

# DRUG SHORTAGES: ROOT CAUSES AND POTENTIAL SOLUTIONS



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# Drug Shortage Mission

- Our mission is to prevent, mitigate and alleviate drug shortages
- Patient and practitioner access to life-saving medication is our #1 priority
- Drug Shortage Staff works with professional organizations, patient groups, clinicians and other stakeholders (DEA, CMS, EMA ..etc.)

## Brief History

- Part of FDA's Center for Drug Evaluation & Research (CDER)
- Drug Shortage Program began in 1999
- 2011- President Obama signed *Executive Order 13588-Reducing Prescription Drug Shortages*
- 2012-Requirements to Industry For Early Notifications Under Section 506C of the FD&C Act  
Food and Drug Administration Safety and Innovation Act (FDASIA)
- CDER Drug Shortage Program (DSP) changed to Drug Shortage Staff (DSS) in 2012
- Moved under the CDER Office of the Center Director in 2014

# FDA Drug Shortage Staff (DSS)

**Drug Shortage Staff:** The program office that is designated by FDA to oversee and facilitate the resolution of all drug shortage situations

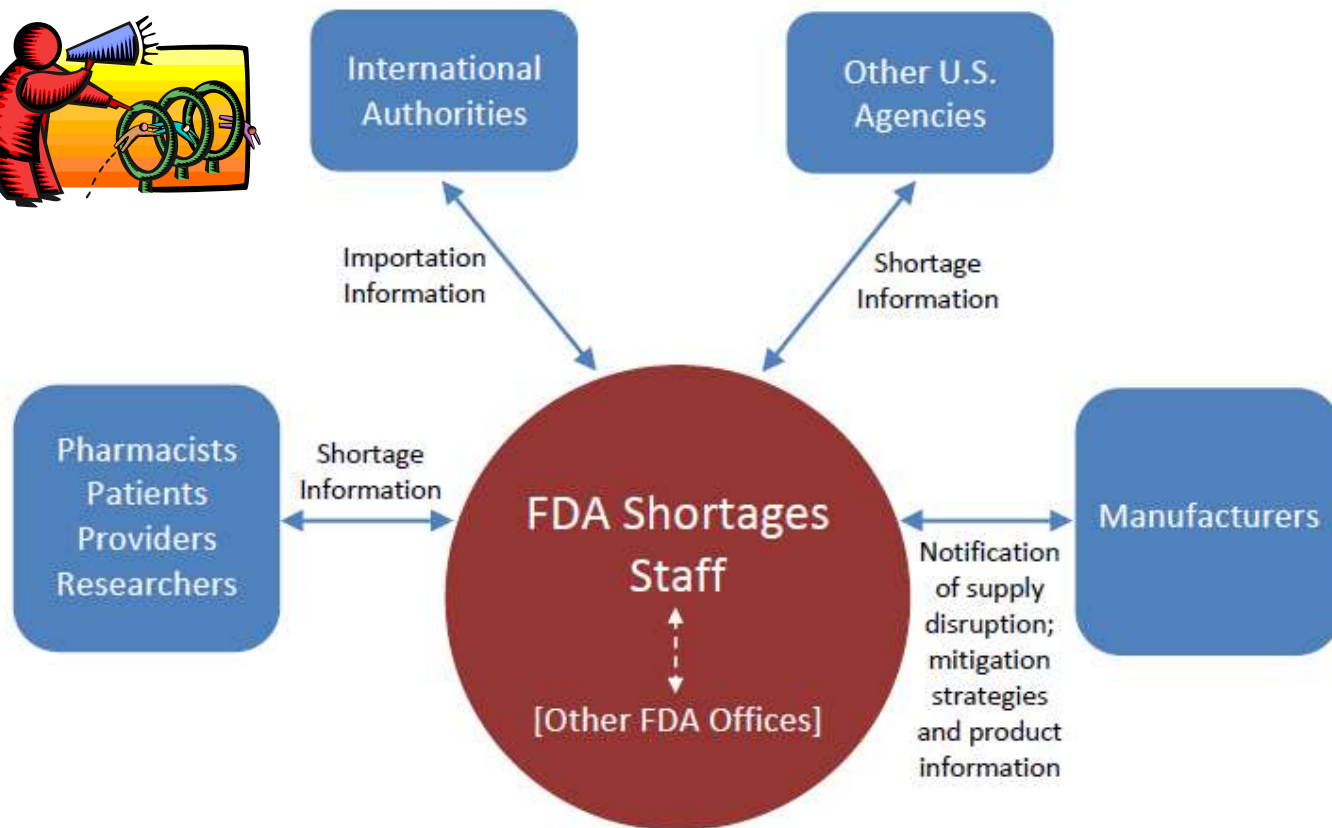
**DSS serves to support FDA's mission of ensuring that safe and effective drugs are available to patients**

