U.S. FOOD & DRUG ADMINISTRATION

February 24, 2022

(b) (4)

Dear (b) (4)

This letter is to inform you that the notification that you submitted, on behalf of SyncoZymes (Shanghai) Co., Ltd., 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 December 27, 2021. Additional information was received on February 1 and 14, 2022. Your notification concerns the new dietary ingredient "beta-nicotinamide mononucleotide (β-NMN)" that you intend to market as a bulk dietary ingredient.

According to your notification, the conditions of use are, "Take with water. 300 mg per person per day divided into 1 or 2 doses; at any time of the day." The target population is "Adults."

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.

FDA has carefully considered the information in your submission and we have significant concerns about the evidence on which you rely to support your conclusion that a dietary supplement containing your new dietary ingredient, "beta-nicotinamide mononucleotide (β-NMN)," will reasonably be expected to be safe under the conditions of use described in your notification.

**U.S. Food and Drug Administration**
**5001 Campus Drive**
**College Park, MD 20740**
**www.fda.gov**

FDA was unable to establish the safety of your new dietary ingredient, "beta-nicotinamide mononucleotide (β-NMN)," based on the history of use information provided in your notification. For example, your notification stated that β-NMN is a naturally occurring ingredient in various food sources at different levels; however, this exposure is several times lower compared to your maximum proposed serving level of 300 mg/day. Based on the various low levels of NMN from food sources compared with your new dietary ingredient, it is unclear how your maximum serving level relates to history of use of NMN in food. In addition, your notification stated that there are dietary supplements containing NMN on the market in Japan since 2020; however, the duration of marketing for these products is less than two years; which is inadequate time to establish the absence of adverse events. Therefore, it is unclear how NMN in the diet is qualitatively and quantitatively related to the proposed serving level of your new dietary ingredient.

FDA was unable to establish the safety of your new dietary ingredient, "beta-nicotinamide mononucleotide (β-NMN)," based on the other evidence of safety provided in your notification. For example, your notification provided several pre-clinical and clinical studies that were conducted on other forms of β-NMN such as NMN or nicotinamide riboside (NR); however, your notification did not establish how the test articles used in these studies are quantitively and qualitatively related to your new dietary ingredient. Based on the above, FDA was unable to establish the safety of your new dietary ingredient under the proposed conditions of use. Therefore, it is unclear how this other evidence of safety information will establish the basis of the safety of your new dietary ingredient under the proposed conditions of use.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that your new dietary ingredient, "beta-nicotinamide mononucleotide (β-NMN)", when used under the suggested conditions of use, will reasonably be expected to be safe. Therefore, a product containing your new dietary ingredient may be adulterated under 21 U.S.C. § 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury. Introduction of such a product into interstate commerce is prohibited under 21 U.S.C. § 331(a) and (v).

Your notification will be kept confidential for 90 days after the filing date of December 27, 2021. After the 90-day date, the notification will be placed on public display at www.regulations.gov as new dietary ingredient notification report number 1240. 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 Steven Casper, Ph.D., Division of Research and Evaluation by email: NDITEAM@fda.hhs.gov.

Sincerely,

Ali A. Abdel-rahman -S

Digitally signed by Ali A. Abdel-rahman -S
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