



Report on Drug Shortages for Calendar Year 2016

Required by

Section 1002 of the Food and Drug Administration Safety and Innovation Act

Food and Drug Administration
Department of Health and Human Services

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Commissioner of Food and Drugs

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EXECUTIVE SUMMARY

This fourth annual report to Congress summarizes the major actions taken by the Food and Drug Administration (FDA) during the first three quarters of 2016 to prevent or mitigate drug shortages¹ in the United States. Because drug shortages can pose a significant public health threat that can delay, and in some cases even deny, critically needed care for patients, shortages remain a top priority for FDA. As a result of actions by the President, Congress, and FDA, manufacturers are notifying FDA about potential shortages earlier than in the past. Early notification of potential shortages gives FDA additional time to work with sponsors and other stakeholders to identify ways to maintain treatment options and prevent a shortage. Using a range of available tools, including regulatory flexibility and discretion when appropriate, FDA's Center for Biologics Evaluation and Research (CBER) and FDA's Center for Drug Evaluation and Research (CDER) worked with manufacturers to successfully prevent 63 shortages from January 1 to September 30, 2016. In addition, the number of new shortages tracked by CBER and CDER for this same time period is 21, compared to a peak of 251 *new shortages during the full calendar year of 2011*.²

Based on our experience to date and the data on drug shortages presented in this report, FDA believes that the requirements related to early notification of potential shortages and FDA's own actions are helping to reduce the threat and impact of drug shortages. FDA will continue to prioritize this important public health issue, working to ensure the availability of necessary drugs and biological products for the American public.

¹ For purposes of this report, the term "drug shortage" includes shortages of human drug and biological products. The report may individually refer to shortages tracked by FDA's Center for Drug Evaluation and Research or FDA's Center for Biologics Evaluation and Research, if the context requires distinguishing between these.

² This fourth annual report to Congress addresses all covered drug and biological products. This includes all drugs within the meaning of section 506C(h)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), as well as other products tracked by CDER's Drug Shortage Staff, such as biological products approved under section 505 of the FD&C Act. This also includes biological products licensed under section 351 of the Public Health Service Act and tracked by CBER's Office of Compliance and Biologics Quality, such as vaccines and blood products. See Appendix 2 for a breakdown of 2016 CBER and CDER numbers.

INTRODUCTION

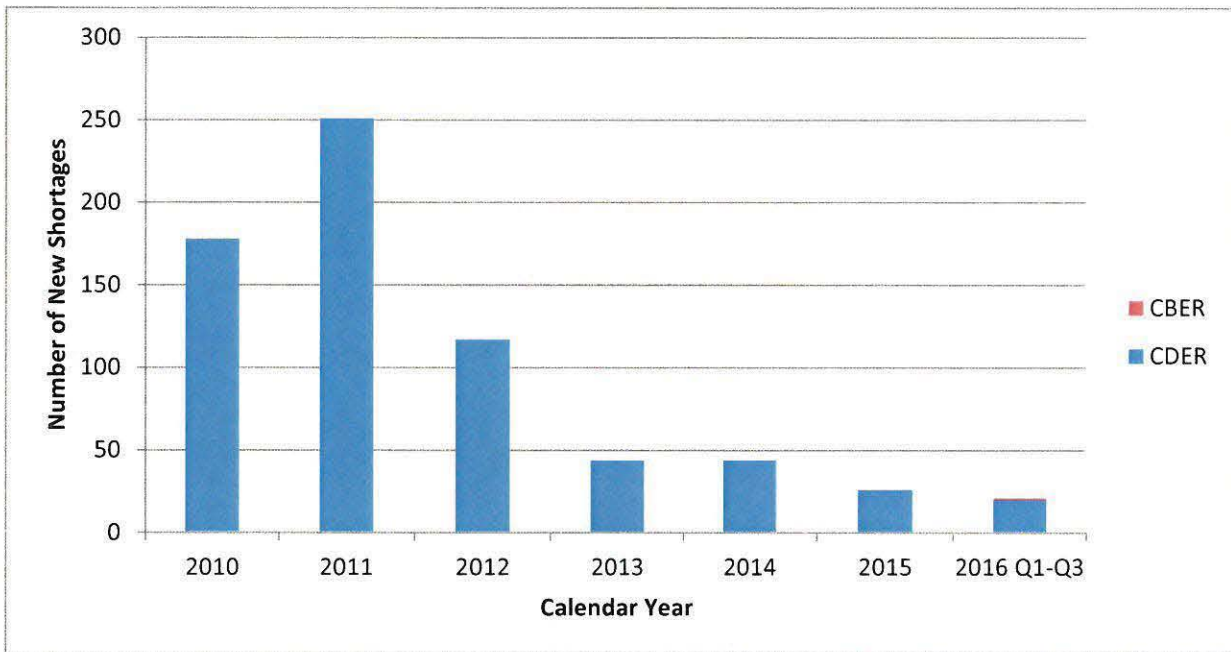
The Food and Drug Administration Safety and Innovation Act (FDASIA) was enacted on July 9, 2012. Title X of FDASIA, which addresses drug shortages, took effect on the date of enactment and, among other things, amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 301 et seq.) by updating section 506C. Section 506C sets forth the requirement that manufacturers notify FDA of a permanent discontinuance or interruption in the production of certain prescription drugs that are life-saving, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition. In addition, section 1002 of Title X of FDASIA added section 506C-1 to the FD&C Act, requiring FDA to file a report to Congress at the end of each calendar year on drug shortages. FDA is submitting this annual report to fulfill its obligations under section 506C-1. The report provides background about drug shortages and FDA efforts to address them to date. FDA also responds to the specific issues listed under section 506C-1. The analyses reflect data collected and evaluated by FDA's Center for Biologics Evaluation and Research (CBER) and FDA's Center for Drug Evaluation and Research (CDER) from January 1, 2016, through September 30, 2016. This report also summarizes some important ongoing activities FDA believes will help to address drug shortages in the future. A list of definitions and three appendices, which includes the statutory language regarding annual reporting on drug shortages and the breakdown of data supplied by CBER and CDER, are included at the end of this report.

