FDA Releases New Draft Guidance on Compounded Drugs

On December 10, U.S. Food and Drug Administration (FDA) Commissioner Scott Gottlieb, MD, and Deputy Commissioner Anna Abram released a statement on new efforts by the agency to ensure the quality of compounded drugs. Gottlieb reported that the FDA continues to implement its January 2018 Compounding Priorities Plan (https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm592795.htm), originally issued as a partial response to incidents of contamination and resulting injury and death from products produced at compounding facilities. "We're especially focused on the importance of ensuring compounded product quality," said Gottlieb in the statement. "Through enforcement actions, we've been addressing insanitary conditions and manufacturing quality issues at compounders' facilities across the country. More activities are planned, and we've stepped up our collaborative work with the Department of Justice. But preventing problems before they put patient safety at risk is our key objective to protect consumers."

The statement reiterated persistent concerns about compliance with current good manufacturing practice (CGMP) by larger outsourcing facilities that often operate on a broad scale with products distributed across the country. Gottlieb and Abram announced updates to the draft guidance related to compounding facilities (https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM403496.pdf).

The aims of the new guidance are to outline practices for drugs produced under CGMP requirements by outsourcing facilities, recognize differences in drug production between outsourcing facilities and conventional drug manufacturers, and provide clarity on quality assurance, maintenance of suitable facilities, sterility, stability testing, and beyond-use or expiration dates for products that do not go through the FDA drug approval process. The revisions also address stakeholder concerns that smaller orders for compounded substances might be adversely affected.

In addition to the release of the revised draft guidance, Gottlieb and Abram also announced a public meeting to be held on May 21 at the FDA's White Oak campus in Silver Spring, MD. The meeting is intended to solicit comments on the potential impact of the guidance, if finalized, on outsourcing facilities supplying compounded drugs for office stock. Health care professionals, outsourcing facilities, entities considering becoming outsourcing facilities, and other interested parties will have the opportunity to present to the FDA their perspectives on the ways in which they will be affected by guidance revisions. The FDA hopes to gain additional clarity from stakeholders on outsourcing facility production of office stock products, the fulfillment of smaller orders of these office stock products, and the production of products with beyond-use dating desired by providers, among other topics. The agency is also soliciting public comments through its website (https://www.federalregister.gov/documents/2018/12/11/2018-26725/the-food-and-drug-administrations-proposed-current-good-manufacturing-practice-policies-for).

The December 10 statement emphasized the need to help mitigate risk and ensure quality for patients while also effectively providing patients and clinicians with access to compounded products made under appropriate production standards. Gottlieb and Abrams indicated that the FDA remains concerned about "far too much" unsafe activity in the compounding sector, including at facilities that have not registered with FDA as outsourcing facilities but continue to distribute office stock products. The agency will continue to conduct risk-based inspection and enforcement efforts at compounders not registered as outsourcing facilities, especially if they appear to be distributing compounded sterile drugs nationwide without valid patient-specific prescriptions, and will take action against facilities with deficient practices.

The statement also noted that soon the FDA will further define what substances can be used in compounded products by traditional compounders. A final rule will be issued identifying the criteria to be used to evaluate bulk drug substances for the bulk drug list that may be used in compounding under section 503A of the Federal Food, Drug, and Cosmetic Act. This final rule will also identify bulk substances the agency has evaluated and will or will not place on the 503A bulks list.

Two days after issuing the statement on compounded drugs, the FDA released a second statement from Gottlieb on a broader agency effort to ensure drug supply safety through updated guidance on data quality and integrity associated with drug manufacturing. The new guidance, issued under the title "Data Integrity and Compliance with Drug CGMP: Questions and Answers" (https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM495891.pdf) is an update of previous 2016 policy. The guidance covers the design, operation, and monitoring of systems and controls to maintain data integrity. The revised recommendations are aimed at helping manufacturers address identified data integrity lapses, implement best practices to address gaps that can create risks to data integrity, and ensure consistent awareness and commitment to data integrity.