

United States House of Representatives Energy and Commerce Committee

Subcommittee on Health

Hearing: “Examining Implementation of the Compounding Quality Act”

Written Testimony of:

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On Behalf of the National Community Pharmacists Association (NCPA)

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Chairman Burgess, Ranking Member Green and Members of the Subcommittee:

Thank you for conducting this hearing on compounding and providing me the opportunity to share my views and personal experiences. My name is Jake Olson and I am a pharmacist owner of four pharmacies located in the Children’s Hospital of Wisconsin and their outlying specialty clinics in the greater Milwaukee area.

In 2003 I opened Skywalk Pharmacy as the first independently owned community pharmacy located in a children’s hospital in the United States to serve the unique needs of pediatric patients. My pharmacies specialize in patients with cystic fibrosis, oncology, and organ transplants with a focus on specialty and compounded medications. On average, we fill 500 prescriptions amongst my 4 locations, only for children.

Of those 500 prescriptions, we compound roughly 100 of those per day by primarily taking tablets and capsules approved for adults, and making them into a liquid to be dosed correctly for a child. I am a member of the National Community Pharmacists Association (NCPA) and serve on NCPA's Compounding Steering Committee.

NCPA represents America's community pharmacists, including the owners of more than 22,000 independent community pharmacies. Together they represent an \$80 billion health care marketplace and employ more than 250,000 individuals on a full or part-time basis. I am here today as a healthcare provider and small business owner to present some of my experiences and those of my fellow independent pharmacists, focusing on quality compounded preparations and patient access.

In this statement, NCPA would like to present our thoughts on important issues surrounding implementation of the Compounding Quality Act. According to a NCPA member survey, over 88% of our members provide some form of compounding services. Also, over 95% of survey respondents stated they do not plan to register as a 503B outsourcing facility. Therefore, most of our members are held to the laws and regulations of section 503A of the Food, Drug, and Cosmetic Act.

Compounding is a backbone of pharmacy practice and for many decades independent community pharmacists have provided millions of adults, children, and animals with access to safe, effective and affordable medications through compounding services. When manufactured drugs aren't an option, independent community pharmacists provide traditional pharmacy compounding to prepare customized medications for patients.

Independent community pharmacies perform a wide variety of compounding services including hormone replacement medications, making suspensions out of tablets and capsules to allow for pediatric patients to receive correctly dosed medications, different dosage forms for patients suffering from intractable nausea and vomiting, and removing allergy causing excipients from commercially available products, to name a few. Compounding services can help bridge the gaps during times of prescription drug shortages, such as those occurring now with oral suspensions used for flu patients.

It is important to note that pharmacist compounding is an integral part of the pharmacy profession and that compounding occurs in many pharmacy settings, including hospitals. All compounding pharmacies should be held to the same standards so that patients have assurance that they are receiving the same quality regardless of whether the compounded medication is from a hospital or community pharmacy.

It is essential that patient access to vital compounded medications is preserved in the patient-physician-pharmacist triad. Providers must be able to choose the best medication for the patient's well-being.

Along with every American, NCPA member pharmacists were horrified by the tragic consequences of the fungal meningitis outbreak triggered by the reckless actions of NECC. We appreciate the thorough, bipartisan approach that this committee undertook to examine what changes, from both the regulatory enforcement and legislative fronts, were necessary to help prevent such an epidemic from recurring, while preserving patient access to essential, customized medications. NCPA subsequently endorsed the bipartisan law that emerged from those efforts, the Compounding Quality Act.

However, because of the FDA's implementation and enforcement of the Compounding Quality Act, providers lack much needed clarity and access to compounded medications has been negatively impacted.

For providers to gain clarity and for access to be ensured, NCPA strongly supports bipartisan legislation, H.R. 2871, *the Preserving Patient Access to Compounded Medications Act*, by Reps. Morgan Griffith (R-Va.) and Henry Cuellar (D-Tex.).