BACKGROUND

Drug shortages can have serious and immediate effects on providing needed therapies to patients, and preventing shortages is a priority for FDA. At the height of the drug shortage crisis, the number of new shortages tracked by CDER quadrupled from approximately 61 shortages in 2005 to more than 250 in 2011.

The following figure shows the number of new drug shortages identified by year from 2010 through September 30, 2016.

Figure 1. Number of New Drug Shortages Per Year, 2010 Through September 30, 2016³



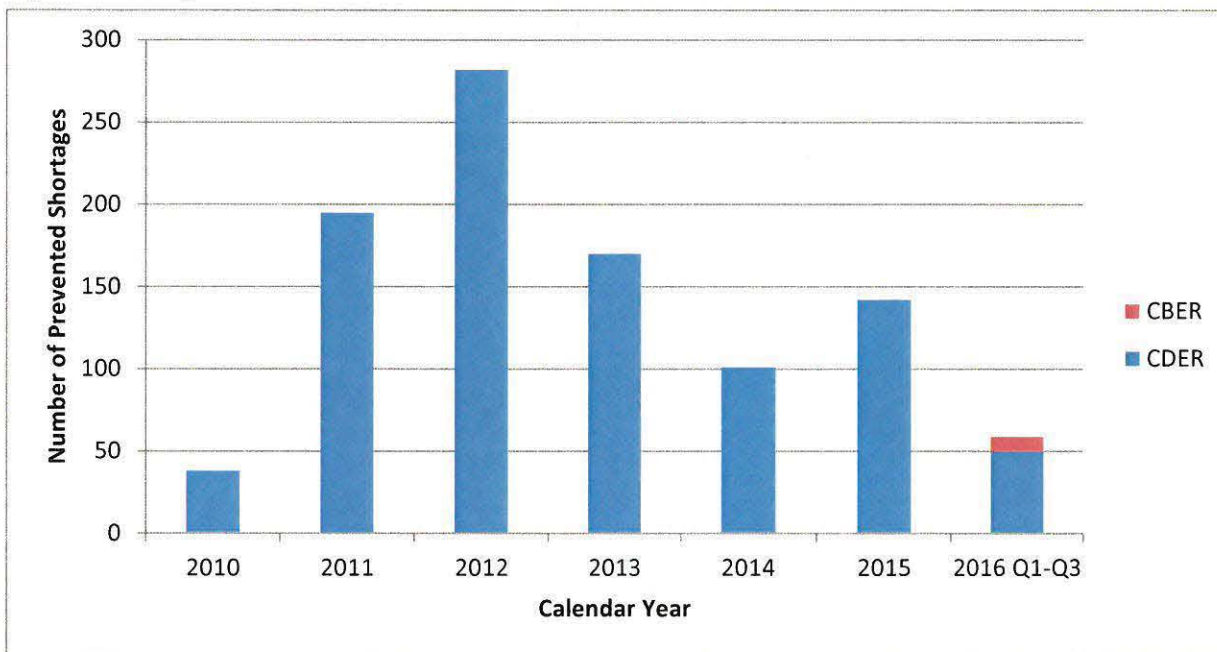
Although the number of new drug shortages has declined since 2011 as a result of work by many groups including the FDA, shortages continue to pose a real challenge to public health. This is especially the case when a shortage involves a critical drug to treat cancer, to provide parenteral nutrition, or to address another serious medical condition, such as the shortage of intravenous saline solution. These shortages can delay or deny needed care for patients, creating a potential lapse in medical care. Shortages can also lead prescribers to use second-line alternatives, which may be less effective or pose additional risks. To prevent these situations from occurring, FDA has used a variety of methods to prevent shortages, working within the confines of the statutory and regulatory framework in place and in partnership with manufacturers and other stakeholders. As tracked by CDER, FDA helped prevent 282 drug shortages in 2012, 170 shortages in 2013, 101 shortages in 2014, and 142 shortages in 2015. In the first three quarters of 2016, FDA helped to prevent 63 shortages as tracked by CBER and CDER.⁴

