April 29, 2024

Food and Drug Administration
10903 New Hampshire Ave
WO 51, Room 2231
Silver Spring, MD 20993

Submitted via e-mail: linda.joy@fda.hhhs.gov; Compounding@fda.hhs.gov

Re: Statement for the Record for FDA Drug Compounding Annual Listening Session on May 14, 2024

Dear Sir or Madam:

The National Community Pharmacists Association (NCPA) welcomes the opportunity to provide a statement for the record to the FDA Drug Compounding Annual Listening Session on May 14. NCPA appreciates the willingness of FDA to engage in discussion with impacted stakeholders and hopes this productive dialogue will continue in the future.

NCPA represents America's community pharmacists, including 19,400 independent community pharmacies. Almost half of all community pharmacies provide long-term care services and play a critical role in ensuring patients have immediate access to medications in both community and long-term care (LTC) settings. Together, our members represent a $94 billion healthcare marketplace, employ 230,000 individuals, and provide an expanding set of healthcare services to millions of patients every day. Our members are small business owners who are among America's most accessible healthcare providers. NCPA hopes that FDA will address our concerns below.

Concerns with Patient Access to cBHT

NCPA expresses concern with maintaining appropriate access to cBHT. An April 2022 meta-analysis in *Menopause: Journal of The North American Menopause Society* concluded that there is no evidence that compounded hormones pose an increased clinical risk compared to FDA-approved products.[1] This article also demonstrates that clinically relevant information regarding cBHT was omitted from the 2020 report[2] that the National Academies of Sciences, Engineering, and Medicine (NASEM) provided to the FDA.

We also re-iterate our arguments made in a September 2020 letter to FDA, jointly written with the National Alliance of State Pharmacy Associations (NASPA) and the Alliance for Pharmacy

[1] See "Menopause publishes cBHT meta-analysis," *Alliance for Pharmacy Compounding.* April 1, 2022. Available at: APC: Menopause publishes cBHT meta-analysis (a4pc.org).

[2] See "The Clinical Utility of Compounded Bioidentical Hormone Therapy: A Review of Safety, Effectiveness, and Use (2020). Available at: The Clinical Utility of Compounded Bioidentical Hormone Therapy: A Review of Safety, Effectiveness, and Use | The National Academies Press.

Compounding (APC).[3] In this letter, we criticize the NASEM report, especially considering that the NASEM committee lacked experts on compounding, and the NASEM report went well beyond its charge, which was to focus on the clinical utility of therapies, particularly when recommending that almost all hormones that are used in cBHT be considered for FDA's difficult to compound list. NCPA and its members who compound hormone therapies have engaged in several advocacy opportunities to gather patient and prescriber feedback on cBHT, including participating in a cBHT testimonial portal conducted by The Partnership for Personalized Prescriptions, as well as a prescriber survey.

Insanitary Conditions Overreach

In November 2020, FDA issued its final guidance *Insanitary Conditions at Compounding Facilities: Guidance for Industry*. Unfortunately, FDA failed to respond to most of the comments NCPA provided on November 26, 2018, when the original draft guidance was released. Now, nearly six years after NCPA submitted comments, there are still unresolved questions regarding the differences between the guidance and the requirements of USP <797>. Specifically, the encouragement of recalls of possibly contaminated product, adequate coverage of hair and skin when compounding drugs in sterile environments, and terms used by the FDA in the guidance left undefined and vague which makes compliance difficult and burdensome for compounders.

Any Future MOU

NCPA welcomes FDA's delay of implementation of the MOU on October 21, 2022 until the effective date of a final rule regarding certain distributions of compounded human drug products and publication of an updated standard MOU.[4] NCPA also supported FDA's past suspension of the October 2020 MOU, its plans to establish a new MOU through rulemaking, and its "plans to further extend the period during which FDA does not intend to enforce the statutory 5 percent limit during the rulemaking process."[5]

NCPA hopes that any future MOU will address our previously stated concerns. First, we hope that states are given sufficient time to assess any conflicts of law, and if they choose to sign, modify existing laws to comply with the MOU. Already, several state boards of pharmacy have raised issues about the potential conflicts between the old MOU and existing state laws regarding confidentiality of information – which conflicts with the reporting requirements of the old MOU. Some of these states have significant patient populations who use compounded drugs.

We also remain concerned about the consequences of not signing the MOU on patient access to essential compounded medications. Pharmacies in states that sign the MOU will be permitted to provide patients with personalized medications unimpeded. In states that choose not to sign, a five percent cap on interstate shipments would be imposed on pharmacies. NCPA is also

[3] See Microsoft Word - Joint Pharmacy Draft Letter to FDA NASEM Report.docx (ncpa.org).
[4] See 2022-22876.pdf (govinfo.gov).
[5] See Memorandum of Understanding Addressing Certain Distributions of Compounded Drugs | FDA.

concerned that patients who rely on compounded medications from pharmacies in states that cannot or do not sign the final MOU deadline will be penalized by disruption of care and inability to receive therapy from their pharmacy of choice.