We greatly appreciate this opportunity to provide our input on these important issues.

1. State Board of Pharmacy Oversight of Pharmacy Compounding is Critical

NCPA has always and will continue to advocate that pharmacy compounding is best regulated by the state Boards of Pharmacy while manufacturing is overseen by the FDA. Pharmacy compounding of medications is an important part of medical care that allows for the dispensing of custom-made medications and should continue to be regulated by state Boards of Pharmacy, as all other medical licensed professional practices are. If the FDA has a concern about an appropriately-licensed pharmacy, then the FDA has the authority to ask the state Board of Pharmacy to work with them to address the issue. If it is found that an entity acting under the guise of a pharmacy has exceeded their state-regulated authority, then the state Boards of Pharmacy should suspend the license of the pharmacy until it complies with state laws and regulations governing compounding or meets FDA standards and registers with the FDA.

2. **FDA Must Reverse Stance on Office-Use Compounding**

Office-use compounding occurs when a pharmacist compounds a limited quantity of a medication that due to medical necessity must be administered in an office or clinical setting by the physician. By prohibiting all office-use compounding by 503A pharmacies, FDA disregards the plain language of Section 503A and the fact that Section 503A permits office-use, as well as disregards Congressional intent that states should continue to oversee traditional compounding practice, including office-use compounding.

The majority of pharmacy practice acts and state regulations authorize some form of office-use compounding. In addition, Congress has weighed in on multiple occasions and in multiple ways reminding FDA that office-use compounding should still be allowed in states that authorize its use. This includes several Statements for the Record that were given and floor speeches that were made during passage of the Drug Quality & Security Act.¹

Appropriators have also been clear with FDA on the issue of office-use and its allowance in the House Reports accompanying the FY2016 and FY2017 Omnibus Appropriations Acts, as well as House Report language in the FY2018 FDA/Agriculture Appropriations Act.

¹ Senator Coburn (OK). “Drug Quality and Security Act.” *Congressional Record* 159: 162 (November 14, 2013) p. S8029.
Senator Boozman (AR). “Drug Quality and Security Act.” *Congressional Record* 159: 164 (November 18, 2013) p. S8073.
Representative Griffith (VA). “Drug Quality and Security Act.” *Congressional Record* 159: 131 (September 28, 2013) p. H5963.
Representative Green (TX). “Drug Quality and Security Act.” *Congressional Record* 159: 131 (September 28, 2013) p. H5963.

Unfortunately, FDA continues to prohibit all office-use compounding by 503A pharmacies, ignoring the plain language of Section 503A, Congressional intent, current state laws or regulations, and even contradicting the FDA's own current draft guidance document "Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act," as well as FDA's previous rationale regarding office-use compounding. This previous rationale includes the FDA circulating in 2012 a draft compliance policy guidance that would have allowed for office-use compounding under 503A, with some restrictions. The relevant statutory language of 503A was not changed by the DQSA, yet FDA is taking the position that the same language now prohibits office-use compounding, even where expressly authorized by state law.

Section 503A limits interstate "distribution" of compounded medications to quantities that do not exceed 5 percent of the total prescription orders dispensed or distributed unless a state enters a MOU with the FDA addressing the distribution of compounds above the 5% threshold.² Based on the statute, this 5% rule is meant to limit what constitutes "distribution" under Section 503A, that is compounding for office-use. Other Federal laws support this construction. For example, the Controlled Substances Act (CSA) permits pharmacies to distribute for office-use without a distributor's license so long as their office-use distribution does not exceed 5%.³

² 21 U.S.C. §353a(3)(B)

³ 21 U.S.C. §802(10)-(11)

The permission contained within the CSA is the same statutory approach set up by Section 503A permitting pharmacies to distribute up to 5% of their compounded medications interstate, e.g., compounds for office-use. Many State laws also adopt a similar 5% rule permitting office-use distribution.⁴

NCPA contends that Congressional intent is very clear in that compounding for office-use is permitted under Section 503A. We fully support the 65 Members of Congress who wrote the FDA in May of 2017 asking that the final office-use guidance be rescinded and that the FDA work with stakeholders to develop a proposed rule that authorizes office-use compounding by 503A pharmacies when authorized by state law.

