



# Report on Drug Shortages for Calendar Year 2019

Required by

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

U.S. Food and Drug Administration  
Department of Health and Human Services

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Date

## Table of Contents

<b>EXECUTIVE SUMMARY .....</b>	<b>1</b>
<b>INTRODUCTION.....</b>	<b>2</b>
<b>BACKGROUND .....</b>	<b>2</b>
1. Executive Order 13588 – Reducing Prescription Drug Shortages.....	4
2. FDASIA .....	5
3. Inter-agency Drug Shortage Task Force .....	5
<b>DATA SOURCES USED IN THIS REPORT .....</b>	<b>6</b>
<b>ANNUAL REPORTING REQUIREMENTS PER SECTION 506C-1 .....</b>	<b>6</b>
<b>CONTINUED DRUG SHORTAGES EFFORTS IN 2019.....</b>	<b>12</b>
Inter-agency Drug Shortage Task Force’s Report.....	12
<b>CONCLUSION .....</b>	<b>14</b>
<b>APPENDIX 1.....</b>	<b>15</b>
<b>APPENDIX 2.....</b>	<b>16</b>
<b>APPENDIX 3.....</b>	<b>17</b>
<b>APPENDIX 4.....</b>	<b>18</b>

## EXECUTIVE SUMMARY

This seventh annual report to Congress summarizes the major actions taken by the U.S. Food and Drug Administration (FDA) during calendar year (CY) 2019 to prevent or mitigate drug shortages<sup>1</sup> in the United States.<sup>2</sup> 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 154 shortages from January 1 to December 31, 2019. In addition, the number of new shortages tracked by CBER and CDER for this same period (i.e., during CY 2019) was 51, compared to a peak of 251 new shortages during CY 2011.<sup>3</sup>

Based on FDA's 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.

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<sup>1</sup> In this report, the term "drug shortage" includes shortages of human drug and biological products. This report individually refers to shortages tracked by FDA's Center for Drug Evaluation and Research or FDA's Center for Biologics Evaluation and Research when the context requires distinguishing between these Centers.

<sup>2</sup> Because this report covers FDA's response to drug shortages during CY 2019, this report does not cover FDA's activities related to the shortage threat posed by the coronavirus disease (COVID-19). (Information about FDA's response to COVID-19 is available on FDA's website at <https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/coronavirus-disease-2019-covid-19>.)

<sup>3</sup> This seventh 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 CBER's and CDER's 2019 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 the U.S. Food and Drug Administration (FDA or the Agency) 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.<sup>4</sup> FDA is submitting this annual report to fulfill its obligations under section 506C-1.

This report provides a background on drug shortages<sup>5</sup> and FDA's efforts to address them to date. This report also responds to the specific issues listed under section 506C-1. The analyses included in this report 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, 2019, through December 31, 2019.<sup>6</sup> 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 additional 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 calendar year from 2010 through December 31, 2019.

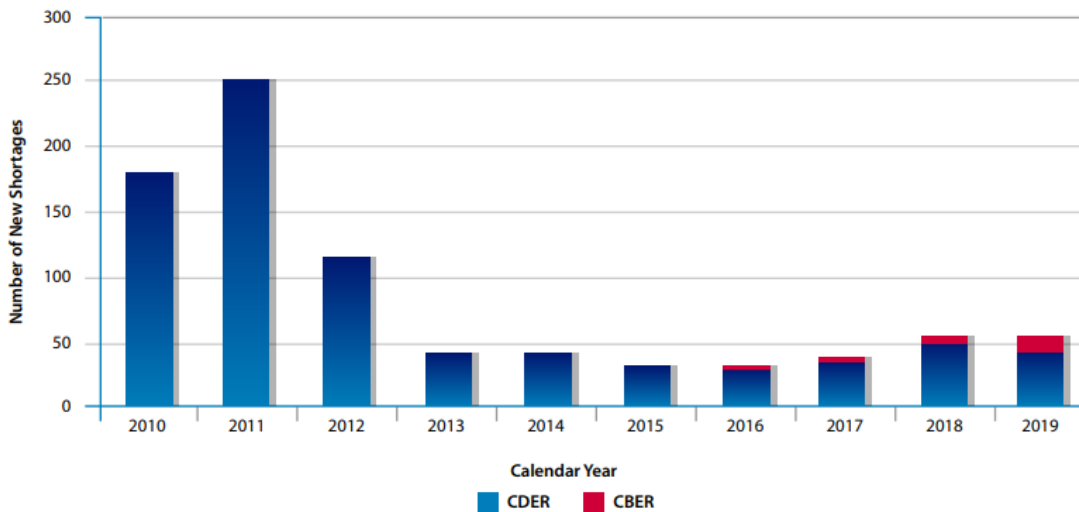
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<sup>4</sup> Section 506C-1 of the FD&C Act initially required the annual report on drug shortages to be submitted to Congress "not later than the end of each calendar year." To meet this deadline, the annual reports submitted to Congress presented data and information on drug shortages gathered during the first three quarters of the calendar year. The 21<sup>st</sup> 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 ...."

