U. S. Department of Justice
Drug Enforcement Administration

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Marcia Crosse
Director, Health Care
U.S. Government Accountability Office
441 G Street NW
Washington, DC 20548

Dear Ms. Crosse:

The Drug Enforcement Administration (DEA) provides the following comments to the Government Accountability Office (GAO) report entitled "*Controlled Substances: Better Management of the Quota Process and Enhanced Coordination between DEA and FDA Needed to Address Drug Shortages*" (GAO-15-202).

It is important to note that the titled conclusion of the report is inconsistent with the GAO finding that it cannot establish either a "causal relationship between shortages of drugs containing controlled substances and DEA's management of the quota setting process" (Draft, p. 45) or that DEA coordination with the U.S. Food and Drug Administration (FDA) adversely affected the availability of drug products containing controlled substances.[1]

Introduction

The DEA agrees that prescription drug abuse is a nationwide epidemic and more must be done to prevent, detect, and deter the diversion of pharmaceutical controlled substances that supply drug addiction and abuse. The DEA role in this effort is as the primary agency responsible for coordinating the drug law enforcement activities of the United States. The Diversion Control Program (DCP) is a strategic component of the DEA's law enforcement mission. The DEA Office of Diversion Control administers the DCP and implements and enforces Titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. 21 U.S.C. 801–971. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, but are collectively referred to as the "Controlled Substances Act" or the "CSA." The CSA and its implementing regulations are designed to prevent, detect, and deter the diversion of controlled substances and listed chemicals into the illicit market while

[1] See Draft, p. 34 (stating GAO "cannot confirm whether DEA's lack of timeliness in establishing annual and supplemental quotas has caused or exacerbated shortages"); p. 40 (stating "DEA and FDA have not established a sufficiently collaborative relationship, which *could* hinder their abilities to effectively coordinate *future* shortages") (emphasis added).

establishing the total quantity of each basic class[2] of controlled substance in schedules I and II and for ephedrine, pseudoephedrine, and phenylpropanolamine to be manufactured each year to provide for the estimated medical, scientific, research, and industrial needs of the United States, for lawful export requirements, and for the establishment and maintenance of reserve stocks. This is a delicate balance.

One way that DEA provides for the estimated medical, scientific, research, and industrial needs of the United States is to establish an aggregate, nationwide quota for each basic class of schedule I and II controlled substance (referred to as the Aggregate Production Quota, or "APQ") and to authorize individual quotas (referred to as manufacturing quota and procurement quota). It is important to understand that DEA authorizes quota only at the manufacturer level for those entities that manufacture active pharmaceutical ingredients (API), those entities that manufacture substances into dosage forms, and those entities that repackage or re-label drug products that contain schedule I or II controlled substances. Once the aggregate quota is established and a particular manufacturer is

[2] "Basic class" means, as to controlled substances listed in Schedules I and II:
(1) Each of the opiates, including its isomers, esters, ethers, salts, and salts of isomers, esters, and ethers whenever the existence of such isomers, esters, ethers, and salts is possible within the specific chemical designation, listed in §1308.11(b) of this chapter;
(2) Each of the opium derivatives, including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation, listed in §1308.11(c) of this chapter;
(3) Each of the hallucinogenic substances, including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation, listed in §1308.11(d) of this chapter;
(4) Each of the following substances, whether produced directly or indirectly by extraction from substances of vegetable origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis:
(i) Opium, including raw opium, opium extracts, opium fluid extracts, powdered opium, granulated opium, deodorized opium and tincture of opium;
(ii) Apomorphine;
(iii) Codeine;
(iv) Etorphine hydrochloride;
(v) Ethylmorphine;
(vi) Hydrocodone;
(vii) Hydromorphone;
(viii) Metopon;
(ix) Morphine;
(x) Oxycodone;
(xi) Oxymorphone;
(xii) Thebaine;
(xiii) Mixed alkaloids of opium listed in §1308.12(b)(2) of this chapter;
(xiv) Cocaine; and
(xv) Ecgonine;
(5) Each of the opiates, including its isomers, esters, ethers, salts, and salts of isomers, esters, and ethers whenever the existence of such isomers, esters, ethers, and salts is possible within the specific chemical designation, listed in §1308.12(c) of this chapter; and
(6) Methamphetamine, its salts, isomers, and salts of its isomers;
(7) Amphetamine, its salts, optical isomers, and salts of its optical isomers;
(8) Phenmetrazine and its salts;
(9) Methylphenidate;
(10) Each of the substances having a depressant effect on the central nervous system, including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation, listed in §1308.12(e) of this chapter. 21 C.F.R. § 1300.01(b).

