

Summary of Proceedings

March 18-19, 2015, Inter-governmental Working Meeting on Compounding

On March 18-19, 2015, the U.S. Food and Drug Administration (FDA) convened its third inter-governmental working meeting of state government officials (including the District of Columbia and Puerto Rico). Attendees included officials from the state Boards of Pharmacy and Health Departments and organizations that represent state officials, including the National Association of Boards of Pharmacy (NABP) and the Association of State and Territorial Health Officials (ASTHO).

The purpose of this meeting was to discuss oversight of compounding, including implementation of the Drug Quality and Security Act (DQSA), and to identify opportunities to better protect the public health by strengthening oversight of compounders through improved federal-state collaboration.

FDA previously held inter-governmental working meetings with state officials and their designated representatives in December 2012 and in March 2014. FDA initiated these meetings after the 2012 fungal meningitis outbreak associated with contaminated compounded drugs, involving illnesses and deaths across many states.

The meeting included discussions of the following topics:

Compounding Regulatory Policy Update

FDA began the March 2015 meeting by providing an update on recent developments in the policy area, as well as other DQSA implementation efforts. Since enactment of the DQSA, FDA had published three final guidance documents, ten draft guidance documents, a draft standard memorandum of understanding under section 503A, and a proposed rule concerning the list of drugs that have been withdrawn or removed from the market for reasons of safety or effectiveness. FDA also held the first meeting of the newly reconstituted Pharmacy Compounding Advisory Committee.

FDA described in detail the following four draft guidance documents that the agency issued in February 2015:

- “For Entities Considering Whether to Register as Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act,” which is to provide an entity considering whether to register with the FDA as an outsourcing facility with information about the regulatory impact of registering;
- “Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities,” which proposes conditions under which FDA would not intend to take action for violations of certain sections of the Federal Food, Drug, and Cosmetic Act (FD&C Act) when a pharmacy, Federal facility, or outsourcing facility repackages certain human drug products;
- “Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application (BLA),” which proposes conditions under which FDA would not intend to take action for violations of certain sections of the FD&C Act when a pharmacy, Federal facility, or outsourcing facility mixes, dilutes, or repackages certain biological products; and

- “Adverse Event Reporting for Outsourcing Facilities under Section 503B of the Federal Food, Drug, and Cosmetic Act,” which concerns adverse event reporting for outsourcing facilities.

FDA answered questions and encouraged the states to submit comments to the public dockets that were established for these draft guidances.

Interstate Distribution of Compounded Drugs Under Section 503A and the Draft Standard Memorandum of Understanding (MOU) between FDA and the States

Officials from FDA, the states, and NABP discussed the draft standard MOU that FDA issued for public comment in February 2015, and states provided some comments on the draft. FDA described the conditions under section 503A relating to the MOU, noting that after the final MOU is made available for signature and FDA begins to enforce this condition, a licensed pharmacist, pharmacy, or physician located within a state that has not signed an MOU with FDA cannot distribute (or cause to be distributed) compounded drugs out of the state in which they are compounded that exceed 5% of the total prescription orders dispensed or distributed by that pharmacy or physician. FDA described the provisions of section 503A that specify what the MOU must address.

State officials discussed their views on the draft MOU, including aspects of the draft MOU that they felt needed clarification or presented challenges. For example, some state officials suggested defining “units” of compounded human drug products and further clarifying the calculation of “inordinate amounts.” They also discussed issues involving the application of the MOU to physicians who compound as well as pharmacies, including which state agency or official would sign the MOU. Some questioned whether their states could commit to enforcing the terms of the MOU within their current legal framework. State officials were also concerned about resource constraints, which may impede states’ ability to investigate complaints associated with human drugs distributed out of their state and to determine whether pharmacies are distributing “inordinate amounts” of human drug products out of state.

FDA encouraged the states to submit written comments to the public docket that FDA established for the draft MOU. FDA will consider the issues raised at the intergovernmental working meeting as well as any comments submitted to the docket and will consult with NABP in developing the final MOU.

