

REPORT TO CONGRESS

Second Annual Report on Drug Shortages
for Calendar Year 2014

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

Public Law 112-144

Department of Health and Human Services
Food and Drug Administration

EXECUTIVE SUMMARY

The Food and Drug Administration Safety and Innovation Act (FDASIA) was enacted on July 9, 2012. Under FDASIA, manufacturers are required to notify FDA of a permanent discontinuance or interruption in the production of certain prescription drugs that are lifesaving, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition. FDASIA requires that FDA file a report to Congress at the end of each calendar year on drug shortages. This is the second annual report submitted by FDA to fulfill its obligations under FDASIA.

Drug shortages remain a significant public health issue in the United States and a top priority for FDA. To address them, FDA works with manufacturers to help prevent shortages from occurring and to mitigate the impact of shortages that cannot be prevented. 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 2014, FDA helped prevent 78 potential new shortages. As a result of successes the Agency's work in preventing and mitigating drug shortages, as well as efforts by industry and other partners, we saw 5 fewer new drug shortages in the first three quarters of 2014, compared to the same period in 2013 (33 vs. 38).

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 for the American public.

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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. 355) 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 lifesaving, 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. In this annual report, FDA provides some background about drug shortages and FDA efforts to address them to date. FDA will then respond to the specific issues listed under 506C-1. These analyses will reflect data collected and evaluated by the Center for Drug Evaluation and Research (CDER) from January 1, 2014, through September 30, 2014.¹ To provide a more comprehensive view of CDER's efforts to manage drug shortages, this report includes data for all products tracked by CDER's Drug Shortage Staff (DSS).² This report also summarizes some important ongoing activities FDA believes will help to address drug shortages in the future. A list of definitions and the statutory language regarding annual reporting on drug shortages is 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 new shortages in 2005 to more than 250 in 2011. Although that number significantly decreased to 117 new shortages in 2012 and 44 in 2013, drug 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 recent 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 things

¹ Please note that these data are derived from the time period beginning January 1, 2014, and ending September 26, 2014, due to the shutdown of Document Archiving, Reporting & Regulatory Tracking System (DARRTS) and migration of data into the new CDER Informatics Platform, which occurred on September 27, 2014.

² This includes drugs within the meaning of section 506C(h)(1), 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. In the future, FDA's annual reports on shortages may include data on biological products licensed under section 351 of the Public Health Service Act, including those tracked by the Center for Biologics Evaluation and Research (CBER), such as vaccines and blood products.

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 discussed below.³ FDA helped prevent 282 drug shortages in 2012, 170 shortages in 2013, and 78 shortages in the first three quarters of 2014.

Several actions have been taken in recent years that have 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.”⁴ 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 lifesaving medicines, including through notifications and expedited reviews, as appropriate.

2. Interim Final Rule and Draft Guidance for Industry on Drug Shortages

In December 2011, FDA responded to this presidential directive by publishing an interim final rule (IFR)⁵ that amended existing early notification requirements. The IFR amended FDA’s regulations related to early notification to improve the likelihood of FDA receiving advance notification of a potential drug shortage, a critical step in the process of preventing or mitigating a shortage. As a companion to the IFR, in February 2012, FDA issued a draft guidance for industry entitled *Notification to FDA of Issues that May Result in a Prescription Drug or Biological Product Shortage*.⁶ The draft guidance

³ Examples of FDA’s mitigation strategies to address drug shortages can be found at <http://www.fda.gov/Drugs/DrugSafety/ucm382255.htm>, <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>, and <http://www.fda.gov/Drugs/NewsEvents/ucm401553.htm>.

⁴ Executive Order 13588, available at <http://www.whitehouse.gov/the-press-office/2011/10/31/executive-order-reducing-prescription-drug-shortages>.

