U.S. FOOD & DRUG ADMINISTRATION

(b) (4)

Dear (b) (4)

This letter is to inform you that the Food and Drug Administration filed the notification that you submitted, pursuant to 21 United States Code (U.S.C.) § 350b(a)(2) (section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)), on June 2, 2020. Your notification concerns a new dietary ingredient that you call "Oleandrin" and intend to market as a bulk dietary ingredient for use in dietary supplement products.

According to your notification, the conditions of use are: "A single serving size is 6.25 micrograms per 0.5 milliliters taken by mouth, limit of 4 servings/day, maximum total daily intake level not to exceed 2 milliliters (25 micrograms/day). Oleandrin is intended for adults only, it is not intended for children, and it should not be used by individuals under the age of 18 years."

Under 21 U.S.C. § 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under 21 U.S.C. § 350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21 U.S.C. § 342(f)(1)(B) (section 402(f)(1)(B) of the Act) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

FDA has carefully considered the information in your notification and other published reports and determined that "Oleandrin" is excluded from the definition of a dietary supplement under 21 U.S.C. § 321(ff)(3)(B)(ii) (section 201(ff)(3)(B)(ii) of the Act). The definition of a dietary supplement is set forth in 21 U.S.C. § 321(ff) (section 201(ff) of the Act), which states in relevant part:

> (ff) The term 'dietary supplement' ... (3) does ... (B) not include – …

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> (ii) an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public,
>
> which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this chapter.

FDA has concluded that the "Oleandrin" has been authorized for investigation as a new drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public. Further, FDA has carefully reviewed the information provided in your submission and other available information and has not identified any evidence to demonstrate that "Oleandrin" was marketed as a dietary supplement or as a food prior to such authorization. Therefore, "Oleandrin" is excluded from the definition of dietary supplement under 21 U.S.C. § 321(ff)(3)(B)(ii) and may not be marketed as or in a dietary supplement.

We also note that, even if "Oleandrin" was not excluded from the definition of dietary supplement, the agency has significant concerns about the evidence included in your submission as a basis for concluding that a dietary supplement containing "Oleandrin" will reasonably be expected to be safe under the conditions of use described in your notification. For example, while your submission cited to a history of medicinal use of *Nerium oleander* extracts and clinical and pre-clinical studies of certain *N. oleander* preparations, your submission did not provide sufficient information to establish that the information that you rely on as evidence of safety is qualitatively and quantitatively related to the ingredient, when used under the proposed conditions of use, as indicated in your submission. Furthermore, studies performed in advanced cancer patients generally cannot establish the safety of your ingredient in its intended population of normal healthy adults, and you did not provide any information to indicate that such extrapolation between different populations would be scientifically valid. For these reasons, the information in your submission indicates that, even if your ingredient, "Oleandrin," were not excluded from the definition of a dietary supplement, your notification does not provide an adequate basis to conclude that a dietary supplement containing the ingredient, "Oleandrin," when used under the conditions recommended or suggested in the labeling of your product, will reasonably be expected to be safe. Therefore, if it were a dietary supplement, a product containing your ingredient, "Oleandrin," may be adulterated under 21 U.S.C. § 342(f)(1)(B) (section 402(f)(1)(B) of the Act).

Your notification will be kept confidential for 90 days after the filing date of June 2, 2020. After the 90-day date, the notification will be placed on public display at www.regulations.gov as new dietary ingredient notification report number 1157. Prior to that date, you may wish to identify in writing specifically what information you believe is trade secret or confidential commercial information and include an explanation of the basis for this belief.

If you have any questions concerning this matter, please contact CDR Jeanne Skanchy, R.Ph., Evaluation and Research Staff, at (240) 402-8790 and by email: NDITEAM@fda.hhs.gov.

Sincerely,

Ali A. Abdel-rahman -S

Digitally signed by Ali A. Abdel-rahman -S
Date: 2020.08.14 17:25:06 -04'00'

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