Registration of Outsourcing Facilities

FDA and state officials discussed the implications of the different treatment of outsourcing facilities under different states’ laws. Under section 503B of the FD&C Act (federal law), an outsourcing facility is not required to be a licensed pharmacy. State officials indicated that the fact that section 503B neither requires nor precludes an outsourcing facility from being a state-licensed pharmacy creates opportunities for inconsistencies in how various states regulate these entities.

Some states require an outsourcing facility to obtain a pharmacy license to operate within the state, and other states do not license outsourcing facilities as pharmacies. Rather, they may license them under a different category, such as wholesalers or manufacturers. In addition, some states license outsourcing facilities as both manufacturers and wholesalers if they distribute non-patient specific drugs, and as pharmacies if they dispense drugs to individual patients. Because outsourcing facilities

may or not be licensed pharmacies and may or may not obtain patient specific prescriptions, these inconsistencies pose challenges to outsourcing facilities as well as regulators. Participants expressed interest in gathering information in a more systematic way about the various state approaches.

Many states enacted new pharmacy laws after the 2012 fungal meningitis outbreak, but have not yet amended them since enactment of the DQSA in 2013 to address outsourcing facilities. Although there may always be certain differences among state laws, several state officials indicated that additional discussion, and possibly a “model” law, could help them to adopt more consistent laws and regulations concerning state pharmacy licensure and related state requirements for outsourcing facilities.

States are also considering how to inspect outsourcing facilities that are licensed as pharmacies. Many states inspect state-licensed pharmacies for compliance with the standards of United States Pharmacopeia (USP) Chapters <795> and <797>, but outsourcing facilities are subject to CGMP requirements. Although FDA inspects outsourcing facilities for compliance with the provisions of section 503B and CGMP requirements, several states indicated that they are unable to rely solely on FDA’s inspections because these inspections may not cover issues that are specific to individual states’ pharmacy laws and regulations, such as pharmacist to technician ratios or state prescription labeling and dispensing requirements. State officials asked FDA for clarification about the differences between USP <795> and <797> standards and CGMP requirements applicable to outsourcing facilities.

Information Sharing and Disclosure

FDA officials reviewed the framework under which they are able to share information with the states. For example, although the Freedom of Information Act (FOIA) provides for disclosure of many FDA records with the public, there are exemptions to the FOIA, as well as other laws and regulations governing disclosure, under which the Agency either can or must withhold information (e.g., confidential commercial, trade secret, pre-decisional, personal privacy, and law enforcement records). Certain non-public information can be shared with state officials who are either commissioned by FDA or have signed a “20.88” confidentiality agreement. State and FDA officials again agreed that there is a need to have good information-sharing practices for the oversight of compounding pharmacies, particularly when there is an outbreak that might require immediate state action to protect the public health.

FDA and state officials discussed the progress made on improving and clarifying information sharing and disclosure issues since last year’s meeting. One improvement discussed was the Single-Signature [20.88 Long-Term Drug Compounding Information Sharing Agreement](#). The new draft agreement, now available for states to sign, lasts for five years rather than one year and only needs to be signed by one official who can sign for a state Board of Pharmacy or other agency involved in the protection of public health rather than by each individual staff member who would receive information. FDA also presented the [“Compounding Domestic Inspection and Information Sharing Chart”](#), a tool that it created to describe what categories of information are gathered during or after an FDA inspection, what types of non-public information might be included in the various categories of information, and the conditions under which such non-public information can be shared with a state.

Many states indicated that they either have or would like to enter into an information sharing agreement with FDA, but some said they are unable to do so because of their own disclosure laws that prevent them from committing to the terms of the 20.88 agreement in its current form. For example, some states

operate under “sunshine” laws, which can present challenges to complying with Federal non-disclosure rules. In addition, the states and FDA discussed the commissioning process whereby a state official can become commissioned and receive unredacted information from FDA. Some state officials described the process for becoming commissioned as burdensome, and also cited state disclosure rules as preventing them from becoming commissioned. Some state officials also said obtaining information as a commissioned official presented problems because commissioned individuals cannot further disclose certain information to their staff or superiors if they are not commissioned, or use the information to bring a state enforcement action. However, other state officials noted that even though the non-public information that they obtain as commissioned officials cannot be shared with others who are not commissioned, the information may prompt them to initiate their own independent state investigations into issues that they would not have otherwise known about.