⁵ See <http://www.gpo.gov/fdsys/pkg/FR-2011-12-19/html/2011-32354.htm>. The IFR is a final rule implementing the pre-FDASIA section 506C. FDASIA significantly amended section 506C and requires FDA to initiate a new rulemaking process to implement the amended section 506C. On November 4, 2013, FDA published a proposed rule for public comment to implement the drug shortages provisions of FDASIA and withdraw the IFR (78 FR 65904, available at <https://www.federalregister.gov/articles/2013/11/04/2013-25956/permanent-discontinuance-or-interruption-in-manufacturing-of-certain-drug-or-biological-products>). Once finalized, the rule will supersede the IFR.

⁶ FDA’s guidances are available on its Guidance Web site at <http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234622.htm>. Comments on this draft guidance

was issued for public comment and: (1) further discussed FDA's interpretation of the mandatory reporting requirements under section 506C of the FD&C Act and FDA's related regulations; (2) explained a policy of encouraging additional voluntary reporting; and (3) acknowledged that manufacturers play a primary role in preventing or responding to drug shortages and that many shortages arise from quality or other issues experienced during the manufacturing process. These quality issues may result in interruptions or other adjustments in manufacturing that may adversely affect market supply. Other factors affecting shortages may include delays in acquiring critical raw materials or components, import delays, or unexpected increases in demand.

3. FDA Safety and Innovation Act

With the passage of FDASIA, 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 covered prescription drugs* (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. In 2014, FDA sent the first two letters and posted them, along with the responses from the manufacturers, on its website. 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 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.

4. 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.

are available online at <http://www.regulations.gov>, Docket No. FDA-2012-D-0140. Before publication of the IFR and draft guidance, FDA published a letter to industry on the same day the Executive Order was issued, reminding manufacturers of their obligation to notify FDA about certain issues and encouraging them to notify FDA of others, even if not required.

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

5. FDA Drug Shortage Proposed Rule

On November 4, 2013, FDA published a proposed rule for public comment to help implement FDASIA's expanded notification requirements. Among other things, as proposed, the rule would extend the notification requirement to most manufacturers of biological products. The proposed rule can be viewed at: <https://www.federalregister.gov/articles/2013/11/04/2013-25956/permanent-discontinuance-or-interruption-in-manufacturing-of-certain-drug-or-biological-products>.

DATA SOURCES USED IN THIS REPORT

The data used to fulfill the reporting requirements of FD&C Act § 506C-1 are collected by several program areas within FDA, sometimes for reasons that are broader than the FDA response to drug shortages. Tracking the data for reporting requirements related to drugs (the number of drugs in shortage) is within the purview of DSS. Similarly, DSS tracks information about notifications and their source (and, therefore, the number of reporting manufacturers). 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. 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 regulatory and scientific evaluation and justification, are tracked by CDER's Office of Compliance. CDER staff across offices work closely together to compile the appropriate data and prepare the Report to Congress.

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 from 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 2014, FDA was notified of 125 potential shortage situations by 52 different manufacturers.⁸

⁸ As noted above, this report includes data on all products tracked by CDER's Drug Shortage Staff.

Requirement 2: Describe the communication between FDA field investigators and CDER’s Office of Compliance and Drug Shortage Program, including FDA’s procedures for enabling and ensuring such communication

CDER’s Office of Compliance (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 groups have separate, but interrelated, functions with respect to drug shortages. These offices communicate regularly with DSS on potential warning letters and enforcement actions. 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 that may have a detrimental impact on product availability during an inspection, information regarding the observations and the products manufactured can be relayed to CDER immediately, so that the 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 CDER/OC, ORA issued Field Management Directive #15, Product Shortage Communication (Field Management Directive (FMD) #15), in July 2012. FMD #15 established drug shortage coordinators in ORA, and now 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 enforcement discretion 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 for a batch(es) of product initially not meeting established standards.

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 year⁹**

In the first three quarters of 2014¹⁰, 100 applications were provided expedited review, as described below:

- CDER's Office of Generic Drugs (OGD) expedited the review of 87 applications, including 60 abbreviated new drug applications and 27 supplemental applications.
 - CDER's Office of Biological Products (OBP) expedited the review of 2 supplemental applications.
 - CDER's Office of New Drug Quality Assessment (ONDQA) expedited 11 supplemental applications.
- **List the number of establishment inspections or reinspections related to the mitigation or prevention of a shortage that the Secretary expedited under section 506C(g)(2) during such calendar year¹¹**

Ten inspections occurred that were prioritized to address a drug shortage.¹²

⁹ Includes submissions for abbreviated new drug applications and prior approval supplements (PAS). In some cases, changes being effected (CBE) supplements are also included for new drug applications, where FDA determined that it was appropriate for a CBE to be submitted for a change instead of as a PAS. FDA's answer to requirement 3 includes data on all products tracked by CDER's Drug Shortage Staff.

