March 22, 2024

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

CITIZEN PETITION

The undersigned Petitioners respectfully submit this petition under 21 C.F.R. §§10.20, 10.30 to request that the Commissioner of Food and Drugs issue a guidance stating that over-the-counter ("OTC") vaginal suppositories containing boric acid that are marketed solely with deodorant claims, or claims to reduce vaginal odor, are "cosmetics" and not also "drugs." In the alternative, if the Commissioner decides to deem these products to be "drugs"—Petitioners request that (1) the Commissioner promulgate a regulation classifying any affected products as "drugs"; and (2) at least until such time as that regulation is final, announce a policy of enforcement discretion over any affected products.

The undersigned Petitioners are Vireo Systems and pH-D Feminine Health (collectively "pH-D Feminine"), and pH-D Feminine has long been manufacturing and marketing pH-D Boric Acid Vaginal Suppositories ("pH-D Suppositories"), solely with anti-odor claims, as "cosmetics." pH-D Feminine has done so based on a reasonable understanding that these products are appropriately regulated as "cosmetics" rather than as "drugs." This understanding is supported by (among other things): (1) the definition of "cosmetic" in the Food, Drug and Cosmetic Act ("FDCA") itself,[1] and (2) multiple statements in a 1983 Federal Register notice and a 1994 Federal Register notice, both of which were related to FDA's rulemaking on OTC vaginal drug products, indicating that FDA did not intend to include OTC vaginal products with the active ingredients under consideration at that time (including boric acid) in the OTC drug rulemaking process if they were solely marketed with certain "cosmetic" claims, such as "deodorizing" claims.[2]

In the last few years, pH-D Feminine became concerned that there is confusion within FDA about the regulatory status of our pH-D Suppositories and other similar products discussed in FDA's 1983 and 1994 Federal Register notices. Accordingly, in October 2022, we submitted a citizen petition (the "2022 Citizen Petition") respectfully requesting that the Commissioner of Food and

[1] 21 U.S.C. § 321(i).
[2] 48 Fed. Reg. 46694 (Oct. 13, 1983); 59 Fed. Reg. 5226 (Feb. 3, 1994); *see also* Vireo Systems and pH-D Feminine's Citizen Petition to FDA, dated October 17, 2022 ("2022 Citizen Petition"); we ask that the 2022 Citizen Petition be incorporated into the record.

Drugs issue a guidance for industry and FDA staff stating *that all OTC vaginal products marketed solely as deodorants, or to reduce vaginal odor, are "cosmetics" and not also "drugs*."[3] In the alternative, we requested that: (1) the Commissioner promulgate a regulation re-classifying any affected products; and (2) at least until such time as that regulation is final, announce a policy of enforcement discretion over any affected products.

We acknowledge FDA's response to the 2022 Citizen Petition, dated March 4, 2024, and we understand that our requests in that citizen petition have been denied.[4] It is our understanding that FDA denied those requests largely because (1) the Agency does not interpret its past statements in the 1994 Federal Register notice at issue as suggesting that *all* OTC vaginal products marketed solely with deodorizing, or reduced odor, claims are "cosmetics," and (2) the Agency believes that the determination of whether a specific OTC vaginal product marketed solely with deodorant, or reduced odor, claims is a "cosmetic" or a "drug" is a fact-specific, product-by-product determination.

With respect, we disagree with FDA's interpretation of its 1994 Federal Register notice. For the reasons explained below, we read the 1994 Federal Register notice and the 1983 Federal Register notice together, to create, at a minimum, a reasonable expectation that OTC vaginal products (at least those with the active ingredients, like boric acid, that were being considered at the time) that are solely marketed with deodorizing claims, are "cosmetics," *regardless of active ingredient*.[5]

In any event, we now respectfully ask that the Commissioner consider the more specific question of whether OTC vaginal suppositories that contain boric acid, which are marketed solely with deodorizing, or reduced odor, claims are "cosmetics" and not also "drugs."

ACTION REQUESTED

The undersigned Petitioners respectfully request that the Commissioner of Food and Drugs issue a guidance stating that OTC vaginal suppositories containing boric acid, that are marketed solely with deodorant claims, or claims to reduce vaginal odor, are "cosmetics" and not also "drugs."

