

**Testimony before the Committee on Energy and Commerce  
Subcommittee on Health  
United States House of Representatives  
May 22, 2013**

**The Pew Charitable Trusts**

Dear Chairman Pitts, Ranking Member Pallone and members of the Subcommittee,

Thank you for the opportunity to testify on the need for federal legislation to improve the safety of compounded medicines.

My name is Gabrielle Cosel. I work on pharmaceutical quality and safety at the Pew Charitable Trusts, an independent, nonpartisan research and public policy organization.

Pharmacists have always compounded medicines – it is the origin of the profession – but many of the activities we refer to as compounding today are far removed from the traditional practice of preparing individualized medicines for one patient at a time. Some compounders today produce large volumes of drugs and ship them to clinics and hospitals across the country.

In recent months, this committee has repeatedly stressed the responsibility of FDA to ensure the safety of activities that depart from traditional compounding and are more akin to manufacturing. I will focus today on a regulatory framework that clarifies the Agency’s role, ensures that limited resources are used wisely, and sets clear expectations of the industry. First, though, it is important to understand the risks we face.

**Examining the risks**

The epidemic caused by the New England Compounding Center highlights the dangers to patients from compounded drugs. As of May 6, that outbreak has been associated with 55 deaths and 741 serious infections in 20 states.

But what happened at NECC is not an isolated incident. I have included with my testimony a Pew summary that describes 19 additional pharmacy compounding errors since 2001.<sup>1</sup>

These errors caused serious injuries and deaths in at least 29 different states. The list includes 22 additional deaths, as well as serious infections – meningitis, bloodstream, and at least 38 patients who suffered partial or complete loss of vision. It also includes patients harmed by sub-potent or super-potent doses. For example, three people in Oregon and Washington who died after receiving drugs from Texas – intravenous injections for back pain that were *eight times* the labeled strength.<sup>2</sup>

Recent inspections of compounders raise further concern: For example, two months ago, the FDA announced a recall of all of the products manufactured by a New Jersey compounder because of potential mold contamination. The FDA press release referred to “visible particulate contaminants” in what was supposed to be a sterile product.<sup>3</sup> Also this year, a Georgia compounder conducted a nationwide recall of sterile products after reports of serious eye infections.<sup>4</sup>

Compounding errors can cause exponentially greater harms if the product has been produced in mass quantities. There are companies today that compound thousands of packages or vials of medicine and ship them to buyers all over the country, going well beyond the traditional practice of a pharmacist making a single drug in response to a specific prescription for a specific patient. These activities have outgrown the state regulatory structures established to oversee them.

Congress, through section 503(A) of the Food, Drug and Cosmetic Act, already recognizes FDA's responsibility to oversee some compounding activities. Today, we urge you to amend certain elements of this provision to ensure its effectiveness and provide greater clarity on state and federal roles. We urge the following elements:

- 1. When appropriate, large-scale compounding should be subject to higher quality standards – specifically applicable Good Manufacturing Practices (GMPs),**
- 2. FDA is the appropriate agency to oversee GMPs, and states should not exercise redundant oversight,**
- 3. Patients must be protected by ensuring that compounders do not undermine “gold standard” FDA-approved drugs.**

Today, compounding quality standards are set by states. Some states incorporate United States Pharmacopeia standards for sterile and non-sterile compounding (USP chapters 797 and 795, respectively), but experts at a recent pharmacy compounding summit co-hosted by Pew, the American Hospital Association (AHA), and the American Society of Health-System Pharmacists (ASHP) stressed that USP compounding standards were developed for use in pharmacies and are not suitable for larger-scale production.

Compounding large volumes of repeated batches of medicines implies standardized processes that should be subject to appropriate quality standards such as those outlined in current Good Manufacturing Practices (cGMPs) for drug manufacturers.

For example, cGMP requires manufacturers to validate systems and processes to ensure that medicines meet consistent quality and safety standards. Process validation becomes increasingly important as the same drug is compounded in repeat batches. In addition, USP 797 does not require the testing of a drug's starting ingredients, while cGMP does. And expiration dates are set for a manufactured drug based on extensive stability testing. But a beyond-use date for a compounded medicine may in some cases be set by referencing published studies of drugs that may not conform exactly to the compounded product.<sup>5,6</sup> GMPs are developed by the FDA, and the agency is best placed to enforce them.

Facilities that produce large volumes of sterile products, or carry out particularly high-risk compounding, such as manufacturing from a non-sterile bulk ingredient, should be required to register with the FDA. FDA should issue a regulation clarifying the criteria for registration. As with pharmaceutical manufacturing, FDA should inspect compounding facilities on an ongoing basis, with a frequency based on risk.

To avoid an unfunded mandate, the FDA will need adequate resources to conduct ongoing inspections of registered facilities. These resources should be provided through facility fees.

