July 17, 2023

The Honorable Jeff Duncan
U.S. House of Representatives
Washington, D.C. 20515

Dear Representative Duncan:

Thank you for your letter of April 27, 2023, in which you expressed your opinion that the Food and Drug Administration (FDA or we) should hold a public hearing under 21 CFR Part 15 to "clarify the Food and Drug Administration's position on the use of Nicotinamide Mononucleotide (NMN) in dietary supplements." Your letter also asked several questions related to NMN that are addressed below.

While we appreciate your interest in the FDA's regulation of dietary supplements, we do not plan to hold a public hearing under 21 CFR Part 15, which governs informal hearings before the Commissioner or a designee. Unless the Federal Food, Drug, and Cosmetic Act (FD&C Act) or FDA regulations specifically provide for a hearing on a particular matter, which is not the case here, the decision whether to grant a hearing is entrusted to the Commissioner's discretion. Section(a) provides that the procedures governing a Part 15 hearing apply when the Commissioner concludes "as a matter of discretion, that it is in the public interest to permit persons to present information and views at a public hearing…." When deciding whether a Part 15 hearing would be in the public interest, the Commissioner typically considers, among other factors, whether interested persons have other opportunities to present information and views on the topic in question.

On March 6, 2023, FDA received a citizen petition from the Natural Products Association and the Alliance for Natural Health USA, asking us to reconsider our view on whether products containing NMN are dietary supplements. The citizen petition was posted to Regulations.gov and a docket (FDA-2023-P-0872-0001) was opened to receive public comment. In light of this opportunity for the public to provide information and views that FDA will consider as part of our work in reviewing and responding to the citizen petition, we do not believe that it is in the public interest to hold a public hearing on this matter.

In addition, your letter asked several questions related to NMN. Some of the questions you raise are actively under consideration as part of our review of the March 6, 2023, citizen petition. Accordingly, we are still in the process of giving these questions serious consideration as part of our obligation to carefully and thoroughly review citizen petitions under 21 CFR 10.30. We commit to further respond to your office when we have responded to the petition.

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1. Has the FDA contacted e-commerce platforms regarding the sale of NMN?

The Center for Food Safety and Applied Nutrition's Office of Dietary Supplement Programs and other FDA components that have a role in regulating products marketed as dietary supplements have confirmed that FDA has not contacted any e-commerce platforms regarding the sale of NMN-containing products.

2(a). How many structure-function claims notifications have been submitted to the FDA for review for NMN products under new dietary ingredient notifications (NDINs) requirements, and how many did the FDA determine inappropriate marketing?

Structure/function claim notifications are submitted under section 403(r)(6) of the FD&C Act (21 U.S.C. 343(r)(6)) and 21 CFR 101.93(a). These notifications are not required to list all of the ingredients in the product, and FDA's files do not track the notifications by ingredient. However, our best estimate as of May 10, 2023, is that FDA has received at least 42 structure/function claim notifications for NMN-containing products and has raised objections in at least 10 of the notification responses. According to our typical practice, structure/function notifications and our responses are periodically posted to Regulations.gov.[1]

FDA reviews structure/function claim notifications under the criteria in section 403(r)(6) of the FD&C Act, which focus on the subject matter of the claim. Our review generally does not include an evaluation of the ingredients in the product for which the claim is made. Further, FDA's response to a structure/function claim notification is not required or intended to be an all-inclusive statement of issues that may exist in connection with that product. Thus, FDA's silence on an ingredient's regulatory status in a response to a structure/function claim notification, or the lack of an FDA response to a structure/function notification, should not be read as a statement that the ingredient is lawful for use in dietary supplements.

We note that structure/function claim notifications are not submitted under the new dietary ingredient notification requirements. Structure/function claim notifications are required by section 403(r)(6) of the FD&C Act and 21 CFR 101.93(a), whereas new dietary ingredient notifications are required by section 413(a) of the FD&C Act (21 U.S.C. 350b(a)) and 21 CFR 190.6.

[1] Structure/function claim notifications are posted under different docket numbers depending on when they were submitted and whether FDA responded. To view claim notifications that resulted in a courtesy letter, type "FDA-1997-S-0006" in the search box on regulations.gov. Claim notifications that were submitted to FDA after 2012 and did not receive a response are separated by year; to view those notifications, please include the four-digit year in the following search term: FDA-YEAR-S-0024. For example, if you are looking for notifications submitted in 2022, you would type "FDA-2022-S-0024" in the search box on www.regulations.gov. Notifications are generally posted in the docket between 60-90 days after they have been processed and reviewed.

