



Report on Drug Shortages for Calendar Year 2017

Required by

Section 506C-1 of the Federal Food, Drug, and Cosmetic Act

Food and Drug Administration
Department of Health and Human Services

_____ Date _____

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Commissioner of Food and Drugs

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EXECUTIVE SUMMARY

This fifth annual report to Congress summarizes the major actions taken by the Food and Drug Administration (FDA) during calendar year (CY) 2017 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 manufacturers 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 145 shortages from January 1 to December 31, 2017. In addition, the number of new shortages tracked by CBER and CDER for this same period is 39, 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 fifth 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 3 for a breakdown of 2017 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 an annual report to Congress on drug shortages.³ 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, 2017, through December 31, 2017. 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 include 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.

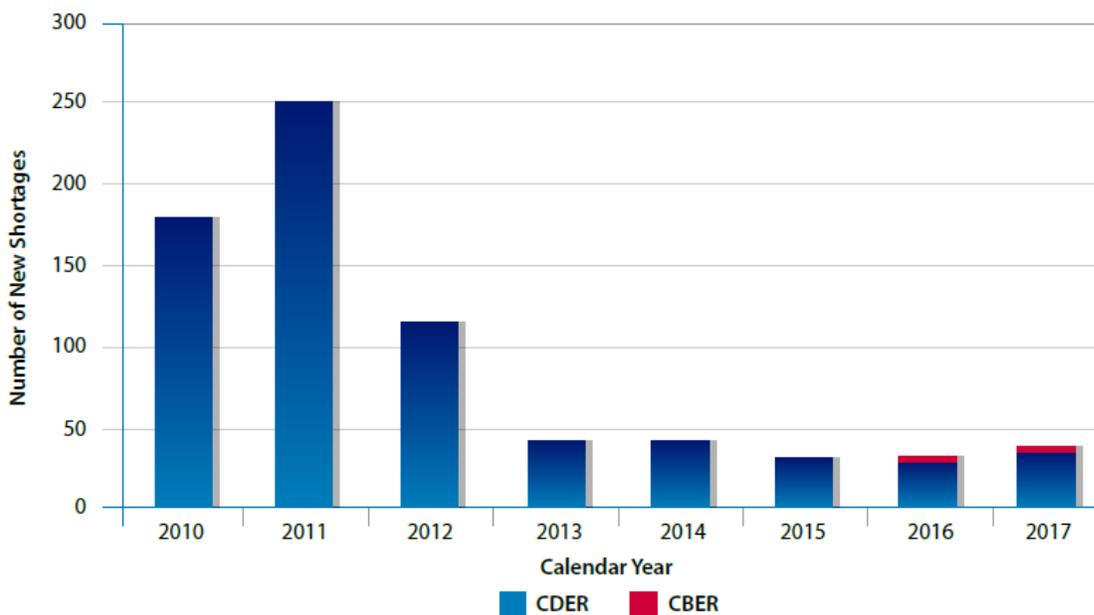
BACKGROUND

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 December 31, 2017.

³ Section 506C-1 of the FD&C Act initially required the annual report on drug shortages to be submitted to Congress "not later than the end of each calendar year." To meet this deadline, the annual reports submitted to Congress presented data and information on drug shortages gathered during the first three quarters of the calendar year. The 21st Century Cures Act, which was enacted on December 13, 2016, amended section 506C-1 to require that "[n]ot later than March 31 of each calendar year, 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, with respect to the preceding calendar year, on drug shortages..."

Figure 1. Number of New Drug Shortages Per Year, 2010 - 2017⁴



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. While there has been a steady decrease in new shortages over the past few years, 2017 has been a challenging year for shortages. First, there was a major manufacturer who shut down a facility for remediation purposes resulting in loss of manufacturing capacity needed for the supplies of numerous products. Critically, disruptions were also caused in the Fall of 2017 by Hurricanes Harvey, Irma, and Maria—the latter of which ravaged Puerto Rico, an island that is home to numerous manufacturing facilities. This created delays in the release of some products, resulting in both new shortages as well as the worsening of existing shortages. FDA’s efforts to respond to the hurricanes are summarized later in the report.