authorized to manufacture a specific amount of a basic class of controlled substance, DEA cannot require the manufacturer to manufacture API or a specific drug product, or distribute that substance down through the supply chain. Furthermore, a bulk manufacturer may extract or synthesize API in an authorized calendar year, and hold it in inventory until any subsequent calendar year. Of equal importance, the CSA prohibits DEA from establishing quotas in terms of individual pharmaceutical dosage forms prepared from or containing such a controlled substance. 21 U.S.C. § 826(a). These limitations are critical to understanding the effect that quota can have on the availability of a specific drug product at the retail level or at the emergency medical service (EMS) provider level. The failure to appreciate these limitations is the fatal flaw in the GAO report.

Another fundamental weakness in the GAO report is the failure to account for the fact that "shortage" means different things to different entities, and without accounting for this distinction, the GAO report is misleading with respect to the effect that the DEA quota process can have on patient care. To identify trends in shortages of drugs containing controlled substances, GAO analyzed University of Utah Drug Information Service (UUDIS) data. UUDIS broadly defines a "shortage" as a supply issue that affects how pharmacies prepare and dispense a product or that influences patient care when prescribers must choose an alternative therapy because of a supply issue. A UUDIS "critical shortage" occurs when alternative medications are unavailable, the shortages affect multiple manufacturers, or the shortages are widely reported. In addition, UUDIS information is based on national drug codes (NDCs) rather than the basic class of controlled substance contained within a specific drug product. NDCs are identifiers that are unique to a particular manufacturer, drug product, dosage form, dosage strength, and package size. Accordingly, a single basic class of controlled substance will be represented by many different NDCs. Statistics and analysis based on the NDC, rather than the basic class of controlled substance, could dramatically distort the actual number of shortages that could be attributed to quota.

From September 2006 through July 2012, the FDA defined a "drug shortage" as a "situation in which the total supply of all clinically interchangeable versions of an FDA-regulated drug is inadequate to meet the current or projected demand at the user level."[3] (FDA CDER MAPP 6003.1, Sept. 26, 2006). FDA changed their definition in September 2014 to align with the definition in the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA) to "a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug." Although this new definition is materially different from the definition applicable during the period in review (2011 and 2012), the GAO report uses the 2014 definition in its analysis.

In contrast to the UUDIS and FDA, which view shortages in the context of patient-level availability, DEA views shortages in the context of manufacturer-level quota. Accordingly, a shortage within DEA's jurisdiction is the lack of sufficient quota available for bulk or dosage form manufacturers to manufacture a basic class of a schedule I or II controlled substance. This perspective is the result of the CSA prohibition against establishing quotas in terms of individual

[3] The GAO report discusses DEA's concern with the reliability of information posted on FDA's drug shortage website. During the period under review, DEA was concerned that FDA did not adhere to the applicable definition of "drug shortage" because FDA was listing drug products in shortage when clinically interchangeable drug products were available. Other inaccuracies included reporting that some distributors experienced a shortage due to quota or lack of API, yet distributors do not receive quota.

pharmaceutical dosage forms prepared from or containing a controlled substance, together with the mandate to limit the supply of controlled substances available for diversion, and the inability to require a manufacturer to manufacture a specific API or drug product or require the distribution of controlled substance drug products downstream. Accordingly, if alternative forms of a drug product are available (e.g., brand, generic, or other clinically interchangeable drug products), or if manufacturers have quota authorization, the DEA cannot remedy any patient-level shortage (e.g., inadequate supply at the retail level or EMS provider level) by increasing the aggregate or authorizing more quota at the manufacturer level. GAO fails to emphasize and account for these fundamental distinctions in its review of the potential effect of the quota process on the availability of drug products containing schedule II controlled substances.