In the alternative, if the Commissioner decides to deem these products to be "drugs"—Petitioners request that (1) the Commissioner promulgate a regulation classifying affected products as "drugs"; and (2) at least until such time as that regulation is final, announce a policy of enforcement discretion over any affected products.

STATEMENT OF GROUNDS

As you are aware, the FDCA defines cosmetics, in relevant part, as "articles intended to be . . . introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, [or] promoting attractiveness . . . ."[6] By comparison, the Act defines "drugs" as

[3] *See* Citizen Petition submitted to FDA by Vireo Systems and pH-D Feminine Health, Oct. 17, 2022.
[4] *See* FDA Response to Citizen Petition submitted to FDA by Vireo Systems and pH-D Feminine Health, Oct. 17, 2022, dated March 4, 2024, Docket No. FDA-2022-P-2571.
[5] *See generally,* 48 Fed. Reg. 46694 (Oct. 13, 1983).
[6] 21 U.S.C. § 321(i).

articles "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or "intended to affect the structure or any function of the body."[7]

FDA assesses a product's intended use by looking at the objective intent of the labeling, advertising and promotion, and any relevant source of evidence (direct and circumstantial).[8] Specifically, FDA will consider: (1) "expressions"—such as labeling claims and representations, advertising matter, and oral or written statements by persons responsible for the labeling, or their representatives; (2) the design or composition of the article; and (3) circumstances surrounding the sale or distribution of the article.[9] The indicia that FDA will consider in determining whether a product is a "drug" or "cosmetic" are not in dispute.

I. FDA's 1983 and 1994 Federal Register Notices Related to Its Review of OTC Vaginal Products Indicate that Boric Acid Vaginal Suppositories, When Marketed Solely with Deodorizing, or Reduced Odor, Claims are "Cosmetics" and Not Also "Drugs"

On October 13, 1983, FDA issued an advanced notice of proposed rulemaking ("ANPRM"), based on the recommendations of the Advisory Review Panel on OTC Contraceptives and Other Vaginal Drug Products.[10] The panel was established to review the data submitted in response to an FDA request for data on the safety and efficacy of such products that were being marketed at the time, and to prepare a report on the safety, efficacy, and labeling of those products.[11] As part of that review, the panel considered "[l]abeled ingredients contained in OTC vaginal *drug* products," including boric acid.[12] The panel, also, for the first time defined the term "vaginal suppository" as follows:

> "A vaginal suppository is a small globular mass, designed for easy introduction into the vagina. It is usually made of two major components—a vehicle and one or more chemical agents. It is solid at room temperature and either liquifies at body temperature or dissolves in vaginal fluids. Vaginal suppositories are designed to be used for one or more of the following purposes; (1) *Producing soothing and refreshing effects, (2) deodorizing*, (3) relieving minor irritations, (4) reducing the number of pathogenic microorganisms, (5) altering the pH so as to encourage the growth of normal vaginal flora, or (6) producing an astringent effect."[13]

Shortly thereafter in the 1983 Federal Register notice, the panel noted that the classification of a product

> "as a drug or a cosmetic is determined by both the type of claim made for the product and the type and strength of ingredients present in the product. If an active ingredient is present in a therapeutic concentration, the product is a drug,

[7] *Id.* § 321(g)
[8] *See* 21 C.F.R. § 201.128.
[9] *Id.*
[10] 48 Fed. Reg. 46694 (Oct. 13, 1983).
[11] *See id.* 46696.
[12] 48 Fed. Reg. at 46698.
[13] *Id.* at 46701.

> even if that product does not claim to produce the effect which will result from the action of the therapeutically effective ingredient."

Notwithstanding those observations, the panel went on to state that as "a result of its extensive deliberation" it concluded that *vaginal products which make only "producing soothing and refreshing effects" claims or "deodorizing" claims—"are not under the purview of this Panel and do not require testing for effectiveness."*[14]

We believe that it is reasonable to interpret these statements together as indicating that—even though FDA considers both product composition and marketing claims as indicia of intended use—the panel considered vaginal suppositories (at least those with active ingredients that were then being considered by the panel), which solely make claims regarding the product's soothing and refreshing effects or deodorizing claims, to be "cosmetics," not "drugs," *regardless of active ingredient*.[15] We interpret FDA's conclusion that vaginal products that make deodorizing claims are "not under the purview of this Panel" as indicating that the active ingredients considered by the panel, do not, alone, subject the products to review as OTC drugs. Although we acknowledge, that this conclusion could be interpreted to suggest that FDA will make case-by-case determinations regarding the regulatory status of such products, it is very difficult (if not impossible) to read the Agency's conclusion that these products "do not require testing for effectiveness," as suggesting anything other than that—these products are not "drugs," regardless of active ingredient.