3. Not All Office-Use Compounding Needs Can be Met by Outsourcing Facilities

NCPA is very concerned that FDA has taken the position that health care providers can easily obtain all needs for office-use compounds via Section 503B outsourcing facilities. 503B outsourcing facilities provide an important function in meeting the needs of healthcare providers and patients, however outsourcing facilities are not able to meet the entire office-use market nor are they able to replace the role of traditional compounding pharmacies practicing under Section 503A.

⁴ Wisc. Stat. §450.01(23)(e); Wisc. Admin. Code Pharm. §13.02(11)(e); 12 Alaska Admin. Code §52.695(5)(A); Ariz. Stat. §32-1981(7)(d)

Because of the requirements placed on outsourcing facilities (limited to positive list, clinical need, cGMP validation procedures) and the cost of complying with cGMP, outsourcing facilities are not able to compound in small batches, thus limiting the role they can play in meeting immediate patient needs for compounds. As an example, outsourcing facilities have told us that when an ophthalmologist or urologist needs a sterile compound which is not a common formula for that facility they must refer the clinic to a 503A pharmacy.

NCPA has continually offered FDA input regarding compounded medications that are needed by providers in office settings.

The following is a non-exhaustive list of both non-sterile and sterile compounded office-use products that community healthcare providers rely on from our members. As discussed above, 503B outsourcing facilities are not able to provide many commonly needed office-use products, and by prohibiting 503A pharmacies to compound for office-use, FDA is severely limiting access to these products.

- Anesthetic gels/creams for dental, ENT and dermatology practices. In the past, practices could keep a jar/pump or tube of these available in the office for when patients needed them. The patient-specific requirement has created several issues. MDs may not know what the patient needs until they are seen. If they need to do a procedure, now the patient must schedule a second visit because they don't have the anesthetic available in the office. This creates waste. Many patients only need a small amount, but when a patient-specific prescription is generated it is typically for 30 to 60 grams. Depending on the procedure the MD may only use 5 grams for the patient.

- Erectile Dysfunction injections (Tri-mix, Quad-mix). The first dose of these medications is always given in the office to determine the best formulation and dosage. Now patients are forced to buy it before the physician has tried it and they must transport it (sometimes refrigerated) to the office for their first dose. If it doesn't work, they must buy another prescription. The importance of the physician-patient interaction, including counseling and education, at the time of the office visit necessitates the medication be on hand to ensure access to the right dosage of medication at the right time.
- Phenol and Cantharidin both used in podiatry and dermatology. These are items that like anesthetic gels are easily kept in office for when a patient presents and needs them. They use a very small amount on each patient. Having a patient-specific prescription for a whole bottle is wasteful and again causes delay in treatment.
- Ophthalmic injections and "emergency" eye drops. The physician does not know when a patient will present with a need for these items. Pharmacies often get frantic phone calls at the end of the day for these medications. Literally waiting until the next day could cause loss of vision. Many times, the MD is forced to admit the patient to the hospital if they cannot locate these items within a few hours.
- Iontophoresis solutions for use in physical therapy (Potassium Iodide, Dexamethasone).
- Pain creams for hand therapists in a Hand, Shoulder & Elbow Surgical group. Mostly Ketoprofen, Gabapentin, and Lidocaine.

- Children's dentistry (Hydroxyzine Pamoate Suspension for anxiety).
- Chemical peels for dermatologists.
- Anesthetics for numbing prior to laser resurfacing.
- Lidocaine/Oxymetazoline for nasal rinsing in office.
- Phenol for inner ear procedure.

