FDA Regulatory Actions Involving Drug Compounding

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Potential Actions

- Recommend Voluntary Recalls
- Warning Letters
- State Referral Letters
- Injunctions

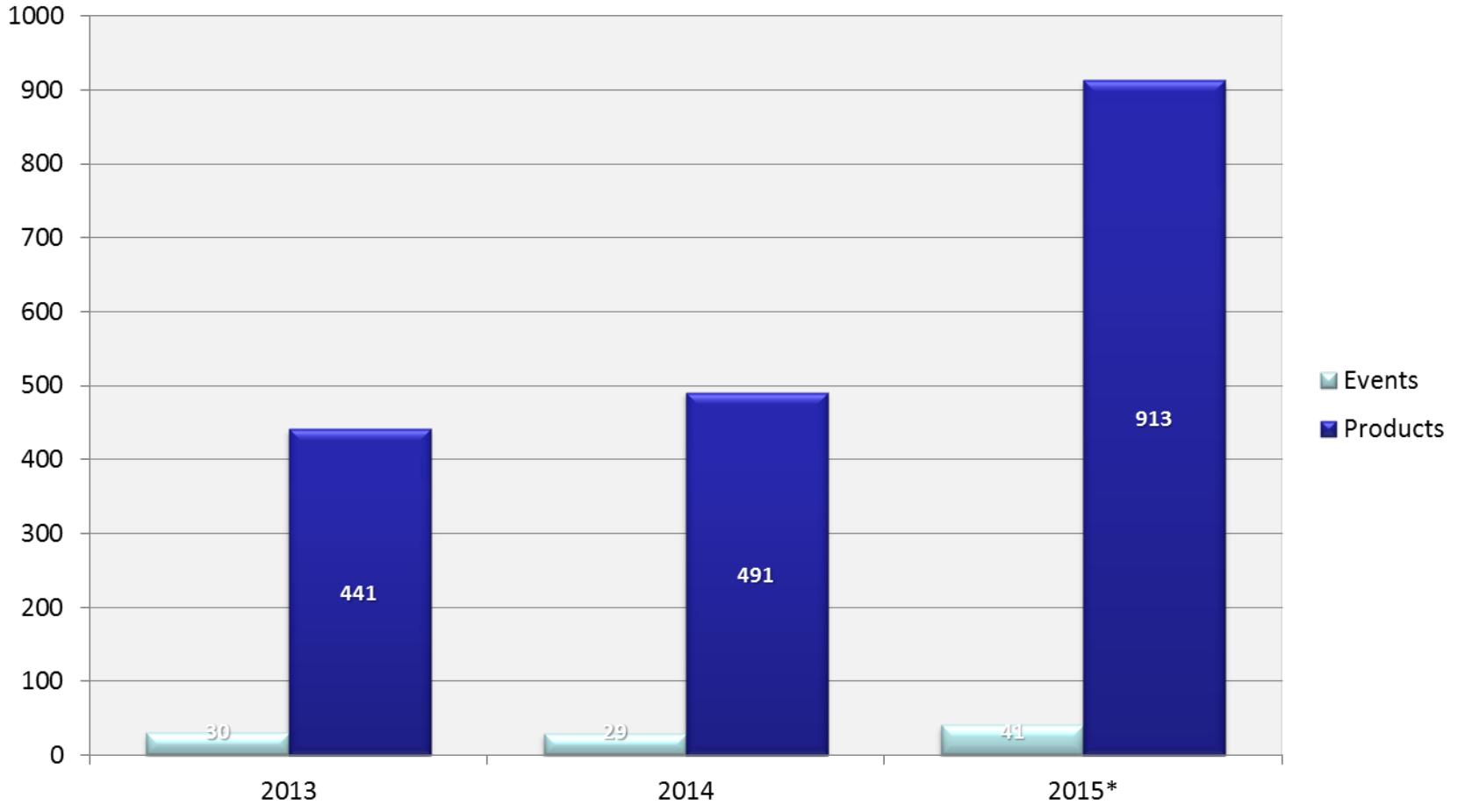
Some Factors to Consider

- Risk to public health
  - Lack of sterility assurance
  - Actual contamination
- Prior violations and likelihood of firm compliance
- How easily can the violations be corrected
- Firm's willingness to take voluntary action

Voluntary Actions

- Recalls
  - Since October 2012 there have been over 100 recall events involving compounded drugs, many due to conditions and practices resulting in a lack of drug sterility assurance
    - Some recalls overseen by FDA, others overseen by the state
    - FY 2013 – 30 recall events
    - FY 2014 – 29 recall events
    - FY 2015 – 41 recall events
  - Since October 2012 FDA has issued 3 letters formally asking firms to recall compounded drugs after they refused informal requests

Compounding Recalls FY 13-15*



The total number of products is misrepresented in some events. A large number of products were characterized as 1 product described as "all products".

