FDA's Role in Preventing and Mitigating Drug Shortages

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Generic Drug Forum

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Objectives

- Describe FDA's role in the prevention and mitigation of drug shortages and the role of the Drug Shortage Staff.
- Understand the ongoing reasons for drug shortages as well as new challenges to the U.S. drug supply.

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-FDASIA legislation – requires Early Notifications of supply disruption for certain products
- CDER Drug Shortage Program (DSP) changed to Drug Shortage Staff (DSS) in 2012
- Moved under the CDER Office of the Center Director in 2014
- Additional shortage staff in other Centers (e.g. CBER, CDRH)
- Coronavirus Aid, Relief, and Economic Security Act (CARES Act) 2020

FDA Drug Shortage Staff

CDER Drug Shortage Staff (DSS): The program office designated by FDA to oversee and facilitate the resolution of all drug shortage situations (MAPP 4190.1)

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)

Often working across manufacturers, facilities, and issues – multiple moving parts, urgency

→ Maintain availability while minimizing risk to patients

How does the FDA determine if a drug is in shortage?

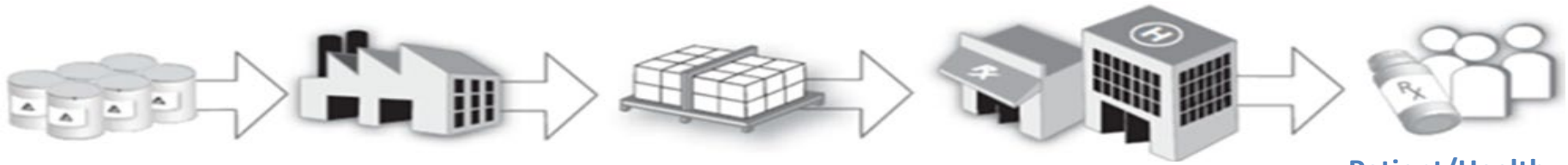
Drug Shortage Defined

A period of time when the demand or projected demand for the drug *within the United States* exceeds the supply of the drug (section 506C of the FD&C Act, 21 CFR 314.81).

Covered drugs: a drug that is life-supporting, life-sustaining, or intended for use in the prevention or treatment of a debilitating* disease or condition, including any such drug used in emergency medical care or during surgery or any such drug that is critical to the public health during a public health emergency declared by the Secretary.

*Per 80 FR 38915, FDA equates "debilitating" with "serious" found in 21 CFR 312.300

Drug Supply Chain – 1st Tier



Supplier

Manufacturer

Wholesaler

Pharmacy/Hospital

Patient/Health Care Provider

Inventory/Production Data:
Voluntarily Supplied
Supply Interruptions:
Required per FDASIA

