

## Summary of Proceedings

### March 20-21, 2014, Inter-governmental Working Meeting on Pharmacy Compounding

On March 20-21, 2014, the U.S. Food and Drug Administration (FDA) convened an inter-governmental working meeting of state government officials, including officials from the District of Columbia and Puerto Rico.

Attendees included officials from Boards of Pharmacy, Health Departments, the Centers for Disease Control and Prevention (CDC), and representatives from organizations that represent state officials, including the National Association of Boards of Pharmacy (NABP), the Association of State and Territorial Health Officials (ASTHO), and the National Conference of State Legislatures (NCSL).

During this meeting, participants discussed oversight of compounding pharmacies and implementation of the Drug Quality and Security Act (DQSA). The DQSA, P.L. 113-54, was signed into law on November 27, 2013, and contains provisions relating to federal and state oversight of compounded human drugs.

The purpose of this meeting was to identify opportunities to better protect the public health by strengthening oversight of compounders, including through improved federal-state collaboration.

FDA previously held an inter-governmental working meeting with state officials and their designated representatives in December 2012. That meeting came in the wake of a fungal meningitis outbreak associated with contaminated compounded drugs, involving many illnesses and deaths across many states.

#### ***Overview of Compounding Quality Act and FDA's Plans for Implementation.***

FDA officials began the March 2014 meeting by providing an overview of the DQSA and the compounding provisions in section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

FDA officials described section 503A, which was enacted in 1997 and describes the conditions under which certain drugs compounded by a licensed pharmacist or physician may be entitled to exemptions from three sections of the FD&C Act: current good manufacturing practice (CGMP), labeling with adequate directions for use, and new drug approval (sections 501(a)(2)(B), 502(f)(1), and 505 of the FD&C Act, respectively).

FDA described how the DQSA removed the unconstitutional advertising and solicitation provisions from [section 503A](#) of the FD&C Act, which removed uncertainty regarding the validity of this section and clarified that it applies to compounders nationwide. FDA stated that to be eligible for these exemptions from the FD&C Act, the drugs must be compounded by a licensed pharmacist in a state-licensed pharmacy or Federal facility or by a licensed physician, and dispensed pursuant to a prescription for an identified individual patient.

FDA also described new [section 503B](#) added to the FD&C Act by the DQSA, which created a new category of [outsourcing facilities](#) that may compound and distribute sterile drug products without receiving prescriptions for individual patients.

FDA stated that a firm may elect to be an outsourcing facility by voluntarily registering with FDA, paying a registration fee, and complying with all provisions of section 503B of the FD&C Act.

FDA noted that such outsourcing facilities are subject to FDA standards (e.g., CGMP) and oversight (e.g., inspection according to a risk-based schedule).

FDA officials also discussed some of its implementation activities since the enactment of the DQSA. For example, the Agency published [three draft guidance documents](#) that address: (1) how a compounder can register under section 503B as an outsourcing facility; (2) how outsourcing facilities should report required information to FDA about products they produce; and (3) provisions of section 503A that require rulemaking or other FDA actions to implement, including the development of a bulk drug substances list, a “difficult to compound” list, and a standard memorandum of understanding between FDA and the states.

In addition, FDA published [three Federal Register notices](#) soliciting nominations for lists of bulk drug substances that can be used to compound drug products and drug products that cannot be compounded because they are “difficult to compound.”<sup>1</sup>

The meeting also included discussions of the following topics:

***Federal/State Communications.***

FDA officials described the framework under which they are able to share information with the states. State and FDA officials 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.

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.

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<sup>1</sup> FDA published three Federal Register Notices soliciting nominations for lists including: (1) the list of drug products that present demonstrable difficulties for compounding under sections 503A and 503B; (2) the list of bulk drug substances that may be used to compound drug products under section 503A; and (3) the list of bulk drug substances that may be used to compound drug products under section 503B (based on clinical need).