<sup>5</sup> In this report, the term "drug shortage" includes shortages of human drug and biological products.

<sup>6</sup> This report individually refers to shortages tracked by CBER and CDER when the context requires distinguishing between these Centers.

**Figure 1. Number of New Drug Shortages Per Year, 2010 - 2019<sup>7</sup>**



Although the number of new drug shortages has declined since 2011 as a result of work by many groups including FDA, shortages continue to pose a real challenge to public health. This is especially the case when the shortage involves a critical drug to treat cancer, to provide parenteral nutrition, or to address another serious medical condition, such as the shortage of blood pressure medications. While there has been a steady decrease in new shortages over the past few years, CY 2019 has been a challenging year for shortages. FDA continues to see the lingering effects from the closing of two facilities by major drug manufacturers for remediation purposes in 2017 and 2018, which resulted in the loss of manufacturing capacity needed for the supplies of numerous drug products.

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 statutory and regulatory framework in place and in partnership with manufacturers and other stakeholders. Situations such as the Nitrosamine Impurity Investigation are examples of how the Agency has taken steps to ensure safety while also working to both

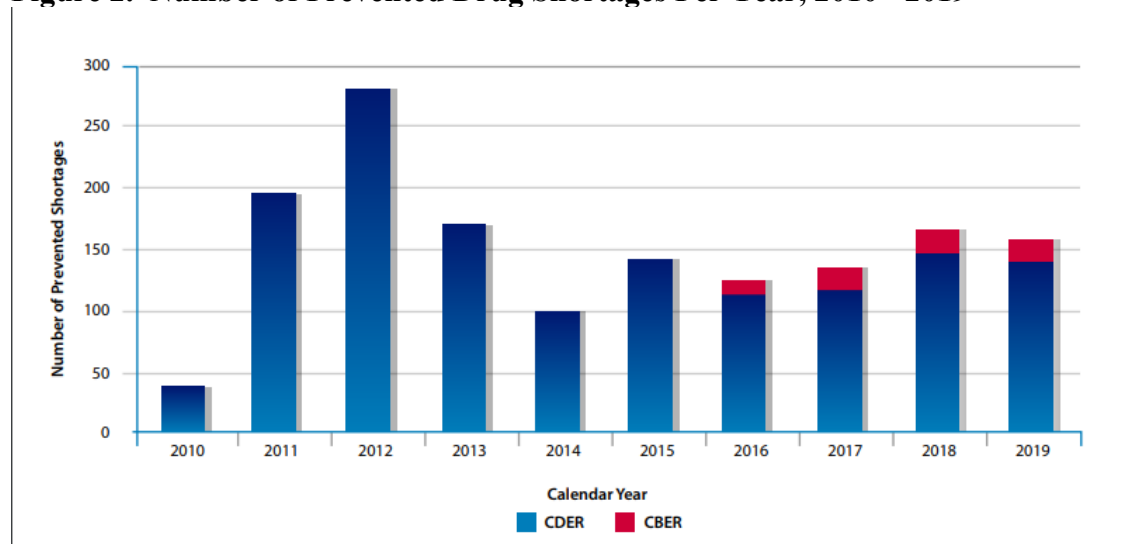
<sup>7</sup> This seventh annual report to Congress is the fourth year to include reporting for both drug and biological products. This includes all drugs within the meaning of section 506C(h)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), as well as other products tracked by CDER's Drug 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 CBER's and CDER's CY 2019 numbers.

mitigate and prevent future shortages using tools such as expedited reviews and inspections.<sup>8</sup>

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. As tracked by CBER and CDER, FDA helped prevent 126 shortages in 2016, 145 in 2017, 160 in 2018, and 154 in 2019.<sup>9</sup>

The following figure shows the number of prevented drug shortages, identified by calendar year, from 2010 through 2019.

**Figure 2. Number of Prevented Drug Shortages Per Year, 2010 - 2019**



Many actions, including the following, have been taken that are helping FDA address drug shortages.

