linking agents, and hydrazines. Such substances may be detected using <i>E. coli</i> WP2 strains or <i>S. typhimurium</i> TA 102, which have an AT base pair at the primary reversion site. To detect cross-linking mutagens, it may be preferable to include TA 102 or a DNA repair-deficient strain of <i>E. coli</i> , such as WP2 or WP2 (pKM101). The guideline specifies a recommended combination of strains (<i>S. typhimurium</i> TA 1535; <i>S. typhimurium</i> TA 1537 or TA 97a or TA 97; <i>S. typhimurium</i> TA 98; <i>S. typhimurium</i> TA 100; and <i>E. coli</i> WP2 uvrA or <i>E. coli</i> WP2 uvrA (pKM101) or <i>S. typhimurium</i> TA 102).
Duration of exposure	48 hours at 37°C	90±2 minutes at 37±2°C (preincubation period with test article or controls); 48-72 hours at 37°C (plate incubation period)	For the preincubation method, cultures should be incubated for 20 minutes or more at 30-37°C prior to mixing with top agar. All plates should be incubated at 37°C for 48 to 72 hours.
Time of assessment	Number of revertant colonies/plate was counted after 48 hours incubation	Number of revertant colonies counted after 48-72 hours incubation (plates that were not counted immediately were stored at 2-8°C)	All plates should be incubated at 37°C for 48 to 72 hours. After the incubation period, the number of revertant colonies per plate is counted.
Type of assessment	Revertant colonies counted using a colony counter. <u>Criteria for a positive result:</u> Increased revertants/plate compared to controls; statistical analysis (Student's t-test tables) was used to determine the minimum vapor concentration that significantly increased the number of revertant colonies.	Revertant colonies counted either entirely by automated colony counter or entirely by hand (except positive controls). <u>Criteria for a positive result:</u> Dose-related increases in the numbers of revertants/plate in at least one strain over a minimum of two increasing concentrations of 1-BP; at least 3-fold increase in revertants for <i>S. typhimurium</i> strains TA 1535 and 1537 and at least 2-fold increases for all other strains.	After the incubation period, the number of revertant colonies per plate is counted (method of counting not specified). Criteria for determining a positive result include a concentration-related increase over the range tested and/or a reproducible increase at one or more concentrations in at least one strain with or without activation. Biological relevance should be considered first; statistical methods may be used but should not be the only determining factor. Any result that does not meet these criteria is considered negative. Data

Metric	Barber et al. (1981)	BioReliance (2015)	OECD (1997)
			should be presented as the mean number of revertant colonies per plate and standard deviation. There is no requirement for verification of a clear positive result. Equivocal results should be clarified by modifying experimental conditions, whenever possible. Negative results need to be confirmed on a case-by-case basis; if not confirmed, justification should be provided.

GLC = gas-liquid chromatography; GC = gas chromatography

J.5.8 Metabolism, Structure-Activity Relationships and Mechanism/Mode of Action

Studies in experimental animals and humans indicate that 1-BP can be absorbed following inhalation, oral, or dermal exposure (Cheever et al., 2009; NIOSH, 2007). Metabolism studies show that oxidation by P450 enzymes (e.g., CYP2E1) and glutathione conjugation are the primary metabolic pathways (Garner et al., 2006; Ishidao et al., 2002). Over 20 metabolites have been identified in rodent studies, including the four metabolites that can be detected in urine samples of workers exposed to 1-BP (Hanley et al., 2009). Besides being a direct-acting alkylating agent, 1-BP may be converted to either of two epoxide metabolites, glycidol and propylene oxide, by oxidation followed by cyclization of the resulting alpha-bromohydrin intermediates. Both the 2- and 3- positions on 1-bromopropane are susceptible to oxidation by cytochrome P450 (NTP, 2013b). Oxidation at the 3-position results in the formation of 3-bromo-1-propanol. Further oxidation of this intermediate at the 2-position yields 3-bromo-1,2-propanediol, which can cyclize to form glycidol. Propylene oxide may be formed by a similar, though shorter pathway. Oxidation of 1-bromopropane at the 2-position yields 1-bromo-2-propanol. This bromohydrin intermediate may then be cyclized to form propylene oxide. Glycidol was detected in urine of rats exposed 6 hours/day to 1-BP by inhalation for 3 to 12 weeks (Ishidao et al., 2002). Metabolic pathways by which propylene oxide may be generated from 1-BP are shown in Jones and Walsh (1979), NTP (2013b), and IARC (2018) and a pathway by which glycidol may be generated from 1-BP is shown in IARC (2018). Epoxide intermediates such as propylene oxide and glycidol are expected to have more mutagenic activity than 1-BP (IARC, 2018, 2000, 1994).

