June 3, 2022

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

Submitted via e-mail: navdeep.bhandari@fda.hhs.gov; jacquin.jones@fda.hhs.gov; Compounding@fda.hhs.gov

Re: Statement for the Record for FDA Drug Compounding Annual Listening Session on June 17, 2022

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 June 17. 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 $67 billion healthcare marketplace, employ 215,000 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.

Timeline of FDA's PCAC meeting

NCPA expresses concern regarding the unreasonably condensed timeline and review process surrounding its June 8, 2022, PCAC meeting. For the PCAC meeting, it is extremely onerous to review the 876-page PCAC packet one week before the list of speakers is due to FDA, and two weeks before nominator slides are due. And NCPA finds it unreasonable that FDA published the PCAC packet only after NCPA sent a letter requesting the release of this information.

The process of sending PCAC materials, and the brief review time, impedes physician and stakeholder participation in the process and makes it more difficult for nominators to address the breadth of issues raised in FDA's evaluation. For example, the advisory committees are set up such that they don't have to provide these materials very far in advance, and only need to

announce the meeting at least 15 calendar days in advance.[1] The accelerated timeline employed by FDA is inappropriate to create a robust discussion on the future of the availability of the compounding agents at issue for patient care. While nominators can speak to these agents, it has often been years since the original nominations were submitted. Nominators would therefore appreciate more time to gather the most recent and relevant research. The nominators also need more time to review FDA's lengthy analyses.

Therefore, NCPA believes that nominators should have at least three weeks from the release of the FDA packet to the due date for speakers, and an additional two weeks to the due date for slides. NCPA does not understand why slides need to be turned in a week before the meeting, when FDA is already giving nominators a short timeline.

Implementation of GFI 256

NCPA is grateful for FDA's Center for Veterinary Medicine (CVM)'s willingness to participate in productive conversations on the GFI. However, we question whether ongoing conversations on the GFI will lead to patient-centered change.

NCPA reiterates concern with GFI #256, issued in its final form by FDA in April.[2] Our concerns are similar to the concerns we expressed in comments to FDA to the draft GFI #256 in October 2020, and to GFI #230, which the Agency issued in 2015 and withdrew in 2017 following serious objections from stakeholders, such as veterinarians, pharmacists, and pet owners. In addition, in the final appropriations bills for FY2017 and FY2018, Congress included report language asserting that GFI #230 exceeded FDA's statutory authority. This final GFI #256 will likely inhibit veterinarians from properly treating their animal patients. Our additional comments will focus on issues we believe will lead to decreased access to compounds for veterinary use and undermine the triad of care that exists between prescribers, pharmacists, and animal patients.

For the reasons stated below and in earlier provided comments, NCPA continues to request the FDA withdraw GFI #256.

1. **The final guidance misinterprets federal law and regulations issued by the FDA.**

Federal law is silent on compounding for animals from active pharmaceutical ingredients (APIs). It remains incongruent to have federal law say you can compound with APIs for humans but have FDA interpretation that would disallow this for animals except in limited circumstances.

[1] https://www.fda.gov/advisory-committees/about-advisory-committees/common-questions-and-answers-about-fda-advisory-committee-meetings
[2] "#256: Compounding Animal Drugs from Bulk Drug Substances - Guidance for Industry," April 22, 2022. *Food and Drug Administration.* Available at: https://www.fda.gov/media/132567/download.

Furthermore, FDA's stated logic that compounding from APIs for animals is not in federal law and is thus illegal creates a legal uncertainty for FDA's lists for office stock; these lists are also not grounded in any statutory authority.

NCPA requests FDA review these current regulations and draft new guidance which respects this shared authority in the compounding space.

2. **FDA's Animal Office Stock Compounding Lists Essentially Approve Compounding in Those Instances, Yet FDA Takes Position that Animal Compounding Is Not Allowed**

As noted in the final GFI #256, FDA established a public docket in November 2019 for interested parties to nominate bulk drug substances to a list (the List) of bulk drug substances for compounding office stock drugs for use in nonfood-producing animals or antidotes for food-producing animals (the List) and comment on nominated and evaluated bulk drug substances. On April 14, 2022, FDA expanded these nominations to include drugs compounded for use as sedatives or anesthetics for free-ranging wildlife species, and rearranged the List into two separate lists as described above. In this way, FDA's list for animal office stock compounding has essentially created approved specific compounds with indications. This is inconsistent with FDA policy that compounds cannot have indications, as indications are for approved drugs.