State officials expressed concerns that the framework for sharing information is too limiting. For example, many states operate under their own disclosure laws, such as “sunshine” laws, which can present challenges to entering into 20.88 confidentiality agreements or complying with Federal non-disclosure rules.

In addition, the commissioning route for disclosure was described as limiting because the person who is commissioned cannot further disclose the information to their superiors if they are not commissioned, or use it to bring a state enforcement action.

Furthermore, the 20.88 agreements contain strict non-disclosure language that states that disclosure of certain shared information could be a criminal violation of federal law, and some state officials are reluctant to enter into 20.88 agreements because of this.

Some state officials noted that although the states could conduct their own inspections, it is not efficient for the states to have to duplicate FDA inspection efforts to obtain information necessary to bring an enforcement action. They cited duplicating product sampling and laboratory testing of the samples as one example of this. They also cited the need to obtain the information in a timely way to support immediate action when necessary.

Several state officials indicated they need more clarity on what constitutes confidential commercial information (CCI).

FDA and state officials agreed to work together to explore better ways to share information consistent with Federal and state law. Specifically, FDA will reexamine the language in 20.88 agreements to determine whether it can be modified in any way to remove disincentives to signing such agreements.

FDA also will work with the states to determine what types of information gathered during or after an FDA inspection might be necessary for a state to take rapid enforcement action to protect the public health, and explore whether that information can be made available more quickly so the states can use it.

### ***Inspections of Sterile Compounding Facilities and Enforcement.***

FDA officials discussed the inspections of sterile drug compounding facilities and post-inspection action(s), which may include warning letters, state referral letters, or injunctions.

Under FDA’s inspection program, there are opportunities for continued collaboration with the states in for-cause, surveillance, and follow-up inspections of compounding pharmacies and outsourcing facilities.

Some state officials expressed concerns about whether inspections are to be conducted jointly, or in parallel, and what the differences between the two models are. FDA agreed to work with the states to clarify the differences. State officials welcomed the opportunity to partner with FDA and expressed an interest in FDA providing training for state inspectors.

FDA and state officials also discussed FDA’s ability to provide support for state actions resulting from information gathered during FDA and joint FDA and state inspections, including witnesses

and affidavits. State officials recommended that to improve communications, FDA should alert the states before posting [inspection observations](#) (captured in the Form FDA 483) and issuing warning letters.

FDA indicated that it would inspect outsourcing facilities according to a risk-based schedule, as required by the DQSA, and that the establishment fees were predicated on an inspection every three years. Several state officials indicated that was not adequate and inspections should be conducted every six months to a year. FDA said it would consider whether it could conduct the inspections more frequently.

***Regulating interstate distribution of compounded drugs pursuant to section 503A under a Memorandum of Understanding (MOU) with FDA.***

Officials from FDA, the states, and the NABP discussed the standard MOU that the Agency is required to develop under section 503A of the FD&C Act that addresses the interstate shipment of compounded products and the investigation of complaints by the states related to compounded drugs.

FDA described the requirements under section 503A, noting that 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 interstate that exceed 5% of the total prescription orders dispensed or distributed by that pharmacy or physician.

FDA described the provisions of section 503A that allow a licensed pharmacist or physician located in a state that has signed an MOU to exceed the 5% limit, and the requirement that the MOU address the interstate distribution of “inordinate amounts.”

FDA described the issues it may address when drafting the MOU such as how FDA should define “inordinate amounts” (e.g., as a percentage or an absolute amount), whether the MOU should take into account contiguous states, and how the MOU should address investigations of complaints (including what constitutes appropriate investigation of complaints).

FDA solicited views of the states on these issues and obtained a variety of views. Certain state officials said that they were not particularly concerned with a strict definition of “inordinate amounts” because in their experience, the interstate shipment of compounded drug products is either a very small component or nearly the entire business of a compounding pharmacy.

Some state officials expressed views favoring defining inordinate amounts in terms of a specific percentage, and at least one participant did not think FDA needed to establish an MOU at all. FDA indicated it would consider the input received during the meeting in developing the MOU.