*** = Quarter 4**

Voluntary Actions: Examples

- In May 2015, Montana Compounding Pharmacy and Wellness Center ceased operations and recalled all sterile products within expiry after FDA investigators identified, during a surveillance inspection, deviations including: the use of non-sterile drinking water dispensed from a top-loaded bottled water dispenser for use in making injectable drug products; the use of non-sterile, non-pharmaceutical grade ingredients in making injectable drug products; and dog beds, dog fences, and dog hairs within the facility, including in close proximity to the compounding room.

- In September 2015, Medistat (an outsourcing facility) ceased sterile operations and recalled all sterile products within expiry after an FDA inspection of the facility revealed a lack of sterility assurance. FDA had received several reports of adverse events potentially associated with drug products compounded by the firm.

Voluntary Actions

- Four outsourcing facilities have recalled compounded products
- Recall events by outsourcing facilities are included on FDA's list of outsourcing facilities

http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm378645.htm

Warning Letters

- Advisory actions – provide notice
- Communicate the Agency's position
- Issued to achieve voluntary and prompt corrective action
- Generally used when there is no history of repeat violations

Warning Letters

- FDA has issued over 60 warning letters since October 2012
- Many of the warning letters describe violations associated with insanitary conditions

Warning Letters

Warning letters to facilities not registered as outsourcing facilities under section 503B may also include other violations of the Federal Food, Drug, and Cosmetic Act, and if the firm does not compound in accordance with the conditions of section 503A, these may include violations of requirements for new drug approval, labeling with adequate directions for use, and current good manufacturing practice

Warning Letters

- Warning letters to facilities registered as outsourcing facilities under section 503B may also include:
  - Violations of current good manufacturing practice (CGMP) requirements (independent of 503B compliance)
  - Failure to meet the conditions of section 503B, such as
    - Failure to include appropriate labeling
    - Failure to submit required product reports

Warning Letters

- Outsourcing facilities received about 20 of the 60 warning letters issued since October 2012
- Several of the outsourcing facilities that received warning letters subsequently deregistered with FDA
- Unapproved new drug and misbranding charges are included in warning letters to outsourcing facilities that fail to meet the conditions of section 503B

Warning Letters: Examples

- Some examples of deviations from adequate sterile practices and conditions cited in recent warning letters include:
  - Mold in unopened vials of purportedly sterile products
  - Production of sterile drugs with exposed skin
  - Failure to use a sporicidal agent to disinfect the ISO 5 area
  - No environmental monitoring during periods of sterile drug production
  - Use of non-sterile cleaning and disinfecting agents in aseptic processing areas

State Referral Letters

- State Referral Letters:
  - Sent to State Board of Pharmacy in the state in which the FDA-inspected compounding pharmacy is located when a
    - Pharmacy apparently compounds drugs in accordance with the provisions of section 503A (e.g., obtains prescriptions for identified individual patients); and
    - Pharmacy has promised to correct deviations, and they are readily correctable
  - FDA has issued approximately 20 state referral letters

Injunctions

- To prevent further production and/or distribution of adulterated, misbranded, and/or unapproved new drug products and to correct the root cause of the violations
- The firm has a history of significant violations and has not made corrections

Injunction Process

- FDA drafts referral letter, complaint, and consent decree and submits to the Department of Justice (DOJ)
- DOJ determines whether to pursue the case
- May issue “sign or sue” letter
- Attempt to negotiate consent decree
- File complaint in court

Compounding Injunction Cases Since 2012

- On June 28, 2013, a federal judge entered a consent decree of permanent injunction against MedPrep Consulting (Tinton Falls, NJ) and the company's president and owner.

- On December 4, 2014, a federal judge entered a consent decree of permanent injunction against Main Street Family Pharmacy (Newborn, TN) and the company's co-owners. In addition, Main Street and one of its co-owners pleaded guilty to a misdemeanor criminal violation of the FD&C Act.

- On March 10, 2015, a federal judge entered a consent decree of permanent injunction against Specialty Compounding (Cedar Park, TX) and the company's co-owners.

- The firms in each case manufactured purportedly sterile injectable drug products that tested positive for bacterial contamination.

Compounding Criminal Cases Since 2012

- On December 16, 2014, a grand jury returned a 131-count criminal indictment in connection with the New England Compounding Center (NECC) and 2012 nationwide fungal meningitis outbreak. The owner and head pharmacist of NECC and its supervisory pharmacist were charged with 25 acts of second-degree murder, among other criminal acts, and 12 others were charged with additional crimes, including FDCA violations.

- On February 20, 2015, the Government unsealed a 37-count indictment charging Med Prep, its president and owner, and its pharmacist-in-charge, with wire fraud and violations of the FDCA for introducing adulterated and misbranded drugs into interstate commerce with the intent to defraud and mislead the FDA and Med Prep's customers.

Inter-governmental Working Meeting on Drug Compounding and DSCSA

U.S. Food and Drug Administration
Silver Spring, Maryland

November 16-17, 2015