Summary of Proceedings
October 10-11, 2019, Inter-governmental Working Meeting on Compounding

The U.S. Food and Drug Administration convened its eighth inter-governmental working meeting with state government officials, October 10 and 11, 2019, at the agency's White Oak campus in Maryland. Attendees included officials from state boards of pharmacy and state health departments and representatives from the National Association of Boards of Pharmacy (NABP).

The purpose of this meeting was to continue discussions about compounding oversight, including efforts to support implementing the Compounding Quality Act (CQA) (Title I of the Drug Quality and Security Act (DQSA)), and further explore opportunities to protect the public health through federal-state collaboration and policy and regulatory discussions.

Officials from 43 states, in addition to the District of Columbia and the U.S. Virgin Islands, attended the 2019 inter-governmental working meeting on compounding.

FDA previously held inter-governmental working meetings on compounding with state officials and their designated representatives in December 2012, March 2014, March 2015, November 2015, September 2016, September 2017 and September 2018. FDA initiated these meetings after the 2012 fungal meningitis outbreak associated with contaminated compounded drugs, which led to deaths and serious illnesses across the country.

Compounding Policy Updates
FDA kicked off the meeting with a policy update on the nine compounding policy documents the agency issued in 2019. The agency also shared an overview of its collaborative projects with the University of Maryland and Johns Hopkins University, which will inform the agency's evaluation of bulk drug substances for the 503B bulks list. The policy documents discussed include the revised draft insanitary conditions guidance, the revised draft FDA-State Standard Memorandum of Understanding (MOU) and the draft guidance related to hospital and health system compounding.

FDA-State Standard Memorandum of Understanding Update
FDA summarized the 2018 revised draft standard MOU, including changes made to address stakeholder concerns about potential impacts to patient access. Under the 2015 draft MOU, the states would agree to take action against a compounder that distributed inordinate amounts of its compounded drugs interstate. FDA proposed in the 2015 draft, that distribution interstate of compounded drugs equal to or greater than 30 percent of compounded and non-compounded drugs dispensed or distributed both intrastate and interstate by the compounder, during a calendar month, would be inordinate.

Under the revised draft MOU, states would agree to identify compounders that distribute interstate more than 50 percent of the number of prescription orders for compounded drugs distributed or dispensed both intrastate and interstate during a calendar month and report certain information to FDA about those compounders and their compounded drugs.

FDA and states discussed the revised draft MOU, including certain state questions about how the revised draft MOU addresses physician compounding and related reporting expectations. Some states also expressed concerns about legal considerations that may impede signature by the state. FDA expressed it was revising the revised draft MOU to address concerns states expressed about potential

barriers to entering into the MOU. FDA reiterated the statutory 5 percent limit only applies to traditional pharmacy compounders located in states that do not sign the MOU.

Information-Sharing System for Distribution of Compounded Drugs Interstate
The National Association of Boards of Pharmacy (NABP) discussed receipt of FDA's cooperative agreement grant entitled "Information Sharing Systems for State-Regulated Drug Compounding Activities." NABP explained the grant will fund creation of an information sharing system that will help increase understanding of the distribution interstate of compounded drugs and help track quality or safety issues related to compounded drugs sent across state lines. NABP explained the system will provide a mechanism to facilitate state reporting to FDA under the MOU and will also provide compounding pharmacies with the ability to self-report their compounding activities. The ultimate goal of the system is to provide data that will inform oversight decisions, enabling FDA and states to better prioritize resources to help identify and address compounding pharmacies that pose the highest risk to patients.

The development work for the information-sharing system is to be completed in three phases:

1. building the data system based on existing NABP systems,
2. gathering, auditing and analyzing information after the system is operational and
3. preparing a final report for FDA.

Good Manufacturing Practices for Outsourcing Facilities
FDA discussed revision 1 of the draft guidance on current good manufacturing practices (CGMP) for outsourcing facilities, providing conditions under which the agency generally does not intend to take regulatory action against an outsourcing facility regarding certain CGMP requirements. This guidance reflects FDA's intent to recognize the differences between outsourcing facilities and conventional drug manufacturers, while maintaining the minimum standards necessary to protect patients from the risks of contaminated or otherwise substandard compounded drugs. The agency explained the draft guidance proposes enforcement discretion policies regarding reduced end-product release testing, stability testing and reserve sample retention for certain lower-risk compounding activities. However, the draft guidance seeks to retain robust production controls regardless of risk.

FDA reviewed certain CGMP topics in greater depth, including sterility assurance, process validation, process design and development and qualification of components, container-closures and equipment. The agency discussed the responsibilities of the quality unit under CGMP and that outsourcing facilities are responsible for the work contract facilities and contract testing laboratories do for them. In addition, inspectional observations were discussed.

State Legislative and Regulatory Updates
A number of state boards of pharmacy joined a panel session describing recent state legislative and regulatory update efforts related to drug compounding in various stages of advancement.

- One state board of pharmacy described efforts to develop a new tool to assist with pharmacy licensing, as well as plans to establish a specific license for hospital cleanrooms. In this state, licensees submit information, including a sterile compounding reporting form, an environmental action monitoring report, serious event reports and a defective drug preparation log.

