Drug Shortages: Root Causes and Potential Solutions

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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

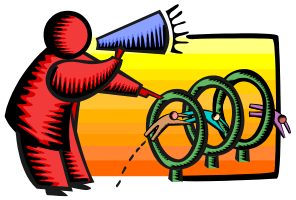
DSS serves to support FDA's mission of ensuring that safe and effective drugs are available to patients

- 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



Data Comparison: CDER Drug Shortage vs ASHP Website

- FDA receives information provided by manufacturers
- ASHP receives information from practitioners unable to get product
- FDA does not consider a product to be in shortage if one or more manufacturers are able to supply the full market demand for the product
- ASHP's Drug Shortage website provides information about which manufacturers have the drug available and which ones do not, since supply chain disruptions may occur when all previous manufacturers are not yet back on the market

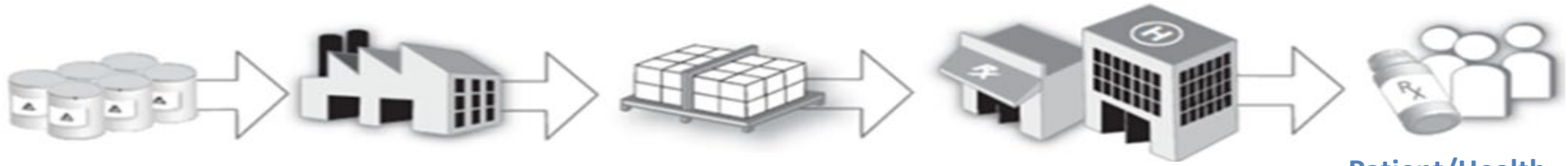
Contrasting the FDA (CDER) and ASHP Drug Shortage Websites: What are the differences?		
	FDA	**ASHP**
Purpose	Provides information obtained from manufacturers about current shortages, estimated duration, and discontinuations and provides information about FDA's and other stakeholders' roles in addressing and preventing shortages	Notification of new shortages and status of ongoing shortages; drug shortage management resources
Audience	Public	Healthcare practitioners
Scope of shortage list	All drugs are listed that are confirmed to be a national shortage by FDA. A shortage is considered to be the period of time when the demand for the drug within the United States exceeds the supply of the drug. **Note:** A separate shortage webpage[i] for vaccines and some biologics is maintained by the Center for Biologics Evaluation and Research.	All drug and biologic shortages reported and confirmed with manufacturer that are national in impact. **Note:** ASHP frequently lists more shortages than FDA.
Source of shortage report	Manufacturers notify FDA of production disruption and voluntarily provided updates. Reports are also received from ASHP and from public via drugshortages@cder.fda.gov **Note:** Manufacturer-provided information represents shortage status at drug firm level	Voluntary reports from practitioners, patients, pharmaceutical industry representatives and others **Note 1:** Information is updated based on release dates from manufacturers. **Note 2:** Reports reflect status at healthcare provider level.
Criteria for inclusion on list	Manufacturers cannot meet current market demand for the drug based on information provided by manufacturers and market sales research	(1) Shortage is verified with manufacturers and (2) affects how pharmacy prepares or dispenses a product, or (3) requires use of alternative drugs, which may affect patient care
Criteria for resolving shortage	One or more manufacturers are in production and able to meet full market demand	All manufacturers of the drug restore all formulations and dosage sizes to full availability. **Note:** Product are listed despite partial or restricted availability as supply chain disruptions can result in intermittent shortages at the provider or patient level
Reason for shortage	Provided by manufacturers using reasons required by legislation.[ii] FDA encourages firms to provide additional information about reasons and other information which, if proprietary, is nondisclosable without the firms' permission.	Provided by manufacturer, if willing to disclose. **Note:** May differ from FDA's due to different sources of information and legislation requiring FDA to use specified reasons
Other information	Estimated duration, links to regulatory information such as recalls and Dear Healthcare Provider Letters	Estimated duration, list of available products, implications for patient care and safety, shortage management strategies, therapeutic alternatives

Developed by: Food and Drug Administration Drug Shortage Staff, American Society of Health-System Pharmacists, and the University of Utah Drug Information Service. August 2014

[i] URL : http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/Shortages/ucm351921.htm

[ii] From the Food and Drug Administration Safety and Innovation Act. 2012. A reason selected from the following categories must be provided for each drug on the shortage list: (a) Requirements related to complying with good manufacturing practices (b) Regulatory delay (c) Shortage of an active ingredient (d) Shortage of an inactive ingredient component (e) Discontinuation of the manufacture of the drug (f) Delay in shipping of the drug (g) Demand increase for the drug.

