Center of Excellence Hospital and Health System Compounding Under Section 503A of the FD&C Act

September 8, 2022

Tracy Rupp, PharmD, MPH, BCPS

CDER Office of Compounding Quality and Compliance

Briefing Overview

- Background
  - Basics
  - Challenge
  - Section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act) -- Patient Specific Prescriptions
- Hospital and Health System Compounding
  - Draft Guidance (2016): Geographical consideration
    - 1 mile radius
  - **Revised Draft Guidance (2021):** Time based and additional considerations
    - 24 hours

The Basics

Compounded Drugs:

- are not reviewed by FDA for safety, effectiveness, or manufacturing quality before marketing
- can qualify for exemptions from key provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act) if certain conditions are met
- can serve an important role for patients for whom an FDA-approved drug is not appropriate or available

The Challenge

- Ensuring continued access to compounded drugs for patients who need them, while also protecting patients from the risks of contaminated or otherwise harmful products
- **We continue to face the real risk of another major public health emergency caused by poor quality compounded drugs**

Statutory Framework

Drugs compounded under Section 503A (pharmacies, physicians)	Drugs compounded under Section 503B (Outsourcing Facilities)

• Conditions to qualify for exemptions – e.g.:
  • Patient specific prescriptions -- 503A(a)
  • "Compounds the drug product using bulk drug substances…that…" -- 503A(b)(1)(A)
  • "Does not compound regularly or in inordinate amounts … any drug products that are essentially copies of a commercially available drug product" -- 503A(b)(1)(D)
• Not subject to CGMP if conditions are met
• MOU between FDA/States
	• Conditions to qualify for exemptions -- e.g.:
	  • "The drug is compounded in an outsourcing facility that does not compound using bulk drug substances …, unless…" -- 503B(a)(2)
	  • "The drug is not essentially a copy of one or more approved drugs" -- 503B(a)(5)
	  • Prohibition on wholesaling -- 503B(a)(8)
	  • Labeling provisions -- 503B(a)(10)
	• No patient-specific prescriptions required (can produce office stock)
	• Subject to CGMP
	• Requirements for registration, reports of drugs compounded, adverse event reporting -- section 503B(b)

Hospital and Health System Compounding Under Section 503A of the FD&C Act

2016 Draft Guidance

- Proposed policy provided that FDA does not intend to take action if a hospital pharmacy distributes compounded drug products without first receiving a patient-specific prescription or order as long as certain conditions were met, including:
  - Compounded drug products are distributed only to healthcare facilities that are owned and controlled by the same entity that owns and controls the hospital pharmacy and that are **located within a 1-mile radius** of the compounding pharmacy

Hospital and Health System Compounding Under Section 503A of the FD&C Act

2021 Revised Draft Guidance

- Published October 2021
- The policies proposed in the revised draft guidance are based on FDA's current understanding of risks
- The revised draft guidance, when finalized, will:
  - Describe how FDA intends to apply certain provisions of section 503A of the FD&C Act to human drug products compounded by state-licensed pharmacies that are not outsourcing facilities for distribution within a hospital or **health system**:[1]

Prescription requirement

Essentially copies provision

[1] **Health system** means, for purposes of the revised draft guidance, "…an organization, that includes at least one hospital and at least one group of physicians that provides comprehensive care (including primary and specialty care) who are connected with each other and with the hospital through common ownership or joint management" (See *Compendium of U.S. Health Systems,* Agency for Healthcare Research and Quality, 2018. Available at: https://www.ahrq.gov/chsp/data-resources/compendium.html.

Section 503A Conditions: Prescription Requirement

- FDA recognizes that hospital and health systems may sometimes maintain supplies of non-patient-specific compounded drugs, including “sterile” drugs, outside of the pharmacy (e.g., in the emergency department), ready to administer to patients
  - These drug products are generally compounded and sent out of the hospital or health system’s pharmacy before the receipt of a patient-specific prescription, which would not satisfy the prescription requirement in section 503A
- Certain characteristics of hospital and health system pharmacies can differentiate them from other compounding pharmacies, and from conventional manufacturers. These include limited scope of distribution and shared recordkeeping systems and oversight

Section 503A Conditions: Prescription Requirement

- Outsourcing facilities can compound non-patient-specific drug products and are subject to more stringent quality standards
- FDA recognizes that outsourcing facilities may not always be able to meet medical needs for non-patient-specific compounded drug products to be used in hospitals and health systems
- On the other hand, a health system pharmacy that compounds drug products without patient-specific prescriptions for facilities within its health system could function as a large manufacturing operation without the standards that normally apply to conventional manufacturers to help ensure drug quality, safety, and effectiveness, and without the protections afforded by the prescription requirement in section 503A of the FD&C Act

