Inter-governmental Working Meeting on Drug Compounding and DSCSA

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

November 16-17, 2015

Compounding Regulatory Policy Update

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Accomplishments

- Status of rules, guidances, and MOU
- Pharmacy Compounding Advisory Committee (PCAC)
- Stakeholder listening sessions

Rulemaking in progress

- Working to finalize rule on additions and modifications to the list of drug products that have been withdrawn or removed from the market for reasons of safety or effectiveness (currently codified in 21 CFR 216.24)
  - Proposed rule published July 2, 2014
  - Discussed with PCAC in February, 2015
- Working on new proposed rule to add four drug products to the withdrawn or removed list based on discussions with the PCAC in June, 2015
- Working on 503A bulks list proposed rule

Guidances

- Published two final guidances:
  - Guidance for Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act
  - Adverse Event Reporting for Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act

Guidances, cont'd

- Published two new draft guidances:
  - Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act
  - Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act
  - Comment period closes December 28, 2015

503A Bulk Drug Substances

A licensed pharmacist or licensed physician can compound a drug product under section 503A using bulk drug substances that:

- Comply with the standards of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph, if a monograph exists, and the USP chapter on pharmacy compounding;
- If such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary; or
- If such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, appears on a list developed by the Secretary through regulations issued by the Secretary under subsection (c) of section 503A.

See section 503A(b)(1)(A)(i) of the FD&C Act

503B Bulk Drug Substances

- An outsourcing facility must not compound drug products using a bulk drug substance unless:
  (1) the substance appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need, (see section 503B(a)(2)(A)(i) of the FD&C Act); or
  (2) the drug product compounded from such bulk drug substance appears on the drug shortage list in effect under section 506E of the FD&C Act at the time of compounding, distribution, and dispensing (see section 503B(a)(2)(A)(ii) of the FD&C Act).

Each draft guidance references four lists which were published on the FDA website

- List 1: Bulk drug substances under evaluation;
- List 2: Bulk drug substances that raise safety concerns;
- List 3: Bulk drug substances nominated without adequate support; and
- List 4: Bulk drug substances that may not be used to compound drug products (to be developed).
- 503A and 503B have the same four categories of interim lists but lists include different drugs because of the different criteria, different substances nominated, and different processes for developing the bulks lists under 503A and 503B

Interim Policy – 503A Draft Guidance

- Until the substance has been considered and dealt with in a final rule as being included, or in the preamble of the final rule as not included on the 503A bulks list, FDA does not intend to take action against a compounder under section 503A that is compounding with bulk drug substances on List 1 provided that several conditions are met.
- List 1 includes substances nominated with sufficient supporting information for FDA to evaluate them and that have not been identified by FDA as a substance that appears to present safety concerns (which are listed on List 2).

Interim Policy – 503B Draft Guidance

- Until FDA publishes its final determination in the Federal Register that a bulk drug substance may or may not be used in compounding under section 503B, FDA does not intend to take action against an outsourcing facility that is compounding a drug product using a bulk drug substance that appears on List 1.
- List 1 includes substances nominated with sufficient supporting information for FDA to evaluate them and that have not been identified by FDA as a substance that appears to present safety concerns (which are listed on List 2).

FDA Established New Dockets for Nominations

- FDA established two public dockets (one for 503A and one for 503B) where
  - substances can be re-nominated with sufficient supporting information or
  - nominations can be submitted of bulk drug substances that were not previously nominated
- FDA will consider re-nominated and new substances after completing the reviews of the substances that have already been determined to have been supported with sufficient information to evaluate them.

Other Guidances in Process:

- Working to complete several final guidances after revising in response to comments:
  - Current Good Manufacturing Practice-Interim Guidance for Human Drug Compounding Outsourcing Facilities Under the Federal Food, Drug, and Cosmetic Act
    - Interim guidance until CGMP rules adopted
  - Electronic Product Reporting for Human Drug Compounding Outsourcing Facilities
  - Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities
  - Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application

Pharmacy Compounding Advisory Committee

- Three meetings this year (Feb, June, Oct)
- Discussed 29 candidates for the withdrawn/removed list and two modifications to current list
- Discussed criteria for the 503A bulks list
- Discussed 19 substances nominated for inclusion on the 503A bulks list
- Discussed criteria for the difficult to compound list

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