July XX, 2023

VIA ELECTRONIC TRANSMISSION

The Honorable Robert Califf, MD
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, M.D. 20993

Dear Commissioner Califf:

We write to emphasize the importance of continued access to compounded bioidentical hormone therapies (cBHTs), which millions of Americans rely on to meet their health care needs. In July of 2020, a report from the National Academies of Sciences, Engineering, and Medicine (NASEM) recommended considering many commonly compounded hormones for the U.S. Food and Drug Administration's (FDA) Difficult to Compound List, which would make it unlawful to compound these therapies. We appreciate the FDA's careful consideration of these recommendations, given the consequences for patient access, and encourage the agency not to enact any new policies that would limit access to commonly compounded hormones before thoroughly engaging with stakeholders and establishing a strategy to ensure patients continue to have access to their medications.

Doctors and patients rely on compounded hormones when a FDA-approved drug product will not meet their unique needs, and available evidence suggests compounded hormones can help alleviate patient symptoms. For example, in a 2013 peer-reviewed journal article, researchers found that administration of cBHT in doses targeted to physiologic reference ranges administered in a daily dose significantly relieved menopausal symptoms in peri/postmenopausal women.[1] Similarly, a 2014 article describes how sublingual cBHT is effective in reducing vasomotor, mood, and quality-of-life symptoms experienced in post-menopausal women.[2] The NASEM report acknowledges that "[m]illions of men and women use cBHTs to alleviate symptoms associated with age-related hormone changes, such as hot flashes in menopause, or low muscle mass due to decreased testosterone."[3] Unfortunately, this same report's

[1] Stephenson K, Neuenschwander PF, Kurdowska AK, The effects of compounded bioidentical transdermal hormone therapy on hemostatic, inflammatory, immune factors; cardiovascular biomarkers; quality-of-life measures; and health outcomes in perimenopausal and postmenopausal women, *Int J Pharm Compd.* 2013 Jan-Feb;17(1):74-85, PMID: 23627249, https://pubmed.ncbi.nlm.nih.gov/23627249/.
[2] Ruiz, AD, and Daniels KR, The effectiveness of sublingual and topical compounded bioidentical hormone replacement therapy in postmenopausal women: an observational cohort study, *Int J Pharm Compd.* 2014 Jan-Feb;18(1):70-7, PMID: 24881343, https://pubmed.ncbi.nlm.nih.gov/24881343/.
[3] National Academies of Sciences, Engineering, and Medicine, The Clinical Utility of Compounded Bioidentical Hormone Therapy: A Review of Safety, Effectiveness, and Use, 2020, Washington, DC: The National Academies Press, https://doi.org/10.17226/25791.

recommendations would interfere with the practice of medicine and restrict access to these important products.

FDA has long acknowledged that its scope does not extend to regulating the practice of medicine, and we encourage the agency to not upend treatment for the millions of men and women who rely on compounded hormones because their doctors have determined they are a more appropriate medication.[4] It is important to note that patients often choose cBHTs because they prefer them and because their physicians recommend cBHTs as the best course of treatment for them. A 2015 article in *Menopause,* the journal of the North American Menopause Society, described two surveys that "were conducted to quantify the use of (cBHT) among perimenopausal and postmenopausal women in the United States, to assess women's knowledge of (cBHT) versus Food and Drug Administration-approved hormone therapy, and to gather information on menopausal experience."[5] In the first study, 89 percent of the 801 respondents claimed that cBHTs provided "moderate or significant relief;" in relieving menopausal symptoms and in the second study, 83 percent of the 2,044 respondents described their experience using cBHTs as being "extremely effective, very effective, or somewhat effective." Over 90 percent of respondents in the first study and 63 percent of respondents in the second study stated that they used cBHTs because their physician recommended them. The NASEM report recommendations would eliminate or restrict access to cBHTs, even when such therapies would otherwise be recommended by physicians and preferred by patients.

Given the importance of cBHTs to patients, we believe consultation with prescribers, compounders, and patients should be a critical component of any effort to develop a new policy related to cBHTs. As the FDA works to improve patient access to safe and effective medications, we urge the agency to engage with patients and stakeholders and establish a strategy to ensure patients continue to have access to their compounded medications before acting to develop new policies based on the NASEM recommendations.

Thank you for taking these concerns into account. We look forward to your response.

Sincerely,

[4] U.S. Food and Drug Administration (FDA), About FDA: Patient Q&A, accessed March 29, 2023, https://www.fda.gov/media/151975/download.

[5] Pinkerton, JoAnn V. MD, Santoro, Nanette MD, Compounded bioidentical hormone therapy: identifying use trends and knowledge gaps among US women, *Menopause. 2015 Sep; 22(9): 926–936,* doi: 10.1097/GME.0000000000000420.