The following figure shows the number of prevented drug shortages identified by year from 2010 through September 30, 2016.

³ This fourth annual report to Congress is the first year to include both reporting for those covered drug and biologic products. See Appendix 2 for a breakdown of 2016 CBER and CDER numbers.

⁴ See supra n. 2.

Figure 2. Number of Prevented Drug Shortages Per Year, 2010 Through September 30, 2016⁵



Several actions have been taken in recent years that helped FDA address drug shortages.

1. Executive Order 13588 – Reducing Prescription Drug Shortages

In response to a dramatic increase in shortages, on October 31, 2011, the President issued Executive Order 13588, recognizing that “shortages of pharmaceutical drugs pose a serious and growing threat to public health...endanger patient safety...burden doctors, hospitals, pharmacists, and patients...and increase health care costs.”⁶ The Executive Order acknowledged the need for a “multifaceted approach” to address the many different factors that contribute to drug shortages. The Executive Order directed FDA to take steps to help prevent and reduce current and future disruptions in the supply of life-saving medicines, including notifications and expedited reviews, as appropriate.

⁵ This fourth annual report to Congress is the first year to include both reporting for those covered drug and biologic products. See Appendix 2 for a breakdown of 2016 CBER and CDER numbers.

⁶ Executive Order 13588, available at <http://www.whitehouse.gov/the-press-office/2011/10/31/executive-order-reducing-prescription-drug-shortages>.

2. FDA Safety and Innovation Act

With the passage of FDASIA on July 9, 2012, FDA was given important new authorities related to drug shortages. For example, section 1001 of FDASIA broadened the scope of the early notification provisions by requiring manufacturers of *all prescription drugs* that are life-supporting, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition (whether approved or unapproved) to notify FDA of a permanent discontinuance or temporary interruption in manufacturing. FDASIA also allowed FDA to require, by regulation, early notification of discontinuances or interruptions in manufacturing of biologics. FDASIA requires FDA to send a non-compliance letter to firms that fail to notify FDA in accordance with section 506C, as amended by FDASIA. FDA sent the first two letters in 2014, and posted the letters and the responses from the manufacturers on its website. As described in more detail below, two additional non-compliance letters were sent during the first three quarters of 2016. Section 506C also authorizes FDA to expedite reviews of drug applications and supplemental applications and to expedite inspections that could help mitigate a shortage. Other FDASIA requirements with respect to prescription drug shortages include improving FDA's internal and external communications about shortages, improving communication between FDA and the Drug Enforcement Administration (DEA) regarding shortages of controlled substances, and developing a strategic plan to enhance FDA's response to preventing and mitigating drug shortages.

3. FDA Strategic Plan to Prevent and Mitigate Shortages

On October 31, 2013, FDA issued its *Strategic Plan for Preventing and Mitigating Drug Shortages*.⁷ The plan contains details on the origin of drug shortages, FDA's processes and procedures for helping to prevent or mitigate shortages, and FDA's strategy for strengthening those processes and procedures. The plan also recommends actions that other stakeholders can consider to help prevent shortages.