¹⁰ These data are derived from the time period beginning January 1, 2014, and ending September 26, 2014, due to the shutdown of DARRTS and migration of data into the new CDER Informatics Platform, which occurred on September 27, 2014.

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

¹² Note that not all submissions to OGD, ONDQA, and OBP require inspections, but that some submissions can involve multiple sites, which may require inspections.

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 things, 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 are developing a memorandum of understanding (MOU). The MOU will set forth steps and procedures, including identifying contacts, for efficiently tracking and exchanging relevant information. At present, FDA and DEA are finalizing details regarding the scope of information that will be tracked and exchanged and the process for implementing identified steps and procedures.

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 a supply of approved drugs, 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 2014, FDA has exercised regulatory flexibility and discretion in 30 instances, affecting 31 products.¹³ The following are examples of situations in which FDA has exercised regulatory flexibility and discretion to prevent or mitigate a shortage:

- FDA has used temporary regulatory flexibility and discretion for medically necessary products that present quality issues through the use of measures to

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.

- 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, including foreign sources, of medically necessary drugs in rare instances when all alternative approaches have been applied.

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, website 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 two letters under section 506C(f). The first letter was sent on May 22, 2014, to Bristol-Myers Squibb Company and CordenPharma Latina S.p.A, and the second letter was sent on August 26, 2014, to Mylan Institutional LLC and Agila Specialties Private Limited. The letters sent by FDA and the responses received from the manufacturers are available on FDA's website.

¹⁴ Links to letters of Non-Compliance With Notification Requirement can be found at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm403902.htm>

Requirement 7: Specify the number of drug shortages occurring during 2014 (the first three quarters of 2014)

Using data from CDER's drug shortage database,¹⁵ the number of new shortages significantly decreased, from 117 in 2012 to 44 in 2013. Data indicate that this trend is continuing into 2014. As of September 30, 2014, 33 new drug shortages have been identified. Another important figure to look into and mitigate is the number of ongoing or persistent shortages that have yet to be resolved from previous years. At the end of the CY 2013, FDA identified 97 ongoing shortages. As of September 30, 2014, there were 73 ongoing shortages.

HIGHLIGHTS OF FDA WORK IN 2014 ON DRUG SHORTAGES

1. Drug Shortage Data System

FDA continues to improve its system for data tracking and analysis for drug shortages and has put into place a new system called the Drug Shortage Data System (DSDS). FDA believes this system is responsive to the recent Government Accountability Office (GAO) report on drug shortages,¹⁶ which made recommendations to further enhance the tracking of drug shortage data.

The new system enhances the efficiency and consistency of drug shortage data entry. The system standardizes key data elements and adds automated data integrity checks to ensure that data are accurate and complete for analysis. The system also centralizes various databases currently used by DSS to assess the potential impact of shortages. For example, DSDS imports drug sales data to show which products are currently marketed and the market share for those products. This simplifies the data entry process (because it auto-populates certain fields) and streamlines the basic research conducted by DSS when a shortage or potential shortage is reported.

DSDS is not yet fully integrated with other CDER data systems, such as the FDA Drug Shortage website database, Document Archiving, Reporting, and Regulatory Tracking System, or Compliance Management System. This means that 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. Also, DSDS is not designed to predict whether a manufacturer or product is at risk of shortage. Its primary function is to streamline day-to-day research, data entry, and data management for DSS. FDA is continuing to integrate DSDS with other CDER data systems to improve its drug shortage tracking and reporting capabilities.

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

¹⁶ GAO's report can be found at <http://www.gao.gov/assets/670/660785.pdf>.