- Another state board of pharmacy described current processes including requiring sterile compounding licenses and inspection of outsourcing facilities. They also described work to update board regulations related to compounding and handling hazardous drugs.
- A third board of pharmacy discussed their risk-based inspection strategy, implementation of a 2015 rule to require compounding pharmacies to be in compliance with United States Pharmacopeial Convention (USP) chapters <797> and <795> and their ongoing preparation for USP chapter revisions. The state also shared that it will inspect all sterile compounding pharmacies every 18 months, regardless of state-assigned risk classification, beginning in December 2019.

Compounding Incidents
FDA described its process regarding incidents related to compounded drugs, including how adverse event and complaint reports are received and investigated by FDA, and actions taken to facilitate resolution. FDA also described compounding risk alerts and explained this information is to inform health care professionals, compounders and patients about adverse events and other drug quality issues related to compounded drugs.

Drug Supply Chain Security Act Implementation
FDA provided an update on implementing the Drug Supply Chain Security Act (DSCSA), which establishes traceability requirements for the pharmaceutical supply chain. FDA described the DSCSA's serialization requirements for 2D barcodes, which went into effect in 2018, and product verification requirements, which went into effect in 2019. FDA explained these requirements will support product verification at the "unit" level, and are key to an interoperable, fully electronic traceability system. FDA stated it continues to work on regulations for wholesalers and third-party logistics providers. FDA also described the pilot project program launched to help the agency and industry identify the system attributes needed to implement traceability requirements.

FDA Inspections and Enforcement Update, and FDA Form 483 Walk Through
FDA provided an update on oversight, including enforcement activities. In fiscal year 2018, FDA conducted 129 compounding facility inspections, including 86 inspections of facilities seeking to compound drugs under section 503A of the Federal Food, Drug and Cosmetic Act, 43 inspections of outsourcing facilities and 50 recall events involving compounded drugs. Over the same time period, FDA issued 34 warning letters and 28 letters referring inspectional findings to the state regulatory agency. In addition, FDA worked with the Department of Justice on civil and criminal enforcement actions and provided four examples of consent decrees of permanent injunction.

FDA presented case examples of FDA Form 483s to describe identifying imminent health hazards during inspections that may lead FDA to recommend compounders recall a drug. FDA shared the most common reason for recall recommendations is lack of sterility assurance. Other examples of imminent health risks that may lead to FDA recommending recall include super-potent drugs, poor conditions in aseptic processing areas, extensive beyond-use dates or factors that could present concern for microbial contamination in compounded drugs.

Breakout Session and Tabletop Discussion Summaries
FDA and state representatives discussed opportunities for optimizing FDA-state interactions, potential mechanisms to improve information sharing between FDA and states, approaches undertaken by states to utilize information provided by the agency such as FDA Form 483 observations or other information

provided to support regulatory action and emerging drug compounding issues or trends encountered by states during breakout sessions.

States reported that listening sessions and conference calls are generally helpful and requested more information in frequently asked questions format. States reported they use the outsourcing facility product reports and would like access to information on outsourcing facility drug recalls. States shared they cannot always easily identify specific drug recall information, including the compounder's addresses or which states have received drugs subject to the recall. States also reported it is difficult to find specific information such as inspection and Form FDA 483 information on FDA's website and requested access to written responses between compounders and FDA regarding inspectional findings.

States identified emerging compounding trends involving cannabidiol, biologics and implanted hormones. States also discussed gaps in state inspector training and opportunities for increased sterile compounding training for state inspectors. States asked for further clarification around commissioned personnel agreements and what can be shared in establishment inspection reports.

Outsourcing Facility Challenges and Compounding Quality Center of Excellence
The meeting concluded with an FDA presentation about challenges outsourcing facilities have faced with facility licensure, inspections, CGMP enforcement and state disciplinary actions. Based on input from outsourcing facilities, FDA reported some states are enforcing CGMP requirements in a manner that is inconsistent with the policies described in FDA's revised draft guidance on CGMP for outsourcing facilities, and others are basing state-level disciplinary measures on observations described in FDA Form 483s. FDA explained information such as FDA Form 483 observations are not final agency actions.

FDA also provided an overview on the Compounding Quality Center of Excellence focused on improving the overall quality of compounded drugs produced by outsourcing facilities. The Compounding Quality Center of Excellence provides training courses for outsourcing facility staff covering sterile processing, investigations and corrective action procedures, environmental and personnel monitoring and cleanroom design, and will host a conference geared to outsourcing facilities and stakeholders, including state regulators, hospitals and other pharmacies interested in becoming outsourcing facilities.

October 10-11, 2019 Inter-governmental Working Meeting Action Items

- FDA will strive to provide timely inquiry responses and encourage states to participate in the commissioning process
- FDA will identify improved ways to enhance incident information sharing through a centralized compounding mailbox
- FDA will identify opportunities to improve information accessibility on our website
- FDA will provide training opportunities for states and other opportunities related to the Compounding Quality Center of Excellence