DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

February 27, 2014

Michael Carome, M.D.
Sarah Sorscher, J.D., M.P.H
1600 20th St., NW
Washington, DC 20009

Dear Dr. Carome and Ms. Sorscher:

Thank you for your letter dated December 17, 2013 to Commissioner Hamburg, which discusses your concerns about the Food and Drug Administration's (FDA or Agency) recent public announcements on compounding. You state in your letter that these announcements may "give the false impression that drugs manufactured by outsourcing facilities will now be subject to the same federal oversight as FDA-approved drugs, which will in turn lead health care providers to purchase and prescribe the products as substitutes for FDA-approved products" and "appear to be a broad endorsement of pharmaceutical products produced by outsourcing facilities, even in cases in which FDA-approved products are also available to treat patients." In your letter, you request that FDA correct the public statements we have made since the passage of the Drug Quality and Security Act (DQSA) to more accurately reflect the differences between drugs compounded by outsourcers and FDA-approved drugs. You also encourage FDA to educate the medical community on the risks associated with compounded products versus FDA-approved drugs.

We agree that it is important to convey to the public the differences between compounded and FDA-approved drugs. FDA has clearly stated its position with regard to compounded drugs, both in the recent letters sent to more than 6,000 healthcare entities that may purchase compounded drugs and to governors, boards of pharmacy, and state health officials in all 50 States, as well as in statements posted on our web page. In those letters, Commissioner Hamburg said:

> When a drug is FDA-approved, patients are assured that FDA has reviewed the safety and efficacy of the drug and the adequacy of the manufacturing process to produce a quality product. Because they do not go through the drug approval process, compounded drugs do not provide such assurance and, therefore, should only be used when an FDA-approved product is not available to meet the medical needs of an individual patient.[1]

[1] *See* "Letters to Stakeholders," at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm380596.htm.

In questions and answers posted on FDA's web page in early December 2013,[2] FDA states that compounded drugs are not FDA-approved, that the Agency does not verify the safety or effectiveness of compounded drugs, and that compounded drugs lack an FDA finding of manufacturing quality before such drugs are marketed (Compounding Q&A, Question 4). FDA also stated that there can be health risks associated with compounded drugs that do not meet federal quality standards (Compounding Q&A, Question 5). For example, compounded drugs made using poor quality practices may be sub- or super-potent, contaminated, or otherwise adulterated. Additional health risks include the possibility that patients will use ineffective compounded drugs instead of FDA-approved drugs that have been shown to be safe and effective (Compounding Q&A, Question 5).

In addition, in more recent communications posted on its web page regarding outsourcing facilities, FDA has clarified what drugs produced by outsourcing facilities are and are not. For example, the information about registered outsourcing facilities includes the following question and answer:

4. **If FDA has inspected a human drug compounding outsourcing facility, can I be sure that the drugs I purchase from that facility are safe?**

Drugs made by compounders, including those made at human drug compounding outsourcing facilities, are NOT FDA-approved. This means that they have not undergone the same premarket review as approved drugs. They lack an FDA review of safety and efficacy and of manufacturing quality. Therefore, when an FDA-approved drug is commercially available, FDA recommends that practitioners prescribe the FDA-approved drug rather than a compounded drug unless the prescribing practitioner has determined that a compounded product is necessary for the particular patient and would provide a significant difference for the patient as compared to the FDA-approved commercially available drug product.

Although the drugs will not be FDA approved, purchasers of drugs compounded at a registered outsourcing facility that has had a recent satisfactory FDA inspection will have some assurance that the conditions at that facility met applicable current good manufacturing practice standards at the time of the inspection, and the compounded drugs are labeled with the required information. It should be noted, however, that FDA inspections are just a snapshot in time. Conditions at the facility can change at any time. And FDA only reviews a small sample of the records available at a facility during an inspection and must draw conclusions about the conditions and practices at the facility from that small sample of records. Purchasers should look at other available information about the facility that can provide them with additional insight with regard to the facility's operations. [3]

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[2] *See* "Compounding and the FDA: Questions and Answers," at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm339764.htm.

[3] *See* "Registered Outsourcing Facilities," at http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm378645.htm.

These and the other questions and answers posted on the web clearly state FDA's position with regard to registered outsourcing facilities.

FDA will continue to work with stakeholders, including the medical community, to encourage the appropriate use and oversight of compounded drugs. We look forward to continued interactions with you on this topic.

Sincerely,

Janet Woodcock, M.D
Director
Center for Drug Evaluation and Research