4. Final Rule – Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products

On July 8, 2015, FDA published a final rule to implement certain drug shortages provisions of section 506C, as amended by FDASIA.⁸ Among other requirements, the rule requires all applicants of covered approved drug or biological products, including certain applicants of blood or blood components for transfusion, and all manufacturers of covered drug products marketed without an approved application to notify FDA electronically of a permanent discontinuance or an interruption in manufacturing of the product that is likely to lead to a meaningful disruption in supply (or a significant disruption in supply for blood or blood components) of the product in the United States.

⁷ To view the Strategic Plan and related information, visit <http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf>.

⁸ 80 FR 38915 (July 8, 2015). See also 21 CFR 310.306, 314.81, and 600.82.

The rule became effective on September 8, 2015. As noted above, this fourth annual report to Congress includes reporting for all covered drug and biological products.

DATA SOURCES USED IN THIS REPORT

The data used to fulfill the reporting requirements of section 506C-1 are collected by several program areas within FDA,. Tracking the data for reporting requirements related to drugs and biological products (the number of products in shortage) is within the purview of CBER's Office of Compliance and Biologics Quality (CBER/OCBQ) and the Drug Shortage Staff (DSS). Similarly, CBER/OCBQ and DSS track information about notifications and their source (and, therefore, the number of reporting manufacturers). In contrast, reporting requirements related to expedited review are tied to specific *submissions* by manufacturers that are experiencing production disruptions or manufacturers that are adding or expanding their production capabilities to address a specific shortage. CBER and CDER offices reviewing these submissions track which reviews and related inspections they expedite as a part of a larger set of activities related to their review of submissions. Other reporting requirements for this report relate to instances of regulatory flexibility and discretion. These specific cases, all requiring separate regulatory and scientific evaluation and justification, are tracked by CBER/OCBQ and CDER's Office of Compliance (CDER/OC).

ANNUAL REPORT REQUIREMENTS PER 506C-1

Section 1002 of Title X of FDASIA added section 506C-1 to the FD&C Act, requiring FDA to file a report to Congress on drug shortages at the end of each calendar year.

The statutory requirements for the report are as follows.

Requirement 1: Specify the number of manufacturers that submitted a notification to the Secretary under section 506C(a) during such calendar year.

For the first three quarters of calendar year 2016, FDA was notified of 186 potential drug and biological product shortage situations by 67 different manufacturers.

Requirement 2: Describe the communication between FDA field investigators and CDER/OC and DSS, including FDA's procedures for enabling and ensuring such communication.

CDER/OC and the FDA field investigators in the Office of Regulatory Affairs (ORA) are crucial to FDA's prompt response to a drug shortage. These two groups have separate functions with respect to drug shortages. Consistent with sections 506D(b) and (c) of the FD&C Act, CDER/OC communicates with DSS on warning letter and enforcement action recommendations being reviewed within CDER/OC. FDA field investigators in ORA typically conduct inspections at manufacturing facilities and report on their findings. If the investigators identify actions or activities during an inspection that

warrant a warning letter or enforcement action that could reasonably be anticipated to lead to a meaningful disruption in the supply of a drug, information regarding the observations and the products manufactured can be relayed to CDER/OC immediately so that DSS can begin to assess the supply situation for those products. These procedures are critical to FDA's efforts to prevent and mitigate a potential drug shortage.

To facilitate communications between ORA and FDA medical product centers, which include CBER and CDER, ORA issued Field Management Directive (FMD) #15 in July 2012. FMD #15 established drug shortage coordinators in ORA so that each FDA field district has a District Drug Shortage Coordinator who serves as the point of contact between ORA and FDA's medical product centers. The District Drug Shortage Coordinator is responsible for notifying the relevant FDA center of any issue that has the potential to lead to a product shortage (e.g., information obtained during an inspection or other field activities). FMD #15 clarified communication roles, responsibilities, and expectations related to potential and current product shortage situations between ORA and the centers.

Requirement 3: List the major actions taken by the Secretary to prevent or mitigate drug shortages.

Mitigation efforts begin once FDA has confirmed that a shortage exists or could occur. The actions FDA can take to prevent or mitigate a shortage include, as appropriate:

- Identify the extent of the shortfall and determine if other manufacturers are willing and able to increase production to make up the gap;
- Expedite FDA inspections and reviews of submissions from manufacturers attempting to restore production;
- Expedite FDA inspections and reviews of submissions from competing manufacturers who are interested in starting new production or increasing existing production of products in shortage;
- Exercise temporary regulatory flexibility for new sources of medically necessary drugs;
- Work with the affected manufacturers to ensure adequate investigation into the root cause of the shortage; and
- Develop risk mitigation measures, such as the use of sterile filters, to allow individual batches of a drug product initially not meeting established standards to be released.

