Update on 503A Memorandum of Understanding

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Statutory Basis for MOU

- Section 503A: 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

Statutory Basis for MOU (cont'd)

- 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"
- FDA directed to develop standard MOU in consultation with NABP

MOU History

- 1999 - FDA published a draft standard MOU for comment
- FDA received over 6,000 comments on the draft
- Because of the Supreme Court decision in 2002, MOU was never finalized
- When DQSA enacted, FDA began again to implement this condition of 503A
- Interstate distribution conditions do not apply to 503B outsourcing facilities

Why is interstate distribution a concern?

- State-licensed pharmacies primarily overseen by states
- Congress did not intend for compounders operating under the exemptions in section 503A to grow into conventional manufacturing operations making unapproved drugs and operating a substantial portion of their business interstate
- If a substantial proportion of a compounder's drugs are distributed outside of a State's borders, adequate regulation of those drugs can pose logistical, regulatory, and financial challenges to State regulators; can be difficult to investigate and address multi-state outbreaks
- If a poor performing pharmacy locates in a lax state or a state with insufficient resources, puts patients in other states at risk

Provisions of Draft Standard MOU

- With regard to investigation of complaints, states that sign MOU would agree to:
  - Investigate complaints about compounded drugs made in the state and distributed outside state (previous MOU said all complaints, not just interstate);
  - Complaints to be investigated include adverse drug experiences and product quality issues that, if left uncorrected, could lead to potential public health risks or safety concerns
  - Details of investigation left to the states

Provisions of Draft Standard MOU (cont'd 2)

- State would agree to:
  - Take action to make sure compounder determines root cause of the problem and addresses it
  - Notify FDA within 72 hours of complaint if involves potential public health risk or immediate safety concern,
  - Provide FDA with an initial assessment of the validity of the complaint, and actions taken or planned to address the complaint, and certain other information about the complaint

Provisions of Draft Standard MOU (cont'd 4)

Inordinate amount: if number of units of compounded human drug products distributed interstate during any calendar MONTH is $\geq$ 30% of the number of units of compounded and non-compounded drug products distributed or dispensed both intrastate and interstate by pharmacy during that calendar month

Provisions of Draft Standard MOU (cont'd 5)

- FDA does not intend to include in the calculation of inordinate amounts those prescriptions dispensed to a patient or patient's agent where the patient or patient's agent carries the drug across state lines after it has been dispensed at the facility in which it is compounded
- FDA did not provide for an exception for drugs distributed within 50 mile radius to contiguous states because it included higher percentage for inordinate amounts and clarified that carrying across state lines was excluded from the calculation

Provisions of Draft Standard MOU (cont'd 3)

- With regard to "inordinate amounts" of drugs shipped interstate, states that sign MOU would agree to:
  - Review records during inspections of compounding pharmacies to determine whether they are distributing inordinate amounts of compounded drug interstate
  - Notify FDA if they identify an entity who is distributing inordinate amounts interstate, and provide information about the entity, the evidence of interstate shipment of inordinate amounts, and a description of any action taken to address the distribution
  - Take action regarding that entity

Comments on the Draft Standard MOU

- Over 3,000 comments submitted
- Significant comments included:
  - Definition of inordinate amounts will eliminate access to needed drugs; should not include drugs dispensed according to a prescription
- 15 State BOPs commented. Issues included:
  - Burden on the states regarding handling of complaints, reviewing records for inordinate amounts
  - Procedural issues (e.g., who can sign, termination of MOU)
  - MOU should describe what FDA agrees to do

STATE PRESENTATIONS

Access Issues

- Would a higher percentage for inordinate amounts (e.g., 50%) address access issues? Would this raise safety concerns?
  - For compounded drugs distributed to contiguous states, what percentage is shipped as opposed to picked up? If drugs are shipped, does it really matter that they are shipped to contiguous states?
  - What medical need is met by specialty pharmacies that do 100% compounding and ship > 50% interstate?
  - Should special exceptions be provided for long-term care facilities? Health systems? How can they be distinguished from other types of compounding facilities?
- What if those that ship "inordinate amounts" were only required to register or meet other requirements?

State Burden Issues

- Handling of complaints (sec. III.a.5)
  - 72 hour timeframe for reporting to FDA any complaint involving drug distributed out of state involving public health risk or immediate safety concern, such as serious AE or product quality issue
    - Assessment of validity of complaint
    - Plans to address

State Burden Issues, cont'd

- Investigations of complaints
  - Investigations will determine whether potential public health risk or safety concern and confirm any risk or safety concern associated with the product is adequately contained (i.e., there is no ongoing risk to the public) (sec.III.a.3)
  - In accordance with State law, state will take appropriate action to ensure that the compounder determines the root cause and undertakes corrective action to eliminate any identified public health risk (sec. III.a.4)

State Burden Issues, cont'd

- Record review to determine inordinate amounts (sec. III.b.1)
  - Do states know which pharmacies in the state ship interstate and how much they ship?
  - Are pharmacies required to keep records of prescriptions picked up or shipped under current law?
  - How are office stock laws that are based on a percentage or other amount enforced by the states? Record reviews?
  - Could states require pharmacies that ship interstate to keep records or report to states on amounts shipped interstate?
  - States could then audit rather than full record review

Other Issues

- Should the MOU describe FDA agreements?
  - Share information with the states about complaints?
  - Take action concerning inordinate amounts?
  - Other?