### 1. Executive Order 13588 – Reducing Prescription Drug Shortages

In response to a dramatic increase in shortages, the President issued Executive Order 13588 on October 31, 2011, 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.”<sup>10</sup> 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

<sup>8</sup> See <https://www.fda.gov/drugs/drug-safety-and-availability/information-about-nitrosamine-impurities-medications>.

<sup>9</sup> See supra n. 3.

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

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.

## 2. FDASIA

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 amended the FD&C Act to broaden 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 the manufacturing of biologics.<sup>11</sup>

FDASIA requires FDA to send a non-compliance letter to firms that fail to notify FDA in accordance with section 506C of the FD&C Act. FDA sent the first two letters in 2014, an additional two letters in 2016, three in 2018, and one in 2019. If FDA concludes that there is or is likely to be a drug shortage covered by section 506C, as amended, that section authorizes FDA to expedite its reviews of abbreviated new drug applications (ANDAs), supplemental new drug applications, and supplemental ANDAs and to expedite inspections that could help mitigate or prevent that shortage.<sup>12</sup>

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. Inter-agency Drug Shortage Task Force

In response to a request in June 2018 from 31 U.S. Senators and 104 members of the House of Representatives, the Commissioner of Food and Drugs established the inter-agency Drug Shortage Task Force to determine the root causes of drug shortages and develop recommendations to address them. The task force took a comprehensive look at all drivers of drug shortages and identified potential ways to prevent or mitigate them in the future. To ensure FDA did not overlook any drivers or solutions, the task force included not only senior leaders from FDA but also leaders from the Centers for Medicare & Medicaid Services (CMS) and the Department of Veterans Affairs (VA). Collectively, CMS and the VA provide or pay for prescription medicines for millions of Americans. The Department of Defense, the Federal Trade Commission, and the Office

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<sup>11</sup> See section 506C(i)(3) of the FD&C Act; see also 21 CFR 600.82 and 80 FR 38915 (July 8, 2015).

<sup>12</sup> The FDA Reauthorization Act of 2017 (Pub. L. 115-52) enacted on August 18, 2017, amended the FD&C Act to add section 505(j)(11), requiring FDA to prioritize its review of certain original aANDAs for drugs that have been included on the list of drugs in shortage under section 506E of the FD&C Act.

of the Assistant Secretary for Preparedness and Response (within the U.S. Department of Health and Human Services (HHS)) were also represented on the task force.<sup>13</sup> The task force invited public participation through a public meeting on November 27, 2018; established a docket to receive comments; and invited stakeholders to a series of listening sessions. As discussed below, in October 2019, the task force issued its report, *Drug Shortages: Root Causes and Potential Solutions*, that identifies root causes of drug shortages and offers recommendations for government and industry to address them.<sup>14</sup>

## **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. For instance, 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). CBER/OCBQ and DSS similarly track information about drug shortage notifications and their sources (and, therefore, the number of reporting manufacturers).

In contrast, section 506C-1 reporting requirements related to FDA's expedited review are tied to specific *submissions* by manufacturers that are experiencing production disruptions or by manufacturers that are adding or expanding their production capabilities to address a specific shortage. CBER's and CDER's offices reviewing these submissions track which reviews and related inspections they have expedited as a part of a larger set of activities related to their review of submissions.

Other section 506C-1 reporting requirements for this report relate to instances of regulatory flexibility and discretion. These specific instances, all requiring separate regulatory and scientific evaluations and justifications, are tracked by CBER/OCBQ and CDER's Office of Compliance (CDER/OC).

## **ANNUAL REPORTING REQUIREMENTS PER SECTION 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 for each calendar year.

The statutory requirements for this congressional report and the data addressing those requirements are as follows.

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<sup>13</sup> The task force also consulted with officials from the Defense Advanced Research Projects Agency, the U.S. Department of the Treasury, and the DEA.

<sup>14</sup> The report was updated on February 21, 2020, to include a revised economic analysis about production increases and supply restoration after a shortage. The report is available at <https://www.fda.gov/media/131130/download>.



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

For CY 2019, FDA was notified of 575 potential drug and biological product shortage situations by 109 different manufacturers.

