Current Topics in Sterile Compounding: The Drug Quality and Security Act

EDUCATIONAL OBJECTIVES
Upon completion of this activity, participants will be better able to:
1. Discuss the issues that led to the introduction and passage of the Drug Quality and Security Act (DQSA);
2. List the provisions for compounding and outsourcing facilities stipulated in the DQSA;
3. Compare and contrast the definitions of compounding and outsourcing facilities provided in Sections 503A and 503B of the Federal Food, Drug & Cosmetic Act (FDCA); and
4. Describe the process for becoming an outsourcing facility under Section 503B of the FDCA.

Post-Test/Rationale

1. Which of the following is TRUE regarding the Drug Quality and Security Act (DQSA)?
   A. The DQSA created Section 503A of the Food, Drug, and Cosmetic Act (FDCA)
   B. The DQSA amended Section 503B of the FDCA, which was originally created by the Food and Drug Administration Modernization Act (FDAMA) in 1997
   C. The DQSA removed the advertising clauses of FDAMA***
   D. The DQSA was enacted in response to deaths related to inappropriately compounded sulfanilamide elixir

Correct Answer: C
The DQSA was enacted primarily in response to an outbreak of fungal meningitis among patients who received products compounded at the New England Compounding Center. Title I of the DQSA amends Section 503A and clarifies federal authority of compounding and defines “traditional compounders.” Title I also creates Section 503B of the FDCA, which addresses outsourcing facilities. The Food and Drug Administration Modernization Act (FDAMA) of 1997 created Section 503A of the FDCA and distinguished manufacturing from compounding activities that could be completed by pharmacies. The DQSA removes advertising and promotion clauses of the original Section 503A that were rendered unconstitutional.

2. The DQSA addresses which of the following practices?
   A. The manufacturing of sterile drugs for veterinary use
   B. The dispensing of non-sterile drugs for human use
   C. The compounding of sterile drugs for human use***
   D. The prescribing of drugs for investigational use

Correct Answer: C
The DQSA provides guidance for the compounding of sterile and non-sterile drugs; it only applies to drugs for human use and not drugs for veterinary use; veterinary products are regulated under the Animal Medicinal Drug Use Clarification Act of 1994. Investigational drugs are also excluded from the DQSA.
3. Which of the following Titles of the DQSA is correctly matched to its intent or purpose?

A. Title I: defines traditional compounding pharmacies and outsourcing facilities***
B. Title I: increases the amount of interstate commerce in which a pharmacy can participate
C. Title II: establishes a ‘track and trace’ system of drug distribution over the next 10 years to increase prosecution related to counterfeit medicines
D. Title II: provides standards for non-sterile compounding

Correct Answer: A

Title I is also known as the Compounding Quality Act, which clarifies federal authority of compounding, defines “traditional compounders” under Section 503A of the FDCA, and creates Section 503B of the FDCA, which addresses outsourcing facilities. Title II is the Drug Supply Chain Security Act, which defines terms in the drug supply chains in the United States under Section 581 of the FDCA and establishes a ‘track-and-trace’ system of prescription drugs under Section 582 of the FDCA in an effort to reduce the availability of counterfeit drugs.

4. Which of the following is required for pharmacies who intend to engage in compounding, as defined in Section 503A of the DQSA?

A. The final compounded product must be approved by the Pharmacy Compounding Advisory Committee
B. The ingredients in the compounded product must have monographs available that confirm strength, purity, and quality***
C. The product must be compounded in multiple dosage forms
D. The compounded product must be identical to a product currently on the market

Correct Answer: B

All ingredients used for compounding should comply with standards for strength, purity, and quality established by USP or National Formulary (NF) monographs or be a component of an FDA-approved human drug product. The PCAC only provides advice to FDA and recommends drugs and substances to be included on compounding lists that are supplied to pharmacies, including "Do Not Compound," "Demonstrably Difficult," and "Approved Bulk Drug Substances" lists. Products that are essentially copies of commercially available drug products cannot be compounded under Section 503A.

5. The PCAC has recommended that which of the following drugs be included on the “Do Not Compound” list?

A. Ophthalmic solutions of bromfenac sodium
B. Acetaminophen with less than or equal to 325 mg per dosage unit
C. Rosuvastatin
D. Propoxyphene***

Correct Answer: D
Several drugs have been recommended for the "Do Not Compound" list on the basis of safety and/or efficacy concerns. The PCAC recommended that some drug products included on the list have modifiers related to dose, route of administration, indication, or patient population. The current “Do Not Compound” list is available in Table 1.