Mice appear to have a greater capacity to oxidize 1-BP than rats (Garner et al., 2006). This species difference in metabolic capacity may explain why mice were found to be more sensitive to 1-BP toxicity than rats. The identified or putative reactive intermediates for 1-BP include the epoxides noted above (glycidol, and propylene oxide), α -bromohydrin and 2-oxo-1-BP (NTP, 2014; Ishidao et al., 2002; Mitchell et al., 1998). Detoxification of 1-BP metabolites occurs primarily via glutathione-S-transferase (GST) -mediated conjugation with glutathione (NTP, 2014; Liu et al., 2009; Garner et al., 2006).

1-BP is expected to be a good alkylating agent because bromine is a good leaving group. Two of its closest homologs, bromoethane and 1-bromobutane, were both shown to be mutagenic in the Ames Salmonella test; in both cases, use of desiccators was needed to show positive results ([NTP, 1989b](#); [Simmon et al., 1977](#)). Bromoethane is a known carcinogen via the inhalation route of exposure ([NTP, 1989b](#)), whereas 1-bromobutane has not been tested for carcinogenic activity. 1-BP is a relatively soft electrophile which is expected to preferentially react with sulfhydryl (-SH) residues on glutathione and proteins before binding to DNA. Besides being a direct-acting alkylating agent, 1-BP may be metabolically activated to genotoxic intermediates (see above). A number of other structurally-related halogenated alkanes such as 1,2-dibromoethane (ethylene dibromide) ([IARC, 1999e](#)), dichloromethane ([IARC, 1999d](#)), 1,2-dichloroethane ([IARC, 1999b](#)), 1,2-dibromo-3-chloropropane ([IARC, 1999a](#)) and 1,2,3-trichloropropane ([IARC, 1999c](#)) have been classified as “probably carcinogenic to humans (group 2A)” or “possibly carcinogenic to human carcinogens” (group 2B) by the International Agency for Research on Cancer; however, some of these chemicals may have different mechanisms.

The mechanism/mode of action for 1-BP carcinogenesis is not clearly understood. More research is needed to identify key molecular events. Since 1-BP can induce tumors in multiple organs and can act directly as an alkylating agent, as well as indirectly via metabolically-activated reactive intermediates such as glycidol and propylene oxide, it may have different mechanisms in different target organs. Whereas the reasonably available data/information and the weight of the scientific evidence provide some support for a MMOA for 1-BP carcinogenesis, at least three additional mechanisms, oxidative stress, immunosuppression, and cell proliferation may contribute to the multi-stage process of carcinogenesis ([NTP, 2013b](#)).

As discussed in the previous section on genotoxicity, 1-BP and its genotoxic reactive intermediates can induce DNA mutations and/or chromosome aberrations. Although the results are not as clear cut for 1-BP itself, some of the discrepancies may be explained by testing limitations. Available structure-activity relationship analyses support the genotoxic potential of 1-BP. The induction of tumors in multiple targets by 1-BP is also a common characteristic of genotoxic carcinogens. DNA binding studies show formation of N⁷-propyl guanine adducts by 1-BP, although these specific adducts are not known to result in mutations. Overall, the weight of scientific evidence for a MMOA for 1-BP carcinogenesis is suggestive but inconclusive.

Oxidative stress due to cellular glutathione depletion could contribute to the carcinogenicity of 1-BP ([Morgan et al., 2011](#)). Oxidative stress is an important epigenetic mechanism that can contribute to all three stages of carcinogenesis - oxidation can induce initiation (as a result of DNA damage), promotion (as a result of compensatory cell proliferation in response to cell necrosis), and progression (via oxidative changes in signal transduction and gene expression; *rev.* ([Woo and Lai, 2003](#))). Exposure to 1-BP has also been shown to deplete glutathione in various tissues (*e.g.*, ([Liu et al., 2009](#); [Lee et al., 2007](#); [Wang et al., 2003](#))), which can lead to a loss of protection against electrophiles.

