# Pharmacy Compounding Under FDAMA

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# Topics

- General compounding requirements - physician, patient, pharmacist triad
- Bulk drug requirements
- Inactive ingredients
- Lists of drugs that may not be compounded
- Memorandum of Understanding

# New Section 503A

Added to FD&C Act by FDAMA Section 127

- Provides exemption from sections 505, 501(a)(2)(B), and 502(f)(1) for pharmacy compounding that meets certain requirements specified in the statute

# Basic Requirements

- Drug product must be compounded:
  - For an identified individual patient
  - Based on unsolicited receipt of a valid prescription order, or a notation, approved by the prescribing practitioner, that a compounded product is necessary for the identified patient
  - By a licensed pharmacist in a State licensed pharmacy, or by a physician

# Basic Requirements

- Drug products may be compounded in limited quantities before receipt of prescription if
  - 1) History of receiving such orders and
  - 2) Established relationship between pharmacist or physician and individual patient or physician who will write order

# Requirements for Bulk Drugs

- Bulk drug substances used in compounding must be:
  - In compliance with applicable USP/NF monograph, if one exists, and
  - USP chapter on pharmacy compounding OR

# Requirements for Bulk Drugs

- If no monograph, must be a component of an FDA approved drug, OR
- Must appear on a list of bulk drug substances developed by FDA

# List of Bulk Drug Substances Acceptable for Pharmacy Compounding

- Nominations were solicited by FR in April, 1998
- Nominations evaluated and presented to Advisory Committee
- Proposed rule published January 7, 1999 (64 FR 996)
- Proposed to put 20 substances on list; 10 still under review
- Comment period closed March 23, 1999; 193 comments received; most on the aminopyridines
- After evaluating comments, FDA will prepare final rule

# Criteria for Inclusion on Bulks List

- Chemical characterization of the substance
- Safety of the substance
- Historical use of the substance in pharmacy compounding
- Available evidence of effectiveness or lack of effectiveness, if such evidence exists

# Other Bulk Drug Requirements

- Must be manufactured at a registered establishment
- Must be accompanied by a valid certificate of analysis

# Inactive Ingredients

- Other ingredients must comply with applicable USP/NF monographs, if they exist, and the USP chapter on pharmacy compounding

# Products Withdrawn Because Unsafe or Ineffective

- May not compound:
  - Drug products that appear on a list of products that have been withdrawn or removed from the market because found unsafe or ineffective

# List of Drugs Withdrawn or Removed from the Market for Safety/Efficacy

- Proposed rule - October 8, 1998
- 60 drugs proposed for inclusion on list based on safety
- Comment period closed November 23, 1998; few comments
- Final rule - March 8, 1999; 59 drugs included on list
- FDA will update list periodically if other drugs removed for safety

# Commercially Available Drug Products

- May not compound:
  - Regularly or in inordinate amounts, drug products that are essentially copies of commercially available drug products

# Difficult to Compound Drug Products

- May not compound:
  - Drug products identified by regulation as presenting demonstrable difficulties for compounding that reasonably demonstrate an adverse effect on safety or effectiveness

# Advertising and Promotion

- The compounding pharmacy, pharmacist or physician may not advertise or promote the compounding of any particular drug, class of drug, or type of drug, although they may advertise the compounding service

# Interstate Shipment of Compounded Drug Products

- Interstate distribution of compounded products may not exceed 5% of total Rx orders dispensed unless compounding is in a State that has entered into a Memorandum of Understanding

# MOU Provisions

- MOU is to address the distribution of inordinate amounts of compounded drug products interstate and

- Provide for appropriate investigation by a State agency of complaints related to compounded drug products distributed out of state

# Definition of Inordinate Amounts

- Number of compounded Rx dispensed or distributed interstate annually by pharmacy ≥ 20% of total number of Rx dispensed or distributed by the pharmacy

- Number of compounded Rx dispensed or distributed annually is ≤ 20% but Rx for one product distributed interstate is ≥ 5% of total number of Rx dispensed or distributed

# Complaint Investigations

- Types of complaints that should be investigated:
  - Reports of serious adverse drug experiences
  - Alleged violations of FD&C Act including compounding that does not qualify for the exemptions in section 503A

# Complaint Investigations

- States have primary responsibility for collecting data and investigating complaints about compounded products

- States agree to investigate complaints about compounded products shipped interstate in accordance with applicable state statutes, regulations, and procedures

# Complaint Investigations

- States to take regulatory action in accordance with State statutes, regulations, and admin procedures
- Maintain records for at least three years
- Meet and share information periodically with FDA about complaints and investigations

# Enforcement Guidance

- November 23, 1998, Notice of Availability of Guidance Document published (63 FR 64723)
- Recognizes the need for enforcement policy during transition to full implementation
- E.g., FDA won't take action against a pharmacist who ships interstate compounded products that represent more than 5% of his or her total prescriptions until a standard MOU has been issued and States have had an opportunity to enter into an agreement with FDA
- Similar provisions for other rules and documents under development

# TASKS SUMMARY

- Develop a list of bulk drug substances acceptable for pharmacy compounding
- Develop list of drugs that may not be compounded because withdrawn for safety/efficacy
- Identify drugs that may not be compounded because demonstrably difficult to compound
- Develop standard MOU with States
- Develop general regulations implementing statute