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

CDER/OC and FDA's 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. CDER/OC communicates with DSS on warning letter and enforcement action recommendations being reviewed within that office. FDA's 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's 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 identified during an inspection or other field activities that has the potential to lead to a product shortage. In addition, 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 confirms 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's inspections and reviews of submissions submitted by affected manufacturers attempting to restore production;

- Expedite FDA’s inspections and reviews of submissions from competing entities who are interested in starting new production or increasing existing production of products in shortage;
- Expedite the release of lots of certain licensed biological products regulated by CBER or CDER;<sup>15</sup>
- Review requests for extensions of expiration dating;
- Exercise temporary regulatory flexibility for new sources of medically necessary drugs;
- Work with the affected manufacturers to ensure adequate investigations into the root cause of the shortage;
- Develop risk mitigation measures to allow individual batches of a drug product to be released even when quality assurance requirements were not met; and
- Establish communication channels with stakeholders and other interested parties.

FDA can use one or more of these mitigation tools or seek to develop other options within its legal authority depending on the severity of the potential shortage and the surrounding circumstances. When selecting specific tools, FDA continues to work with manufacturers to tailor their responses to the specific situations. 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 224 submissions in 2019.<sup>16</sup>

- **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.<sup>17</sup>**

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<sup>15</sup> FDA may require manufacturers to submit for review and confirmatory testing samples of any lot of any licensed biological product, together with the protocols showing results of applicable tests when deemed necessary for the safety, purity, or potency of the product. See 21 CFR 610.1 and 610.2.

<sup>16</sup> See Appendix 4 for a breakdown of submission types.

<sup>17</sup> Includes prioritized inspections or site reviews for new applications or supplements that were granted an expedited review due to a drug shortage.

FDA prioritized 17 establishment inspections to address drug shortages in 2019.<sup>18</sup>

***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 DEA in efforts to prevent or mitigate the shortage. Among other duties, DEA is responsible both for setting aggregate limits on the amount of certain controlled substances 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.<sup>19</sup> DSS has reached out to DEA on two occasions this past year in regard to potential shortage situations.

***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 first priority is to ensure patients have access to safe, effective, and high quality drugs even when a drug is in shortage. FDA's preferred solution to any shortage situation is to help ensure that there is a supply of approved drugs and biological products sufficient to meet patient demand, as well as to be able to meet the appropriate quality, safety, and efficacy standards of those products. 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 within its legal authority for certain situations in order to prevent or mitigate a shortage situation. In certain shortage situations, the temporary exercise of regulatory flexibility and discretion has proven to be an important tool in alleviating a drug shortage and ensuring access to treatment options for patients in critical need.

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<sup>18</sup> Note that not all submissions to FDA require inspections, but some submissions may involve multiple sites that require multiple inspections.

<sup>19</sup> The MOU can be found at <https://www.fda.gov/about-fda/domestic-mous/mou-225-15-11>.

During CY 2019, FDA exercised regulatory flexibility and discretion in 54 instances, affecting 56 products.<sup>20</sup> Examples of situations in which FDA exercised regulatory flexibility and discretion to prevent or mitigate a shortage are listed below:

- FDA exercised temporary regulatory flexibility and discretion, such as the following, for medically necessary products that presented quality issues:
  - 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 exercised temporary regulatory flexibility and discretion with respect to the 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 exercised 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.

***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,<sup>21</sup> 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.

Since 2014, FDA has issued eight non-compliance letters under section 506C(f). In CY 2019, in particular, a letter was sent to Pfizer/Hospira, Inc., on December 5, 2019. The

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<sup>20</sup> One instance of regulatory flexibility may affect more than one product. Conversely, a shortage of one product may involve multiple instances of regulatory flexibility to mitigate the issue.

<sup>21</sup> Links to letters of non-compliance with notification requirements can be found at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm403902.htm>.

letter sent by FDA and the response received from the manufacturer are available on FDA's website.

**Requirement 7: Specify the number of drug shortages occurring during 2019.**

The data from CDER's drug shortage database<sup>22</sup> shows that the number of new shortages has significantly decreased in recent years, with 117 in 2012, 44 in 2013, 44 in 2014, 26 in 2015, and 26 in 2016. Unfortunately, this downward trend did not continue in subsequent years, as previously discussed. Two large drug manufacturers closed manufacturing facilities for remediation purposes in 2017 and 2018, and these closures resulted in the loss of manufacturing capacity needed for the supplies of numerous drug products. In 2017, there were a total of 39 new drug and biological product shortages identified; in 2018, 54 were identified, and in 2019 there were 51 new drug shortages.<sup>23</sup>