3. **The GFI fails to properly recognize and accommodate animal drug shortages.**

FDA notes in the final guidance that it will "apply its process" to mitigate animal drugs that are temporarily in shortage. FDA further stipulates that "actions may include working with drug manufacturers and others in the animal health industry, speeding up the animal drug review and approval process, encouraging sponsors of alternate products to increase production, or refraining from taking action against imports of foreign-approved versions of the drug product."[3]

However, these processes fail to address the impact on animal patient care a shortage might have and impedes compounders from serving the needs of those patients. Additionally, the procedures established by FDA are inadequate to determine what is currently in shortage in the market.

4. **Compliance requirements set unobtainable standard for compounders to assess inactive ingredients.**

According to the final GFI, FDA generally does not intend to take enforcement action against the compounding of animal drugs from bulk drug substances as office stock for nonfood-producing animals for violations of the requirements for animal drug approval, adequate

[3] "#256: Compounding Animal Drugs from Bulk Drug Substances - Guidance for Industry," April 22, 2022. *Food and Drug Administration*. Available at: https://www.fda.gov/media/132567/download.

directions for use, and current good manufacturing practice (CGMP) when certain circumstances are present, including that "All bulk drug substances, inactive ingredients, and finished drug products used in compounding meet the standards set in any applicable USP-NF monograph and comply with other FD&C Act requirements for drug components."[4] This sets an unobtainable standard for compounders. Compounders do not have the ability to assess inactive ingredients, as the package inserts for manufactured animal drug products do not disclose them.[5]

5. **Conclusion.**

NCPA appreciates the opportunity to share with you our additional comments and suggestions to the final GFI #256. For the reasons stated above and previously submitted, we urge FDA to withdraw the final GFI #256 as it did with its previous draft (GFI #230), which the Agency issued in 2015 and withdrew in 2017. NCPA is committed to working with FDA and other industry stakeholders in promoting efforts to preserve veterinary and human patient access to medically necessary compounded medications.

Concerns with patient access to cBHT

NCPA expresses concern with maintaining appropriate access to cBHT. An April 2022 article 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.[6] This article also demonstrates that clinically relevant information regarding cBHRT was omitted from the report.

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 Compounding (A4PC).[7] 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, 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.

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[4] "#256: Compounding Animal Drugs from Bulk Drug Substances - Guidance for Industry," April 22, 2022. *Food and Drug Administration.* Available at: https://www.fda.gov/media/132567/download.

[5] One example is Vetmedin. While the package insert discusses the active ingredient it does not disclose the inactive ingredients. See: https://www.bi-vetmedica.com/sites/default/files/dam/internet/ah/vetmedica/com_EN/product_files/vetmedin/vetmedin_label.pdf. On the other hand, human drug products list all the ingredients including the inactive ingredients. See Section 11, the Description, here for example: https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/019777s064lbl.pdf.

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

[7] See Microsoft Word - Joint Pharmacy Draft Letter to FDA NASEM Report.docx (ncpa.org).

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. There are still unresolved questions regarding the difference 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.

NCPA strongly supports addition of glutathione to the 503A Bulks List

NCPA strongly supports the inclusion of glutathione on the 503A Bulks List, and originally nominated it for inclusion in 2014. NCPA disagrees with FDA's recommendation that glutathione not be included on the 503A Bulks List. NCPA supports the testimony of A.J. Day, PharmD, Vice President of Clinical Services at PCCA, given to PCAC on June 8, 2022.

As indicated in the FDA briefing packet, NCPA strongly supports the addition of glutathione for chemotherapy-induced neuropathy and cystic fibrosis.[8]

Any Future MOU

NCPA welcomes FDA's delay of the MOU to October 27, 2022, the 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."[9]

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

[8] https://www.fda.gov/media/158541/download, page 544-546.
[9] 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. That being said, 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.[10]

NCPA supports the Patient Access to Urgent-Use Pharmacy Compounding Act (HR 3662), 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.[11]

Adverse Event Reporting

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

[10] https://www.fda.gov/media/137125/download.
[11] H.R.3662 - 117th Congress (2021-2022): Patient Access to Urgent-Use Pharmacy Compounding Act of 2021 | Congress.gov | Library of Congress.

Conclusion

NCPA feels 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 June 17 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