November 4, 2022

(b) (4)

Dear (b) (4)

This letter is in further response to the notifications (NDIN 1240 and 1247) that you submitted for the new dietary ingredient "β-nicotinamide mononucleotide" (NMN) on behalf of SyncoZymes (Shanghai) Co., Ltd. As you know, we responded to NDIN 1240 with a letter of acknowledgement and objections on December 27, 2021; and in response to NDIN 1247, we acknowledged receipt and filing of your notification without objection on May 16, 2022.

Based on new information that came to light when we were reviewing another notification, FDA initiated a review of past notification responses for NMN and concluded that NMN is excluded from the definition of a dietary supplement. This means that NMN may not be marketed as or in a dietary supplement. The reasons for this conclusion are explained below.

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 beenFDA has reviewed NMN, 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 available to us 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 available to us and has

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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. Today we are sending letters communicating this conclusion simultaneously to all firms that have submitted an NDI notification for NMN. The reasons for our conclusion are further explained in FDA's supplemental response letter to NDIN 1259, which will be posted here after any confidential information has been redacted: NDIN 1259.

This response supersedes the earlier responses you received to NDIN 1240 and NDIN 1247. If you have information about the marketing of NMN as a dietary supplement or as a food that you would like to submit to us, please send it to NDITEAM@fda.hhs.gov with a reference to the NDIN number. Any documentation sent should include the date on which the marketing occurred.

If you have any questions concerning this matter please contact us at NDITEAM@fda.hhs.gov.

Sincerely,

Philip Yeager -S Digitally signed by Philip Yeager -S
Date: 2022.11.04 17:17:37 -04'00'

R. Philip Yeager, PhD, JD, DABT
Director
Division of Research and Evaluation
Office of Dietary Supplement Programs
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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