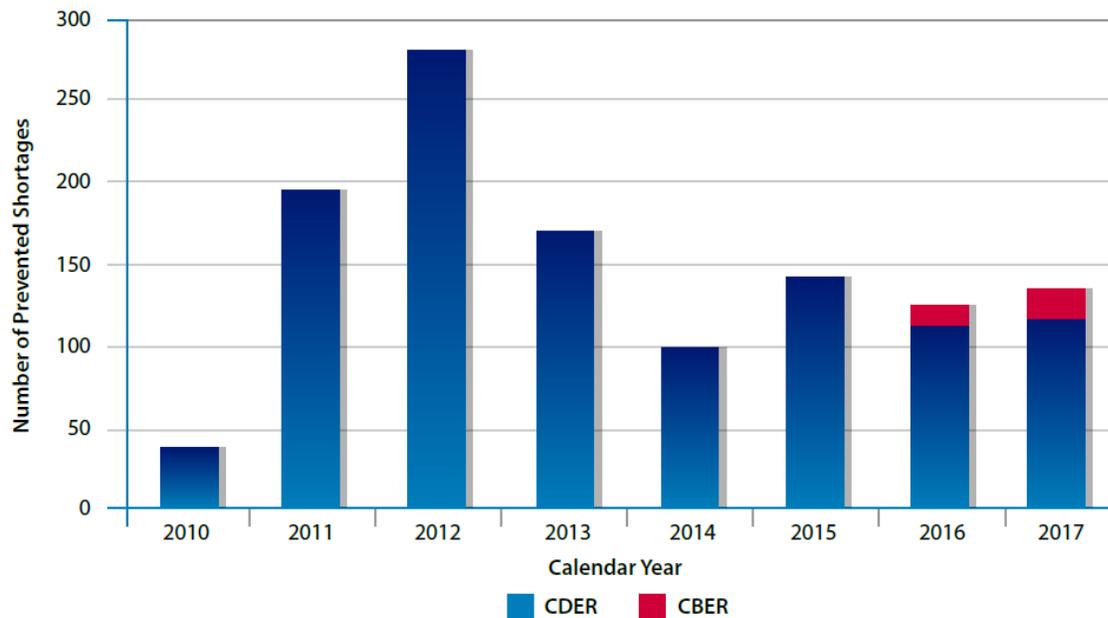
Shortages can delay or deny needed care for patients, creating a potential lapse in medical care. Shortages can also lead prescribers to use second-line alternatives, which may be less effective or pose additional risks. As summarized below, to prevent these situations from occurring, FDA has used a 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

⁴ This fifth annual report to Congress is the second year to include reporting for both drug and biologic products. See Appendix 3 for a breakdown of 2017 CBER and CDER numbers.

in 2015. In 2016, FDA, as tracked by CBER and CDER, helped to prevent 126 shortages; in 2017, the Agency helped to prevent 145 shortages.⁵

The following figure shows the number of prevented drug shortages identified by year from 2010 through 2017.

Figure 2. Number of Prevented Drug Shortages Per Year, 2010 - 2017⁶



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.”⁷ 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 See supra n. 2.

⁶ This fifth annual report to Congress is the second year to include reporting for both drug and biologic products. See Appendix 3 for a breakdown of 2017 CBER and CDER numbers.

⁷ 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 an additional two letters in 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*.⁸ 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 shortage provisions of section 506C, as amended by FDASIA.⁹ 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. The rule became effective on September 8, 2015. As noted above, last year's report to Congress was the first to include reporting for all covered drug and biological products.

⁸ To view the strategic plan and related information, visit <http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf>.

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

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 CDER's 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 and the data addressing those requirements 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 calendar year 2017, FDA was notified of 520 potential drug and biological product shortage situations by 86 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. For example, if the investigators identify actions or activities during an inspection that may have a detrimental impact on product availability, information

regarding the observations and the products manufactured can be relayed to CDER 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 attempting to restore production;
- Expedite FDA inspections and reviews of submissions from competing entities 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, to allow individual batches of a drug product to be released even when quality assurance requirements were not met.