FDA can use one or more of these mitigation tools, or seek to develop other options, depending on the severity of the potential shortage and the surrounding circumstances. When selecting specific tools, FDA continues to work with the manufacturer to tailor its

response to the specific situation. As a part of these actions, FDA also frequently communicates available information about a potential shortage or existing shortage to affected stakeholders and monitors the shortage until it has been resolved.

- **List the number of applications and supplements for which the Secretary expedited review under section 506C(g)(1) during such calendar year.**

FDA expedited the review of 102 submissions in the first three quarters of 2016.⁹

- **List the number of establishment inspections or reinspections related to mitigation or prevention of a shortage that the Secretary expedited under section 506C(g)(2) during such calendar year.**¹⁰

Ten FDA inspections were prioritized to address a drug shortage in the first three quarters of 2016.¹¹

Requirement 4: Describe the coordination between FDA and DEA to prevent or alleviate drug shortages.

If a drug at risk of shortage is a controlled substance, FDA works closely with DEA in efforts to prevent or mitigate its shortage. Among other issues, DEA is responsible for setting aggregate limits on the amount of each controlled substance that may be manufactured and for allocating to each manufacturer a specific percentage of the aggregate limit (a quota). This tight control over controlled-substance products requires FDA and DEA to coordinate when a shortage of a controlled substance is looming. For example, FDA may work with DEA to enable a manufacturer to increase its allotted quota if this step would help avoid a shortage of the product.

Recognizing this need, FDASIA included provisions on improved coordination and communication between FDA and DEA regarding a potential shortage of a controlled substance. To help streamline and improve communications, FDA and DEA developed a memorandum of understanding (MOU). The MOU sets forth steps and procedures, including identifying contacts, for efficiently tracking and exchanging relevant information.¹²

⁹ See Appendix 3 for a breakdown of submission types.

¹⁰ Includes prioritized inspections or site reviews for new applications or supplements, which were granted expedited review due to drug shortage.

¹¹ Note that not all submissions to FDA require inspections, but some submissions may involve multiple sites that require multiple inspections.

¹² The MOU can be found at <http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm440091.htm>.

Requirement 5: Identify the number of (and describe) instances in which FDA exercised regulatory flexibility and discretion to prevent or alleviate a drug shortage.

FDA's standards of safety, efficacy, and quality do not change in a shortage situation. FDA's preferred solution to a shortage is to help ensure that there is a supply of approved drugs and biological products sufficient to meet patient demand, as well as meet the appropriate quality, safety, and efficacy standards. However, FDA recognizes that there can also be risks to patients if treatment options are not available for critical conditions and understands the importance of using appropriate tools for a given situation to prevent or mitigate a shortage. In appropriate cases, the temporary exercise of regulatory flexibility and discretion has proven to be an important tool in ensuring access to treatment options for patients in critical need.

During the first three quarters of calendar year 2016, FDA has exercised regulatory flexibility and discretion in 25 instances, affecting 15 products.¹³ Examples of situations in which FDA has exercised regulatory flexibility and discretion to prevent or mitigate a shortage are listed below:

- FDA has used temporary regulatory flexibility and discretion for medically necessary products that present quality issues through the use of measures to mitigate the risks associated with those products when weighed against the risk to patients of not receiving the drug, as follows:
 - Filters are supplied with a product to remove particulate matter,
 - Extra testing for product quality or identity is done at the manufacturing facility before releasing the product into the marketplace,
 - Third-party oversight of production is instituted to monitor quality issues, and
 - Special instructions are provided to health care professionals/patients.
- FDA has used temporary regulatory flexibility and discretion with regard to continued distribution of a drug product to mitigate or resolve a drug shortage while FDA reviews a supplement/proposed change to address a problem with the drug product.
- FDA has used temporary regulatory flexibility and discretion with regard to new sources of medically necessary drugs, including FDA-registered foreign sources, in rare instances when all alternative approaches have been exhausted.

¹³ One instance of regulatory flexibility may affect more than one product. Conversely, a shortage of one product may involve multiple instances of regulatory flexibility.

- FDA has permitted expanded access to investigational drugs for treatment use under an investigational new drug application (IND) (21 CFR 312.315(a)(3)(ii)) to mitigate a shortage of an approved drug product.

Requirement 6: List the names of manufacturers issued letters under section 506C(f).