2(b). What number of FDA enforcement actions were taken to address the marketing of NMN products by companies attempting to receive an NDIN for NMN-containing products?

None.

2(c). What was the date when the FDA identified NMN being used in consumer products in the United States, both as a drug and as a dietary supplement or ingredient?

We cannot provide a date when FDA identified NMN being used as a drug in consumer products in the United States because NMN has not been approved as a new drug in the United States.

Regarding the use of NMN as or in a dietary supplement in the United States, FDA is currently evaluating the available information relating to the date NMN was first marketed as a dietary supplement or food as part of our review of the March 6, 2023, citizen petition, which presents questions regarding these dates and whether NMN is excluded from the dietary supplement definition under section 201(ff)(3)(B) of the FD&C Act (21 U.S.C. 321(ff)(3)(B)). Once we have finished our evaluation of this matter and reached a determination with respect to the pertinent questions, we will respond to the petitioners and will further respond to your office regarding this issue.

2(c)(i). For NMN-containing products referenced by the FDA, please provide the analysis of the composition of the NMN present in the application for approval as a drug and the NMN dietary supplement composition.

As explained in the answer to question 2(c), NMN has not been approved as a new drug in the United States. In general, consistent with applicable statutes and regulations, FDA is prohibited from disclosing whether an unapproved new drug application for a particular substance exists and from disclosing data or information in an unapproved application (see, e.g., 21 CFR 20.61, 314.430(b)-(d)). Therefore, we cannot confirm or deny whether we have received an application for approval of NMN as a new drug, and we cannot provide any analysis of the composition of NMN presented in such an application, if one exists.

Further, the laws and regulations governing dietary supplements do not require manufacturers or distributors to notify FDA of the composition of their dietary supplements, except when a new dietary ingredient notification is required. NDI notifications must include a description of the dietary supplement that contains the new dietary ingredient (see 21 CFR 190.6(b)(3)). To date, FDA has received and responded to

eight NDI notifications related to NMN. These notifications and our responses are publicly available on Regulations.gov.[2]

2(d). What is the FDA's position on whether NMN would be banned from formulated dietary supplements under the drug exclusion criteria when the statute did not allow the FDA to remove products from the marketplace to the transparent advantage of a company marketing a drug with NMN as the active ingredient?

The question you raise here about FDA's position on whether NMN is excluded from the dietary supplement definition, and therefore not lawful for use in or as a dietary supplement, is substantively similar to questions raised in the March 6, 2023, petition currently under FDA review. FDA is carefully reviewing these questions as part of our process to review citizen petitions under 21 CFR 10.30. Once we have finished our evaluation of this matter and reached a determination with respect to the pertinent questions, we will respond to the petitioners and will further respond to your office.

2(e). Does the FDA intend to remove the more than 600 NMN-containing products listed on the Dietary Supplement Label Database maintained by NIH from consumer access?

The question you raise here about whether FDA intends to remove NMN products from the market presupposes that the main issue raised in the March 6, 2023, petition, whether NMN is lawful for use in or as a dietary supplement, has already been resolved. However, as noted in our answer to question 2(d), FDA is still reviewing this question as part of our process to review citizen petitions under 21 CFR 10.30. Once we have finished our evaluation of this matter and reached a determination, we will respond to the petitioners and will further respond to your office.

We note that as of May 2023 our count of NMN-containing products in NIH's Dietary Supplement Label Database (DSLD) returned fewer than 300 product labels.

[2] See NDI notifications 1174, 1189, 1234, 1240, 1247, 1259, 1265, 1267. In accordance with section 413(a) of the FD&C Act and 21 CFR 190.6(e), FDA keeps the existence and contents of NDI notifications confidential for 90 days after receipt. After the 90th day, FDA places the notification on public display by posting it at regulations.gov, except for any information that is trade secret or confidential commercial information. To view an NDI notification, type "NDI xxxx" in the search box on regulations.gov, where xxxx is the NDI notification number assigned. For example, if you are looking for NDI notification 1267, you would type "NDI 1267" in the search box on www.regulations.gov.

FDA focuses our limited compliance and enforcement resources based on risk and public health priorities. It would not be appropriate for FDA to comment on what, if any, enforcement actions we might seek to take regarding products containing NMN.

Sincerely,

Kimberlee Trzeciak -S

Digitally signed by Kimberlee R. Trzeciak -S
Date: 2023.07.17 21:53:33 -04'00'

Kimberlee Trzeciak
Associate Commissioner for
Legislative Affairs