4. FDA Must Clearly Differentiate Between “Distribute” and “Dispense” In the MOU

NCPA remains concerned that FDA continues to use the term “distribute” and “dispense” in an interchangeable manner, when in fact these terms are distinct and clearly defined in both Federal and State law. In Section 503A, Congress did use the words “distribute” and “dispense” as mutually exclusive categories, in the same sentence, and separated them by “or.”⁵ Congress used the two words in the same sentence to mean two different things, as they have repeatedly used these two terms to mean different things.⁶ NCPA requests that FDA follow the intent of Congress and treat these two terms as separate and distinct activities.

⁵ 21 U.S.C. §353a(3)(B)(ii)

⁶ FDCA §581(5), 21 U.S.C. §802(10)-(11), and 21 CFR §208.3

By defining “distribution” to include dispensing in the MOU, FDA disregards the plain language of Section 503A and the fact that Section 503A permits office-use, as well as disregards Congressional intent that states should continue to oversee traditional compounding practice. In the availability notice of the draft MOU, FDA states “interstate distributions of compounded drug products would count toward the 30 percent limit whether or not the compounded drug products satisfied the prescription condition, or other conditions, in section 503A of the FD&C Act.”⁷ FDA also states, “under our draft standard MOU, a distribution occurs when a compounded drug leaves the facility where it was made, regardless of whether the drug is also deemed to be dispensed.”⁸

NCPA disagrees with FDA’s inclusion of “dispensing” in the definition of “distribution,” as the plain language of Section 503A does not support this conclusion. Section 503A states that the MOU should address the “distribution of inordinate amounts of compounded drug products interstate and provide for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State.”⁹ There is no allowance in the statute for FDA to address dispensing in the MOU.

NCPA also disagrees with FDA’s reasoning behind including “dispensing” in the definition of “distribution.” That is, Congress did use the words “distribute” and “dispense” as mutually exclusive categories, in the same sentence, and separated them by “or.”¹⁰

⁷ 80 Fed. Reg. 8877

⁸ *Id.*

⁹ 21 U.S.C. §353a(3)(B)(i)

¹⁰ 21 U.S.C. §353a(3)(B)(ii)

Therefore, FDA’s assertion that there is nothing “to suggest that Congress understood distributed and dispensed to be mutually exclusive categories rather than overlapping categories” is not persuasive. Congress used the two words in the same sentence to mean two different things, as they have repeatedly used these two terms to mean different things.¹¹

FDA should follow the plain language of the statute when developing the final MOU as directed by Congress, and ensure that the MOU only addresses “the distribution of inordinate amounts of compounded drug products interstate.”¹² FDA should not include the interstate dispensing of compounded drugs in the definition of distribution, and instead leave the practice of dispensing compounded drugs to oversight by the States, as Congress intended.

By not allowing 503A pharmacies to compound for office-use, the current MOU eliminates all non-sterile office-use compounding and severely limits access to sterile office-use compounding.

NCPA is very concerned that FDA is attempting to regulate traditional compounding pharmacies and the patient-specific compounds they dispense through the MOU process. FDA, with the proposed MOU, would have the authority to oversee traditional compounding pharmacy practice based solely on the location of a patient.

¹¹ FDCA §581(5), 21 U.S.C. §802(10)-(11), and 21 CFR §208.3

¹² 21 U.S.C. §353a(3)(B)(i)

Many pharmacies specialize in specific treatment areas and because of their expertise, these pharmacies have relationships with doctors and patients in wide geographic areas, are registered in multiple states, and ship their medications. Under the draft MOU, most would involuntarily be deemed an outsourcing facility by FDA. In some cases, these pharmacies may not compound sterile products, and therefore would not be eligible to become an outsourcing facility.

Also, based on the current proposed threshold and how it's calculated, pharmacies that provide only compounds, and no general non-compounded prescription products, will always be at a great disadvantage when calculating what constitutes an "inordinate amount of compounded human drug products interstate". Some NCPA members are compounding-only pharmacies, and do not dispense any non-compounded prescriptions, and therefore would be at a mathematical disadvantage to their colleagues who have "hybrid" pharmacies, i.e. those that provide both traditional prescription services in addition to compounds.