Under section 506C(f) of the FD&C Act, if a manufacturer fails to provide notification of a discontinuance or interruption in manufacturing as required by section 506C, FDA must issue a letter to that manufacturer stating that the notification requirement was not met. The manufacturer is required to respond to FDA's letter within 30 calendar days, providing the reason for noncompliance and the required information on the discontinuance or interruption. Within 45 calendar days of its original letter to the manufacturer, FDA is required to post that letter and any response received on FDA's website,¹⁴ with appropriate redactions to protect trade secrets or confidential commercial information, unless FDA determines that the original notification was issued in error or, after review of the manufacturer's response, that the manufacturer had a reasonable basis for not notifying FDA as required.

To date, FDA has issued four non-compliance letters under section 506C(f). In 2016, two letters were sent on April 19, 2016, to Par Pharmaceutical and Teva Pharmaceuticals. The letters sent by FDA and the responses received from the manufacturers are available on FDA's website.

Requirement 7: Specify the number of drug shortages occurring during 2016 (the first three quarters of 2016).

The data from CDER's drug shortage database¹⁵ shows that the number of new shortages has significantly decreased in recent years, from 117 in 2012 to 44 in 2013, 44 in 2014, and 26 in 2015. Data indicate that this trend continued into 2016. As of September 30, 2016, there were a total of 21 new drug and biological product shortages identified.¹⁶ In the first three quarters of 2016, FDA prevented 63 drug and biological product shortages.

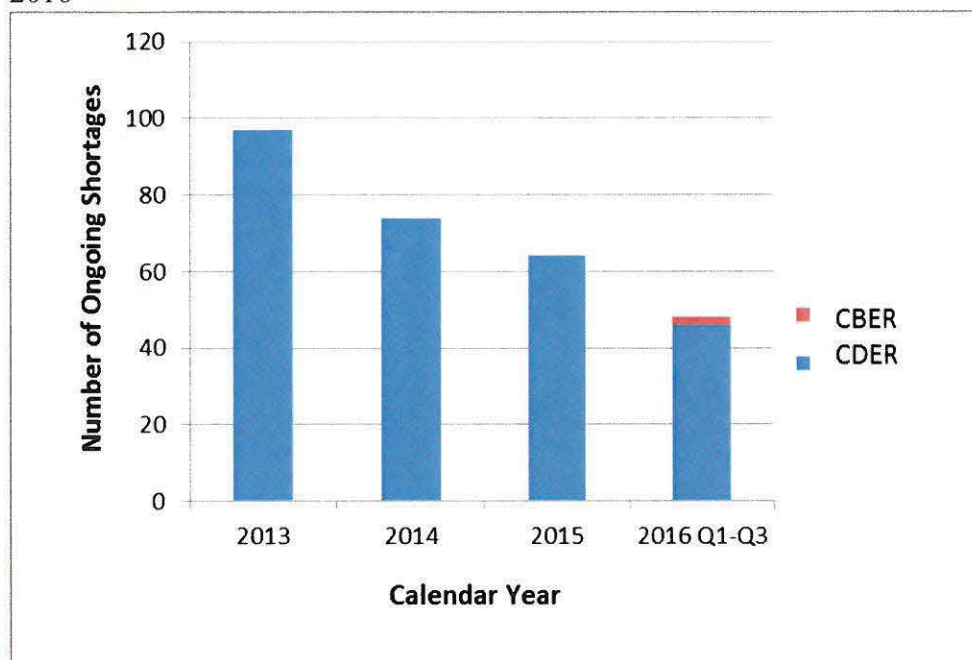
Another data point to note is the number of ongoing shortages yet to be resolved from previous years. FDA identified 97 ongoing CDER-tracked shortages at the end of CY 2013, 74 ongoing CDER-tracked shortages at the end of CY 2014, and 64 ongoing CDER-tracked shortages at the end of CY 2015. As of September 30, 2016, there were 48 ongoing shortages, the lowest number since FDA started collecting such data.

¹⁴ Links to letters of non-compliance with notification requirement can be found at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm403902.htm>.

¹⁵ CDER's drug shortage statistics can be found at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050796.htm>.

¹⁶ See Appendix 2 for a breakdown of 2016 CBER and CDER numbers.