Sales/Market Share Data:
Reported to FDA via annual report and other channels

Inventory/Supply Interruptions:
Voluntarily Supplied

Public Notifications:
FDA Drug Shortages email account

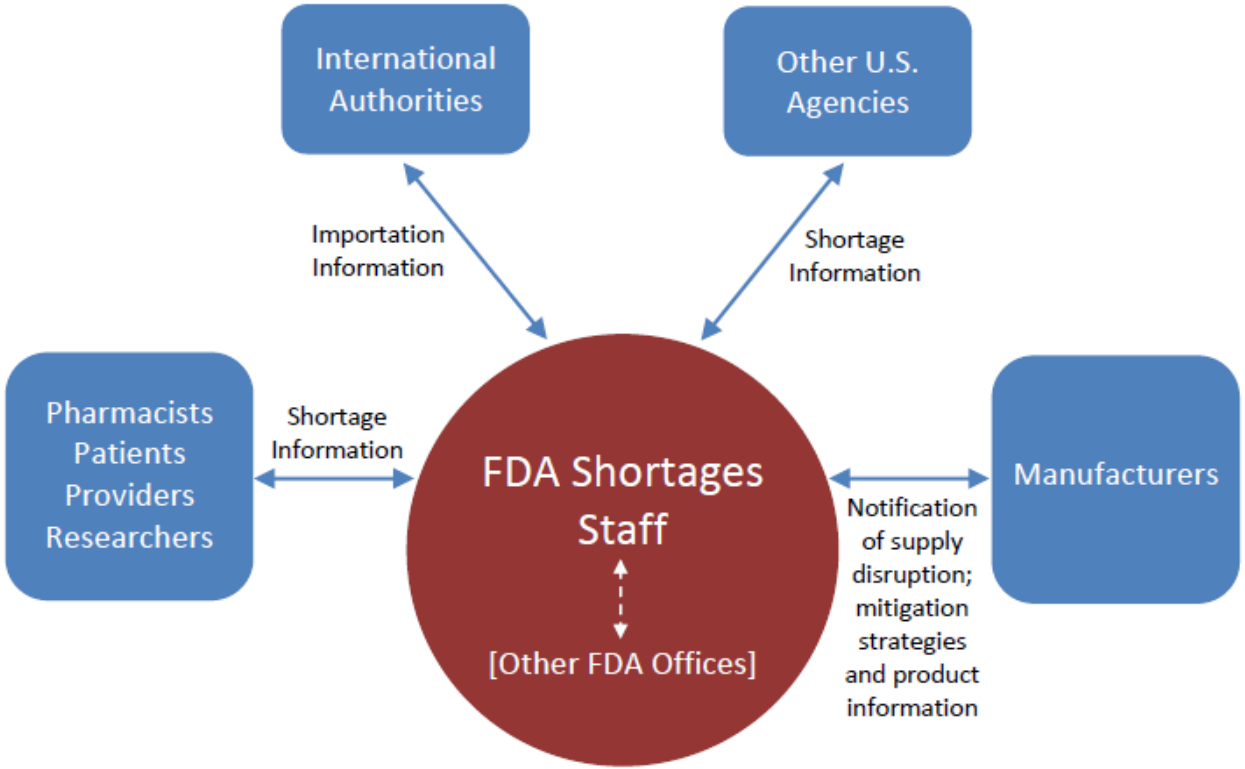
Notification Requirements Under Section 506C of the FD&C Act and FDA Regulations

Manufacturers and applicants and of certain finished drugs and biological products are required to notify FDA (drugshortages@fda.hhs.gov) of:

- a permanent discontinuance in the *manufacture* of such products,
- an interruption in the *manufacture* of such products that is likely to lead to a meaningful disruption in supply of those products in the United States,
- a permanent discontinuance in the *manufacture* of API for such products, or
- an interruption in the *manufacture* of API for such products that is likely to lead to a meaningful disruption in the supply of the API for those products.

See also 80 FR 38915, 21 CFR 314.81, Guidance for Industry.

FDA Drug Shortage Staff - Key Communications



Strategic Plan for Preventing and Mitigating Drug Shortages (2013)

FDA Drug Shortage Staff - Actions

MAPP 4190.1

- Monitoring: When DSS receives notice from industry, other FDA offices, professional organizations, health care providers, or patients regarding potential or actual drug shortages, it is assigned to a staff member for follow up.
- Evaluation: DSS reviews current market share data and information across all manufacturers of the drug in the U.S. market to determine if there is a drug shortage concern.
- Coordination: DSS oversees CDER activities and communications to address the drug shortage concern.
- Posting: If DSS confirms that a drug shortage exists, DSS may post this information on the CDER Drug Shortage list (per section 506E of the FD&C Act) and will continue to follow up to resolution.

What can FDA do to help mitigate, prevent, or limit drug shortages?

Opportunities and Limitations with Shortages

FDA will work closely with manufacturers to address problems

We can advise, assist, and expedite inspections and reviews, but the manufacturer must address the root cause

What we CAN require:

- Notification prior to a disruption in a manufacturer's own supply (section 506C of the FD&C Act)
  - Manufacturing interruptions
  - Discontinuations
- Notification of certain quality events or manufacturing changes

What we CANNOT require:

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

FDA Drug Shortage Staff - Actions

MAPP 4190.1

- DSS evaluation to confirm a potential drug shortage concern, in particular with medically necessary drugs
- Once confirmed, DSS works across all manufacturers of the drug marketed in the U.S. by:
  - Prompting manufacturers to communicate closely on production and demand
  - Expediting reviews and inspections (per section 506C of the FD&C Act)
  - Exercising regulatory flexibility based on benefit-risk, e.g. lot-specific release and in rare cases, exercising temporary enforcement discretion to import supply from other countries under certain contingencies as necessary