Some simplified examples can illustrate how the above distinctions can skew shortage conclusions. If there is an unmet patient need for hydromorphone 10 mg/mL, 1 mL vials, UUDIS and FDA would qualify it as a shortage. However, DEA would not consider there to be a shortage within its jurisdiction if the 10 mg/mL, 5 mL vials are available. Similarly, DEA would not consider there to be a shortage if the brand name version of a particular drug product is unavailable, if the generic version of the drug product is available. Also, there would be no shortage in DEA's jurisdiction if there is hydromorphone quota available in the APQ (i.e., the annual APQ has not been exhausted) and manufacturers are not requesting additional quota, or if manufacturers with authorized hydromorphone quota are not manufacturing their quota allotment or are not distributing the manufactured hydromorphone downstream.

Further comments regarding the GAO report are focused on the following three main areas and are discussed below: method of conducting investigation; method of data analysis; and GAO conclusions.

Method of conducting investigation:

Generally, the Congressional requesters sought to "better understand the impact of DEA quotas on patients with emergency medical and critical care conditions and traumatic injuries, and the extent to which DEA policies and regulations may impede the ability of physicians and health care providers to mitigate a shortage of a drug on any of the applicable schedules." Specifically, GAO was asked to particularly focus on shortages of drugs containing controlled substances used by EMS providers and to treat attention deficit hyperactivity disorder (ADHD). GAO did not evaluate the flow of specific controlled substances from the point of quota request and authorization to manufacture, or from the point of manufacture to distribution to the retail level, using available data from the Automation of Reports and Consolidated Orders System (ARCOS) and Year End Reporting and Quota Management System (YERS/QMS).

GAO was aware of which manufacturers self-reported shortages to FDA claiming the shortage was due to quota, and which specific drug products were reported in shortage due to quota, yet GAO did not investigate each manufacturer's quota allotment or usage, the manufacturer's manufacturing and distribution practices, whether the manufacturer provided adequate justification for quota, or if the manufacturer asked for quota before or after reporting the shortage. In fact, GAO did not attempt to determine whether "shortages" actually existed because of a lack of quota. GAO was not without the tools to determine the answer to this question. After a protracted and contentious

negotiation regarding the data that DEA could release to GAO to conduct this investigation, DEA and GAO reached an agreement wherein DEA provided specified information from ARCOS and YERS/QMS. ARCOS and YERS/QMS data could have provided GAO with a full view of the distribution of schedule II controlled substances by manufacturers and distributors, from the point of bulk manufacture, to dosage form manufacture, and down to distribution to the retail level. Instead, GAO simply reported manufacturers' anecdotal complaints about the quota process' effect on shortages.

Amphetamine is a schedule II controlled substance and is used to treat ADHD, among other things, and it was reported to be in shortage during the review period. GAO requested ARCOS information pertaining to 17 specific NDCs, all of the amphetamine basic class. However, the 17 requested NDCs represented only a small fraction of the available market supply. The DEA estimated that there were 48 other amphetamine-containing drug products, 25 of which were manufactured and distributed during the period under review. GAO did not request ARCOS data on the other available amphetamine-containing products on the market, and GAO did not discuss in its report any findings relative to the 17 requested NDCs. The ARCOS information, combined with information from YERS/QMS, is crucial to determining whether sufficient API was manufactured, whether the API was distributed downstream by bulk manufacturers, whether dosage form manufacturers were manufacturing drug products in accordance with their quota applications, whether dosage form manufacturers were distributing drug products downstream and if so, where, and whether controlled substances were being held at the manufacturer level or destroyed rather than placed into the supply chain.