Figure 3. Number of Ongoing Drug Shortages Per Year, 2013 Through September 30, 2016¹⁷



CONTINUED DRUG SHORTAGES EFFORTS IN 2016

1. DSS Shortage Tracker

FDA continues to improve its system for data tracking and analysis for drug shortages and last year put into place a system called the CDER Shortage Tracker, which is housed within Panorama, a CDER Platform. This system addressed certain recommendations in the 2014 Government Accountability Office (GAO) report on drug shortages for further enhancing the tracking of drug shortage data.¹⁸ The primary function of the CDER Shortage Tracker is to streamline day-to-day work to identify and mitigate shortages, including research, data entry, and data management for DSS. The CDER Shortage Tracker is not designed to predict whether a manufacturer or product is at risk of shortage.

While we have been able to link Shortage Tracker to the CDER Informatics Platform, certain processes, such as receiving notifications under section 506C of the FD&C Act and updating the FDA Drug Shortage website, still require manual input spanning multiple platforms. The next goal for DSS is to launch an external collaboration portal for industry. The CDER Direct NextGen Collaboration Portal will enable sponsors to

¹⁷ This fourth annual report to Congress is the first year to include both reporting for those covered drug and biologic products. See Appendix 2 for a breakdown of 2016 CBER and CDER numbers.

¹⁸ GAO's report can be found at <http://www.gao.gov/assets/670/660785.pdf>.

submit drug shortage notifications to FDA based on FDA-validated product information, such as National Drug Code (NDC), active ingredient, and product name. The Portal will allow industry users to log in, enter their shortage information, and submit notifications directly into the CDER Shortage Tracker. This online capability will help to minimize manual data entry and track notifications for better drug shortage monitoring and mitigation. FDA is currently piloting the NextGen Collaboration Portal and anticipates making it available for broader use in 2017.

2. FDA Public Communications Regarding Drug Shortages

In March 2015, FDA launched its first mobile application (app) that provided the public with easier and faster access to important information about drug shortages. The free mobile app is an innovative tool designed to identify current drug shortages, resolved shortages, and the discontinuations of drug products. The app provides health care professionals and pharmacists with real-time information about drug shortages to help them make treatment decisions. Users of this app can search or browse by a drug's brand name, generic name, active ingredient, or therapeutic category. The app can also be used to report a suspected drug shortage or supply issue to FDA. The mobile app was further enhanced in August 2016 for Android devices. Android device users are able to receive notifications when there is new or updated information about a shortage of a drug product or about a drug within selected therapeutic categories. As of September 30, 2016, there have been almost 32,500 installs of the Drug Shortage App.

Further outreach during the first three quarters of 2016 included seven presentations given to professional and patient advocacy organizations, industry and trade associations, as well as stakeholder groups.

3. FDA Drug Shortage Assistance Award

In September 2014, FDA created the FDA Drug Shortage Assistance Award¹⁹ to publicly recognize drug companies and manufacturers that have demonstrated a commitment to preventing or alleviating drug shortages of medically necessary drugs. This award recognizes efforts of drug manufacturers who, while maintaining federally mandated quality standards, have worked in cooperation with FDA and implemented strategies to help provide a steady supply of medically necessary drugs for patients at a time when critical drug shortages pose a challenge for health care providers and patients nationwide. FDA hopes that shining a spotlight on the efforts of drug manufacturers that have gone above and beyond in this area will encourage other manufacturers to follow suit.

On April 14, 2016, FDA issued its third Drug Shortage Assistance Award to Eurohealth International Sarl, a subsidiary of Hikma Pharmaceuticals for its efforts related to the shortages of Thiotepea for injection and phentolamine mesylate for injection.

¹⁹ Link to FDA Drug Shortage Assistance Award information can be found at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm415807.htm>.

4. FDA Internal Efforts Regarding Drug Shortages

The recent establishment of the Office of Pharmaceutical Quality (OPQ) within CDER created a single unit dedicated to product quality by improving FDA's oversight of quality throughout the lifecycle of a drug product. DSS has important and frequent interactions with OPQ as well as CDER/OC to assess drug shortage risk at manufacturing sites as a preventative effort to address shortages.

DSS also works closely with CDER's Office of Generic Drugs (OGD) on shortage mitigation and prevention efforts and, when a product quality review is involved, DSS and OGD work with OPQ to ensure coordination across offices. OGD works expeditiously to review and approve abbreviated new drug applications (ANDAs) and ANDA supplements for drug products that are in shortage.

Likewise, CBER/OCBQ has procedures similar to CDER/OC and DSS, and works closely with all CBER product review offices concerning shortage mitigation and prevention efforts. CBER/OCBQ also works to facilitate and ensure coordination across CBER product review offices.

