CDER Drug Shortage Program

Agenda

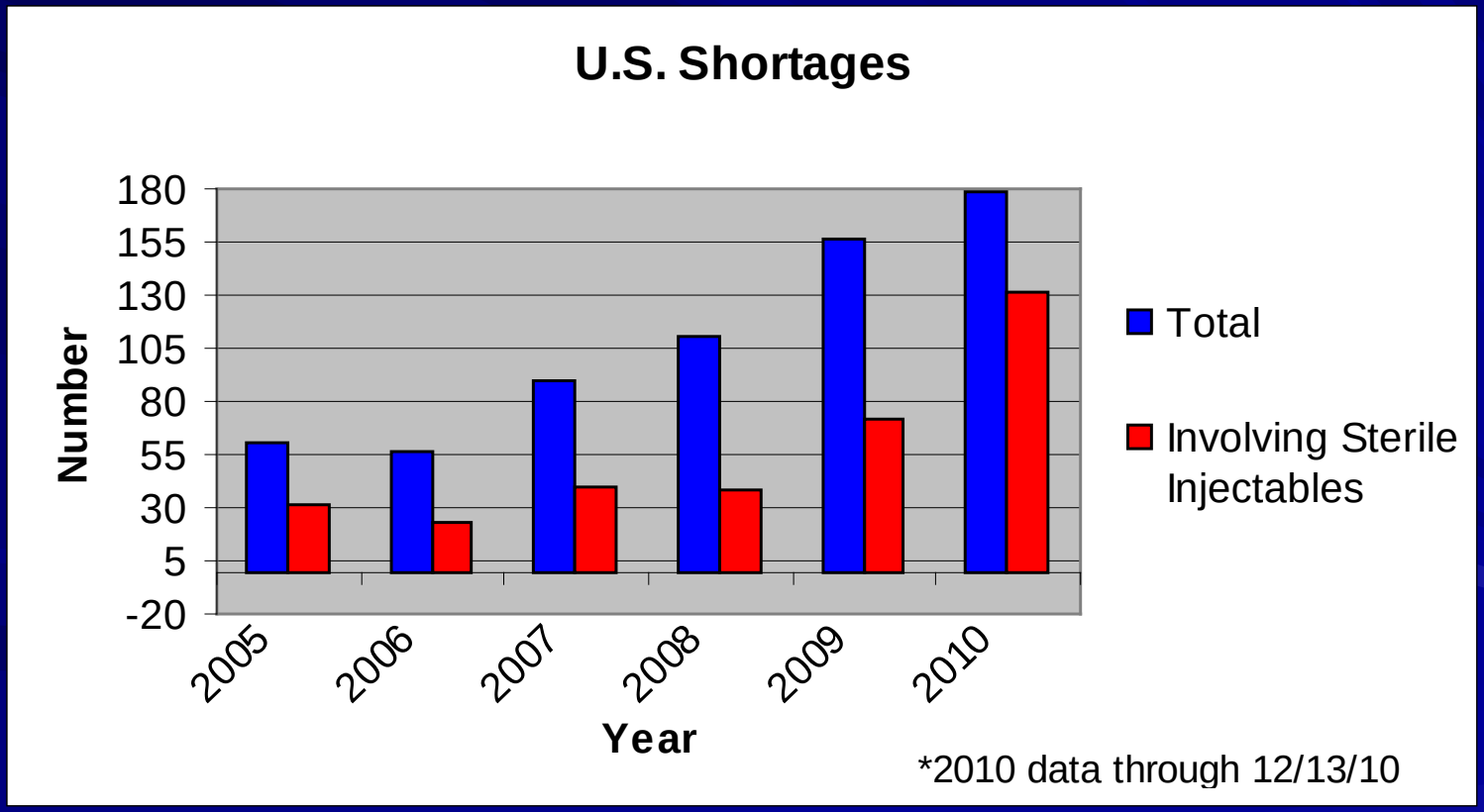
- **Shortage Trends**
- **Shortage Process and Medical Necessity (MN) Determination**
- **FDA’s Role**
- **Key Issues**