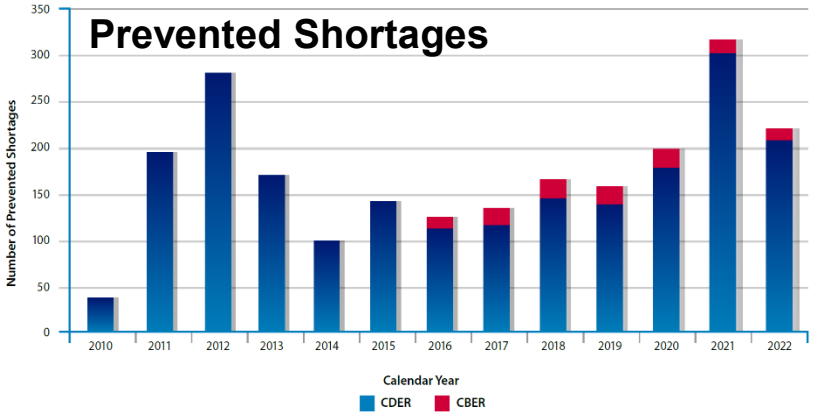
→ Maintain availability while minimizing risk to patients

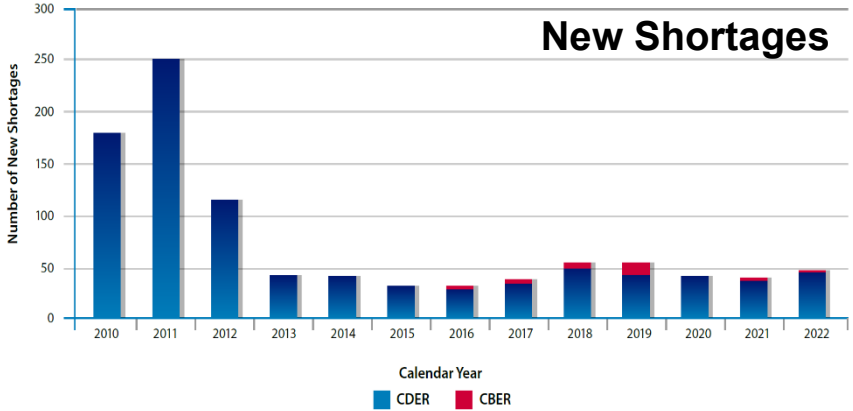
FDA Toolbox

- Proactive outreach through CDER NextGen Drug Shortage Emergency Event Portal
- 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
    - 3rd party oversight of production
    - Special instructions for safe use
    - Extension of expiration dating
- 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
  - Dextrose 5% in Water, SWFI, Technetium injection, IV Saline Solution, Hydromorphone Injection, Potassium Chloride injection, Sodium Bicarbonate Injection, Bupivacaine Injection, Cefotaxime Injection
  - Past importation of Foscarnet and Thiotepa lead to new US approvals

Early Notification is Key to Prevention

- Through ongoing dialogue/work with industry the number of prevented shortages continues to grow, while new drug shortages remain flat
- Depending on the precipitating events, some drug shortages can endure for months to years (e.g., plant remediations and agency approvals).
- The earlier this work begins the greater the likelihood a shortage can be prevented, or the most severe impacts mitigated