CONCLUSION

Drug shortages remain a significant public health issue in the United States and a top priority for FDA. To address them, FDA is working with other partners to help prevent shortages from occurring and to mitigate the impact of shortages that cannot be prevented. As a part of this work, early and open dialogue between FDA and manufacturers is critical to our success. Because of important actions taken by the President and Congress, FDA has been able to learn of possible shortages before they occur and take steps to prevent or mitigate them. During the first three quarters of 2016, FDA helped prevent 63 potential new shortages, and there were only 21 new shortages for the first three quarters of 2016.²⁰ While important progress has been made in preventing drug shortages from occurring, and decreases have been seen in the total numbers of shortages, FDA continues to work to ensure that patients in the United States will have access to the medicines they need. This report reflects FDA's commitment to continue our important work to prevent or mitigate drug shortages.

²⁰ This fourth annual report to Congress is the first year to include both reporting for those covered drug and biologic products. See Appendix 2 for a breakdown of 2016 CBER and CDER numbers.

DEFINITIONS

Drug Shortage: A *drug shortage* means a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug.

Biological Product Shortage: A *biological product shortage* means a period of time when the demand or projected demand for the biological product within the United States exceeds the supply of the biological product.

Meaningful Disruption: A *meaningful disruption* means a change in production that is reasonably likely to lead to a reduction in the supply of a drug or biological product by a manufacturer that is more than negligible and affects the ability of the manufacturer to fill orders or meet expected demand for its product. A meaningful disruption is not an interruption in manufacturing due to matters such as routine maintenance and does not include insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time.

Significant Disruption: A *significant disruption* means a change in production that is reasonably likely to lead to a reduction in the supply of blood or blood components by a manufacturer that substantially affects the ability of the manufacturer to fill orders or meet expected demand for its product. A significant disruption does not include interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time.

Life Supporting or Life Sustaining: *Life supporting* or *life sustaining* is used to describe a drug or biological product that is essential to, or that yields information that is essential to, the restoration or continuation of a bodily function important to the continuation of human life.

APPENDIX 1

SEC. 506C–1. ANNUAL REPORTING ON DRUG SHORTAGES.

(a) ANNUAL REPORTS TO CONGRESS.—Not later than the end of calendar year 2013, and not later than the end of each calendar year thereafter, the Secretary shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate a report on drug shortages that—

(1) specifies the number of manufacturers that submitted a notification to the Secretary under section 506C(a) during such calendar year;

(2) describes the communication between the field investigators of the Food and Drug Administration and the staff of the Center for Drug Evaluation and Research’s Office of Compliance and Drug Shortage Program, including the Food and Drug Administration’s procedures for enabling and ensuring such communication;

(3) (A) lists the major actions taken by the Secretary to prevent or mitigate the drug shortages described in paragraph (7);

(B) in the list under subparagraph (A), includes—

(i) the number of applications and supplements for which the Secretary expedited review under section 506C(g)(1) during such calendar year; and

(ii) the number of establishment inspections or reinspections that the Secretary expedited under section 506C(g)(2) during such calendar year;

(4) describes the coordination between the Food and Drug Administration and the Drug Enforcement Administration on efforts to prevent or alleviate drug shortages;

(5) identifies the number of and describes the instances in which the Food and Drug Administration exercised regulatory flexibility and discretion to prevent or alleviate a drug shortage;

(6) lists the names of manufacturers that were issued letters under section 506C(f); and

(7) specifies the number of drug shortages occurring during such calendar year, as identified by the Secretary.

APPENDIX 2

Breakdown of CDER and CBER Shortage Numbers, Q1-Q3, 2016

	CDER	CBER
NEW SHORTAGES	20	1
PREVENTED SHORTAGES	54	9
ONGOING SHORTAGES	46	2
NOTIFICATIONS	162	24
NO. OF MANUFACTURERS NOTIFYING	50	17
ACTIONS TAKEN TO MITIGATE SHORTAGES		
REGULATORY FLEXIBILITY AND DISCRETION	24	1
EXPEDITED REVIEWS	96	6
EXPEDITED INSPECTIONS	10	0

APPENDIX 3

Breakdown of Expedited Reviews by Submission Type

	EXPEDITED REVIEWS
CDER NDA/NDA SUPPLEMENTS	17
CDER ANDA/ANDA SUPPLEMENTS	78
CDER BLA/BLA SUPPLEMENTS	1
CBER BLA/BLA SUPPLEMENTS	6