- Facilitate temporary and long-term strategies to address shortages
- Coordinate for timely and comprehensive risk/benefit decisions
- Distribute information (web posting, professional organizations, e.g. ASHP)

**Often working across suppliers, facilities, and issues - multiple moving parts, urgency**

→ Maintain availability while minimizing risk to patients

# FDA Drug Shortage Staff - Key Communications



# Notification REQUIREMENTS Under Section 506C of the FD&C Act AND FDA REGULATIONS



Manufacturers are required to notify the FDA of a permanent discontinuance in the manufacture of a covered drug or an interruption of the manufacture of a covered drug that is likely to lead to a meaningful disruption in the supply of the drug in the United States

- “At least 6 months in advance of the date of the permanent discontinuance or interruption in manufacturing; or, if 6 months’ advance notice is not possible no later than 5 business days after the...permanent discontinuance or interruption in manufacturing occurs”
- Not limited to medically necessary products
- Regardless of market share, or number of companies marketing, or wholesaler volumes



# Drug Shortage Defined

## **Drug Shortage:**

A period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug. In general, the DSS focuses on shortages of medically necessary products that have a significant effect on public health.

# Medical Necessity

“A medically necessary drug product is a product that is used to treat or prevent a serious disease or medical condition for which there is no other alternative drug, available in adequate supply, that is judged by medical staff to be an adequate substitute.”

\*Although the agency focuses on medically necessary drugs, all potential shortages are evaluated to help determine the possible public health impact.

# Manufacturers Report on Potential Impact to Supply

**At the time of any change in manufacturing** that may lead to a reduction in supply of a product\*, e.g.:

- Plans for upgrade or remediation
- Manufacturing issues
- Raw material batch failures
- Particulate issues
- Sterility issues

\*Note, product refers to a specific strength, dosage form, and route of administration



# Manufacturers Report on Potential Impact to Supply

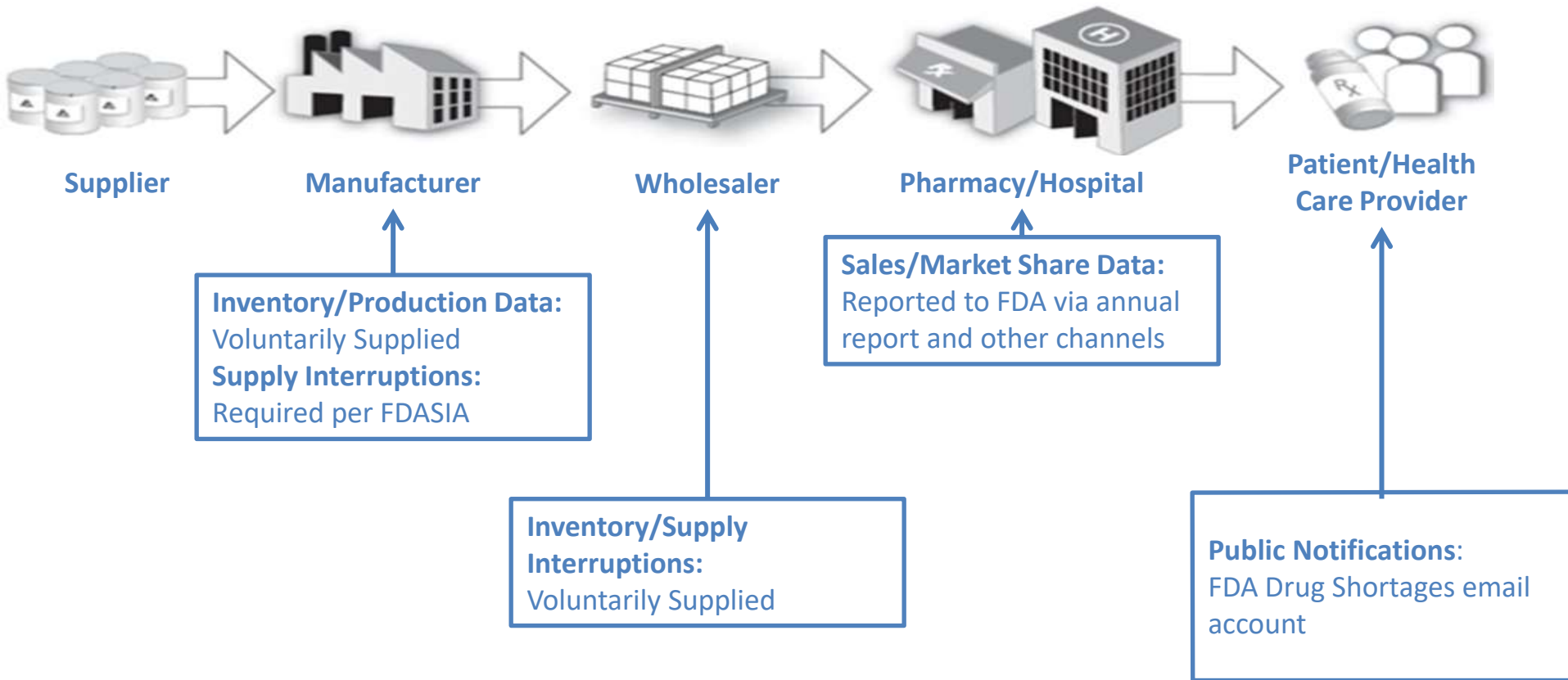
The FDA logo is located in the top right corner of the slide. It consists of the letters "FDA" in white, bold, sans-serif font, set against a blue square background. The slide itself has a decorative background of overlapping blue and white geometric shapes on the right side.

