APhA
American Pharmacists Association

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Director, Office of Compounding Quality and Compliance

c/o Director, Division of Prescription Drugs
Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: FDA Drug Compounding Annual Listening Session - Pharmacy Organizations

Dear Gail:

The American Pharmacists Association (APhA) is pleased to submit comments to today's FDA annual Drug Compounding Listening Session.

APhA is the only organization advancing the entire pharmacy profession. Our expert staff and strong volunteer leadership, including many experienced pharmacists, allow us to deliver vital leadership to help pharmacists, pharmaceutical scientists, student pharmacists, and pharmacy technicians find success and satisfaction in their work while advocating for changes that benefit them, their patients, and their communities. We offer the following recommendations developed with input from our members, including feedback from our APhA Academy of Pharmacy Practice and Management (APhA-APPM) Compounding Pharmacy Special Interest Group (SIG), consisting of over 5,000 members, and Nuclear Pharmacy Practice SIG, consisting of over 2,200 members.

Maintain and Enhance Compounding Flexibilities Under the PHE to Address Current and Future Drug Shortages

As stated last year, APhA applauds FDA's actions during the pandemic, in particular FDA's guidances aimed at easing drug shortages, which permitted hospital and community

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compounding pharmacists to have more flexibility than ever before in meeting both providers' and patients' needs during the public health emergency (PHE).

Many of our hospital compounding pharmacist members have told us FDA's compounding flexibility was the only reason hospitals were able to keep up with patient demand.

Accordingly, flexibility to compound medications under both sections 503A and 503B are likely to be necessary for the foreseeable future. Compounding pharmacists stand ready to provide needed medications for COVID-19 treatment and drugs in shortage in the U.S. because of this global crisis. As FDA understands, compounding pharmacies can help meet the increased demands for these products to prevent and mitigate shortages.

Accordingly, we urge FDA to continue to leverage the flexibility the agency has granted for pharmacists to compound medications in shortage under 503A and 503B for hospitalized patients without patient-specific prescriptions to continue to address COVID-19 and beyond the PHE to ensure readiness to address future pandemics and public health needs. FDA should also expand this flexibility to any additional drugs in shortage for all medically necessary conditions. Permitting pharmacists to compound drugs for all drugs in shortage during and after the pandemic will help ensure our nation's hospitals and other providers have the medications they need without disruption and be able to focus their efforts on patient care.

Feedback on Guidance for Industry #256: Compounding Animal Drugs from Bulk Drug Substances (GFI #256) in Non-Food Producing Animals

APhA refers FDA to the comments of our Compounding SIG coordinator Natalie Young, PharmD, FACVP. We also hope that FDA continues to consider our feedback and APhA as a resource when considering bulk substance nominations in the future.

We do note "[w]hile GFI #256 is "guidance," from the FDA, and even by the FDA's own statements is not legally binding and is to provide the FDA's current policy on whether or not they would take enforcement action or not, GFI #256 has the effect of creating state regulations that must be followed as already numerous third-party accreditation bodies are requiring documentation of compliance with the guidance. And we expect state regulatory bodies to also reference the guidance in their enforcement actions."

This provides notable concerns with GFI #256:

- Federal law via Section 503A of the Food, Drug and Cosmetic Act (FDCA) already sets criteria for using active pharmaceutical ingredient (API)s to compound human medications. Our members have difficulty understanding why this would be permitted for people, but not for animals except under limited circumstances.

- FDA has created multiple lists for office use veterinary medications, without statutory authority.