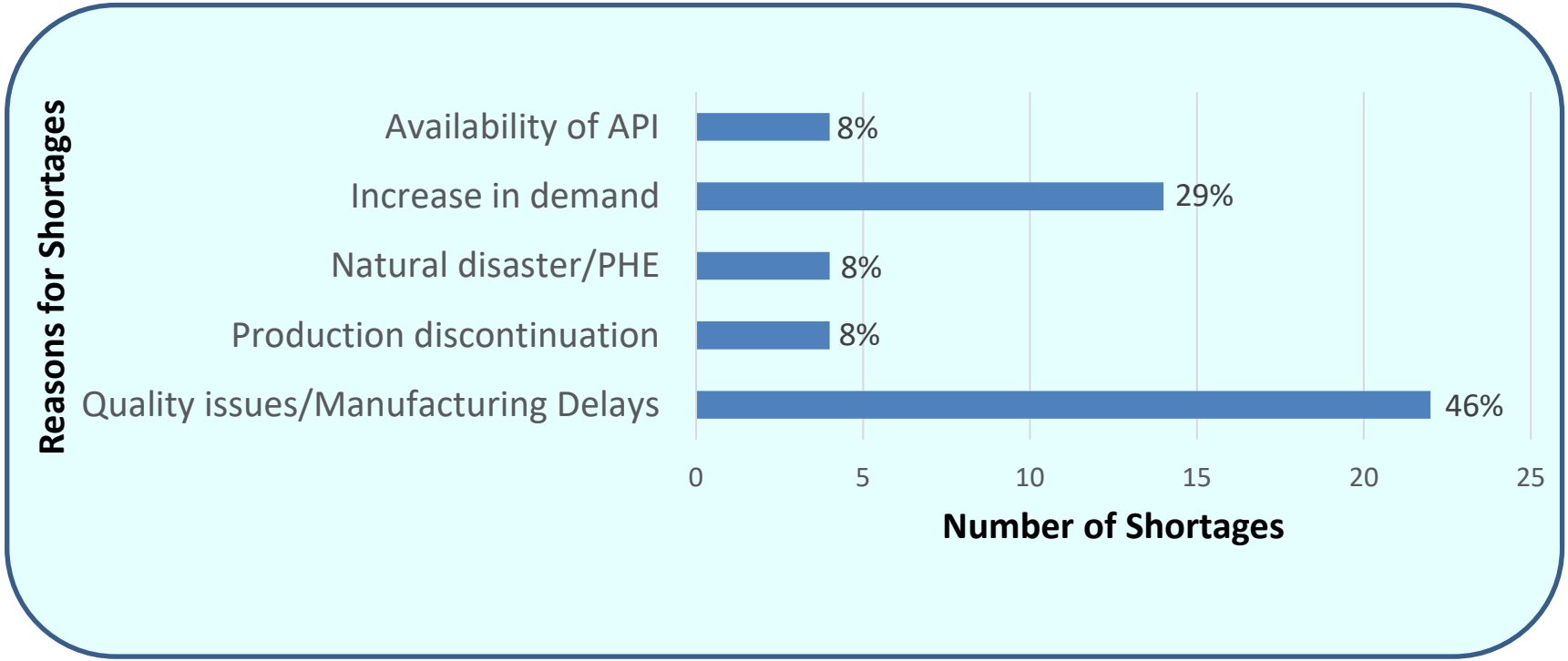
Annual Report on Drug Shortages for Calendar Year 2022

Challenges to Prevention and Mitigation

Drug shortages cannot always be prevented

- Unanticipated events occur
  - Public Health Emergency
  - Manufacturing breakdown
  - Natural disaster (hurricanes, floods)
- Sometimes other manufacturers are not able to meet the shortfall
- If systemic issues are present, the plant may have to close to repair
- DSS can encourage the manufacturer to implement an allocation plan and reserve emergency supply

Reasons for New Shortages in CY 2022



Current Challenges

- **Increased demand -** IV narcotics, IV fluids, ADHD drugs, weight loss drugs, Tripledemic-related medications, etc.
- **Competition on manufacturing lines and in facilities** due to limited capacity and vaccines/related products being made on the same lines
- **Loss of overall market capacity -** recent bankruptcy, other plant closures
- **Industry-wide short supply of manufacturing components** (e.g., filters) and other commodities (glass, vials, stoppers, bags)
- **New quality-related issues found on inspection**
- **Impurities** - such as nitrosamines
- **Natural disasters -** tornado impact at the Pfizer NC facility, current hurricane season, etc.
- **Economic and commercial** - lack of market certainty to support investments in continuous improvement

What can industry do to help decrease drug shortages?

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
- Adopt more mature quality management practices

Additional Solutions

- **Risk Management Plans** are required for certain products as part of the CARES Act of 2020. FDA issued a Guidance for Industry on what should be included in these plans including having a backup plan for when there's a manufacturing failure or demand increases
- **Redundancy in manufacturing** and suppliers – encouraging industry to have "warm" lines and components and supplies at the ready for critical drugs
- **More capacity**, additional manufacturers making critical drugs, especially generics at risk of shortage
- Focus on **Quality Management Maturity** and continuous improvement

"**We have got to fix the core economics** if we're going to get this situation fixed."
– Dr. Robert Califf, FDA Commissioner, May 11, 2023

Thank You!

Drug Shortage Public Notifications (portal)
https://cdernextgenportal.fda.gov/publicportal/s/dsm-submission

Drug Shortage List (webpage)
https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm

To Report a Shortage
drugshortages@fda.hhs.gov
(240) 402-7770

Questions?