***FDA asking manufacturers to notify FDA ahead***, not as, or after, they are unable to fill orders or unable to meet expected demand

## Best Practices

“We have placed the following product(s) on hold pending an investigation. Due to the investigation being in progress and the completion date being not estimated at this time, we wanted to inform Drug Shortage of this potential for a supply interruption.”

# Drug Supply Chain – 1st Tier



# Opportunities and Challenges to Assist with Shortages

## FDA will work closely with manufacturers to address problems

- We can advise, assist, and expedite inspections and reviews, but the manufacturer must fix the problem

### What we CAN require:

- Notification by manufacturers (FDASIA)
  - Supply disruptions
  - Delays
  - Discontinuations
  - Notification of certain manufacturing changes

### What we CANNOT require:

- A company to make a drug
- A company to make more of a drug
- How much of a drug is distributed and which purchasers will be given priority



# The Agency's Approach to Prevention and Mitigation

**Early notification is key!!**

- Prioritize products that are medically necessary
- Risk/Benefit of the drug in question
- Maintain availability while minimizing risk to patients
- Work with firms to address problems
  - We can advise, assist, and expedite inspections and reviews, but the manufacturer must fix the problem

# The Agency's Approach to Prevention and Mitigation

- Drug shortages cannot always be prevented
  - Unanticipated events occur
    - Manufacturing breakdown or natural disaster (Hurricanes & Floods)
  - Sometimes alternate manufacturer may not make up production shortfall
  - If systemic issues present, the plant may have to close to repair
  - The FDA and the manufacturer can work together to encourage smart distribution (*allocation*)

# FDA Toolbox



- Communicate possible shortage concerns on a market shortfall to other suppliers
- Prompts firms to look at demand and supply
- Regulatory Discretion:
  - Manufacture of medically necessary products during remediation
  - Use of additional safety controls
    - Filters with injectable products to remove particulate concerns
    - Extra testing at plant
    - 3<sup>rd</sup> party oversight of production
    - Special instructions for safe use

# FDA Toolbox

## **Expedited review of company proposals**

New manufacturing sites, increased expiry date, new raw material source, changes in specifications, etc.