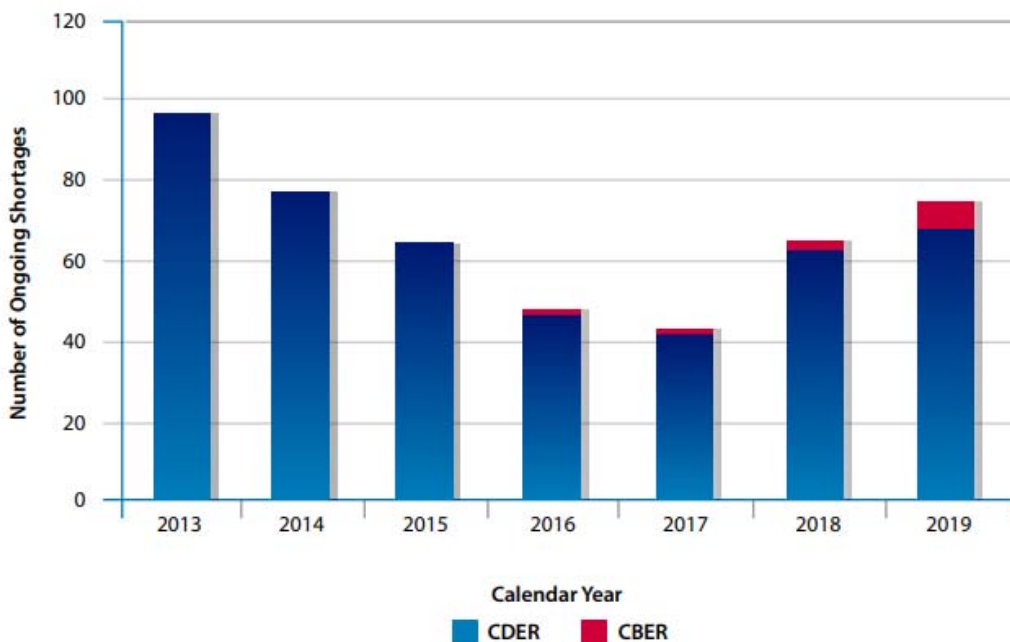
Another data point to note is the number of ongoing shortages yet to be resolved from previous years. FDA identified 97 ongoing CDER-tracked shortages at the end of CY 2013, 74 ongoing CDER-tracked shortages at the end of CY 2014, 64 ongoing CDER-tracked shortages at the end of CY 2015, 48 ongoing CBER- and CDER-tracked shortages at the end of CY 2016, 41 ongoing CBER- and CDER-tracked shortages at the end of CY 2017, and 67 ongoing shortages for CY 2018. As of December 31, 2019, there were 76 ongoing CBER- and CDER-tracked shortages. This increase is also due to the previously discussed closures of manufacturing facilities for remediation purposes.

**Figure 3. Number of Ongoing Drug Shortages Per Year, 2013 - 2019**

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<sup>22</sup> CDER's drug shortage statistics can be found at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050796.htm>.

<sup>23</sup> See Appendix 3 for a breakdown of CBER's and CDER's CY 2019 numbers.



## CONTINUED DRUG SHORTAGES EFFORTS IN 2019

### Inter-agency Drug Shortage Task Force’s Report

As mentioned above, in June 2018, 31 U.S. Senators and 107 members of the House of Representatives asked the Commissioner of Food and Drugs to expand the Drug Shortage Task Force (created by FDASIA<sup>24</sup>), to work with stakeholders and other federal agencies to determine the root causes of drug shortages, and to develop recommendations to ensure that the appropriate supplies of essential medications are always available. The work of this task force resulted in a final report that was published in October 2019 and updated in February 2020. This report, entitled *Drug Shortages: Root Causes and Potential Solutions*, contains the task force’s analysis of root causes and recommendations for addressing them. Although the focus of the report is on human drugs,<sup>25</sup> many of the same concerns mentioned in the report apply to veterinary medicines used to treat service, companion, and food-producing animals.<sup>26</sup>

The report relies on information from stakeholders, published research, and an economic analysis of market conditions affecting drug shortages. After reviewing FDA’s analysis,

<sup>24</sup> See section 506D(a)(1)(A) of the FD&C Act.

<sup>25</sup> See section 506C(h)(1) of the FD&C Act.

<sup>26</sup> Under certain conditions, the Animal Medicinal Drug Use Clarification Act of 1994 allows for the use of approved human drugs in animals. Because veterinarians, especially those in the companion animal field, often use human drugs in their patients, shortages of human drugs can affect veterinary medicine.

published research studies, and stakeholder input, the task force identified the following three major root causes of drug shortages:

- Root Cause 1: Lack of Incentives to Produce Less Profitable Drugs;
- Root Cause 2: Market Does Not Recognize and Reward Manufacturers for Mature Quality Management Systems; and
- Root Cause 3: Logistical and Regulatory Challenges Make It Difficult for the Market to Recover After a Disruption.

