AHPA
AMERICAN HERBAL PRODUCTS ASSOCIATION

April 19, 2023

Cara Welch, Ph.D.
Director, Office of Dietary Supplement Programs
CFSAN/FDA
Via email: cara.welch@fda.hhs.gov

Re: FDA's allegation that the labeled presence of *Pinellia ternata* renders a dietary supplement "adulterated" under 21 C.F.R. § 119.1

Dear Dr. Welch:

I write to follow up again on FDA's allegation of adulteration under 21 U.S.C. § 342(f)(1)(A) due to the listing of the ingredient *Pinellia ternata* on the label of a company's dietary supplement product. The allegation was included in a February 23, 2022, Warning Letter FDA issued to Princess Lifestyles LLC, which cited 21 C.F.R. § 119.1, the federal regulation that declares "dietary supplements containing ephedrine alkaloids" to be "adulterated," as the basis for the allegation. In support of this allegation, the Warning Letter identified *Pinellia ternata* as "a dietary ingredient which contains ephedrine alkaloids."

AHPA is now in receipt of information obtained through FOIA requests indicating that FDA did not take samples of or analyze the subject product to determine the presence of ephedrine alkaloids prior to the February 2022 issuance of the Warning Letter. The information received in response to these FOIA requests also indicates that, when this sampling and analysis did occur, in September and October 2022, respectively, FDA's lab reported that the sample "did not show the presence for [sic] any ephedrine alkaloid at or above the detection threshold of 0.5 ug/g."

In previous correspondence on this matter dated February 8, 2023, you stated as follows:

> "As a general matter, FDA agrees that the determination of a dietary supplement as adulterated under 21 CFR 119.1 should be based on the product containing ephedrine alkaloids. In the absence of clear evidence that a product contains ephedrine alkaloids, FDA agrees that such a product would not be adulterated under 21 CFR 119.1.
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> "… Based on our current review, it is our opinion that the publications[1] confirming both the presence and, in another case, the absence of ephedrine alkaloids in *P.*

[1] This statement responded to my previous correspondence, dated December 23, 2022, that cited three scientific publications that had reported results of analysis of materials identified as *Pinellia ternata*: (1) Fang L, Xie J, Lin L, Tian M, and Row KH. 2020. Multi-phase extraction of ephedrine from Pinellia ternata and herbal medicine using molecular imprinted polymer coated ionic liquid-based silica. *Phytochem Anal* 31:242–251. https://doi.org/10.1002/pca.2888; (2) Oshio H, Tsukui M, and Matsuoka T. 1978. Isolation of *l*-Ephedrine From "Pinelliae Tuber." *Chem Pharm Bull* (Tokyo) 26:2096–2097; and (3) Yahagi T, Atsumi T, Mano S et al. 2021. Quality evaluation of Pinellia tuber by LC-TOF/MS targeted to ephedrine. *J Nat Med* 75:692–698.

> *ternata* were not to the level of scientific rigor typically expected to definitively conclude that a particular substance is a constituent of a botanical."

I appreciate the clarification you provided in this statement. In the meantime, however, I have been informed that Amazon has required at least one company to remove a dietary supplement product due to the inclusion of *Pinellia ternata* as an ingredient. Amazon's action presumably stems from FDA's erroneous Warning Letter allegation that a product containing the herb qualified as "adulterated" when, in fact, the Agency had made no finding that the product contained ephedrine alkaloids.

I am therefore now requesting that FDA issue a public correction to more specifically clarify that the February 2022 Warning Letter to Princess Lifestyles LLC erred in alleging that the company's product labeled as containing *Pinellia ternata* was "adulterated" under 21 C.F.R. § 119.1 and that the Agency has subsequently determined that this product did not, in fact, contain ephedrine alkaloids. Absent such a specific statement, I am concerned that Amazon, and possibly other retailers, will continue to require removal of products labeled as containing *Pinellia ternata*, even though that ingredient is a lawful dietary ingredient if it does not contain ephedrine alkaloids. An additional concern is that private plaintiffs will bring frivolous litigation against marketers of products labeled as containing *Pinellia ternata* based only on the erroneous allegation of adulteration in the above-cited Warning Letter.

I will greatly appreciate your attention to this request, which I hope you will find to be reasonable and necessary. Please let me know if you would like to schedule a time to discuss this further.

Sincerely,

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https://doi.org/10.1007/s11418-021-01485-2. I note that, in 2004, one of these publications (Oshio et al.) served as the Agency's sole basis for asserting in preamble language that "[o]ther plant sources that contain ephedrine alkaloids include ... *Pinellia ternate* (Thunb.) Makino." From your February 8, 2023, correspondence, I understand that FDA now considers this publication to lack the "scientific rigor typically expected to definitively conclude that a particular substance is a constituent of a botanical."