Specifically, we are concerned that the arbitrary cap provides no protections for patients who live in different parts of the country throughout the year or those that may live in states with smaller populations. They and the physicians who treat them would potentially not be able to obtain the compounds they need simply because they do not live in the same state with the pharmacy that they need to provide their medication.

The lack of any protections for border pharmacies is also of great concern to NCPA. FDA does not consider location of the pharmacy in the proposed MOU.

Many NCPA members are in areas, both urban and rural, that border one or more states and by not providing exceptions for these circumstances, FDA is punishing these pharmacies that may ship medications to their patients over state lines. While we appreciate FDA trying to account for some of these situations by allowing for an exemption for patients who drive or walk across state lines to pick up their own medications, this scenario is oftentimes not an option, especially for frail, elderly patients.

5. FDA Must End Inspection Reporting Discrepancies Between Manufacturers and Compounding Pharmacies

When inspected by the FDA, our members pharmacies potentially receive an FDA Form 483. This form is issued after an inspection when the investigator(s) observed any conditions that in their judgement may constitute violations of the Food Drug and Cosmetic Act and related Acts. It is important to note that the compounding inspections that have been conducted to date by the FDA are focused on community-based compounding pharmacies. FDA has inspected only 1 physician compounder and no federal facilities, to our knowledge. We are also unsure how many compounding pharmacies residing in health systems have been conducted but believe this number to be very small or none.

NCPA feels strongly about the quality of compounded medications and after learning of several of our members experiences with FDA inspections and subsequent public posting of Form 483s we sought information on how the inspections were like those of FDA-registered manufacturers. The observations being documented at FDA-registered facilities are very similar to those that FDA publicly reports as unsafe in a compounding environment.

When a Form 483 is presented to a compounding pharmacy, it is also posted by the FDA to the FDA website. Conversely, when perusing the FDA website to search for any Form 483s given to FDA-registered manufacturers, all that can be found are inspection citations and inspectional observation summaries. We have been unable to find any Form 483 for a FDA-registered manufacturer facility posted to the FDA website.

The manufacturer inspection citations are on an excel spreadsheet and list a brief description of the general nature of the violation. The inspectional observation summaries summarize the number of 483s in various fields and you can expand a specific field to see the frequency of the violation. The manufacturers found on these spreadsheets are well-known.

The information posted to the website pertaining to inspections of compounding pharmacies are much more detailed and in depth than those posted for FDA-registered manufacturers. Many of the observations found in compounding pharmacies are the exact same ones found in FDA-registered manufacturing facilities. However, FDA presents the findings of inspections of compounding pharmacies in a much more intense manner than those of registered manufacturers.

While FDA publicizes Form 483s and photographs from compounding pharmacy inspections, we have evidence of several of the same observations from cGMP manufacturers, with no corresponding publicity. This treatment suggests there is intent by the FDA to sway the public to be afraid of compounding.

The observations from inspections of compounding pharmacies have been over generalized as applying to the entire profession. This has led some to believe most of compounding is done in substandard conditions, when this is not the case. These overgeneralizations are detrimental to pharmacies and patients.

Violations do occur in even the most advanced manufacturing processes. Unfortunately, the public is unable to see more details of violations found in FDA-registered facilities as manufacturer 483s are not public information. At the same time, 483s from compounding facilities are publicized.

6. FDA Must Make Key Changes to the Pharmacy Compounding Advisory Committee (PCAC) and Associated Activities

As the FDA and PCAC members continue to consider which drugs nominated will be considered for inclusion on the 503A “positive” list, among other responsibilities, NCPA is committed to working with the FDA and stakeholders on these critical issues. However, we have concerns with the creation, oversight and operation of the PCAC and associated processes.

