Dr. Robert M. Califf
Commissioner of Food and Drugs
U.S. Food and Drug Administration
10903 New Hampshire Avenue WO32-2333
Silver Spring, MD 20993

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Dear Dr. Califf,

I would like to draw your attention to an issue that has impacted me personally and I urge the FDA to remove the black box warning on vaginal estrogen products. This warning continues to unnecessarily deter women and their health care providers from starting life-saving treatment.

Vaginal estrogen has been proven to be a safe treatment for women experiencing the genitourinary syndrome of menopause and lactation. Multiple research studies have been published highlighting the **efficacy and safety of local vaginal estrogen therapy** that effectively reduces urinary tract infections and greatly improves the quality of life for women. During the period when the black box warning was added, deaths related to urinary tract infections have increased by 2.4 times that of infection levels in 1990 (Yang et al. 2022). **Women are dying from UTIs** and complications related to these infections. In light of new data on antibiotic resistance we need to do everything we can to get women preventative care before infection develops (Naghavi et al. 2024).

Vaginal estrogen is safe, even for women with a history of gynecologic and breast cancer history (Meaidi et al. 2024, McVicker et al. 2024, Chambers et al. 2020). We have data that indicates there is little to no systemic absorption of vaginal hormone therapy, making this a safe option for patients with hormone-sensitive cancers (Mitchell et al. 2022). Multiple studies prove that there is no elevated risk of cardiovascular disease with use of vaginal estrogen therapy, in fact it may improve cardiovascular health (Crandell et al 2018, Mikkola et al. 2016).

Vaginal estrogen is effective in reducing urinary tract infections by greater than 50% (Tan-Kim et al. 2023). Guidelines published in 2019 state that "in peri and post menopausal women with recurrent UTIs, clinicians should recommend vaginal estrogen therapy to reduce the risk of future UTIs if there is no contraindication to estrogen therapy" (Anger et al. 2019).

Beyond urinary tract infections, genitourinary syndromes of menopause and lactation cause many patients significant, sometimes extreme discomfort and can greatly reduce the quality of life of many women. In addition to patient comfort, if vaginal estrogen therapy was accessible to more patients (in part, by removing the black box warning label) there is the **potential to reduce medicare spending by billions of dollars annually** on antibiotics and hospitalizations for UTIs (Houston et al. 2024).

This boxed warning not only deters patients from using these therapies, but also scares many medical providers into not administering vaginal estrogen. This is not acceptable given its safety and efficacy.

I urge the FDA to take these points under consideration as you weigh the harm that the boxed warnings continue to cause to women across the nation.

Sincerely,

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My address: _____

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