Our interpretation of the 1983 Federal Register notice is reinforced by the 1994 Federal Register notice, in which FDA sought to withdraw the 1983 ANPRM. In the 1994 Federal Register notice, FDA stated:

> "This action is being taken in part because the agency has determined that *some of the recommended labeling indications relate to cosmetic claims and not drug claims*. In addition, recommended labeling indications and ingredients used for minor irritation, itching, or soreness are not unique to the vaginal area and are already being considered in other OTC drug rulemakings (e.g., antifungal, antimicrobial, and external analgesic)."[16]

In that Federal Register notice FDA also stated:

> "all of the products submitted to the Vaginal Panel were intended for intravaginal use and with the exception of vaginal contraceptives, *the use of these OTC vaginal products, e.g., douches, suppositories, had been for the most part limited to cosmetic purposes, e.g., cleansing, deodorizing, mechanical flushing. Thus, the agency concludes that with the exception of indications relating to minor itching, irritation, and soreness, all other recommended vaginal monograph indications listed in the Vaginal Panel's report (48 FR 46694 at 46729) are cosmetic in nature or outside the scope of the OTC drug*

[14] *Id.*
[15] *See generally,* 48 Fed. Reg. 46694 (Oct. 13, 1983).
[16] 59 Fed. Reg. 5226 (Feb. 3, 1994).

review, e.g., 'Astringent,' 'Removes vaginal discharge," "Removes vaginal secretions," 'Mild detergent action.'"[17]

In its response to the 2022 Citizen Petition, FDA argued that these statements indicate only that the Agency had concluded that the *claims* were "cosmetics" claims—not that the OTC vaginal *products* subject to the OTC review were "cosmetics," not "drugs," when they were marketed solely with "cosmetic" claims. With respect, that explanation is difficult to square for two reasons: (1) the 1983 Federal Register notice indicated that the OTC vaginal products under consideration "do not require testing for effectiveness" when marketed with "cosmetic" claims, indicating that they are not "drugs," and (2) if FDA had believed at the time that the active ingredients under consideration, alone, rendered the products "drugs," then there would have been no reason to exclude the products from the OTC drug review process.

In any event, we acknowledge FDA's response to pH-D Feminine's 2022 Citizen Petition, and that the Agency does not interpret its past statements in the 1994 Federal Register notice as suggesting that *all* OTC vaginal products marketed solely with deodorizing, or reduced odor, claims are "cosmetics." We do not ask FDA to revisit that decision, or even to make a decision as to whether all OTC vaginal products with active ingredients that were considered during the OTC review of vaginal drug products are "cosmetics," not "drugs," if they are marketed solely with deodorant, or reduced odor, claims.

The question at the core of this citizen petition is whether OTC vaginal suppositories containing boric acid that are marketed solely with deodorizing, or reduced odor, claims are in FDA's view "cosmetics" and not also "drugs." We interpret FDA's 1983 and 1994 Federal Register notices, at a minimum, to give rise to a reasonable expectation that these products are "cosmetics" and not also "drugs."

II. Regardless of Whether FDA Agrees with pH-D Feminine's Interpretation of the Agency's 1983 and 1994 Federal Register Notices, We Do Not Believe that There Is Any Reason for FDA to Regulate OTC Vaginal Suppositories Containing Boric Acid, Based Simply on Their Design or Composition, as "Drugs"

Boric acid has never been approved by FDA for use as an active pharmaceutical ingredient in any prescription or nonprescription drug. Moreover, it is our understanding that boric acid suppositories were historically regulated as homeopathic drugs, *only when they were marketed with express "drug" claims* (*e.g.*, to treat yeast infections).

Further, to the extent that boric acid has physiological and/or antimicrobial effects, those effects alone cannot render the boric acid suppositories "drugs." If that were the case, FDA would have to regulate all products that contain ingredients with physiological and/or antimicrobial effects as

[17] *Id.* at 5227.