As summarized in the previous section on genotoxicity, 1-BP did not induce mutations at the *cH* gene of female B6C3F1 transgenic Big Blue® mice following whole-body inhalation exposures to

1-BP vapor concentrations of 62.5, 125, or 250 ppm 5 days/week for 28 days ([Stelljes et al., 2019](#); [Weinberg, 2016](#)); or 7 days/week for 28 days ([Young, 2016](#)). The guideline for transgenic rodent somatic and germ cell gene mutation assays ([OECD, 2013](#)) indicates that daily exposures to test substance are needed in a repeated-dose protocol of at least 28 days based on “observations that mutations accumulate with each treatment.” Thus, the 5 days/week exposure protocol ([Stelljes et al., 2019](#)); [Weinberg, \(2016\)](#) was deficient, but the 7 days/week exposure protocol of [Young \(2016\)](#) conformed to the ([OECD, 2013](#)) guidance to use daily exposures to test substance.

Due to the following issues, the negative Big Blue® rodent mutation assays in female B6C3F1 mice ([Stelljes et al., 2019](#)); [Weinberg, 2016](#); [Young, \(2016\)](#) do not provide definitive evidence against a MMOA of 1-BP carcinogenicity:

- (a) The study protocol was not optimal for detection of mutations because the highest test concentration of 250 ppm was not a Maximum Tolerated Dose (MTD). The MTD is defined as the dose producing signs of toxicity such that higher dose levels, based on the same dosing regimen, would be expected to produce lethality ([OECD, 2013](#)). Given that there were no treatment-related effects on survival, clinical observations, body weights, food consumption, or organ weights, the highest 1-BP test concentration was not an MTD and the study needs to be repeated to include a top concentration at the MTD.
- (b) The studies assessed only females, but it is possible that males may also be sensitive to mutagenicity/carcinogenicity from exposure to 1-BP. Indeed, the NTP ([2011b](#)) 2-year inhalation study found statistically-significant increases in tumor incidence not only in female B6C3F1 mice but also in both male and female F344/N rats.
- (c) The studies assessed only mice, at a maximum 1-BP exposure concentration of 250 ppm, but the 3-month toxicity studies that preceded the NTP 2-year bioassay showed that F344/N rats tolerated a higher repeated-dose inhalation concentration (500 ppm) than B6C3F1 mice (250 ppm). Thus, to provide higher sensitivity for detection of potential mutagenicity in rodents, an additional *in vivo* mutation assay using Big Blue® F344/N rats could be conducted using a higher maximum inhalation concentration than that used in the mouse study, *i.e.*, 500 ppm should be part of the range tested in Big Blue® F344/N rats. According to ([OECD, 2013](#)), “the use of transgenic rat models should be considered,” for example, “when investigating the mechanism of carcinogenesis for a tumor seen only in rats.” The NTP ([2011b](#)) 2-year bioassay of 1-BP reported that neoplasms of skin (in both sexes), large intestines (in females), and pancreas (in males) as well as increased incidences of malignant mesotheliomas (in males) occurred only in F344/N rats, which provides additional justification for 1-BP mutagenicity testing in Big Blue® F344/N rats of both sexes.
- (d) The Big Blue® assay typically evaluates fast and slow mutation fixation/repairing tissue types. The 1-BP studies assessed mutagenicity only in lung, liver and colon but, because of differences in metabolic enzymes/cytochrome p450s among mammalian organs and tissues and different species, several tissues of rats and mice should be sampled for mutations in the Big Blue® rodent mutagenicity assay of 1-BP to minimize the possibility of false negative mutagenicity results. The NTP ([2011b](#)) 2-year study for 1-BP included neoplasm findings for skin, large intestines, lung, and pancreas. Before concluding that a MMOA of 1-BP is not operable for all target sites, additional target sites, including skin, pancreas, and

intestines at a minimum, would need to be assessed for 1-BP in Big Blue® models for both B6C3F1 mice and F344/N rats.