Drug Supply Chain – 1st Tier



Supplier

Manufacturer

Wholesaler

Pharmacy/Hospital

Patient/Health Care Provider

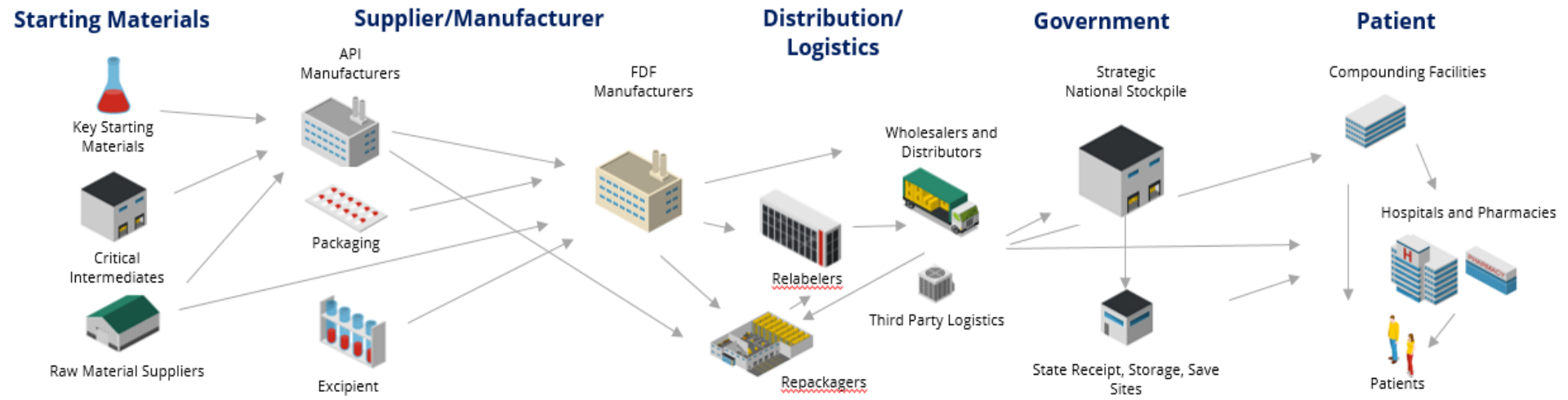
Inventory/Production Data:
Voluntarily Supplied
Supply Interruptions:
Required per FDASIA

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

Illumination – Simplified End-to-End Supply Chain



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

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
- 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, Penicillin G Benzathine Injection
  - Past importation of Foscarnet, Thiotepa, and Cisplatin lead to new US approvals

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

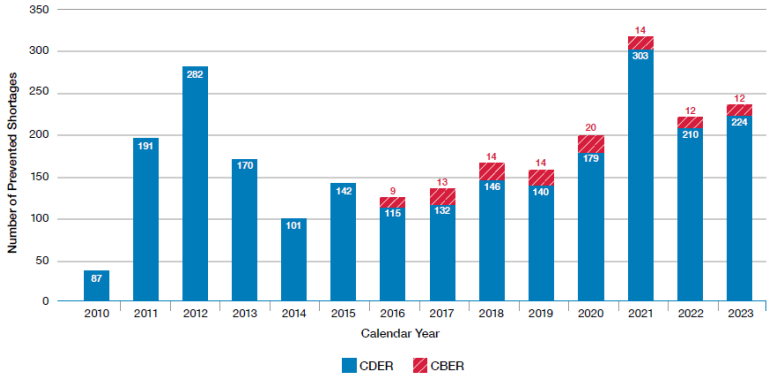
What we CANNOT require:

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

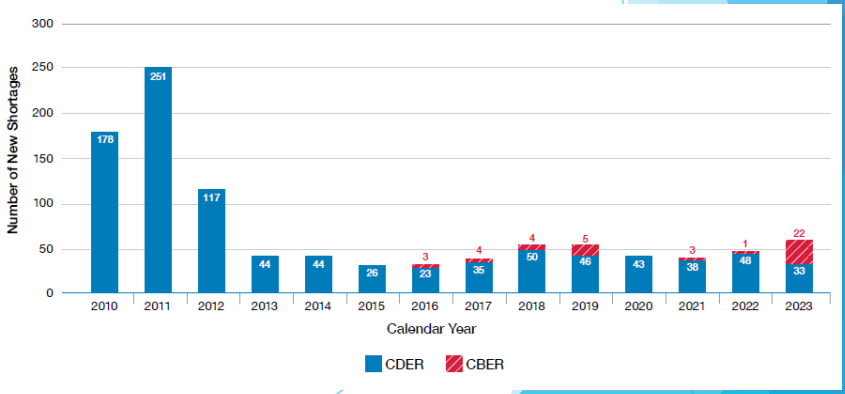
Early Notification is Key to Prevention

- 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

Prevented Shortages



New Shortages



[Annual Report on Drug Shortages for Calendar Year 2023]

Current Drug Shortages and 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

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

Early Notification is Key

- Current law requires manufacturers to notify FDA about a disruption in supply of API or manufacturing that could lead to a shortage
- During COVID we increasingly saw demand driven shortages and that has continued
- CDER has access to sales data, but these are lagging and do not provide good insight into demand
- Currently no requirement for manufacturers to report when increases in demand may lead to a supply shortage

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
- "**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

CARES Drug Amount Reporting: Who, What, and How?

- WHO: To simplify reporting, FDA has limited reporting to the following business operations:
  - FD Manufacture
  - API Manufacture
  - Repack
  - Relabel
  - Transfill
  - Positron Emission Tomography Drug Production
- WHAT: All listed drugs, except for biological products or categories thereof exempted (Blood and blood components for transfusion products, cell and gene therapy products) by an order under section 510(j)(3)(B):
  - Rx and OTC
  - Homeopathic
  - Medical gas
- HOW: Reports should be submitted electronically via the NextGen Portal, available at edm.fda.gov
  - Manually entering the report into the portal directly, or
  - Uploading the report to the portal from a CSV file
  - FDA recommends that drug amount are submitted annually, organized by the amount of drug manufactured each month.

Report a New Shortage via the Portal

Drug Shortage Notifications

For Industry

Industry can notify FDA Drug Shortage Staff of drug and supply shortages via the CDER Direct NextGen Portal.

This portal is intended ONLY for drug manufacturers/applicants. Industry can notify the FDA Drug Shortage Staff of new discontinuances, GMP issues, increase in product demand, recalls, supply interruptions, or other events. If you have any questions, please contact: drugshortages@fda.hhs.gov.

https://cdernextgenportal.fda.gov/

Thank you!

Industry Notification (CDER NextGen Portal)
https://cdernextgenportal.fda.gov/

Public patient/provider notifications (portal)
https://cdernextgenportal.fda.gov/publicportal/s/dsm-submission

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

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

Questions?