October 11, 2022

(b) (4)

Dear (b) (4) :

This letter is to inform you that the notification that you submitted on behalf of Inner Mongolia Kingdomway Pharmaceutical Limited, 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)), was received and filed by the Food and Drug Administration (FDA or we) on July 28, 2022. You submitted an amendment to the notification on September 22, 2022. Your notification concerns a new dietary ingredient, "β-Nicotinamide Mononucleotide" (NMN), that you intend to market as a bulk dietary ingredient for use in dietary supplements.

Your amended notification describes the conditions of use of your ingredient as follows: "Inner Mongolia Kingdomway Pharmaceutical Limited intends that dietary supplements containing its NMN bulk dietary ingredient will be marketed to adults in forms appropriate to dietary supplements (e.g., tablet, capsule, powder) at levels that do not exceed 400 mg NMN per serving or 400 mg NMN per day by adults (e.g., take one 400 mg serving daily, take one 200 mg serving twice daily)."

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) 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.

NMN is an article authorized for investigation as a new drug by the FDA. 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 - (i) an article that is approved as a new drug under section 355 of this title ... or (ii) an article 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, which was not before such approval ... 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.

Under that provision, if an article, in this case NMN, 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, the article may not be marketed as or in a dietary supplement unless the article was marketed as a dietary supplement or as a food before being authorized for investigation as a new drug. FDA has carefully reviewed the information provided in your amended notification and other relevant sources, including our own records, and has determined that NMN was not marketed as a dietary supplement, except unlawfully without an NDI notification, or as a food before FDA authorized it for investigation as a new drug. Further, FDA has carefully considered the information in your amended notification and other relevant sources and has determined that NMN is an article for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public.[1] Accordingly, we conclude that NMN is excluded from the dietary supplement definition under 21 U.S.C. § 321(ff)(3)(B)(ii) and may not be marketed as or in a dietary supplement.

Your notification will be kept confidential for 90 days after the filing date of July 28, 2022. After the 90-day date, the notification will be placed on public display at www.regulations.gov as new dietary ingredient notification report number 1259. Prior to that date, you may wish to identify in writing specifically what information you believe is trade secret or confidential commercial information and an explanation of the basis for this belief.

If you have any questions concerning this matter please contact Markeesa Scales, MPH, Division of Research and Evaluation, by email: NDITEAM@fda.hhs.gov.

Sincerely,

Philip Yeager -S

Digitally signed by Philip Yeager -S
Date: 2022.10.11 17:59:25 -04'00'

R. Philip Yeager, PhD, JD, DABT
Director
Division of Research and Evaluation
Office of Dietary Supplement Programs
Center for Food Safety
and Applied Nutrition

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[1] *See* "A Phase 2a Randomized Controlled Trial of MIB-626 (NAD-boosting Drug) vs. Placebo in Adults With COVID-19 Infection and Early Acute Kidney Injury," available at https://clinicaltrials.gov/ct2/show/study/NCT05038488?term=MIB-626&draw=1&rank=1.
See "A Proof of Concept Trial of a Sirtuin-NAD Activator in Alzheimer's Disease," available at https://clinicaltrials.gov/ct2/show/study/NCT05040321?term=MIB-626&draw=1&rank=2.
See "A Phase 2a Study of NAD+ Precursor Supplementation in Friedreich's Ataxia," available at https://clinicaltrials.gov/ct2/show/study/NCT04817111?term=MIB-626&draw=1&rank=3.