NCPA also disapproves of the way FDA has structured the past MOU. NCPA continues to have issues with both the process and the content of the old MOU – we believe FDA conflates the definitions of "distribute" and "dispense" without Congressional authorization.

The statutory language in section 503A of the FDCA directing FDA to establish an MOU with states requiring reporting of interstate distributions of compounded drugs is now outdated and does not make sense in the context of the establishment of 503B outsourcing facilities under the DQSA. We hope that FDA will work with NCPA, NABP and other pharmacy stakeholders on consensus legislation to update this statute to require reporting by pharmacies of interstate dispensing and distributions of compounded drugs without the need for states to sign an MOU that may conflict with state laws and without the arbitrary and punitive 5% cap in the current law.

Addressing Drug Shortages

NCPA also urges FDA to continue to dialogue with stakeholders on addressing drug shortages. NCPA recommends that FDA adopt a policy to permit 503A compounding pharmacies to be a tertiary supplier of office stock compounded medications when others are unable to provide medications, as shown by the issues with supply during the Public Health Emergency and recognized by the Agency's Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Pharmacy Compounders not Registered as Outsourcing Facilities During the COVID-19 Public Health Emergency Guidance for Industry.[6]

NCPA supports the Patient Access to Urgent-Use Pharmacy Compounding Act (HR 167), which creates a narrow path for 503A to source shortage drugs (on the FDA or ASHP shortage list) to hospitals and clinics when they cannot be acquired from a manufacturer or 503B.[7]

Demonstrably Difficult to Compound Federal Register Notice

FDA has issued a proposed rule[8] to establish criteria for two lists of drug products or categories of drug products that present demonstrable difficulties for compounding (Demonstrable Difficulties for Compounding Lists or DDC Lists) under certain sections of the Federal Food, Drug, and Cosmetic Act. Drug products or categories of drug products that appear on the DDC Lists cannot qualify for certain statutory exemptions, and therefore may not be compounded under,

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[6] https://www.fda.gov/media/137125/download.

[7] H.R.167 - 118th Congress (2023-2024): Patient Access to Urgent-Use Pharmacy Compounding Act of 2023 | Congress.gov | Library of Congress.

[8] See Drug Products or Categories of Drug Products That Present Demonstrable Difficulties for Compounding Under Sections 503A or 503B of the Federal Food, Drug, and Cosmetic Act (March 20, 2024). Federal Register, 19776. Available at: 2024-05801.pdf (govinfo.gov).

either section 503A or section 503B, respectively. FDA is also proposing to establish criteria for evaluating drug products or categories of products for inclusion on one or both lists. For evaluating drug products or categories of drug products for inclusion on the DDC Lists, FDA is proposing to establish the following criteria: the formulation complexity, drug delivery mechanism complexity, dosage form complexity, complexity of achieving or assessing bioavailability, compounding process complexity, and complexity of physicochemical or analytical testing of the drug product or category of drug products. Additionally, FDA is proposing to identify the first three categories of drug products on both DDC Lists: (1) oral solid modified-release drug products that employ coated systems (MRCs), (2) liposome drug products (LDPs), and (3) drug products produced using hot melt extrusion (HMEs).

While most of NCPA's compounders do not compound the above three categories under current technology, our compounders would like to reserve the right to compound such products in the future. Additionally, NCPA opposes this proposed rule, as it does not believe that stakeholders have a sufficient notice and comment period and FDA is seeking to finalize both criteria for creating the drug products for inclusion on the DDC Lists, as well as the actual categories to include on the DDC lists.

FDA's Draft Report and Plan for Guidance Documents, Removing the Public Notice and Comment Period

FDA has also issued a notice of availability and request for comments for removing the comment period for draft guidance. Specifically, FDA sought input on whether there are any additional circumstances, categories of guidance documents, or topics for guidance for which it may be appropriate and consistent with the FD&C Act and FDA's GGP regulation for FDA to consider issuance as a Level 1 guidance document for immediate implementation without prior public comment. [9] Additionally, in the request for comments, FDA stated that for Level 2 guidance documents (i.e., guidance documents that set forth existing practices or minor changes in policy), the FD&C Act and FDA's GGP regulation require that FDA provide for public comment ***upon implementation*** [NCPA emphasis]. [10] Additionally, "FDA does not solicit public comment prior to implementation of Level 2 guidance documents or of Level 1 guidance documents for which "prior public participation is not feasible or appropriate." [11]

NCPA is concerned that if finalized, FDA will use both Level 1 and Level 2 guidance to change compounding policy without proper notice and comment period for stakeholders, including from compounding pharmacies. NCPA did not have the opportunity to comment on this request for

[9] See Food and Drug Administration's Draft Report and Plan on Best Practices for Guidance; Availability (January 3, 2024). Federal Register, 382. Available at: 2023-28872.pdf (govinfo.gov).
[10] See Food and Drug Administration's Draft Report and Plan on Best Practices for Guidance; Availability (January 3, 2024). Federal Register, 381. Available at: 2023-28872.pdf (govinfo.gov).
[11] See Food and Drug Administration's Draft Report and Plan on Best Practices for Guidance Federal Register, 6. Available at: Section 2505 Guidance Report and Plan (fda.gov).

comment, as it did not explicitly mention compounding and thus evaded our search for comment opportunities. NCPA requests that FDA not use Level 1 and Level 2 guidance to circumvent the normal notice and comment period for compounding policies that FDA is considering. Instead, NCPA requests that FDA continue to use sufficient notice and comment periods in the Federal Register for stakeholders to comment on compounding policies prior to finalization.