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 132 submissions in 2017.¹⁰

- **List the number of establishment inspections or re-inspections related to mitigation or prevention of a shortage that the Secretary expedited under section 506C(g)(2) during such calendar year.**¹¹

FDA prioritized 30 establishment inspections to address drug shortages in 2017.¹²

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 the Drug Enforcement Administration (DEA) in efforts to prevent or mitigate the 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.¹³

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

¹⁰ See Appendix 4 for a breakdown of submission types.

¹¹ Includes prioritized inspections or site reviews for new applications or supplements that were granted expedited review due to drug shortage.

¹² Note that not all submissions to FDA require inspections, but some submissions may involve multiple sites that require multiple inspections.

¹³ The MOU can be found at <http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm440091.htm>.

FDA's standards of safety, efficacy, and quality for approval 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; the Agency also 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 CY 2017, FDA exercised regulatory flexibility and discretion in 57 instances, affecting 33 products.¹⁴ Examples of situations in which FDA exercised regulatory flexibility and discretion to prevent or mitigate a shortage are listed below:

- FDA used temporary regulatory flexibility and discretion for medically necessary products that presented 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 were supplied with a product to remove particulate matter,
 - Extra testing for product quality or identity was completed before releasing the product into the marketplace,
 - Third-party oversight of production was instituted to monitor quality issues, and
 - Special instructions were provided to health care professionals and patients.
- FDA used temporary regulatory flexibility and discretion to permit continued distribution of a drug product to mitigate or resolve a drug shortage while FDA reviewed a supplement/proposed change to address a problem with the drug product.
- FDA 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 were exhausted.
- FDA 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).

¹⁴ One instance of regulatory flexibility may affect more than one product. Conversely, a shortage of one product may involve multiple instances of regulatory flexibility.

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,¹⁵ 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). No letters were issued in 2017. 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 2017.

The data from CDER's drug shortage database¹⁶ shows that the number of new shortages has significantly decreased in recent years, from 117 in 2012 to 44 in 2013, 44 in 2014, 26 in 2015, and 26 in 2016. Unfortunately, this downward trend did not continue into 2017, as previously discussed. As of December 31, 2017, there were a total of 39 new drug and biological product shortages identified.¹⁷ In 2017, FDA prevented 135 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, 64 ongoing CDER-tracked shortages at the end of CY 2015, and 48 ongoing CBER and CDER-tracked shortages at the end of CY 2016. As of December 31, 2017, there were 41 ongoing shortages, the lowest number since FDA started collecting such data.