"drugs," including many products marketed as cosmetics that contain lavender, tea tree, or lemon oils,[18] or certain acids, such as acetic, ascorbic, and lactic acids.[19]

In addition, we are not aware of any circumstances of sale or distribution[20] regarding OTC vaginal suppositories containing boric acid that would render the products "drugs." These products are typically sold to consumers at retail establishments that sell other cosmetics, or on-line, like many other cosmetics.

III. FDA Cannot Change the Regulatory Classification of OTC Vaginal Suppositories Containing Boric Acid, Without Issuing a New Regulation

To be clear, the *reclassification* from "cosmetic" to "drug" of OTC vaginal suppositories containing boric acid, which are marketed with "cosmetic" claims, would be a "rule" under the Administrative Procedure Act (APA).[21] Such a reclassification also would be a *legislative* rule because it would have a compulsory effect and expose regulated entities to legal consequences.[22] Indeed, it would establish new standards of duty, such as premarket approval.[23] Therefore, any reclassification could only be effectuated in accordance with notice-and-comment rulemaking under the APA.[24]

Further, even if FDA could successfully argue that reclassifying any OTC vaginal product marketed solely with reduced odor or deodorant claims is not subject to notice-and-comment rulemaking under the APA (and we do not believe that it can), FDA would have to, at a minimum, issue guidance signaling that the Agency has changed its position—in accordance with the Agency's Good Guidance Practices.[25] Good Guidance Practices preclude FDA from "us[ing] documents or other means of communication that are excluded from the definition of guidance document to informally communicate new or different regulatory expectations to a broad public audience for the first time."[26] FDA has publicly communicated in numerous fora its intent to treat odor reduction claims as cosmetic only. Any policy change now would necessitate issuing guidance to communicate FDA's "new" and "different regulatory expectations."

We recognize that FDA, in its response to this citizen petition, may disagree with our interpretation that the 1983 and 1994 Federal Register notices affirmatively classified OTC vaginal suppositories

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[18] A. Kunicka-Styczynska, et al., *Antimicrobial activity of lavender, tea tree and lemon oils in cosmetic preservative systems*, Journal of Applied Microbiology, Nov. 12, 2009, https://sfamjournals.onlinelibrary.wiley.com/doi/10.1111/j.1365-2672.2009.04372.x

[19] Yagnik, et al., Antimicrobial activity of apple cider vinegar against Escherichia coli, Staphylococcus aureus and Candida albicans; downregulating cytokine and microbial protein expression, Sci Rep 2018; 8: 1732 (2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5788933/

[20] The reference to circumstances of sale or distribution refers to common circumstances of sale or distribution regarding those products that are not related to verbal or oral promotion. We are aware of some companies who affirmatively market boric acid vaginal suppositories with "drug" claims (e.g., for treating yeast infections). We agree that when these products are marketed with "drug" claims, they are "drugs."

[21] 5 U.S.C. § 551(5).

[22] *See, e.g.*, *Nat'l Mining Ass'n* v. *McCarthy*, 758 F.3d 243, 250 (D.C. Cir. 2014); *Appalachian Power Co. v. EPA*, 208 F.3d 1015, 1020 (D.C. Cir. 2000).

[23] *See General Motors Corp.* v. *Ruckelshaus*, 742 F.2d 1561, 1563 (D.C. Cir. 1984) (en banc).

[24] *See supra*, at note 22.

[25] 21 C.F.R. § 10.115(e); 21 U.S.C. § 371(h).

[26] 21 C.F.R. § 10.115(e); 21 U.S.C. § 371(h).

containing boric acid, which are marketed only with deodorizing, or reduced odor, claims as "cosmetics" and not also "drugs." Regardless, the two Federal Register notices, together give rise to the reasonable expectation that such products are "cosmetics." Thus, if FDA determines that these products are "drugs," FDA should announce a policy of enforcement discretion over any affected products until such time as FDA has finalized necessary regulations and, as a practical matter, give affected parties sufficient time to conform to new legal requirements.

ENVIRONMENTAL IMPACT

Petitioners claim a categorical exclusion from the requirement of an environmental impact under 21 C.F.R. § 25.30(h).

ECONOMIC IMPACT

Petitioner will submit economic information upon request of the Commissioner. No information is required at this time.

CERTIFICATION

The undersigned certify that, to the best knowledge and belief of the undersigned, this petition and all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

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