Who Regulates Compounding Pharmacies?

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Question

What is a compounding pharmacy and how is it regulated?

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It is easy to differentiate between your local community pharmacy and a large pharmaceutical manufacturer. The pharmacy is viewed as dispensing medications to particular patients with prescriptions from a licensed provider. In contrast, the pharmaceutical manufacturer makes large batches of drug products to be distributed to pharmacy hospitals and other resellers and users of these products.

But there is another entity that falls between these: the compounding pharmacy. To be more precise, the distinctions may best be understood as different types of activities -- dispensing drugs, manufacturing drugs, and compounding drugs -- rather than merely different types of businesses. A pharmacy, which is considered a terminal distributor of dangerous drugs, may be actively dispensing, manufacturing, *and* compounding.

To understand why we have compounding by pharmacies, we should first understand some of the problems that patients encounter when getting prescription medications. Consider that a patient may need, for example, 15 mg of a particular medication to treat a condition. The pharmaceutical manufacturer of the medication may make only 10-mg and 20-mg tablets. To obtain a 15-mg dose, the patient may buy 10-mg tablets, cut them in half, and take 3 of the halved (5 mg) tablets. Although the math works out just fine, many patients resist this approach; they may not want to cut tablets in half or may not be able to cut tablets in half. Furthermore, splitting tablets can lead to imprecise dosing.

So, why doesn't the pharmaceutical manufacturer make a 15-mg tablet? One reason may be money. Although a few patients may require a 15-mg dose, most patients may be treated just fine with a 10-mg or 20-mg dose; there may simply not be enough demand to justify mass production of a 15-mg tablet. At some point, the manufacturer has to draw the proverbial line and produce those products and doses that make economic sense to them.

Seeing this as an opportunity, a compounding pharmacy may begin to prepare the 15-mg tablets -- and do so in a profitable manner which the manufacturer could not or would not do. To use another example, a compounding pharmacy may prepare medications without a particular ingredient to which some patients are allergic, such as coloring agents and dyes. Without the compounding pharmacy, some patients may find themselves "stranded" and unable to obtain the medications they need.

Who Regulates Compounding by Pharmacies?

State boards of pharmacy typically regulate compounding by pharmacies, but federal legislation also plays a role. In the state of Ohio, for example, compounding is defined as preparation, mixing, assembling, packaging, and labeling of 1 or more drugs pursuant to a prescription issued by a licensed health professional authorized to prescribe drugs. [1,2]

Ohio state law also allows compounding in anticipation of orders for drugs pursuant to prescriptions based on routine regularly observed dispensing patterns. This means that a pharmacist may compound medications even though the pharmacist does not yet have a written prescription in hand for those medications, provided that the pharmacist reasonably anticipates receiving prescriptions in the future. This allows the pharmacist to make batches of medications. This is important because compounding can require significant amounts of time to complete and it may be difficult to make very small quantities of particular medications. Under Ohio law, a pharmacy may not sell a compounded drug to another pharmacy or a wholesaler. In Ohio, compounded drug preparations must be assigned beyond-use dates that are based on stability and sterility. [1,2]

State boards of pharmacy can and do enforce regulations pertaining to pharmaceutical compounding. For example, in 2006, the Ohio State Board of Pharmacy took action against Home Medical Enhancement Services, Inc. [3] The Board alleged that the company prepared subpotent medications and did not properly sterilize some compounded medications. The Board alleged that there was fungal contamination in some of the company's pulmonary products. State boards of pharmacy also can and do promulgate and enforce sterile compounding standards. [4]

Renewed Regulatory Interest

The matter of regulating compounding pharmacies (or compounding by pharmacies) and manufacturers recently gained renewed attention when an operation in Massachusetts allegedly prepared and distributed corticosteroids that were administered to patients who subsequently developed serious fungal infections. Some of these patients died. According to reports from the Centers for Disease Control and Prevention, the New England Compounding Center and its sister company Ameridose were involved in the production and eventual recall of methylprednisolone acetate (MPA) and other products in September 2012. [5] The methylprednisolone was particularly prone to sterility concerns because it was produced without antimicrobial preservatives, a common practice for medications injected into the fluid of the central nervous system.

Federal Regulatory Scheme

Since then, there have been calls by some for the Food and Drug Administration (FDA) to regulate operations such as the New England Compounding Center. The suggestion is that involving the federal government in regulating compounding by pharmacies will somehow prevent such incidents in a way that oversight by state agencies does not.

The Food and Drug Administration Modernization Act (FDAMA), [6] enacted November 21, 1997, amended the Federal Food, Drug, and Cosmetic Act relating to the regulation of food, drugs, devices, and biological products. FDAMA exempted individualized compounded drug products from the rigid federal current goods-manufacturing practices. Under federal law, drugs that are not manufactured in conformity with federal current goods-manufacturing practices are deemed to be "adulterated" under 21 U.S.C. 351(a)(2)(B) and subject to federal sanction. Under FDAMA, 21 U.S.C. 351(a)(2)(B) does not apply to a drug product compounded by a licensed pharmacist in a state-licensed pharmacy for an

identified individual patient with a valid prescription order -- or in limited quantities before receipt of the valid prescription order. [7,8] *(Editor's note: In early November, the state of Massachusetts, which had already closed 3 compounding pharmacies since the start of the outbreak, adopted new regulations that will allow the Massachusetts Board of Registration in Pharmacy to track drugs made by compounding pharmacies to determine whether they are acting like a manufacturing facility and thus are subject to FDA oversight. [9])*

Of note, some types of compounding activities are prohibited under federal law. For example, compounding is prohibited when the drug product "presents demonstrable difficulties for compounding that reasonably demonstrate an adverse effect of the safety or effectiveness of that drug product." [8] The FDA issued a concept paper directed to "demonstrable difficulties for compounding." [10]

Federal law also prohibits compounding of drugs removed from the market because such drug products, or 1 or more components, have been found to be unsafe or not effective. [8] Compounding drug products that are essentially copies of a commercially available drug product is also prohibited. [8]

Despite calls for increased federal regulation, as this brief discussion demonstrates, current federal law already governs many aspects of modern compounding by pharmacies.

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