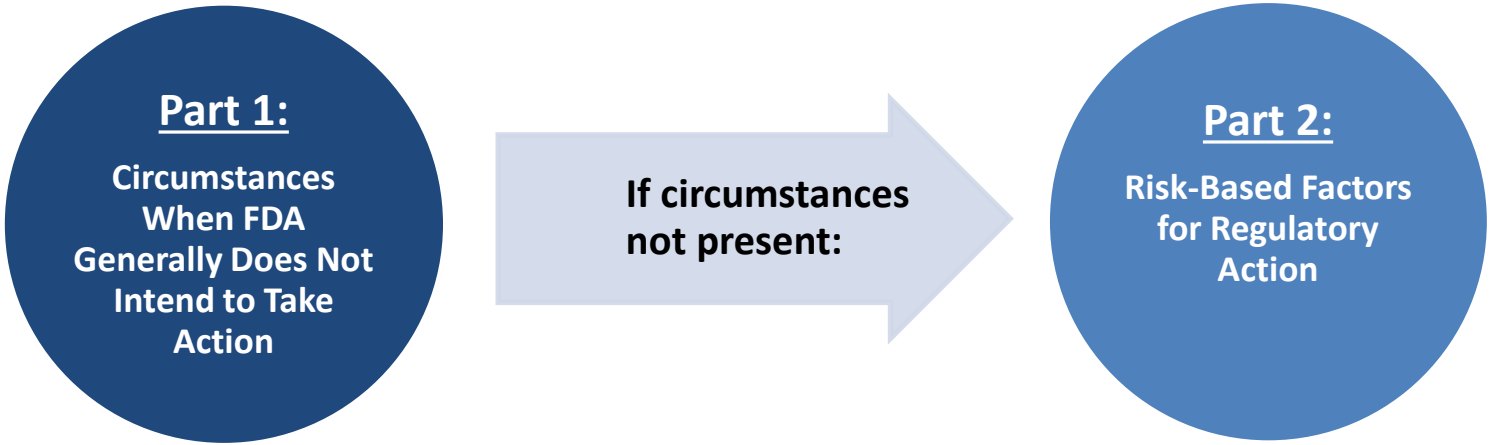
Revised Draft Guidance: Overview

In considering action with respect to the prescription requirement in section 503A of the FD&C Act, FDA intends to proceed on a case-by-case basis, focusing on factors that include:

- Practices that pose the greatest risks to public health
- Practices that threaten the integrity of the drug approval system on which patients depend to protect drug quality
- The important distinction between compounding by outsourcing facilities and hospital and health system pharmacies that are not outsourcing facilities

Revised Draft Guidance: Prescription Requirement Policy

2-Part Compliance Policy



Revised Draft Guidance: Prescription Requirement Policy

Part 1: **The Circumstances Under Which FDA Generally Does Not Intend To Take Action**	1. The compounded drug products are administered only to patients within the hospital or health system;
	2. The compounded drug products are used or discarded within 24 hours of transfer out of the pharmacy; and
	3. The drug products are compounded in accordance with all other applicable requirements of the FD&C Act and FDA regulations (e.g., the drug products are not compounded under insanitary conditions (section 501(a)(2)(A) or misbranded (e.g., section 502(g)).

Revised Draft Guidance: Prescription Requirement Policy

Part 2: **Risk-Based Factors for Regulatory Action**	1. Evidence of poor compounding practices or lack of sterility assurance;
	2. Non-patient-specific compounded drug products not for emergency uses;
	3. Routine, large amounts of non-patient-specific compounded drug products;
	4. Routine interstate distribution of large amounts of non-patient-specific compounded drug products; and
	5. No procedures to obtain non-patient-specific compounded drug products from an outsourcing facility.

Essentially a Copy: Statutory Framework

- Another condition of section 503A of the FD&C Act, is that the drug product must be compounded by a licensed pharmacist or a licensed physician that:
  - "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 further states that:
  - "the term 'essentially a copy of a commercially available drug 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."

Revised Draft Guidance: Essentially a Copy Policy

- In general, FDA intends to apply the policies described in the guidance concerning the "essentially a copy" provision under section 503A of the FD&C Act, *Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act* (January 2018), to drug products compounded by hospital and health system pharmacies that are not outsourcing facilities
- However, the Agency's current thinking is that certain compliance policies described in the 503A copies guidance regarding the documentation of a prescriber's determination of significant difference are appropriately modified when drug products are compounded by hospital and health system pharmacies that are not outsourcing facilities

Hospital and Health System Compounding Under Section 503A of the FD&C Act

Revised Draft Guidance: Essentially a Copy Policy

FDA generally does not intend to take action against a hospital or health system pharmacy that is not an outsourcing facility for compounding a drug product regularly or in inordinate amounts that is essentially a copy of a commercially available drug product if:

- The compounded drug product is administered only to patients within the hospital or health system
- The pharmacy obtains from the prescriber a statement that:
  - specifies a change between the compounded drug product and the commercially available drug product;
  - indicates that the compounded drug product will be administered only to patients for whom the change produces a significant difference from the commercially available drug product; and
  - describes the intended patient population for the compounded drug product;
- A statement is on file for each prescriber that covers each drug product that is compounded; and
- The statement is maintained in the hospital or health system pharmacy to address routine orders for patients for whom the change produces a significant difference.

Useful Links

- Regulatory Policy Information (Guidances, Federal Register notices, Rulemaking)
- FD&C Act Provisions that Apply to Human Drug Compounding
- Compounding Quality Center of Excellence

Questions


FDA
U.S. FOOD & DRUG
ADMINISTRATION