DEA is confident that a review of ARCOS and YERS/QMS data would have established that DEA's administration of the quota process did not cause or exacerbate any shortages of drug products used to treat ADHD in 2011. In 2011, DEA increased the APQ for amphetamine salts by 6,700 kg. A review of the ARCOS and YERS/QMS data for amphetamine salts showed that manufacturers subsequently requested, and DEA authorized, only a very small percentage of this increase. In addition, a significant number of amphetamine dosage units were destroyed throughout 2011, as well as a substantial amount of raw material, and millions of dosage units of ADHD drug treatment products still remained at the distributor and retail level at the end of 2011.

Close review of the ARCOS data would have also refuted manufacturers' assertions about the effects of DEA's timing to establish quotas. For example, manufacturer representatives reported to GAO that the timeline for establishing quotas does not provide manufacturers with enough time to plan for production and order the raw material or API needed to start manufacturing their products at the beginning of the production year. Representatives reported to GAO that they operated solely with what is left in their inventory for the first few months of the production year, "which may be limited because manufacturers operate in a lean manufacturing environment where they carry as little inventory as possible." (Draft, p. 30). This statement from manufacturers is conflicting. Manufacturers complained that they do not have sufficient inventory because of quota and must operate on what is solely remaining in inventory, but then go on to state their business choice to operate in a lean environment where they carry as little inventory as possible. Even so, manufacturers may manufacture API and procure raw material at any time during the year, and not distribute it until the next calendar year because DEA regulations provide for an inventory allowance.

In addition, a review of ARCOS data would have been critical to determining whether the DEA's processing of supplemental quota applications in 2011 caused or exacerbated FDA-reported drug shortages, as alleged by manufacturers. (Draft, p. 30-31). GAO's probability sample of YERS/QMS source documents showed that it took DEA an average of 58 days to respond to supplemental quota applications in 2011 and 2012. (Draft, p. 30-31). GAO also reported that it took DEA 10 days longer, on average, to respond to supplemental quota applications submitted by manufacturers that reported shortages caused by quota in 2011. However, as discussed above, a review of ARCOS and YERS/QMS information would have established that amphetamine manufacturers only sought authorization to manufacture a very small percentage of the mid-year increase.

Method of Data Analysis:

The report's extensive description of the nature and magnitude of shortages (Draft, p. 17) is misleading as it uses a very broad definition of "shortage," using data from two different sources to quantify and explain the consequences of shortages, and then ties these consequences to the very small number of schedule II drug product "shortages" without ever establishing causation between the specific shortage and the quotas for the specific basic class of controlled substance.

GAO found that approximately 10% (168 of 1,575) of the UUDIS shortages from January 2001 through June 2013 involved drug products containing a controlled substance (Draft, p. 17); of these, 57% (96) involved drug products containing schedule II controlled substances (Draft, p. 19), or approximately 6% (96 of 1,575) of the total number of UUDIS shortages. Because UUDIS information is presented according to NDC rather than the basic class, the results (96 shortages of schedule II controlled substances from 2001 to 2013) can dramatically distort the actual number of shortages that could have been attributed to lack of quota in a particular basic class of controlled substance. The results can also be misleading because UUDIS counts a shortage as a period of time; as a result, 45 different drugs containing controlled substances were reported to be in shortage multiple times from January 2001 through June 2013, representing 143 individual shortages. (Draft, p. 19). The data could also be distorted by the fact that GAO analyzed data from YERS/QMS for 2011 and 2012, rather than 2001 to 2013. Analyzing the information regarding the specific drug products and the specific basic class of controlled substance represented by the 96 NDCs, as well as the calendar year that the substances were reported in shortage would have helped to determine the role, if any, that quota played in any shortage.