6. The provision that states that no more than 5% of a pharmacy’s products may be distributed or sold out of state applies to which of the following facilities?
   
   A. Traditional compounding pharmacies, as defined under Section 503A, that have entered into a memorandum of understanding with the state
   B. Traditional pharmacies registered under Section 503A that maintain state-specific compounding licenses***
   C. Outsourcing facilities registered under Section 503B that are located within a health system or group of hospitals
   D. Outsourcing facilities registered under Section 503B that have more than 1 geographic location

Correct Answer: B

Section 503A states that, unless the state where the drug is compounded has entered into a memorandum of understanding (MOU) with FDA, a pharmacy’s products that are distributed out-of-state cannot exceed more than 5% of the total prescription orders dispensed by the pharmacy or the compounding physician. This provision applies to all pharmacies governed by Section 503A, regardless of whether additional licenses are required by the respective state. Section 503B does not place limits on the amount of interstate commerce in which a compounding facility can engage.

7. Which of the following activities is considered “compounding” according to the Food and Drug Administration’s definition of “compounding”?
   
   A. A pharmacy reconstituting a powdered antibiotic
   B. A skilled nursing facility repackaging tablets into unit dose packs
   C. A hospital creating a sterile admixture
   D. A physician using bulk substances to create a new medicinal product for an individual patient***

Correct Answer: D

FDA defines compounding as “…a practice in which a licensed pharmacist, a licensed physician, or, in the case of an outsourcing facility, a person under the supervision of a licensed pharmacist, combines, mixes or alters ingredients of a drug to create a medication tailored to the needs of an individual patient.” Any necessary manipulation ordered in the manufacturer’s FDA-approved labeling, such as the reconstitution of a non-sterile powder or the creation of a sterile product admixture, is not considered compounding by this definition. The United States Pharmacopeia (USP) has an expanded definition of compounding that includes any manipulation of bulk
chemicals or a manufactured product, even if it is prepared according to the instructions appearing in the manufacturer’s approved labeling.

8. Which of the following is TRUE of a pharmacy that decides to register as a 503B outsourcing facility?
   A. The pharmacy must maintain a compounding license issued by its state board of pharmacy
   B. The pharmacy must have an established relationship with physicians and patients
   C. The pharmacy is subject to investigation under a risk-based protocol***
   D. The pharmacy can only compound sterile products

Correct Answer: C
FDA will inspect outsourcing facilities under a risk-based schedule, which includes consideration of the facility’s history, recall history, level of risk for drugs compounded, and if compounding from the drug shortage list, regardless of a specific complaint or safety issue having been identified. Outsourcing facilities are not required to maintain any additional registration, such as a pharmacy license. A compounding entity can be a qualified outsourcing facility if it compounds sterile products, but most of these facilities will likely also be involved in non-sterile compounding. Facilities engaged solely in non-sterile compounding do not qualify to register as an outsourcing facility.

9. What are the minimum requirements to be listed on FDA’s website as a 503B outsourcing facility?
   A. Undergo an inspection by FDA to verify compliance with current good manufacturing practices
   B. Register with FDA and pay the appropriate fees***
   C. Employ at least 2 licensed pharmacists and pass a licensing examination administered by the state board of pharmacy
   D. Pay the appropriate fees and submit a list of products intended for compounding to FDA

Correct Answer: B
Outsourcing facilities must register initially and then annually with FDA. Upon initial registration and payment of all applicable fees, an outsourcing facility can be listed on FDA’s Outsourcing Facilities list. They must submit reports that list the drugs that have been compounded by the facility twice a year.

10. Which of the following is TRUE, when considering the similarities and differences between Sections 503A and 503B of the DQSA?
    A. Both sections prohibit compounding for “office use”
    B. Both sections address requirements for sterile compounding***
    C. Both sections define limits for the quantity of drug that can be compounded at 1 time
D. Both sections allow for the compounding of products involved in drug shortages

Correct Answer: B

Section 503A addresses standards for both sterile and non-sterile compounding; Section 503B only applies to sterile compounding. Compounding of products for “office use” is prohibited under 503A but allowed under 503B. Section 503A offers vague limitations on the amount of product that can be compounding, but Section 503B offers no limitations for quantity. Section 503A prohibits the compounding of products that are currently on the market, regardless of whether they are involved in a drug shortage; few prohibitions exist under 503B.