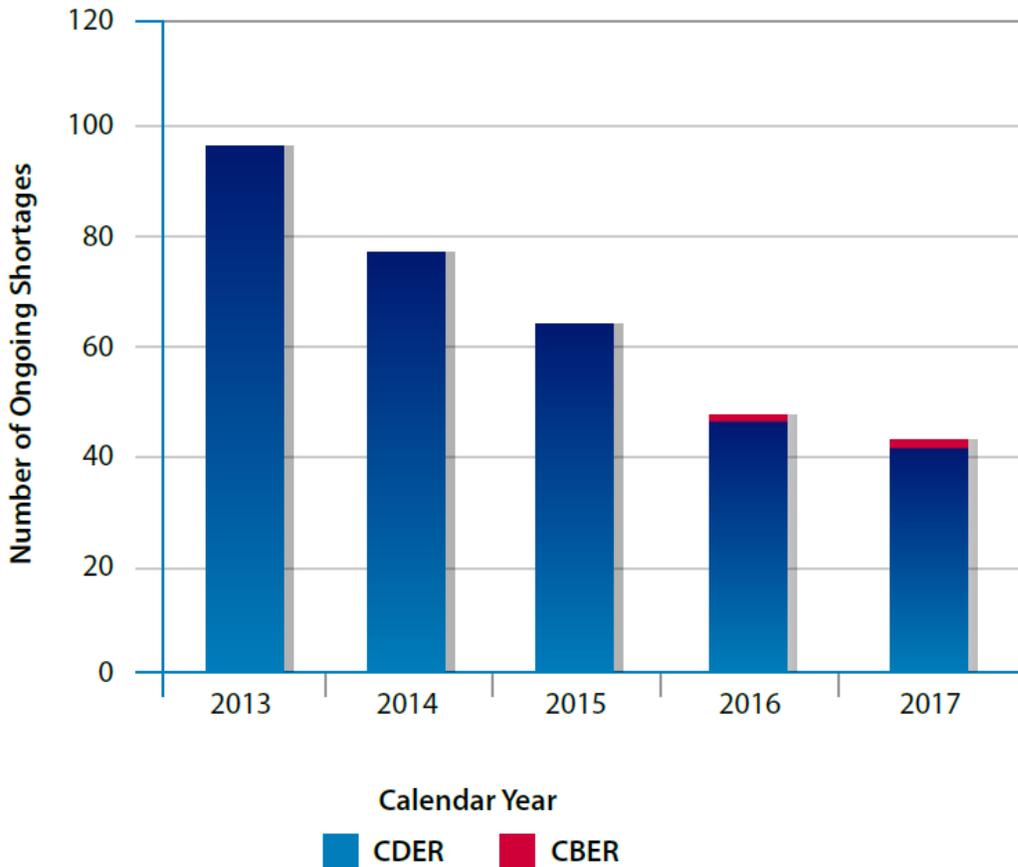
Figure 3. Number of Ongoing Drug Shortages Per Year, 2013 - 2017¹⁸

¹⁵ Links to letters of non-compliance with notification requirement can be found at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm403902.htm>.

¹⁶ CDER's drug shortage statistics can be found at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050796.htm>.

¹⁷ See Appendix 3 for a breakdown of 2017 CBER and CDER numbers.

¹⁸ This fifth annual report to Congress is the first year to include both reporting for those covered drug and biologic products. See Appendix 3 for a breakdown of 2017 CBER and CDER numbers.



CONTINUED DRUG SHORTAGES EFFORTS IN 2017

1. Hurricane Maria and the Impact on Puerto Rico’s Manufacturing Facilities

Hurricane Maria devastated the Caribbean in 2017 and had a major impact on drug manufacturing. The FDA responded to these challenges. Given the extraordinary situation in Puerto Rico, FDA worked closely with local and federal authorities, and the manufacturers of FDA-regulated products with manufacturing facilities located in Puerto Rico, to help address the needs caused by challenges to the basic infrastructure in Puerto Rico after Hurricane Maria made landfall. FDA contacted other federal agencies and local authorities to assist manufacturers in addressing challenges such as gaining access to fuel and/or generators; clearing roads for safe travel and transport; and securing air, sea, and land transport priority for critical raw ingredients. Before the hurricane made landfall, FDA worked to identify potential risks to the drug supply. After the hurricane made landfall, FDA quickly worked with local and federal agencies to perform an assessment of impact.

1. A list of high-priority FDA-regulated products with manufacturing facilities in Puerto Rico was identified.

2. A detailed assessment of the storm's effects on the manufacture of these FDA-regulated products was performed.
3. FDA worked with all manufacturers that have facilities in Puerto Rico to assess the potential impacts on their facilities to avoid—whenever possible—shortages of critical FDA-regulated medical products. During and following the storm, FDA worked with manufacturers to determine whether facilities were damaged or not operational, or if they were still operational and could continue to function and manufacture on generator power.
4. FDA communicated with outside groups and the public with updates concerning the overall situation in Puerto Rico and status of FDA-regulated products manufactured in Puerto Rico.
5. FDA worked with other local and federal agencies to help get needed supplies and infrastructure to critical facilities.