2. FDA Drug Shortage Assistance Award

In September 2014, FDA created the FDA Drug Shortage Assistance Award¹⁷ 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 have worked in cooperation with FDA and have 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, while maintaining federally mandated quality standards. FDA hopes that shining a spotlight on the efforts of drugs manufacturers that have gone above and beyond in this area will encourage other manufacturers to follow suit.

The FDA Drug Shortage Assistance Award will be given to drug manufacturers who have demonstrated a strong commitment to prevent or mitigate a shortage of medically necessary drugs by:

- taking one or more actions to alleviate or prevent a drug shortage, such as increasing production or submitting an application for approval of a drug in shortage;
- making a significant impact on public health; and
- using a facility that was substantially compliant with current good manufacturing practice requirements for at least one inspection prior to the action(s) taken and for the duration of time the candidate used it to manufacture the shortage drug.

A manufacturer must meet additional criteria, including acceptable inspection history of the facilities involved and the manufacturer's overall compliance history. In addition, the shortage at issue cannot be one that the manufacturer played a role in creating.

The recognition is not a seal of approval by FDA, but provides public recognition for a manufacturer's contribution to addressing a critical shortage. This award is given for a specific action or actions taken by a manufacturer to address a critical drug shortage and will have no impact on future inspections or compliance and regulatory actions.

FDA plans to continue to recognize manufacturers with this award based on manufacturers' abilities to meet the criteria.

¹⁷ Link to FDA Drug Shortage Assistance Award can be found at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm415807.htm>.

3. Manual of Policy and Procedures

In September 2014, FDA issued a revised Manual of Policies and Procedures (MAPP) to provide the most transparency in how FDA mitigates and prevents shortages. Although it is an internal tool, it is publicly available.¹⁸ This MAPP outlines the interactions of the various components of FDA that work to respond to drug shortages and establishes CDER's procedures for notification, evaluation, and management of drug shortage situations for all CDER-regulated products, including those studied or marketed under investigational new drug applications, new drug applications, biologics license applications, abbreviated new drug applications, and unapproved drugs marketed without an approved application. Finally, the MAPP outlines the responsibilities of the DSS.

4. Drug Shortage Searchable Database

In June 2014, FDA launched an enhanced drug shortage website. FDA created a searchable database to provide stakeholders with easy access to information about drugs in shortage, such as product availability, supply, and anticipated duration of shortage. The database includes information about current drugs in shortage, resolved shortages, discontinuations, corresponding therapeutic categories, resource information, and relevant links.

5. Improved Coordination with International Agency Counterparts and Other U.S. Agencies

FDA initiated quarterly calls with our international regulatory agency counterparts to share information about drug shortage management and mitigation strategies as well as information about specific shortages that are impacting patients in other countries. FDA has also been working with the Biomedical Advanced Research and Development Authority, as well as the Assistant Secretary for Planning and Evaluation at the Department of Health and Human Services, to explore new methods to assist with critical and imminent drug shortages.

CONCLUSION

Drug shortages remain a significant public health issue in the United States and a top priority for FDA. To address them, FDA works with manufacturers to help prevent shortages from occurring and to mitigate the impact of shortages that cannot be prevented. 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 2014, CDER helped prevent 78 potential

¹⁸ The revised MAPP is available at <http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/manualofpoliciesprocedures/ucm079936.pdf>.

new shortages. As a result of the Agency's work in preventing and mitigating drug shortages, as well as efforts by industry and other partners, we saw 5 fewer new drug shortages in the first three quarters of 2014, compared to the same period in 2013 (33 vs. 38). This report reflects FDA's commitment to continue our work to prevent or mitigate drug shortages. Although important progress has been made in preventing drug shortages from occurring, and decreases have been seen in the total numbers of new shortages, FDA continues to work to ensure that patients in the United States will have access to the medicines they need.

KEY DEFINITIONS USED IN THIS REPORT

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

Meaningful Disruption: A *meaningful disruption* is a change in production that is reasonably likely to lead to a reduction in the supply of a drug 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.

Life Supporting or Life Sustaining: *Life supporting* or *life sustaining* is used to describe a drug 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

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.