In regards to these comments, for congressional intent, we defer to the report language accompanying H.R. 2471 Consolidated (Div. A), Public Law No: 117-103, H. Rept. 117-82:

"The Committee wants to ensure that GFI #256 on animal drug compounding, which FDA issued on November 20, 2019, does not create the same issues that resulted in withdrawal of the previous draft guidance, GFI #230. The Committee expects that any finalized guidance on compounding for animal health will preserve treatment options available to veterinarians, will reflect public input, and will recognize the need for compounded medications by pet owners, animal shelters, zoos and other stakeholders. In addition, the Committee directs FDA to conduct outreach to the veterinary community to explain the application of GFI #256 and how veterinarians will continue to be able to access safe and effective locally-compounded animal drugs."[1]

There is also language in P.L. 117-103, stating:

"The Committee continues to hear concerns that FDA has implemented and enforced the DQSA through guidance for industry documents rather than through the notice and comment rulemaking procedure called for by the underlying statute and the Administrative Procedures Act."

Recognize State Board of Pharmacy Policies on Flavoring of Conventionally Manufactured Commercially Available Medications and Exemption To <795>

Pharmacies continue to be challenged by USP's interpretation that "flavoring is compounding," and thus subject to all the requirements in USP Chapter <795>. APhA has previously requested that USP clarify that custom flavoring of conventionally manufactured liquid medications does not constitute nonsterile compounding. The burden of complying with <795> for one basic

[1] https://www.congress.gov/117/crpt/hrpt82/CRPT-117hrpt82.pdf

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service would be prohibitive for any pharmacy that does not otherwise engage in compounding.

Accordingly, APhA recommends FDA clarify that pharmacies that add flavoring should use the default BUD on the bottle and are not subject to all provisions of USP <795>.

Twenty-five state boards of pharmacy have adopted specific language that permits pharmacists to improve the taste of commercially available medicines with small quantities of flavoring to promote effective medication use by patients. Additionally, the National Association of Board of Pharmacy (NABP), in its Model Pharmacy Act/Rules, ***excludes*** flavorings from its definition of compounding.

Pharmacists today routinely flavor oral liquid medicines for tens of millions of patients, most of whom are children, to successfully improve palatability and compliance, with beneficial results. APhA is concerned that subjecting pharmacies to all of the provisions of <795> could have the unintended consequence of causing harm to the millions of children who rely on flavoring to get the benefit of their medicines. Accordingly, APhA recommends clarifying this exemption from the provisions of <795> that recognizes State Boards of Pharmacy language providing for the simple flavoring of conventionally manufactured commercially available medications.

Review the Peer-Reviewed Study: "Safety and Efficacy of Compounded Bioidentical Hormone Therapy (cBHT) in Perimenopausal and Postmenopausal Women"

We wanted to ensure that you were aware of a new, peer-reviewed study in *Menopause*, the Journal of The North American Menopause Society, titled Safety and efficacy of compounded bioidentical hormone therapy (cBHT) in perimenopausal and postmenopausal women. This systematic review and meta-analysis of randomized controlled trials (RCTs) examined over three thousand full-text articles to identify cBHT-related studies. From those three thousand articles, twenty-nine randomized controlled trials were identified. The twenty-nine studies collected data from over 1,800 patients.

This meta-analysis found that women enrolled in RCTs of up to 12 months in duration did not have adverse changes in lipid profile or glucose metabolism -- two risk factors for cardiovascular disease. In addition, there was no change in endometrial thickness or serious adverse events. Finally, vaginal cBHT was found to significantly improve vaginal atrophy

symptoms. While this analysis sheds some light on the use of cBHT, the authors noted that long-term studies with clinical endpoints would be beneficial.

As you continue to evaluate what, if any, additional steps the FDA will take in response to the National Academies of Science, Engineering, and Mathematics (NASEM) study titled The Clinical Utility of Compounded Bioidentical Hormone Therapy: A Review of Safety, Effectiveness, and Use (2020), we encourage you to keep these new findings in mind and help ensure continued access to these important therapies.

Thank you for considering our recommendations. We look forward to working with FDA to ensure patients have access to the safe and effective compounded medications they need. If you have any questions or require additional information, please contact Michael Baxter, Senior Director of Regulatory Policy, at mbaxter@aphanet.org.

Sincerely,

Ilisa BG Bernstein

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