Alliance for Pharmacy Compounding
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NCPA
NATIONAL COMMUNITY PHARMACISTS ASSOCIATION

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Division of Dockets Management
U.S. Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Docket No. FDA-2025-N-2589
Comments on the Risks and Benefits of Menopause Hormone Therapy

To Whom It May Concern:

On behalf of the Alliance for Pharmacy Compounding and the National Community Pharmacists Association, we appreciate the opportunity to submit comments to the U.S. Food and Drug Administration on the risks and benefits of menopause hormone therapy, as discussed during the July 17, 2025, expert panel and in response to Docket No. FDA-2025-N-2589.

We strongly urge FDA to take a balanced and evidence-informed approach that reflects both the evolving science and the practical realities of patient care. Millions of women rely on hormone therapy to manage the disruptive symptoms and long-term health effects of menopause. Yet for too long, the risks, particularly those suggested by the early findings of the Women's Health Initiative (WHI), have been overstated, while the benefits to bone health, cognitive function, cardiovascular outcomes, and overall quality of life have been underrecognized.

Importantly, compounded hormone therapy plays a critical and irreplaceable role in menopause care for women whose needs are not met by commercially available products. This includes patients who:

- Cannot tolerate inactive ingredients in FDA-approved products due to allergies or sensitivities,
- Require dosages or combinations not available commercially,
- Need alternative routes of administration such as sublingual, topical cream, or vaginal suppository, or
- Require estriol or testosterone therapy, important options for which there are currently *no FDA-approved products available for women*.

The ability to compound low-dose testosterone, estriol, and combination therapies tailored to individual patient needs is not merely a preference—it is, for many women, the only viable option to achieve therapeutic success. These compounded medications are prescribed by licensed clinicians, prepared in regulated pharmacies by trained professionals, and dispensed in accordance with both federal and state law, including standards set forth by the United States Pharmacopeia (USP).

We note with concern that the 2020 National Academies of Science, Engineering and Medicine report commissioned by FDA on the clinical utility of compounded bioidentical hormone therapy (cBHT) reflects significant methodological limitations and potential bias. As detailed in an independent analysis by Berkeley Research Group, the NASEM committee lacked patient-facing clinicians and ignored hundreds of studies and testimonies in favor of a narrow literature review, resulting in a report that fails to accurately characterize the safety, effectiveness, and real-world use of cBHT. It's striking that the NASEM committee only considered 13 studies of only five different cBHT formulations in its review. Eight studies related exclusively to DHEA and three related exclusively to testosterone. In the Report, the committee themselves recognized that the list of cBHT preparations they compiled "presents only a small sample of the universe of cBHT preparations and at best provides a snapshot and limited description of available cBHT preparations."

In line with FDA's request for perspectives on risks and benefits of hormone therapy across key domains, including breast cancer, cardiovascular disease, genitourinary health, bone health, dementia, and how such risks and benefits may vary by age, timing of initiation, duration, hormone type, dosage form, and route of administration, it is important to highlight the growing body of evidence demonstrating the value of compounded options. A recent meta-analysis of 29 randomized controlled trials involving 1,808 perimenopausal and postmenopausal women found that cBHT was not associated with negative changes in lipid profiles or glucose metabolism, nor with increases in endometrial thickness or serious adverse events. On the other hand, compounded vaginal androgens were associated with clear clinical benefits, including significant improvements in vaginal atrophy symptoms and female sexual function scores, outcomes that translate directly to better quality of life. These outcomes were observed alongside findings consistent with data from FDA-approved products regarding hormone level changes. While the authors noted the need for longer-term studies to fully assess cancer and cardiovascular outcomes, the evidence available to date demonstrates that compounded therapies can play an important role in addressing menopause-related conditions, particularly where commercial products do not meet individual patient needs. We urge FDA not to rely on the flawed NASEM report in making determinations about compounded hormone therapy labeling or regulatory policy. Doing so could unjustly restrict access to necessary therapies and undermine the clinical judgment of physicians and pharmacists.

Rather, we encourage FDA to:

- Recognize the important clinical role of compounded hormone therapy for women experiencing menopause,
- Acknowledge the absence of FDA-approved testosterone products for women and the medical necessity of compounded alternatives,

- Respect prescriber autonomy and patient access to individualized therapies as protected under the Federal Food, Drug, and Cosmetic Act, and
- Engage collaboratively with pharmacy and medical stakeholders to improve education, and labeling clarity, without jeopardizing access to needed compounded medications.

The needs of menopausal women are not one-size-fits-all. For many, compounded hormone therapy is not only appropriate, it is essential. We urge FDA to ensure that regulatory approaches preserve access to these therapies and reflect the full scope of current clinical practice.

Respectfully submitted,

Alliance for Pharmacy Compounding
National Community Pharmacists Association