GAO also reported that critical shortages represented 52% (87 of 168) of all shortages of drugs containing controlled substances. (Draft, p. 4, n.6; p. 21). Of the 87 shortages containing controlled substances identified as critical by UUDIS from January 2001 through June 2013, half (44 of 87) involved pain relievers (analgesics). (Draft, p. 20-21). Analgesics can be controlled in schedule II, III, IV, or V. However, GAO does not state whether these products contained schedule II controlled substances subject to quota, or schedule III through V controlled substances not subject to quota. This information, along with the NDCs and basic class of controlled substance involved, would be important in determining the role, if any, quota played in any shortage, particularly with respect to the UUDIS "critical shortages," because the applicable criteria (alternative medications are unavailable, the shortages affect multiple manufacturers, or the shortages are widely reported) are more likely to implicate quota than a standard shortage (a supply issue that affects how pharmacies

prepare and dispense a product or that influences patient care when prescribers must choose an alternative therapy because of a supply issue).

Even so, for the period January 2010 to June 2013, GAO reported that there were 40 FDA-reported shortages of drug products containing schedule II controlled substances, and of those, only seven were alleged to have been caused or exacerbated by quotas. (Draft, p. 30). The remaining 33 reported shortages of drugs containing schedule II controlled substances were caused by other factors that cause shortages of drugs generally such as manufacturing delays, capacity issues, and product quality issues. (Draft, p.30). GAO does not state whether any of these seven shortages occurred during the period in review, 2011 and 2012, nor does GAO indicate which basic class of controlled substance was involved, or whether each shortage involved a different basic class of controlled substance or if a single basic class of controlled substance was involved in several reported shortages. However, GAO contacted the 10 manufacturers that reported the seven shortages from January 2010 to June 2013, and reported that "many" manufacturers stated DEA's lack of timeliness in establishing quotas caused or exacerbated shortages of their drug products. It does not appear that GAO verified these statements with the data it obtained from YERS/QMS or ARCOS. Rather, the cause of these self-reported shortages was substantiated by collecting anecdotal information from manufacturers.

Some drug products specifically mentioned in the report were in shortage due to reasons other than quota. For example, beginning in 2010, a major manufacturer of injectable drug products containing controlled substances voluntarily shut down certain of its production lines and slowed the release of products in certain manufacturing facilities as a result of certain quality issues cited by the FDA. Such interruptions adversely impacted, and continue to adversely impact, the manufacturer's ability to manufacture and sell its products. The availability of all injectables were adversely affected, including substances specifically mentioned in the GAO report as having significant deleterious effects on patient care as a result of shortage, such as fentanyl, hydromorphone, and morphine—all schedule II substances subject to quota. Review of the quota data would have shown that when new manufacturers submitted quota applications to meet the new demand, DEA verified with FDA the supply disruption and acted quickly to authorize quota to the new manufacturers.

In addition, some drug products emphasized by GAO when it reported the effects of drug shortages on treatment and patient care were not drug products subject to quota. For example, GAO references an American Society of Anesthesiologists' survey regarding the effects of drug shortages on anesthesiologists. (Draft, p.24, n.49). The highest frequency of reported shortages were fentanyl (66%), thiopental (40%), succinylcholine (21%), propofol (19%), and pancuronium (15%). As discussed above, fentanyl shortages were due to manufacturing issues. Thiopental is a schedule III controlled substance and thus not subject to quotas; and the remaining three substances are non-controlled substances. In another example, lorazepam injection is a schedule IV controlled substance, and GAO highlighted the adverse consequences of its shortage, indicating that a single shortage of it lasted slightly more than 5 years. (Draft, p. 18). Another consideration GAO ignores is that the benzodiazepines are primarily imported and not manufactured in the United States. Finally, GAO reports that oxycodone oral solution (Draft, p.19), a drug GAO reports is used to treat moderate to severe pain, was in shortage for the longest combined amount of time from January 2001 through June 2013. However, certain oxycodone oral solution drug products were not FDA-approved drugs and could not be lawfully manufactured or distributed until FDA approval in

September, 2014.