- (e) Test chemical exposures of longer than 28 days may be needed for “detecting mutations in slowly proliferating organs” ([OECD, 2013](#)). Further research may be needed to determine if 1-BP exposure periods of more than 28 days are needed for detection of potential mutations in the Big Blue® assay.
- (f) The Big Blue® rodent assay may fail to detect mutagens if the post-exposure fixation time is too short to allow fixing of DNA damage into stable mutations. Likewise, the assay can fail to detect mutagens if a rapid cell turnover in a particular tissue, together with longer post-exposure time, decrease the frequency of cells that carry mutations in reporter genes. As indicated in ([OECD, 2013](#)) administration of the test agent “is usually followed by a period of time, prior to sacrifice, during which the agent is not administered and during which unrepaired DNA lesions are fixed into stable mutations. In the literature, this period has been variously referred to as the manifestation time, fixation time, or expression time.” In the Big Blue® mouse studies of 1-BP, the post-exposure fixation time was 3 days, which may provide adequate sensitivity for detection of mutagenicity in some tissues but not others. ([OECD, 2013](#)) recognizes the issue of potential underestimation of mutagenic potential, noting that the fixation period is tissue-specific and that “maximum mutant frequency may not manifest itself in slowly proliferating tissues” when a 3-day fixation period is used. To address the possibility of underreporting mutagenic potential for slowly proliferating tissues, ([OECD, 2013](#)) indicates that “a later sampling time of 28 days following the 28 day administration period may be more appropriate.” Further research is needed on the lengths of fixation periods needed to manifest mutagenicity in each tissue sampled in future Big Blue® rodent assays of 1-BP.
- (g) The Big Blue® assay lacks a body of data on mutagenic and carcinogenic chemicals with structural similarity to 1-BP. One of the closest homologs of 1-BP, bromoethane, is positive in closed-system testing in the Ames *Salmonella* mutagenicity assay ([NTP, 1989b](#); [Simmon et al., 1977](#)) and is carcinogenic by the inhalation route ([NTP, 1989b](#)). To enhance confidence that the methods used for 1-BP testing in the Big Blue® assays are sufficient to prevent false negative mutagenicity findings, mutagenicity data from Big Blue® assays of rats and mice are needed from independent testing of bromoethane (and other known mutagenic carcinogens with structural similarity to 1-BP) or these 1-BP analogs could be included as potentially-positive controls in additional Big Blue® studies of 1-BP. If mutagenic and carcinogenic structural analogs of 1-BP are not mutagenic in Big Blue® rodent assays, it can be concluded that these assays are not suitable for assessing the mutagenicity of 1-BP.

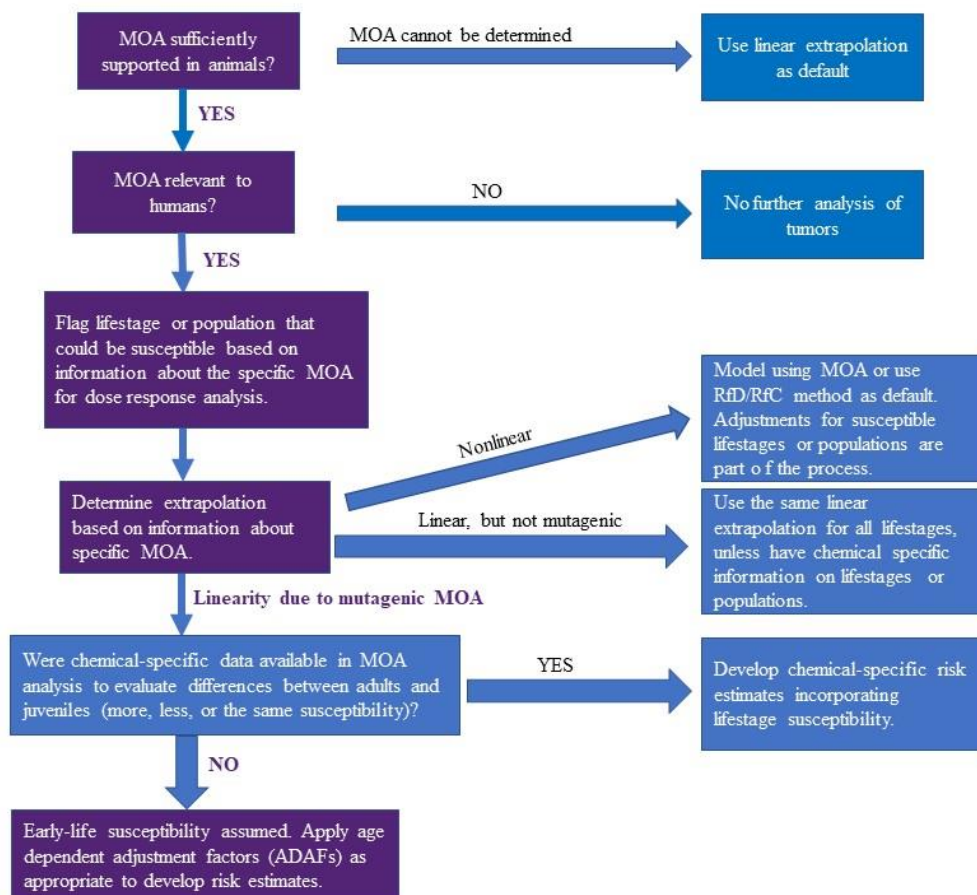
Besides genotoxicity and oxidative stress, 1-BP has been shown to cause immunosuppression in rodents ([Anderson et al., 2010](#); [Lee et al., 2007](#)). Immunosuppression can facilitate tumor progression by lowering the immunosurveillance process against tumor growth. There is also some evidence that 1-BP can cause γ -aminobutyric acid (GABA) dysfunction and thereby impact cell proliferation, differentiation and migration of neuronal cells ([NTP, 2013a](#)).