General Reasons for Shortages

- Manufacturing difficulties/Compliance Issues
- Corporate decisions/discontinuations
- Market Concentration/Limited Capacity
- Bulk drug/API shortage
- Changes in Clinical Practice
- Emergency Situations
- Hospital/Pharmacy based issues

Shortage Trends – Past 6 years

CDER Drug Shortage Data



Shortage Trends - 2010

- 2010 – significantly increased numbers of shortages **178 shortages in 2010 as of 12/15/10**

  (157 in all of 2009)
- Sterile injectables – greater numbers than past years

  74% of 2010 shortages involve sterile injectables
- Critical drugs involved - oncology drugs, succinylcholine, naloxone, furosemide, emergency syringes, etc…

Reasons for Sterile Injectable Shortages - 2010

- 54% - Due to Product Quality issues (includes particulate, microbial contamination, newly identified impurities, stability changes)
- 21% - Due to Delays/Capacity issues (not due to any other reason)
- 11% - Due to Discontinuations
- 5% - Due to raw material (API) issues
- 4 % - Increase in demand due to another shortage
- 3% - Due to loss of manufacturing site
- 2% - Due to component problems/shortage

Trends, Continued

- Older Sterile Injectables
  - Not enough capacity
  - Fewer firms making these products
  - Complex manufacturing process
  - Generally not economically attractive

When one firm has problems or discontinues, a shortage almost always occurs.

Shortage Process – MaPP 6003.1

- Verify that a national shortage exists (Market Share data, confirm availability status with manufacturers)
- Obtain determination of Medical Necessity (MN) from appropriate review divisions(s)
- Facilitate formulation of short term/long term plan for shortage management (e.g. Division(s), Compliance, Company)
- Consider notifications (web posting, notifying professional organizations).

Definition of a Medically Necessary Product

- A product is considered to be medically necessary, if it is used to treat or prevent a serious disease or medical condition, and there is no other adequately available source of that product or alternative product that is judged by medical staff to be an acceptable substitute. "Inconvenience" alone is an insufficient basis to classify a product as a medical necessity.

NOTE: The Drug Shortage Program focuses on Medically Necessary products that have the greatest impact on the public health.

FDA's Role

- Steps FDA takes when there is a shortage:
  - For manufacturing/quality problems – work with the firm to address the issues. Problems may involve very low risk (e.g. wrong expiration date on package) to high risk (particulate in product or sterility issues). Regulatory discretion may be employed to address shortages to mitigate any significant risk to patients.
  - Encourage remaining firms to ramp up.
  - FDA can expedite issues related to addressing shortages (e.g. new manufacturers, increased expiry, increased capacity, new raw material source, changes in specifications).
  - In rare cases, temporary importation (propofol, foscarnet, ethiodol)

What FDA Can't Do

- FDA cannot force a manufacturer to produce a product Manufacturers are not required to report plans to discontinue producing a product unless they are the sole manufacturer of a drug that is life-supporting; life-sustaining; or intended for use in the prevention of a debilitating disease or condition... (21 CFR 314.81 FR published 10/07)
- No penalty for not notifying FDA of a discontinuation.

Discontinuance Regulation

- 21 CFR 314.81 (FR October 2007)
  - A manufacturer that is the sole manufacturer of a drug that is life-supporting; life-sustaining; or intended for use in the prevention of a debilitating disease or condition for which an application has been approved under section 505(b) or 505(j) and that is not a product that was originally derived from human tissue and was replaced by recombinant product, shall notify the Secretary of a discontinuance of the manufacture of the drug at least six (6) months prior to the date of the discontinuance

Key Issues

- Notification from firms is important for all shortage issues (not just sole source and not just those firm determines to be medically necessary)

- Early notification leads to better chance of timely resolution - 38 product shortages prevented in 2010 due to firms notifying FDA in advance

- Timely website postings with helpful information for healthcare professionals and patients regarding reasons for shortages and timelines for resolution

Ways to foster shortage prevention (can't require):

1) commitment to quality –requires investment of resources by firms

2) redundancy of manufacturing/supplies and increased inventory/stockpiling

Shortage Information

- FDA drug shortage website is:
  http://www.fda.gov/Drugs/DrugSafety/default.htm

- To report shortages our e-mail account is Drugshortages@fda.hhs.gov