Compounding and the FDA: Questions and Answers

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What is compounding?

Drug compounding is often regarded as the process of combining, mixing, or altering ingredients to create a medication tailored to the needs of an individual patient. Compounding includes the combining of two or more drugs. Compounded drugs are not FDA-approved.

Why do some patients need compounded drugs?

A drug may be compounded for a patient who cannot be treated with an FDA-approved medication, such as a patient who has an allergy to a certain dye and needs a medication to be made without it, or an elderly patient or a child who cannot swallow a tablet or capsule and needs a medicine in a liquid dosage form. Practitioners in hospitals, clinics, and other health care facilities sometimes provide compounded drugs to patients when an FDA-approved drug is not medically appropriate to treat them.

In these situations, compounding can serve an important patient need. However, some compounders engage in activities that can put patients at risk and/or undermine the drug approval process. For example, FDA has observed that some compounders have made false and misleading statements that compounded drugs are safe and effective, sometimes for the treatment of serious diseases, by incorrectly suggesting the drugs had met the standard for FDA approval.

Are compounded drugs approved by FDA?

Compounded drugs are not FDA-approved. This means that FDA does not verify the safety or effectiveness of compounded drugs. Consumers and health professionals rely on the drug approval process for verification of safety, effectiveness, and quality. Compounded drugs also lack an FDA finding of manufacturing quality before such drugs are marketed.

What are the risks associated with compounded drugs?

Compounded drugs can serve an important medical need for patients, but they do not have the same safety, quality, and effectiveness assurances as approved drugs. Unnecessary use of compounded drugs unnecessarily exposes patients to potentially serious health risks.

Because compounded drugs are not FDA-approved, FDA does not verify their safety, effectiveness, or quality before they are marketed. In addition, poor compounding practices can result in serious drug quality problems, such as contamination or a drug that contains too much active ingredient. This can lead to serious patient injury and death.

FDA has observed troubling conditions during many of its inspections of compounding facilities including toaster ovens used for sterilization, pet beds near sterile compounding areas, and operators handling sterile drug products with exposed skin, which sheds particles and bacteria, among many others.
Compounding drugs under insanitary conditions could lead to widespread patient harm, especially when the compounder engages in large-scale, non-patient specific compounding and distribution. FDA may not be aware of which compounders are making such drugs, and some states may have insufficient resources to adequately oversee them.

In October 2012, the United States faced the most serious outbreak associated with contaminated compounded drugs in recent history. A pharmacy in Massachusetts shipped compounded drugs that were contaminated with a fungus throughout the country, and these drugs were injected into patients' spines and joints. More than 750 people in 20 states developed fungal infections, and more than 60 people died. Approximately 14,000 patients received injections from the lots of contaminated drug product. See 2012 Fungal Meningitis Outbreak: Persons with Fungal Infections Linked to Steroid Injections, by State, Centers for Disease Control and Prevention (https://www.cdc.gov/hai/outbreaks/meningitis-map-large.html) for more information.

Was the 2012 fungal meningitis outbreak an isolated incident?

The 2012 fungal meningitis outbreak was not an isolated event. It was the most serious in a long history of serious adverse events associated with contaminated, super-potent, mislabeled, or otherwise poor quality compounded drugs. In addition, many serious adverse events linked to poor quality compounded drugs, including outbreaks of infections and deaths have occurred since then. And, because most compounders do not report adverse events to FDA, the agency may not be aware of adverse events associated with compounded drugs unless a health care provider or patient voluntarily submits an adverse event report regarding his or her patients or a state official notifies FDA.

Who can compound drugs?

Compounding commonly occurs in pharmacies, although it may also occur in other settings.

Federal law addresses compounding by a licensed pharmacist in a state-licensed pharmacy, or federal facility, or by a physician, as well as compounding by or under the direct supervision of a licensed pharmacist in an outsourcing facility.

Outsourcing facilities are a category of compounders established in 2013 by the Drug Quality and Security Act. Outsourcing facilities are inspected by FDA according to a risk-based schedule and are subject to increased quality standards.

Who inspects facilities that compound drugs?

Various entities may inspect facilities that compound drugs, including state boards of pharmacy and FDA.

Generally, state boards of pharmacy have primary responsibility for the day-to-day oversight of state-licensed pharmacies that are not registered with FDA as outsourcing facilities. FDA does conduct surveillance and for-cause inspections of state-licensed pharmacies that are not registered as outsourcing facilities.

Facilities that register with FDA as outsourcing facilities under section 503B are primarily overseen by FDA and inspected by FDA according to a risk-based schedule.

What quality standards apply to compounded drugs?

Quality requirements for compounded drugs differ depending on the setting where compounding occurs.

Drugs compounded in outsourcing facilities are subject to current good manufacturing practice (CGMP) requirements.

By contrast, drugs compounded by a licensed pharmacist in a state-licensed pharmacy, or federal facility, or by a physician, in accordance with the conditions of section 503A of the FD&C Act, are exempt from compliance with CGMP requirements. These facilities may be subject to less stringent quality standards set in state law or policy. Such standards may differ state to state.

However, regardless of where compounding occurs, whether in a pharmacy, outsourcing facility, or physician's office, other federal requirements apply, including the requirement that drugs not be prepared, packed, or held under insanitary conditions.

How do I submit comments regarding FDA's policies?

For instructions on how to submit comments concerning specific draft or final policy documents (/drugs/compounding/regulatory-policy-information) that FDA has issued, follow the instructions in the *Federal Register* notice announcing the availability of that document. You can search for specific policy documents and their notices of availability on https://www.federalregister.gov (https://www.federalregister.gov).

FDA has also established (/drugs/compounding/fda-establishes-public-docket-drug-compounding) a public docket (https://www.federalregister.gov/documents/2015/03/09/2015-05376/compounding-of-human-drug-products-under-the-federal-food-drug-and-cosmetic-act-establishment-of-a) (FDA–2015–N–0030) to receive information, recommendations, and comments on matters related to the agency's regulation of compounding of human drug products under sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act). This docket is intended for general comments related to human drug compounding that are not specific to documents or issues that are the subject of other dockets.