***State Adverse Event Reporting.***

FDA officials described FDA’s adverse event reporting system, and how it relates to section 503B of the FD&C Act, which requires that outsourcing facilities report adverse events to the Agency.

During the meeting, participants learned about FDA's postmarket drug safety reporting system (MedWatch), how drug safety information is reviewed by FDA, and FDA's process to analyze adverse drug events and medication errors. The databases used to store postmarket drug data contain millions of reports, and the infrastructure required to maintain such systems is substantial.

Reports related to compounding pharmacies comprise a small portion of overall reports and are difficult to track because there is no specific data field that identifies the report as related to a compounded drug product. During compounding outbreak investigations, CDC partners with FDA and states to use available data from MedWatch and other sources to determine the cause of the outbreak.

State officials expressed an interest in working with FDA to gain access to reports submitted to MedWatch and working together to establish state reporting systems that are not duplicative of the federal system, so that it would be less burdensome for reporters.

***State Enforcement Priorities.***

State officials described the challenges they face in overseeing compounding and their enforcement priorities in the wake of the 2012 fungal meningitis outbreak.

States have focused inspections on facilities that compound high risk, sterile products. Several states have hired more inspectors and are training them using NABP and other resources. Some states have also hired NABP to conduct inspections for them.

Many state officials noted that they have begun to require a facility inspection before the registration/licensure of a new sterile compounding pharmacy, as well as before the renewal of the registration/licensure. Some are requiring licensees to pay for these inspections.

States also are taking steps to increase their oversight of out-of-state sterile compounders shipping into their states through other requirements including required reporting of contamination events, recalls, adverse events, and disciplinary actions taken against the compounder or accreditation issues.

Some state officials said they have been encouraging the registration of outsourcing facilities with the FDA.

***State Legislation/Regulation.***

Some states are moving toward comprehensive legislation to provide oversight of compounding, while others are waiting for FDA to implement the DQSA before changing their own laws.

In the meantime, some states have enhanced their pharmacy board capacities through additional funding and staffing. Some of the issues that states are grappling with include whether to permit office use compounding, labeling of compounded products, licensure requirements for firms registered with FDA, exemptions for ophthalmologists and oncologists, and what quality

standards to impose on sterile compounding (e.g., most require compliance with USP 797 standards).

State officials reported that they use terminology, definitions, and categories in their legislative and regulatory frameworks for pharmacy compounding that differ from the FD&C Act. Some states have restructured terminology, definitions and categories to align with those established under the FD&C Act.

**Action Items:**

**Information Sharing:**

1. FDA will reexamine the language in 20.88 agreements to determine whether it can be modified in any way to remove disincentives to signing such agreements.
2. FDA will provide to states more clarity on the commissioning process to facilitate joint oversight. The Agency will consider developing a “how to” guide for states so they may better understand the process.
3. FDA will work with the states to determine what types of information gathered during or after an FDA inspection might be necessary for a state to take rapid enforcement action to protect the public health, and explore whether that information can be made available more quickly so the states can use it.
4. FDA will clarify what types of information acquired during an inspection are considered to be CCI and exempt from disclosure.
5. FDA will consider whether it can provide states with earlier notification of violations before posting a 483 or issuing warning letters.

**Inspections and Enforcement:**

1. FDA will work with states to determine ways to streamline communications. For example, delegating one point of contact for coordination of inspections while providing advanced notification of scheduled inspections.
2. FDA will work with states to clarify the difference between joint and parallel investigations.
3. FDA officials will consider how to provide additional training opportunities to state investigators on how to perform sterile inspections.
4. FDA will consider whether it can inspect outsourcing facilities more frequently than every three years.
5. FDA will work with states on improving the process for supporting the states in enforcement actions, including providing testimony, declarations and affidavits.

**Reporting Adverse Events:**

FDA will consider how best to share with states adverse event reports submitted to the Agency and how to help states establish their own reporting systems that are not duplicative of the federal system.