GAO Conclusions:

Failure to utilize the available information as discussed above, and failure to evaluate and analyze the causes of specific controlled substance shortages lead to an analysis that unfairly linked the quota process to diminished patient care. Even though GAO could not find that shortages occurred because of a lack of quota or because of DEA's administration of the quota process, GAO makes several inferences about a relationship between drug shortages and the quota process. This was accomplished because GAO begins its report with identifying trends in shortages from January 2001 through June 2013, and then examines DEA's administration of the quota process, thereby suggesting the effect of the quota process on shortages. However, GAO only evaluated quota data for 2011 and 2012, and its evaluation is not generalizable to other years.

As discussed above, only seven of 40 FDA-reported shortages of drug products containing schedule II controlled substances were alleged to have been caused or exacerbated by quotas. GAO reports that it cannot confirm that DEA's lack of timeliness caused or exacerbated shortages. However, the tools were available to GAO to refute the specific claims that DEA's administration of the quota process caused or exacerbated shortages.

DEA is confident that its administration of the quota process did not affect a shortage during the period in review because drug product shortages are not limited to products that contain schedule II controlled substances. In fact, for the period January 2010 to June 2013, only 18% (7 of 40) of FDA-reported schedule II drug product shortages implicated quotas. Also, UUDIS data shows that from January 2001 through June 2013, approximately 43% of all reported controlled substance shortages were present in schedule III through V drug products, where quotas are not involved. (Draft, p. 19). In addition, GAO found that, from January 2001 through June 2013, the number of new controlled substance shortages reported each year peaked in 2009 and then declined. (Draft, p. 17-18; fig. 2). The increase in these shortages mimics the pattern found for shortages of all drugs, indicating that the same factors affecting shortages of all drugs are also the same factors affecting shortages of drugs containing controlled substances. It is more likely that a common denominator (or a combination of common denominators) are effecting the similar patterns in shortages amongst controlled substances and non-controlled substances; as well as amongst schedule II controlled substances and schedule III through V controlled substances.

GAO concluded that by not acting "promptly" on supplemental applications, DEA may hinder manufacturers' ability to manufacture schedule II drugs that may help prevent or resolve a shortage. However, as explained above, even if DEA increased the APQ or authorized additional manufacturing or procurement quota, manufacturers must apply for it and actually use it to manufacture the drug products in shortage, and then distribute those products downstream—activities that DEA cannot compel.

DEA Response to Recommendations:

GAO Recommendation (1): Establish controls, such as periodic data checks, to ensure that the YERS/QMS data accurately reflect both manufacturers' quota submissions and DEA's decisions.

Response: The GAO report found that the data error rate was substantially improved from the initial year the process became electronic to the second year (2011 to 2012), dropping from 45% to 10%. (Draft, p. 35). DEA has established policies and procedures to ensure data is accurate. In order to determine the timeliness of responses to submitted requests, there are a number of computer-generated dates, including date submitted, date assigned for review, and date review complete. In order to determine accuracy in quota values being requested and granted there are a series of system-generated flags in YERS/QMS. The flags guide and verify data provided by applicants; and there are flags for internal review, including when a quantity greater than requested is entered. Managers review worksheets for accuracy in summarizing the analysis of the data and supporting documentation provided by the applicant. They then verify that the values contained in the working documents are accurately entered into YERS/QMS. Upon final authorization, managers close the application in YERS/QMS after ensuring that the dates mailed are entered as the authorization letters are scanned and sent to the applicant (via email and U.S. Postal mail). YERS/QMS has a flag to ensure that the date entered is correct.

GAO Recommendation (2): Establish performance measures for DEA related to quotas and ensuring an adequate and uninterrupted supply of controlled substances for legitimate medical use.

Response: DEA recognizes the value in establishing performance measures for personnel reviewing quota applications and will determine whether performance is measurable with regard to processing quotas. Many factors determine how quickly and how accurately a quota application is reviewed and a quota recommended. For example, a single quota application is for one specific basic class; however, each quota request may involve quota for more than one specific drug product containing that basic class. The reasonable amount of time to evaluate each application is highly dependent on how many different factors affect a single request.

GAO Recommendation (3): Monitor and analyze YERS/QMS data to assess DEA's administration of the quota process.