Several known or proposed metabolites of 1-BP have been shown to be mutagenic ([NTP, 2014](#); [IARC, 2000, 1994](#)). For example, both glycidol and propylene oxide are mutagenic in bacteria, yeast, *Drosophila*, and mammalian cells. These compounds have also been shown to induce DNA and chromosomal damage in rodent and human cells, and can form DNA adducts *in vitro*. α -Bromohydrin and 3-bromo-1-propanol were mutagenic in the *S. typhimurium* reversion assay, and 3-bromo-1-propanol and 1-bromo-2-propanol induced DNA damage in *E. coli*. The available *in vivo* test results for glycidol indicate that it induces micronucleus formation, but not chromosomal aberrations in mice. Studies of propylene oxide indicated chromosomal damage evidenced by positive responses for micronucleus induction in mouse bone marrow and chromosomal aberration tests; DNA damage was evident in the sister chromatid exchange (SCE) assay.

Appendix K 1-BP: Mutagenic Mode of Action Analysis

According to the Cancer Guidelines and the Supplemental Guidance for Assessing Susceptibility from Early Life Exposure to Carcinogens ([U.S. EPA, 2005a, b](#)), individuals exposed during early life stages (*i.e.*, development) to carcinogens with a MMOA are assumed to have an increased risk for cancer. The framework for the weight of the scientific evidence for mutagenicity is used to consider the available data ([U.S. EPA, 2005a](#)). Age-Dependent Adjustment Factors (ADAFs) are then applied for carcinogens with a MMOA and/or for carcinogens with available data indicating increased susceptibility after developmental life stage exposure ([U.S. EPA, 2005b](#)) if relevant to potentially exposed populations.

According to the Supplemental Guidance for Assessing Susceptibility from Early Life Exposure to Carcinogens ([U.S. EPA, 2005b](#)); see Figure_Apx K-1 below), chemicals are considered for whether there is a MMOA in animal studies. This figure illustrates the considerations and decision logic for whether ADAFs are applied. For 1-BP, the data are suggestive of a MMOA, but not conclusive. Therefore, linear extrapolation was performed as default and ADAFs were not applied.



Figure_Apx K-1. 1-BP Mutagenic MOA Weight of the Scientific Evidence Determination Following the Supplemental Guidance¹ for Assessing Susceptibility from Early-Life Exposure to Carcinogens

¹EPA’s Guidelines for Carcinogen Risk Assessment ([U.S. EPA, 2005a](#)) includes a framework to establish MOA(s) for a chemical. Purple boxes indicate the decisions made for 1-BP based on the available animal and human cancer studies and mechanistic studies. Blue boxes indicate options in the supplemental guidance that were not supported by the available 1-BP data. The WOE for 1-BP for a mutagenic MOA is suggestive but inconclusive. This figure was adapted from Figure 1-1. Flow chart for early-life risk assessment using mode of action framework in the Supplemental guidance ([U.S. EPA, 2005b](#)).

Table_Apx K-1. Decisions and Justification Relating to Mutagenic Mode of Action Analysis for 1-BP (see Figure 1 from ([U.S. EPA, 2005b](#)))

Decision	Justification	Document; p. #
MOA not sufficiently supported in animals	WOE for MMOA is suggestive but inconclusive.	Section 3.2.4.2

There are uncertainties in the 1-BP database associated with a hypothesized MMOA for carcinogenesis. Data gaps include conclusive information on the mutagenic properties of 1-BP and its metabolites in vitro and in vivo, data on the nature and frequencies of mutations in workers exposed to 1-BP over time, information on variations in susceptibility of the human population to cancer (*e.g.*, related to cyp2E1 polymorphisms or other differences), and associations between developmental life stage exposure and cancer in childhood and adulthood. The available data are not sufficient to establish the molecular initiating and/or key events in the adverse outcome pathway from 1-BP exposure to development of cancer.