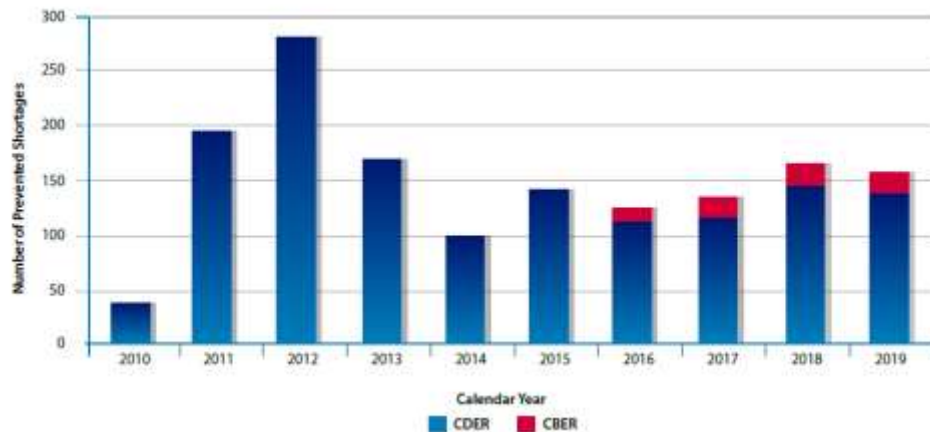
## **In rare cases, temporary exercise of regulatory flexibility and discretion regarding importation from other countries**

2017-2018: Dextrose 5% in Water, SWFI, Technetium injection, IV Saline Solution, Hydromorphone Injection, Potassium Chloride injection, Sodium Bicarbonate injection.

Past importation of Thiotepa lead to new US approvals

# Impact of Early Notifications to the FDA

- Ongoing dialogue/work with industry - high numbers of prevented shortages continue (115 in 2016, 145 in 2017, 160 in 2018)
- Depending on the precipitating events, some drug shortages can endure for months to years. (Ex: Plant remediations and agency approvals)

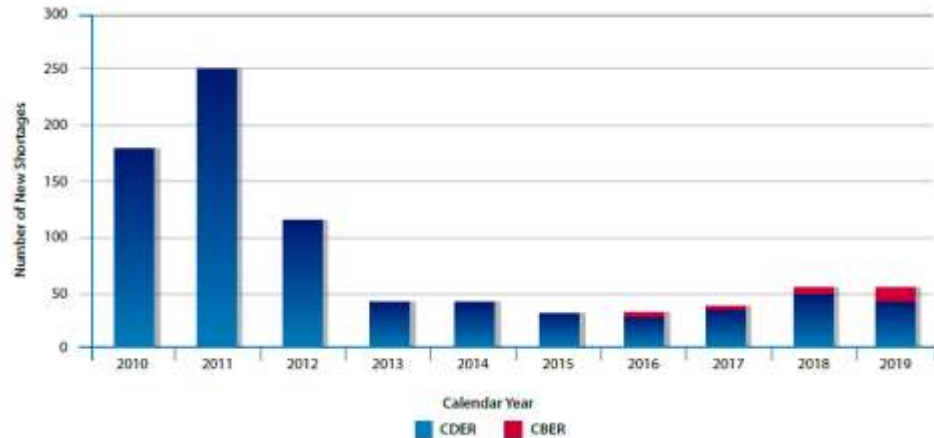


**Total Prevented US Drug Shortages Per Year**



## Current Challenges: Increasing new shortages and persistent shortages

- Shortages peaked in 2011 at 251, and continued to decline through 2016. Shortages rose again in 2017 and 2018 due in part to the 2017 hurricane impact as well as ongoing problems at manufacturers. Numbers of new shortages holding steady in 2019 with 46 new shortages.
- Depending on the precipitating events, some drug shortages can endure for months to years. (Ex: Plant remediations)



**Total New US Drug Shortages Per Year**

# Examples of Current Shortages Affecting Patients

- ▶ Valsartan oral tablets had been in short supply due to the detection of nitrosamine impurities
- ▶ Dexmedetomidine injection due to increase in demand
- ▶ Erwinaze injection continues to be in and out of shortage due to quality issues

# Other Examples of Current Shortages Affecting Patients

- ▶ Injectable hospital drugs including pain medications and local anesthetics
- ▶ Epinephrine autoinjectors
- ▶ Tacrolimus is available, but not from all suppliers

# Role of Industry to Help Prevent and Mitigate Drug Shortages

- Understand the frailties of their supply chain
- Communicate early about potential shortages
- Provide shortage information for posting on FDA website when a shortage is unavoidable
- Provide short term and long term plans for preventing and addressing shortages while maintaining and improving quality
- Work with FDA to minimize shutdowns or slowdowns that will lead to shortages

# Next Steps

FDA announced July 12, 2018, that a new FDA Task Force was implemented to identify more enduring solutions for shortages. A public meeting was held November 27<sup>th</sup>, and additional stakeholder engagement has been conducted. The report was published October 29, 2019.