Response: DEA agrees that monitoring and analyzing YERS/QMS data is important to ensuring proper administration of the quota process. The YERS/QMS data are integrally related for manufacturing and procurement quotas applications and responses. The data are reviewed and monitored constantly when analyzing each quota application. For example, with the APQ set as the maximum of each basic class to be manufactured each year, the quota review process of every manufacturing quota application checks the APQ, amounts issued, pending and remaining. In addition, the manufacturing quota data are analyzed and used with other sources to establish and revise the annual APQs.

GAO Recommendation (4): Establish internal policies for processing quota applications and setting aggregate, annual, and supplemental quotas to ensure that staff conduct these activities consistently and in accordance with the CSA and agency's regulations.

Response: DEA has established policies and procedures for staff administering the quota

procedures. In addition, beginning with 2013 APQs, DEA included an additional 25% of the estimated medical, scientific, and research needs as part of the amount necessary to ensure the establishment and maintenance of reserve stocks. DEA expects that maintaining this reserve in the aggregate production quotas will mitigate adverse public affects if an unforeseen event results in substantial disruption to the amount of controlled substances available to provide for legitimate public need.

GAO Recommendation (5): Expeditiously establish formal policies and procedures to facilitate coordination with FDA as directed by FDASIA, including a specific timeframe in which DEA will be expected to respond to FDA requests to expedite shortage-related quota applications.

Response: DEA shall follow the requirements of FDASIA to respond to requests within 30 days. It should be noted that no special requests for expedited quota review have been forwarded to DEA since enactment of FDASIA in July, 2012. As previously conveyed to GAO, DEA and FDA began negotiating the terms of a new information sharing agreement before this engagement commenced. As of December 15, 2014, the final memorandum of agreement has been routed for signature within DEA.

GAO Recommendation (6): Promptly update the MOU between the two agencies.

Response: As previously conveyed to GAO, DEA and FDA began negotiating the terms of a new information sharing agreement before this engagement commenced. As of December 15, 2014, the final memorandum of agreement has been routed for signature within DEA.

GAO Recommendation (7): Either in the MOU or in a separate agreement, specifically outline what information the agencies will share, and timeframes for sharing such information, in response to a potential or existing drug shortage.

Response: As previously conveyed to GAO, DEA and FDA began negotiating the terms of a new information sharing agreement before this engagement commenced. As of December 15, 2014, the final memorandum of agreement has been routed for signature within DEA. DEA and FDA have engaged in discussions to determine the specific procedures by which information regarding drug shortages shall be exchanged, pursuant to FDASIA. These procedures will be memorialized in a mutually agreeable workplan.

Conclusion:

There can be no doubt that drug shortages adversely affect the public health. Drug shortages occur across the continuum of pharmaceutical characteristics, e.g., brand, generic, controlled, non-controlled, over-the-counter, dosage forms and dosage strengths, analgesics, sedatives, stimulants. Shortages can be caused by a variety of factors, as GAO previously reported in 2011 and 2014. Determining the relationship between retail and EMS level drug product shortages and manufacturing quota is a multifaceted undertaking that particularly requires an understanding of controlled substance manufacturing and distribution practices, an appreciation of how competitive contractual agreements affect the actions of manufacturers, distributors, and patent owners, and how

these dynamics influence the annual forecasting of quota need.

DEA remains committed to establishing production quotas for each basic class of controlled substance in schedule II to be manufactured each year to provide for the estimated medical, scientific, research, and industrial needs of the United States, for lawful export requirements, and for the establishment and maintenance of reserve stocks. Accordingly, DEA appreciates the GAO finding that it cannot establish a causal relationship between shortages of drugs containing controlled substances and DEA's management of the quota setting process.

Should you have any questions regarding this matter or our comments, please contact Michael A. Dixon, Acting Deputy Chief Inspector, Office of Inspections, at (202) 307-4007.

Sincerely,

FOR

Joseph T. Rannazzisi
Deputy Assistant Administrator
Office of Diversion Control

cc: Richard P. Theis
Director, Audit Liaison Group
Internal Review and Evaluation Office
Justice Management Division