One particular focus of the FDA's work after Hurricane Maria was related to the availability of sterile saline solution, a critical drug product used in many clinical situations. Sterile saline solution has been intermittently in shortage for several years as manufacturing capacity has worked to keep up with demand. Hurricane Maria disrupted the manufacturing of sterile saline solution at the Baxter Healthcare Corporation manufacturing facility located in Puerto Rico, resulting in a worsening of the availability of sterile saline solution in the United States. FDA took a variety of actions to address this ongoing shortage:

1. FDA did not object to the temporary importation of sterile saline solutions not approved for use in the United States which were manufactured at Baxter Healthcare Facilities located in Ireland, Australia, Mexico, Canada, and Brazil, nor did the FDA object to the temporary importation of sterile saline solution not approved for use in the United States manufactured at a B. Braun Medical, Inc. manufacturing facility located in Germany.
2. FDA expedited review of drug applications from additional manufacturers of sterile saline solutions to help relieve this shortage. In 2017, the Agency approved sterile saline solutions manufactured by Fresenius Kabi USA, LLC and Laboratorios Grifols, S.A., and the Agency anticipates that availability of these products will help to alleviate the ongoing shortage of sterile saline solutions.
3. FDA has coordinated with outside groups to promote understanding and transparency regarding the saline shortage, including product utilization.
4. FDA has communicated extensively about the shortage of sterile saline solutions.¹⁹

¹⁹ Press announcements from FDA Commissioner Scott Gottlieb on FDA's hurricane response:

2018

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm595020.htm>

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm592617.htm>

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm591391.htm>

2017

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm585720.htm>

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm580290.htm>

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 was 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 can receive notifications when there is new or updated information about a shortage of a drug product or about a drug within selected therapeutic categories. We continue to work to have this feature available in the iOS format as well. As of December 31, 2017, there have been almost 48,000 installs of the Drug Shortage App.

Further outreach during 2017 included 10 presentations given to professional and patient advocacy organizations, industry and trade associations, and stakeholder groups.

3. FDA Drug Shortage Assistance Award

In September 2014, FDA created the FDA Drug Shortage Assistance Award²⁰ 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 December 20, 2017, FDA issued its fourth Drug Shortage Assistance Award to Adienne Pharma & Biotech for its efforts in alleviating a shortage of thiotepa for injection, as well as submitting and obtaining approval for a new drug application for Tepadina (thiotepa) for injection.

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm579493.htm>

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm577338.htm>

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm577112.htm>

²⁰ Information about FDA's Drug Shortage Assistance Award can be found at

<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm415807.htm>.

4. FDA Internal Efforts Regarding Drug Shortages

The 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 preventive effort to address shortages.

DSS also works closely with CDER's Office of Generic Drugs (OGD) and Office of New Drugs (OND) on shortage mitigation and prevention efforts and, when a product quality review is involved, DSS, OGD, and OND work with OPQ to ensure coordination across offices. OGD, OND, and OPQ work expeditiously to review and approve abbreviated and new drug applications, as well as 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 manufacturers and 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 2017, FDA helped prevent 145 potential new shortages, and there were 39 new shortages for 2017. While important progress has been made in preventing drug shortages from occurring, 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.

APPENDIX 1

DEFINITIONS

Drug Shortage: A *drug shortage* means a period 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 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.

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.

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 2

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

(a) ANNUAL REPORTS TO CONGRESS.—Not later than March 31 of each calendar year, 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 with respect to the preceding calendar year 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 3

Breakdown of CDER and CBER Shortage Numbers, 2017

	CDER	CBER
NEW SHORTAGES	35	4
PREVENTED SHORTAGES	132	13
ONGOING SHORTAGES	38	3
NOTIFICATIONS	470	50
NO. OF MANUFACTURERS NOTIFYING	70	23
ACTIONS TAKEN TO MITIGATE SHORTAGES		
REGULATORY FLEXIBILITY AND DISCRETION	55	2
EXPEDITED REVIEWS	116	16
EXPEDITED INSPECTIONS	30	0

APPENDIX 4

Breakdown of Expedited Reviews by Submission Type

	EXPEDITED REVIEWS
CDER NDA/NDA SUPPLEMENTS	43
CDER ANDA/ANDA SUPPLEMENTS	71
CDER BLA/BLA SUPPLEMENTS	2
CBER BLA/BLA SUPPLEMENTS	16