Draft Guidance - Prohibition on Wholesaling Under Section 503B of the Federal Food, Drug, and Cosmetic Act [Docket No. FDA–2023–D–0939]
According to FDA's draft guidance:

> Section 503B(a)(8) of the FD&C Act provides that the prohibition on wholesaling "does not prohibit administration of a drug in a health care setting or dispensing a drug pursuant to a prescription executed in accordance with section 503(b)(1)." FDA interprets this provision to mean that a drug compounded by an outsourcing facility may be eligible for the exemptions in section 503B of the FD&C Act where the drug is distributed directly from an outsourcing facility to a health care facility, such as a hospital or clinic, where the drug is administered to a patient, **or to a State-licensed pharmacy** or Federal facility where the drug is dispensed pursuant to a prescription executed in accordance with section 503(b)(1) of the FD&C Act.[12] [NCPA emphasis]

FDA's policy is likely to create patient access challenges for low volume compounded medications. If outsourcing facilities are selling manufactured-scale compounded products to state-licensed pharmacies, 503A compounders will likely reduce or cease compounding activities. Patients who rely on compounded therapies which may not be suitable for scale production will suffer because without larger volume prescriptions, 503A pharmacies can no longer invest in the quality systems and laboratory to provide the personalized medications for the smaller demand patient populations. This may create unintended consequences where 503As will compound less or may close entirely. This in turn will negatively impact patient access, as more 503As will not be able to provide such compounds to their patients.

There is currently a shortage of 503As doing sterile compounding, particularly in rural and underserved areas. A further decrease in 503A pharmacies performing sterile compounding will further harm patient access. We have a member in Bismarck, North Dakota that is the only 503A left in the state that performs sterile compounding, and his pharmacy also provides compounded medications for patients in Montana and Minnesota. A NCPA member in Jamestown, NY stated that the nearest pharmacy to him that performs sterile compounding is another one of his

[12] See Prohibition on Wholesaling Under Section 503B of the Federal Food, Drug, and Cosmetic Act Guidance for Industry (June 2023). Available at: Prohibition on Wholesaling Under Section 503B of the Federal Food, Drug, and Cosmetic Act (fda.gov).

pharmacies in Erie, PA (60 miles away), followed by one in Buffalo, NY (80 miles away), while there are no sterile compounding pharmacies for hundreds of miles to the east and south.

Additionally, NCPA is further concerned about unintended effects to patient safety. In a traditional relationship the pharmacist who oversees the preparation and dispensing of the customized medication will know about the needs of the patient and prescriber. In this new scenario that FDA is creating, the pharmacy is likely ignorant of compounding details, ingredients, and appropriateness.

Stability Study Delays for USP Category 3 Sterile Compounding

NCPA is concerned with the implementation and enforcement of recent changes to USP Chapter <797>, particularly the requirement that sterile compounding pharmacies have completed stability studies for Compounded Sterile Preparations (CSPs) in Category 3. As a trade association representing compounding pharmacists, we recognize the importance of ensuring CSPs are stable and free from microbial contamination through the expected beyond-use date of the product. We fully support the FDA's efforts to uphold rigorous standards in pharmaceutical compounding.

A complication NCPA has been made aware of is a current and significant delay in obtaining stability test results from the analytical labs. Testing laboratories are experiencing considerably longer turnaround times, largely due to the increased volume of testing requests that the new <797> standard has prompted.

While we acknowledge the importance of ensuring the stability and microbial safety of Compounded Sterile Preparations, we wish to bring your attention to the practical implications of the current testing backlog. Sterile compounders are diligently working toward completing stability studies. However, the extended turnaround times for test results are, in some cases, hindering their ability to comply with the regulatory requirement within the expected timeframe.

Therefore, we urge the FDA to consider the testing backlogs and the impact as FDA is reviewing pharmacies' ability meet the requirements. We are concerned that these delays could impact continuity of care for patients, whose prescriptions for compounded sterile medications may have shorter beyond-use dates during this period.

Additionally, given the diversity in state-level regulations, it is possible that some states may have different requirements or are currently exercising enforcement discretion for pharmacies moving toward full compliance with updated compounding standards.

Adverse Event Reporting

NCPA requests that FDA engage stakeholders in addressing the proper role, responsibilities, and repercussions for adverse event reporting.

Conclusion

NCPA believes there is a path forward on these issues which can meet the needs of patients and compounding pharmacists while ensuring the safety goals of the FDA. NCPA appreciates the opportunity to submit this statement for the record for the May 14 listening session. NCPA is committed to working with FDA and other stakeholders on these important matters. If the agency requires further information or has questions, please contact me at steve.postal@ncpa.org or (703) 600-1178.

Sincerely,

Steve Postal, JD
Director, Policy & Regulatory Affairs
National Community Pharmacists Association