Memorandum of Understanding With the States Under Section 503A

Jane A. Axelrad
Associate Director for Policy
Center for Drug Evaluation and Research

March 20, 2014

Purpose of MOU Provision

- This is one of several provisions of section 503A designed to distinguish between traditional compounding and conventional manufacturing
- Derived from FDA's 1992 Compliance Policy Guide that listed 9 factors to be considered in deciding whether to take action against a pharmacy for activities normally associated with a manufacturer
- One factor was: "Distributing inordinate amounts of compounded products out of state."

Statutory Provision

- Unless the drug product is compounded in a state that has entered into an MOU, a compounder cannot
  - distribute or cause to be distributed compounded drug products outside of the state in which they are compounded in quantities that exceed 5% of the total prescription orders dispensed or distributed by that pharmacy or physician

MOU Requirements

- The MOU must:
  - address “the distribution of inordinate amounts of compounded drug products interstate”; and
  - provide “for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State”

Standard MOU

- The statute does not contemplate 50 individual MOUs
- FDA directed to develop a standard MOU in consultation with NABP

MOU History – 12/23/98 Draft

- In 1999, after consultation with NABP, FDA published a draft standard MOU for comment. Draft MOU provisions:
  - State agreed to investigate complaints of compounded drugs shipped interstate
  - Complaints included reports of serious AEs, alleged violations of the FDCA including compounding that does not qualify for the exemptions in section 503A and compounding of a drug product that is adulterated or misbranded

12/23/98 Draft, cont'd

- Encouraged cooperation with the state into which the drug was shipped and referrals between states, and specified actions to be taken based on findings from investigations
- Asked states to maintain records of complaints and investigations for 3 years
- Disputes between two states could be referred to FDA district offices

12/23/98 Draft - Inordinate Amounts

- Defined “inordinate” in terms of both total Rx and individual products:
  - Number of compounded prescriptions dispensed or distributed interstate annually by a pharmacy or physician is equal to or greater than 20% of the total number of prescriptions dispensed or distributed (including both intrastate and interstate) by such pharmacy or physician; OR
  - The total number of prescriptions so dispensed or distributed was less than 20% but the total amount for one or more individual compounded drug products constituted more than 5% of the total number of Rx’s dispensed or distributed

12/23/98 Draft - Inordinate Amounts

- Distribution to patients interstate but within 50 miles of the compounding pharmacy was excluded from the calculation
- Compounding in response to an emergency was also excluded

Issues for Discussion

- How should FDA define “inordinate amounts” in the MOU? Options include:
  - Percentage
  - Range
  - Absolute amount
  - No amount
  - Per product or total or both
- How can it be made implementable by states and FDA?
- Should it take into account contiguous states? If so, how?

Issues for Discussion, cont'd

- What should the MOU say about the handling of complaints?
  - What complaints should the MOU address? Options:
    - Related to compounded products shipped interstate or all complaints?
    - Limit to complaints related to adverse events (AEs)? Or include quality problems (e.g, contamination, potency) that haven't yet led to AEs? Other types of complaints?

Issues for Discussion, cont'd

- What should the MOU say about what constitutes "appropriate investigation by a State agency of complaints"?
- Should the MOU require the state to notify FDA about complaints? If so, when?
- Should the MOU specify the type of coordination and communication between FDA and states to ensure investigations are appropriate?