



Pharmacy Compounding Legislation and Implementation

50 State Meeting

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Summary of Presentation

- Historical context
- Overview of 503A and 503B
- Implementation Efforts

Compounding by Outsourcers Has Increased

- Hospitals and health care systems compounded drugs in house for own use
- Over the past 15-20 years, hospitals and health care systems have increasingly begun to purchase compounded drugs from outsourcers
- For sterile drugs, compounding batches for multiple facilities, with long BUDs and distributing over long distances increase risks

Section 503A

- 503A describes the conditions under which certain compounded human drug products are entitled to exemptions from three sections of the FDCA requiring:
 - FDA approval prior to marketing (section 505)
 - Compliance with current good manufacturing practice (CGMP) (section 501(a)(2)(B)); and
 - Labeling with adequate directions for use (section 502(f)(1))
- Pharmacies that qualify for the exemptions are primarily regulated by the states, although some Federal requirements still apply (e.g., no insanitary conditions)

Section 503A Requirements

- Compounding performed by licensed pharmacist in a licensed pharmacy or Federal facility, or by licensed physician
- Prescription for an identified individual patient; anticipatory compounding in limited quantities before receipt of prescription

Requirements for Bulk Drug Substances Used to Compound Under 503A

- Bulk drug substances (i.e., active ingredients) used to compound must be:
 - Components of FDA-approved drugs;
 - The subject of a USP monograph; or
 - Appear on a list of bulk drugs developed by FDA of bulk drug substances acceptable for compounding
- In addition:
 - Bulk must be made at an FDA-registered facility;
 - Be accompanied by a Certificate of Analysis (COA)

Other Section 503A Requirements

- Cannot compound drugs that are on an FDA list of drugs that have been withdrawn or removed from the market because they have been found to be unsafe or not effective
- Cannot compound drugs that are on an FDA list of drugs that present demonstrable difficulties for compounding

Other Section 503A Requirements

- Cannot compound regularly or in inordinate amounts what are essentially copies of commercially available products
- Compounder cannot distribute or cause to be distributed interstate more than 5% of the total prescription orders dispensed or distributed by that pharmacy or physician unless they are located in a state that has entered into a Memorandum of Understanding that provides for appropriate investigation of complaints related to drugs distributed outside the state and addresses the distribution of inordinate amounts of compounded drug products interstate

Compounding Quality Act

- Removes certain provisions from section 503A related to solicitation of prescriptions and advertising and promotion that were found to be unconstitutional by the U.S. Supreme Court in 2002.
- Clarifies that section 503A is applicable to compounders nationwide
- Adds new section 503B: “Outsourcing Facilities”

A Registered Outsourcing Facility

- Must comply with CGMP requirements;
- Will be inspected by FDA according to a risk-based schedule; and
- Must meet certain other conditions to be exempt from the new drug approval requirements and the requirements for adequate directions for use.

Outsourcing Facility Conditions

- Registered outsourcing facilities must:
 - Report to FDA twice a year information about the products they compounded during previous six months
 - Report adverse events
 - Label their products with certain information

Other Conditions Similar To Those In 503A

- Outsourcing facilities cannot compound drug products that appear on FDA lists
 - of drug products that have been withdrawn or removed from the market because the drug products or their components have been found to be unsafe or not effective,
 - of drug products that present demonstrable difficulties for compounding,

Other Conditions for Outsourcing Facilities

- The outsourcing facility cannot compound a drug that is essentially a copy of one or more FDA-approved drugs.
- The outsourcing facility cannot compound a drug that is subject to a REMS with elements to assure safe use or from a bulk drug substance that is a component of such drug unless the outsourcing facility demonstrates it will use controls comparable to the REMS

Outsourcing Facility Use of Bulk Drug Substances

- An outsourcing facility may not compound from bulk drug substances –
 - unless the drug it is compounding appears on the FDA drug shortage list, or
 - the bulk drug substance appears on an FDA list identifying the bulk drug substances for which there is a clinical need.

Bulk Drug Substances Used by Outsourcing Facilities

- Bulk drug substances and other ingredients used to compound must comply with USP monographs, if they exist, and bulk drug substances used by outsourcing facilities must come from facilities that have registered with FDA, and be accompanied by a certificate of analysis.

