The Drug Quality & Security Act: What’s Next for Sterile Compounding and Outsourcing

Christopher J. Topoleski, B.A.
Director, Federal Regulatory Affairs
ASHP

Summary of Presentation

- Background
- Overview of the Drug Quality and Security Act (DQSA)
- FDA Implementation of DQSA

Context for the Drug Quality and Security Act

- Hospitals and health care systems historically 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
- NECC tragedy highlighted dangers of unregulated, large scale compounding

Section 503A: Food, Drug, and Cosmetic Act

- Signed into law November 21, 1997
- Section 503A describes the conditions under which certain compounded human drug products are entitled to exemptions from three sections of the FD&C Act 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))
- States primarily regulate pharmacies that qualify for the exemptions

Drug Quality and Security Act (DQSA)

- Signed into law on November 27, 2013
- 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”

Section 503A Requirements

- Compounding performed by licensed pharmacist in a licensed pharmacy or Federal facility, or by licensed physician
- Patient-specific compounding
- Anticipatory compounding permitted in limited quantities
- Requirements for bulk drug substances used to compound
Section 503A Requirements (continued)
- May not compound drugs on an FDA list of drugs that have been withdrawn or removed from the market because they have been found to be unsafe or not effective
- May not compound drugs that are deemed by the FDA to be “demonstrably difficult” to compound

Section 503A Requirements (continued)
- Cannot compound regularly or in inordinate amounts what are essentially copies of commercially available products
- Compounder cannot distribute interstate more than 5% of the total prescription orders dispensed or distributed by that pharmacy absent an MOU between their state and the FDA

A 503B Outsourcing Facility
- Has voluntarily registered with the FDA
- Compounds sterile drugs
- Is not required to obtain a patient-specific prescription prior to compounding
- May remain a licensed pharmacy
- If not a licensed pharmacy, all compounding must be done under the supervision of a licensed pharmacist subject to state licensing laws

A 503B Outsourcing Facility (continued)
- Must comply with CGMP requirements and subject to FDA inspections
- Must report which products they are compounding and any adverse events
- Must pay establishment, annual fees, and reinspection fee if applicable

FDA Implementation of DQSA
  - Proposed Rules
    - List of drugs/drug categories that are demonstrably difficult to compound
    - List of bulk ingredients for compounding (503A)
    - List of bulk ingredients for compounding (503B)
  - Draft Guidance
    - Registering as an outsourcing facility
    - Registering products compounded
    - Withdrawal of 1998 and 2002 CPGs, release of new guidance for traditional compounding under 503A

ASHP Comments to FDA
- ASHP submitted comments on February 3, 2015 on the 503A guidance
  - Office use
  - Compounding of shortage drugs
  - USP chapters
  - Definitions
- ASHP plans to submit comment on the proposed bulk drug and drugs that demonstrate demonstrable difficulties to compound
Future FDA Actions

- Many parts of section 503A require implementation through rulemaking and/or consultation with the Pharmacy Compounding Advisory Committee
  - Establishment of committee to make recommendations to FDA on “demonstrably difficult” list and bulk substances
  - CGMP requirements in 2014
    - Interim draft guidance
    - Final regulations
- FDA to hold 50 State meeting in Q1 of 2014
  - Held initial meeting in December 2012
  - Goal of 2014 meeting is to discuss coordination in light of passage of DQSA

Oversight of Outsourcing Facilities

- As of this February 14, 2014 there were 27 facilities registered under Section 503B representing 24 distinct outsourcing vendors
- FDA will begin inspecting outsourcing facilities, first focusing on those without prior FDA inspection
  - Looking at processes for producing sterile drugs, and
  - Compliance with certain other conditions under section 503B such as the specified labeling requirements

Additional FDA Actions on Oversight of Outsourcing Facilities

- Identification of outsourcers not registered with the FDA under section 503B (risk based)
- Investigation of those not registered as 503B to determine compliance with 503A (compliance with FD&C Act)

New Compounding Regulations: Implications for practice

Bona Benjamin, B.S.Pharm.
Director, Medication-Use Quality Improvement
ASHP

Discussion Topics

As a result of legislation and regulations……
- What is different
- What hasn't changed
- Implications for practice

503A Pharmacy Compounding

Implications for practice:
- Applies to all pharmacies that compound
- Requires individual Rx, professional relationship, limits to advance compounding
- Office use
503A Restrictions
- Bulk substances
  - Not withdrawn because unsafe or not effective
  - Cannot copy “regularly or in inordinate amounts” commercially available drugs (unless clinically indicated for an individual patient)
  - Not “demonstrably difficult”

Implications for practice

Restrictions on what can be compounded
- Copies
  - depends on definition of “commercially available.”
  - No mention of shortage list
- “Demonstrably difficult”
  - Depends on list – long-acting oral drugs, inhalers, lyophilized drugs

Pharmacy Compounding – other

Proposed guidance: Must be in accordance with USP chapters on compounding
- USP 797, 795

USP Standards - Implications for Hospitals
- Is full <797>, <795> compliance feasible?
- Readiness for advanced compounding; extended BUD?
- Resources
  - Trained staff
  - Quality control
  - Equipment
  - Environmental controls
  - Containers and closures
  - Documentation and records

503A “Hot issues” – yet to be resolved
- Interstate distribution
- Office use
- Definitions
- Prohibited substances and formulations
- Who is accountable for dispensing?
Can sterile compounding still be outsourced to compounding pharmacies?

Yes, if......
- Outsourcing drugs admixed per product labeling OR
- Compounding follows USP AND
- In receipt of a prescription for each patient, AND
- Not on any of FDA’s prohibited lists and on its approved ingredients list, AND
- State has MOU or distribution doesn’t exceed 5%

503B Outsourcing Facility
- Does not have to be a pharmacy
- Prescriptions optional
- No limit on interstate distribution
- Can compound copies if in shortage
- Can compound “demonstrably difficult” if “difficulties” resolved

503B Outsourcing Facility
- New significance for “FDA-registered” status
- Recognizes essential role for vendors of sterile compounding services
- Creates a regulatory framework
- Provides FDA assurance of quality

Applies to pharmacies and outsourcers
- Compounded preparations not be resold
- Rxs must be valid (no falsification)
- Advertising or promotion may not be false or misleading

In Summary
- All pharmacies that compound fall under 503A
- Outsourcing facilities are allowed broader scope but are more tightly regulated under 503B
- Whether compounding in-house or outsourcing, health-systems need to understand the implication of 503A and 503B

Questions