Although a complex array of factors contributes to the occurrence and prolongation of drug shortages, the root causes themselves are foundational. They reflect market behavior driven by a search for cost savings in the face of a seemingly inexorable rise in health care spending. Quantifying the extent and effects of drug shortages and addressing the problem over the long term will require the active participation of private sector players – purchasers, intermediaries, and manufacturers – as well as the public sector. To address the identified root causes of shortages, the task force offered the following three recommendations:

- Recommendation 1: Create a Shared Understanding of the Impact of Drug Shortages and the Contracting Practices that May Contribute to Them;
- Recommendation 2: Create a Rating System to Incentivize Drug Manufacturers to Invest in Achieving Quality Management System Maturity; and
- Recommendation 3: Promote Sustainable Private Sector Contracts.

While private sector players are needed to address these root causes, the Agency continues to explore its role, particularly regarding Recommendation 2. Root Cause 2, as noted above, is that the market does not recognize and reward mature quality management systems. Recommendation 2 (i.e., Create a Rating System to Incentivize Drug Manufacturers to Invest in Achieving Quality Management System Maturity) aims to rectify this failure by suggesting the development of a system to measure and rate the quality management maturity of individual manufacturing facilities based on specific objective indicators. This rating would evaluate the robustness of a manufacturing facility's quality system and reward facilities that achieve a high degree of quality system maturity.

Historically, many pharmaceutical manufacturing firms have focused their efforts on compliance with current good manufacturing practices (CGMPs), which include standards for material systems, equipment and facilities, production, laboratory, packaging and labeling, and a quality system. These standards, however, are foundational and set a minimum threshold that companies must achieve in order to be allowed to supply the U.S. marketplace. These standards neither include more advanced levels of quality management, which aim to robustly detect vulnerabilities and address them in order to prevent the occurrence of problems, nor establish a culture that rewards process and system improvements. As companies move from a focus on compliance with CGMPs to institutionalizing continual process and system improvement efforts, these companies begin to advance in quality management maturity.

A rating system could be used to inform purchasers, group purchasing organizations (GPOs), and even consumers about the state of, and commitment to, the quality management maturity of the facility making the drugs they are buying. Pharmaceutical companies could, at their discretion, disclose the rating of the facilities where their drugs are manufactured. GPOs and purchasers could require disclosure of this rating in their contracts with manufacturers. This effort would introduce transparency into the market and provide firms committed to quality management maturity with a competitive advantage, potentially enabling them to obtain sustainable prices as well as grow market share.

As part of the report, the task force also described three legislative proposals that were included in the President's FY 2021 budget to address drug shortages. These proposals include:

- Lengthening expiration dates to mitigate critical drug shortages;
- Improving critical infrastructure by requiring risk management plans; and
- Improving critical infrastructure through improved data sharing.

## **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 the Agency's 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 CY 2019, there were 51 new shortages, and FDA helped prevent 154 potential shortages. 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 its important work to prevent or mitigate drug shortages.



## APPENDIX 1

**Drug Shortage:** A *drug shortage* means a period when the demand or projected demand for a 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 a 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 the 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's and CBER's Shortage Numbers, CY 2019

	<b>CDER</b>	<b>CBER</b>
NEW SHORTAGES	46	5
PREVENTED SHORTAGES	140	14
ONGOING SHORTAGES	68	8
NOTIFICATIONS	540	35
NO. OF MANUFACTURERS NOTIFYING	90	21
<b>ACTIONS TAKEN TO MITIGATE SHORTAGES</b>		
REGULATORY FLEXIBILITY AND DISCRETION	56	1
EXPEDITED REVIEWS	202	22*
EXPEDITED INSPECTIONS	17	0

\* Includes expedited reviews for eight biologics license application (BLA)/BLA supplements and 14 lot-release submissions for CBER-regulated products.

## APPENDIX 4

### Breakdown of Expedited Reviews by Submission Type

	<b>EXPEDITED REVIEWS</b>
CDER NDA/NDA SUPPLEMENTS	53
CDER ANDA/ANDA SUPPLEMENTS	143
CDER BLA/BLA SUPPLEMENTS	6
CBER BLA/BLA SUPPLEMENTS	8*

\* Does not include expedited reviews for the 14 lot-release submissions for CBER-regulated products.