Outsourcing Facility Fees

- An outsourcing facility will not be considered registered until it has paid the applicable annual establishment fee.
- An outsourcing facility may register without paying a fee until September 30, 2014, however, because fees are not required until October 1, 2014.
- Establishment fee is \$15,000 adjusted for inflation and small business reductions
- Statute also authorized reinspection fees

By Definition A Registered Outsourcing Facility

- Is engaged in the compounding of STERILE drugs
- Has elected to register as an outsourcing facility
- Complies with all of the conditions in section 503B
- NOT required to be a licensed pharmacy, but compounding must be by or under the direct supervision of a licensed pharmacist
- May or may not obtain prescriptions for identified individual patients

Compounders That Do Not Register as Outsourcing Facilities

- A compounder that:
 - does not register as an outsourcing facility and comply with the conditions under section 503B, and
 - compounds drugs that do not qualify for the exemptions under section 503A
- Is subject to all of the requirements in the FDCA applicable to conventional manufacturers.

The New Law Leaves Some Issues Unresolved

- Compounders may seek to hide out in the traditional compounding category and escape detection
- The lack of clarity in section 503A over whether a state or FDA has primary responsibility over a particular pharmacy remains

FDA Moving Swiftly to Implement the New Law

- On Dec. 2, FDA issued three draft guidances:
 - Guidance for compounders on how to register under section 503B as an outsourcing facility
 - Guidance for outsourcing facilities on how to report to FDA required information about the products they make
 - Guidance on the sections of 503A that require rulemaking or other FDA action to implement (bulks list, difficult to compound list, MOU)

FDA Solicited Nominations for Lists

- FDA published 3 Federal Register Notices soliciting nominations for:
 - The list of drugs that cannot be compounded under sections 503A and 503B because they are difficult to compound
 - The list of bulk drug substances that may be used to compound under section 503A
 - The list of bulk drug substances that may be used to compound under section 503B (based on clinical need)

Many Issues Remain In 503A and 503B

- Many parts of section 503A require implementation through rulemaking and/or consultation with an Advisory Committee
- FDA working on additional implementing guidance and regulations

FDA Providing Information About Registered Outsourcing Facilities

- We published a list and information about the status of the facilities including: date of last inspection; 483, if any; other action, if any (such as a warning letter); and whether they compound sterile drugs from bulk drug substances
- We also posted Q and A about what it does and does not mean to register as an outsourcing facility
- See:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm378645.htm>

FDA Encouraging Registration

- FDA sent letters to 6,000+ hospitals and health systems encouraging them to purchase compounded drugs from registered outsourcing facilities, if they have a medical need for compounded drugs
 - Letters emphasized why compounded drugs, including those made by an outsourcing facility, should only be used if there is a medical need that can't be met by an FDA-approved drug
- FDA also sent letters to governors, Boards of Health and Boards of Pharmacy encouraging them to consider ways to encourage compounders to register as outsourcing facilities

FDA Working With You

- State partners participated in many recent inspections of compounders; some were initiated at a state's request
- December, 2012, FDA convened a 50 State meeting
- FDA holding this meeting to discuss plans for implementing the law and get input from you on how best to partner to improve oversight of the compounding industry

FDA Working With USP To Improve USP Chapter 797

- FDA participating in the USP Expert Working Group and Expert Panel on the revisions to USP Chapter 797 standards that apply to sterile compounding by compounders not registered as outsourcing facilities

Oversight of Outsourcing Facilities

- FDA has begun inspecting outsourcing facilities, focusing on those that have not been inspected by FDA before they registered
 - Looking at processes for producing sterile drugs, and
 - Compliance with certain other conditions under section 503B such as the specified labeling requirements

Establishing CGMPs for Outsourcing Facilities

- FDA intends to issue draft interim CGMP guidance for outsourcing facilities and ultimately, final requirements in regulations
- FDA intends to post any inspectional observations for outsourcing facilities

Compounders Not Registered as Outsourcing Facilities

- FDA has been conducting inspections of compounding pharmacies for cause (in response to serious adverse event reports, reports of quality problems, and state requests)
- FDA has also been conducting proactive inspections to identify pharmacies with deficient sterile practices
- FDA will continue these efforts as available resources permit