It is important to state that large-scale compounding cannot be addressed simply by asserting these facilities are making unapproved new drugs and requiring them to submit to the New Drug Approval or Abbreviated New Drug Approval process. For example, some large compounders have become a source of intravenous and epidural therapies for hospitals and health systems that do not have the capacity to compound them in-house. Entities that play a role in our health care system should not be left to default or ad-hoc application of full requirements of the FDCA. The regulatory oversight system for these entities should be clearly defined. However, as addressed below, it is important to ensure that compounding does not encourage the sector to produce new drugs that undermine the FDA-approval paradigm.

Under this framework, states may continue to require FDA-registered compounding facilities to hold state pharmacy licenses, but state enforcement of quality standards should be preempted for these facilities. The section 704 provision that exempts pharmacies from the requirement to provide records access to FDA should be removed for registered facilities. Without this authority the FDA will be challenged when it attempts to investigate a facility that should be under its jurisdiction. Such challenges have been well documented. In the wake of deadly meningitis outbreak a Congressional investigation clearly showed that even when the FDA had access to a facility its ability to access records was challenged.<sup>7</sup> Additionally, in March of 2013 the FDA reported that compounders denied FDA investigators access to records in a number of recent cases.<sup>8</sup>

Key safety requirements should also be set at the federal level, such as a “do not compound” list. Congress has already recognized that certain products are not suitable for compounding (frequently cited examples include transdermal delivery systems, biologic products and sustained release formulations) and has given FDA the authority to establish a “do not compound” list. This authority should be maintained and should apply to both FDA-registered and non-registered facilities, as it does now. The section 704 records exemption should also be removed for purposes of enforcing the do not compound list.

It is important to emphasize that compounded drugs do not go through the pre-market approval process that brand and generic drug companies go through to demonstrate safety, efficacy and bioequivalence, along with pre-approval of manufacturing methods and facilities. These are critical systems to protect patients. Because they do not apply to compounders, compounded medicines can never be an adequate substitute for FDA-approved drugs.

Any new federal regulatory scheme must not encourage compounding at the expense of conventional manufacturing. Legislation should be clear that a compounder may not make a copy or a variation of a marketed drug, except when that drug is in shortage or to address specific medical needs of a specific patient. Congress should also prohibit the wholesale of compounded drugs.

Another important safeguard against circumvention of the approvals process is limiting compounding from bulk to only well-characterized and already in-use active ingredients, such as those described by a USP monograph, or those in an existing drug application. These concepts are not new, but are part of current 503A language.

## Conclusion

We thank you for your leadership on this important issue. Congress has long recognized the role of FDA in providing oversight of compounding. It is time to update the Food, Drug and Cosmetic Act to remove ambiguities and create a clear, workable framework to address patient safety.

Thank you for the opportunity to testify, and I welcome your questions.

## References

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<sup>1</sup> The Pew Charitable Trusts. U.S. Illnesses and Deaths Associated With Compounded Medications (2001-Present). April 15, 2013. <http://www.pewhealth.org/other-resource/us-illnesses-and-deaths-associated-with-compounded-medications-85899468587>

<sup>2</sup> U.S. Centers for Disease Control and Prevention. "Deaths from Intravenous Colchicine Resulting from a compounding Pharmacy Error—Oregon and Washington, 2007," Morbidity and Mortality Weekly Report. October 12, 2007. 56(40): 1050-1052. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5640a3.htm>. Accessed January 8, 2013.

<sup>3</sup> Medprep Consulting Inc. "Medprep Consulting Inc. Announces Voluntary Nationwide Recall Of All Lots Of All Compounded Products Due To Potential Mold Contamination." Press Release. March 20, 2013. <http://www.fda.gov/Safety/Recalls/ucm344787.htm>.

<sup>4</sup> U.S. Food and Drug Administration. "FDA alerts health care providers and patients of the nationwide recall of all lots of sterile products distributed by Clinical Specialties Compounding Pharmacy". Press Release. March 21, 2013. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm345019.htm>

<sup>5</sup> United States Pharmacopoeial Convention. USP–NF General Chapter <797> Pharmaceutical Compounding—Sterile Preparations.

<sup>6</sup> 21 CFR 211. Current good manufacturing practice for finished pharmaceuticals.

<sup>7</sup> Committee on Energy & Commerce, Majority Memo. "The Fungal Meningitis Outbreak: could it have been prevented?" Nov 12, 2012. <http://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/Hearings/OI/20121114/HMTG-112-HHRG-IF02-20121114-SD001.pdf>

<sup>8</sup> Hamburg, Margaret A. "FDA Must Have New Authorities to Regulate Pharmacy Compounding." FDA Voice. March 22, 2013. <http://blogs.fda.gov/fdavoices/index.php/2013/03/fda-must-have-new-authorities-to-regulate-pharmacy-compounding/>