Policy Update

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FDA-State Memorandum of Understanding

Statutory Framework: To qualify for the exemptions in section 503A, a drug product must be compounded in a State:

1. That **has entered into an MOU with FDA which addresses the distribution of inordinate amounts of compounded drug products interstate** and provides for appropriate **investigation** by a State agency **of complaints** relating to compounded drug products distributed outside such State (section 503A(b)(3)(B)(i)); or
2. That has not entered into the MOU with FDA and the licensed pharmacist, licensed pharmacy, or licensed physician **distributes** (or causes to be distributed) **compounded drug products out of the State in which they are compounded in quantities that do not exceed 5 percent of the total** prescription orders dispensed or distributed by such pharmacy or physician (section 503A(b)(3)(B)(ii)).

FDA-State Memorandum of Understanding

Development of the MOU to:

- Address distribution of inordinate amounts of compounded human drug products interstate
- Provide for appropriate investigation by a State agency of complaints relating to compounded human drug products distributed outside such State

Versions:

- 1999 Draft MOU
- 2015 Draft MOU
- 2018 Revised Draft MOU
- 2020 Final MOU (not for implementation)

2020 Final MOU (not for implementation)

Inordinate Amount

$$\frac{A}{B} = X, \text{ where:}$$

A = Number of prescription orders for compounded human drug products that the pharmacy distributed interstate during any calendar year

B = The sum of the number of prescription orders for compounded human drug products (i) that the pharmacy sent out of (or caused to be sent out of) the facility in which the drug products were compounded during that same calendar year; plus (ii) the number of prescription orders for compounded human drug products that were dispensed (e.g., picked up by a patient) at the facility in which they were compounded during that same calendar year

If X is greater than 0.5, it is an inordinate amount and is a threshold for certain information identification and reporting under the MOU.

2020 Final MOU (not for implementation)

Investigate Complaints

- Drug products compounded in a state and distributed outside the state
- Adverse Drug Experiences and Product Quality Issues
- State agencies agree to:
  - Investigate complaints
  - Notify FDA

States that do not enter into MOU

- 5% Limit

2020 Final MOU (not for implementation)

Information Sharing Network

- September 2019: FDA entered a cooperative agreement with NABP to develop an information sharing network for use by State agencies to collect and share information pursuant to the MOU
- Intended to help alleviate the resource burden on States

Compounded Drug Products That Are "Essentially Copies" Under Section 503A

Statutory Framework

- To qualify for the exemptions in section 503A, a drug product may be compounded if a licensed pharmacist or physician –
  - Does not compound **regularly or in inordinate amounts** (as defined by FDA) any drug products that are **essentially copies** of a **commercially available** drug product (section 503A(b)(1)(D))

- For the purposes of (1)(D), the term "essentially a copy of a commercially available product does not include
  - a drug product in which there is a **change**, made for an **identified individual patient**, which **produces** for that patient a **significant difference**, as **determined by the prescribing practitioner**, between the compounded drug and the comparable commercially available drug product (section 503A(b)(2)

Compounded Drug Products That Are "Essentially Copies" Under Section 503A

Final guidance: *Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act*

- Regularly or inordinate amounts
- Essentially a copy
- Commercially available
- Unless:
  - Significant difference between compounded drug and comparable commercially available drug
  - Determined by prescriber
  - Identified individual patient

Compounded Drug Products That Are "Essentially Copies" Under Section 503B

Statutory Framework

- To qualify for the exemptions in section 503B, a compounded drug product may not be **essentially a copy of one or more approved drugs**. (section 503B(a)(5))

- The term "essentially a copy of an approved drug" means -
  - a drug that is **identical or nearly identical to an approved drug**, or a marketed drug not subject to section 503(b) and not subject to approval in an application submitted under section 505, **unless,** in the case of an approved drug, **the drug appears on the drug shortage list in effect under section 506E** at the time of compounding, distribution, and dispensing (section 503B(d)(2)(A)); or
  - A drug, a **component** of which **is a bulk drug substance** that **is a component of an approved drug** or a marketed drug that is not subject to section 503(b) and not subject to approval in an application submitted under 505, **unless** there is a **change that produces** for an individual patient a **clinical difference**, as **determined by** the **prescribing practitioner**, between the compounded drug and the comparable approved drug. (section 503B(d)(2)(B))

Compounded Drug Products That Are "Essentially Copies" Under Section 503B

Final guidance: *Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act*.

- **Identical or Nearly Identical to Approved Drug**
  - Active ingredient(s)
  - Route of administration
  - Strength
  - Dosage form; and
  - Excipients

  Unless on Drug Shortage List
- **Bulk Drug Substance – Prescriber Determination of Clinical Difference**
  - if a component of the compounded drug is a bulk drug substance that is also a component of an approved drug or a covered OTC drug, the compounded drug product is essentially a copy unless there is a prescriber determination that there is a change that produces for an individual patient a clinical difference between the compounded drug and the comparable approved drug.


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