Among these concerns are the following:

Inadequate member selection and renewal processes. NCPA remains concerned that none of our nominees to the PCAC were ever contacted. Unfortunately, there is currently not one voting member of the PCAC who compounds for human use daily.

NCPA finds this fact astounding considering the Committee is making recommendations that can vastly impact the practice of compounding. The previous FDA PCAC had at least three pharmacists with current experience and expertise in compounding, one of which specialized in sterile compounding. The FDA should select at a minimum one practicing human compounder on the Committee as a voting member.

Despite Congressional intent and prior FDA actions to include voting members with current expertise and experience in compounding on the PCAC, it is our understanding the Agency has cited potential conflicts of interest in having compounding pharmacists as voting members of the Committee. However, the appearance of impartiality of the Committee could be questioned by voting members whose organizations actively lobby Congress on the very issues they vote upon while serving on the PCAC. We also ask that the FDA provide greater transparency throughout the process of selecting members to serve on the PCAC and make certain that the compounding pharmacy and patient voice of those who depend on these compounded medications are represented.

FDA's insistence that any bulk drug substance not voted onto the positive list can easily be obtained via the investigational new drug (IND) process. This is a cumbersome, timely and expensive process, especially for community health care practitioners who have previously presented their real-life concerns with the IND process to the Committee.

Unequal time allotted for nominators to defend substances and respond to Committee questions. Throughout this entire process, each nominated substance is given a total of 10 minutes to be defended by nominating organizations, and oftentimes nominators will have to split this time up, all while the FDA has unlimited time to present their review and opinions related to the nominated substances. In addition, nominators have a limited time frame to organize their presentations (normally less than 3 weeks), where FDA has months to prepare. NCPA has concerns that FDA allows their own representatives and speakers to participate via conference calls for all PCAC meetings, but has refused our request that stakeholders be allowed to do the same.

FDA's indication that it does not consider USP monographs for dietary supplements to be "applicable" USP or NF monographs, therefore limiting compounding to only USP drug monographs when no basis exists for FDA to exclude USP or NF monographs for dietary supplements. This is of great trouble to NCPA as it defies logic that these substances can be easily obtained by the public at any Costco, Wal-Mart or CVS for example, but in the hands of health care practitioners are not to be trusted. The practice of compounding is built on the patient-physician-pharmacist triad, and there is no better way to oversee the use of these preparations than through this relationship.

A confusing nominating and review process that leaves many unanswered questions for health care practitioners and patients who rely on compounds. NCPA contends that it was premature for the FDA to have solicited nominations for the 503A list, as well as selected six products to consider at the first PCAC meeting, before developing and agreeing on criteria used to develop the list.

In addition, when nominating we were asked for all possible uses of the substances, not the most likely. We are also concerned that the FDA has separated substances in the 503A bulk drug substances interim policy based on nothing more than if the Agency considers that adequate information to evaluate the substance was included as part of the nomination process. Not being able to compound with these substances (included on FDA's 503A List 3) is causing impaired patient access. Not to mention that many of the substances included on List 3 are by FDA's own definition not active pharmaceutical ingredients that should even be under discussion.

Lastly, NCPA has concerns regarding FDA's recommendations for the Difficult to Compound List. It is important that the PCAC keep in mind that while dosage forms under consideration for the List may not be utilized in compounding practices today, there may come a time when technology advances to the point where pharmacies could be able to make these dosage forms. NCPA strongly urges the PCAC to approach the Difficult to Compound List in a very limited way to not stifle future innovation, technology and research.

The intent via Congress of this process was to increase appropriate access to bulk drug substances without a USP/NF monograph or from an FDA approved product. Unfortunately, quite the opposite is occurring.

Conclusion

In summary, NCPA is committed to working with Members of the Health Subcommittee, the FDA, and other stakeholders regarding these important matters. NCPA strongly supports H.R. 2871, *the Preserving Patient Access to Compounded Medications Act* as a much-needed clarification and strengthening of the Compounding Quality Act. We appreciate your consideration of our statement. Thank you.