FDA and state officials also discussed what information FDA may be able to share with a state when FDA receives a report of a serious adverse event or product quality issue associated with a compounded drug, even when there is no disclosure agreement in place, so that the state can initiate its own investigation based on the information. FDA will explore what types of information it can share in such cases and the timeframes in which it can generally share such information.

FDA and the states committed to continue to work together to improve and streamline information sharing to the extent possible.

Inspections of Sterile Compounding Facilities and Enforcement

FDA and state officials discussed inspections of sterile drug compounders, including outsourcing facilities, and the different types of regulatory actions that can result from these inspections. For example, based on findings from an inspection, FDA can issue a warning letter or a letter referring the inspectional findings to the relevant state, or FDA can pursue an enforcement action such as an injunction.

States resources available for inspections vary by state. For example, at least one state is able to inspect all in-state sterile compounding pharmacies as well as out-of-state sterile compounding pharmacies that ship into the state, and at least one other state conducts sampling and analysis programs in addition to inspections and training in sterile processing issues. Other states with more limited resources generally inspect sterile compounding pharmacies only after receiving certain complaints. Some states contract with NABP to conduct the inspections. State officials reiterated the need for FDA to support state regulatory actions by providing expert witness testimony and affidavits, and asked whether they can have access to FDA’s internal evaluations of compounders’ corrective actions. FDA committed to continuing to support states’ cases through testimony and affidavits, as needed, and will explore the circumstances under which FDA can share its evaluations of compounders’ corrective actions.

FDA and state officials committed to continue to work together on opportunities for collaboration in inspections of compounding facilities and in regulatory actions resulting from these inspections.

Animal Drug Compounding

FDA and state officials discussed the current legal and regulatory framework for regulation of animal drug compounding, including inspectional and regulatory challenges. FDA noted that it is working

on a new draft guidance document describing proposed policies with regard to pharmacies that compound animal drugs from bulk drug substances.

March 18-19, 2015 Inter-governmental Working Meeting Action Items:

1. FDA will consider the issues that states described as possible impediments to signing an MOU and aspects of the draft MOU that were identified as needing further clarification. States will also submit these issues as comments to the open docket.
2. FDA will clarify which state agencies or officials would need to sign the MOU, when finalized, if the state decides to sign it, and welcomes state input.
3. NABP will explore the possibility of conducting a survey of state laws and regulations pertaining to compounding to determine how the states are regulating outsourcing facilities and identifying areas of inconsistency that may pose problems. FDA will continue to discuss with the states and NABP ways they could address inconsistencies, including the possibility of a model law that states can review when establishing new laws or regulations to address outsourcing facilities to help promote more uniform outsourcing facility licensure and related requirements.
4. FDA will clarify the differences between USP Chapter <797> and the CGMP requirements that are applicable to outsourcing facilities.
5. FDA will determine whether a modified Information Sharing Agreement could be developed for use in a state with sunshine laws, and what kinds of information could be shared under such an agreement.
6. FDA will determine whether the Single-Signature 20.88 Long-Term Drug Compounding Information Sharing Agreement can be signed by multiple state agencies (for example, both a state Board of Pharmacy and the state attorney general's office).
7. FDA will clarify when a state can use information a commissioned and credentialed state inspector obtained during a joint FDA/state inspection for a state regulatory action.
8. FDA will explore when it can share information with the states from FDA's evaluations of corrective actions that compounders implemented after an inspection or regulatory action, and what can be shared.
9. FDA will explore what types of information it can share with states that do not enter into an information sharing agreement when there is a report of a serious adverse event or product quality issue and the timeframes in which it can generally share such information.
10. FDA will explore how quickly after an inspection it can share information about an outsourcing facility with the states so they can consider the information when licensing the facility.