## **The report identifies three root causes for drug shortages:**

1. Lack of incentives for manufacturers to produce less profitable drugs
2. The market does not recognize and reward manufacturers for “mature quality systems” that focus on continuous improvement and early detection of supply chain issues; and
3. Logistical and regulatory challenges make it difficult for the market to recover from a disruption.

## **The report also recommends enduring solutions to address drug shortages. These solutions include:**

1. Creating a shared understanding of the impact of drug shortages on patients and the contracting practices that may contribute to shortages;
2. Developing a rating system to incentivize drug manufacturers to invest in quality management maturity for their facilities; and
3. Promoting sustainable private sector contracts (e.g., with payers, purchasers, and group purchasing organizations) to make sure there is a reliable supply of medically important drugs.

# Contacts:

Current shortage information updated daily at:

<https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>

To contact DSS:

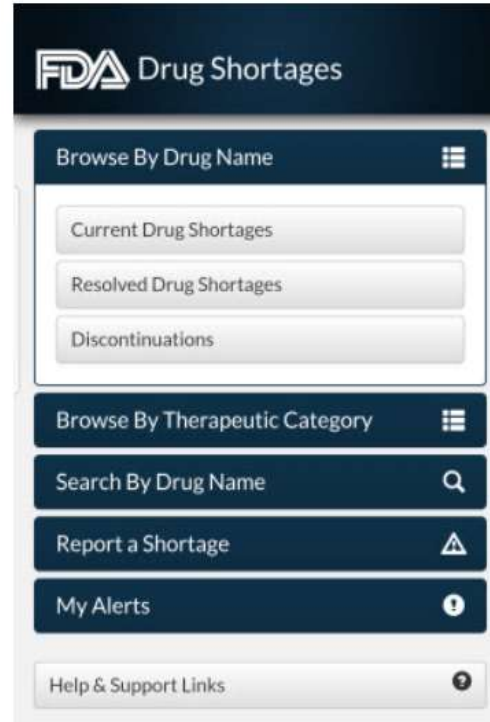
Email: [drugshortages@fda.hhs.gov](mailto:drugshortages@fda.hhs.gov)

FDA Drug Shortages Homepage:

<https://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>

Drug Shortage Mobile APP

## FDA Drug Shortages Mobile App



Receive notifications when there is about a drug product shortage or a therapeutic categories.

[FDA Drug Shortages RSS Feed](#)

# References

- ▶ Explanation of FDA and ASHP shortage posting: <https://www.fda.gov/drugs/drug-shortages/frequently-asked-questions-about-drug-shortages#q1>
- ▶ FDA Sixth Annual Report on Drug Shortages for Calendar Year 2018 <https://www.fda.gov/media/130561/download>
- ▶ FDA Shortages Additional News And information <https://www.fda.gov/drugs/drug-shortages/drug-shortages-additional-news-and-information>
- ▶ Federal Food, Drug, and Cosmetic Act (FD&C Act), Section 506C (21 USC 356c)  
<https://www.gpo.gov/fdsys/pkg/USCODE-2012-title21/pdf/USCODE-2012-title21-chap9-subchapV-partA-sec356c.pdf>
- ▶ Federal Register Final Rule, 80 FR 38915 (July 8, 2015), Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products. <https://www.gpo.gov/fdsys/pkg/FR-2015-07-08/pdf/2015-16659.pdf>. See also 21 CFR 310.306, 314.81, and 600.82.
- ▶ CDER MAPP 4190.1 Rev. 2, Drug Shortage Management (11/1995; Rev. 1, 9/2006; Rev. 2, 9/2014):  
<https://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/ucm079936.pdf>
- ▶ Executive Order 13588 (October 31, 2011), Reducing Prescription Drug Shortages:  
<https://obamawhitehouse.archives.gov/the-press-office/2011/10/31/executive-order-13588-reducing-prescription-drug-shortages>.
- ▶ FDA Strategic Plan for Preventing and Mitigating Drug Shortages:  
<https://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf>
- ▶ Letters of Non-Compliance with Notification Requirement:  
<https://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm403902.htm>