U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR FOOD SAFETY & APPLIED NUTRITION

January 20, 2023

Daniel Fabricant, Ph.D.
President & CEO
Natural Products Association
440 1st Street NW, Suite 520
Washington, DC 20001

Dear Dr. Fabricant:

We have evaluated your request that FDA open a docket to receive information about the earliest marketing of beta-nicotinamide mononucleotide (NMN) in a food or dietary supplement. We are denying this request because interested parties can already submit such information to FDA without a docket dedicated to that purpose, as evidenced by the many submissions FDA has received on this topic from NPA and others.

Except where required by statute or regulation, the opening of a docket is a discretionary act. Outside the rulemaking context, federal agencies are generally free to accept information through other means. Further, the process of opening a docket is generally accompanied by a Federal Register notice describing the type of information the agency is soliciting. We do not believe the publication of a Federal Register notice is warranted at this time. FDA has communicated its conclusion that NMN is excluded from the definition of dietary supplement by letter to all the notifiers who have a new dietary ingredient (NDI) notification on file pertaining to NMN. In these letters, we have invited each notifier to provide any additional evidence they may have regarding the earliest marketing of NMN as a food or dietary supplement. Further, we are aware of media articles covering this matter and have had other communications with interested parties on the matter including, for example, the meeting FDA had with NPA and some of your member companies. We believe the firm-specific communications, along with media articles and other communications with interested parties, have reached the relatively small number of companies that are likely to have records of when NMN was first marketed as a dietary supplement or as a food.

While there are some parallels with vinpocetine, the situations are different in important respects. With vinpocetine, FDA wanted to cast a wide net because vinpocetine had been authorized for investigation as a new drug in 1981, and we anticipated that any relevant evidence of its marketing as a food or dietary supplement would be decades old and would predate internet marketing. Additionally, vinpocetine had been marketed as a dietary supplement for almost 20 years which is another reason why FDA wanted to reach a broad audience. In contrast, NMN appears to be relatively new to the U.S. marketplace; thus, evidence of NMN's marketing should be relatively easy to access.

As you know, NMN is an NDI under section 413(d) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) because it was not marketed in the United States before October 15, 1994. FDA first filed an NDI notification for a dietary supplement containing NMN on December 3, 2020, which means the first date on which a dietary supplement containing NMN could have been lawfully marketed was 75 days later (February 16, 2021) (see section 413(a)(2) of the FD&C Act). FDA is aware of an NMN product (Doctor's Best Instant Whey Protein Concentrate Plus NMN) that was marketed as a conventional food as early as September 2021. However, both February 16, 2021, and September 2021 are after the first date on which NMN was authorized for investigation as a new drug. For FDA to change its conclusion that NMN is excluded from the dietary supplement definition under section 201(ff)(3)(B)(ii) of the FD&C Act, we would need marketing evidence from an earlier date.[1]

Since informing notifiers that NMN is excluded from the dietary supplement definition under section 201(ff)(3)(B)(ii) of the FD&C Act,[2] FDA has received and reviewed a number of submissions from interested parties seeking to change this determination, including several from NPA. Here is a brief summary of the information we have received from NPA to date, with our evaluation of the information.

- A December 21, 2018, announcement by Nutraland USA[3] that their NMN was determined to be generally recognized as safe (GRAS) by an independent review panel. GRAS evaluations concern safety, not marketing, and the date of a GRAS evaluation is not evidence of when an ingredient was first marketed as food.
- Links to two websites[4] selling NMN products labeled as dietary supplements, along with results of a search for NMN products in NIH's Dietary Supplement Label Database (DSLD).[5] Based on our review of these websites and search results, the earliest documented marketing date of an NMN product appears to be August 7, 2018, the date on which ProHealth Longevity NMN Lozenges became available for sale on Amazon.com. However, because NMN is an NDI, the first date on which a dietary supplement containing NMN could have been lawfully marketed was February 16, 2021. Thus, the Amazon listing is merely evidence that NMN was marketed unlawfully without an NDI notification and is not relevant to whether NMN is excluded from the dietary supplement definition. The NIH DSLD search returned some dietary supplements marketed as early as 2012, but based on their labels, those products did not contain NMN as an ingredient. The earliest documented marketing date for an NMN-containing product in the NIH DSLD appears to be June 2020.

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[1] FDA's regulations prohibit us from disclosing the existence of an IND unless it has previously been publicly disclosed or acknowledged. 21 CFR 312.130(a). Accordingly, although we can state our conclusions as to when NMN was first marketed as a dietary supplement or as a food and whether that date was before or after the date NMN was authorized for investigation as a new drug, we cannot specify the date of authorization or identify its source. Details about NMN's authorization as a new drug are documented in FDA's files.

[2] See FDA's supplemental response letter to NDI notification (NDIN) 1259 for an explanation of the agency's basis for concluding that NMN is excluded from the dietary supplement definition.

[3] https://nutralandusa.com/news.

[4] https://www.amazon.com/ProHealth-Longevity-NMN-Lozenges-Pharmaceutical/dp/B07G8QQ986/; https://coastdrink.com/.

[5] https://dsld.od.nih.gov/search/B-Nicotinamide%20Mononucleotide/bWFya2V0X3N0YXR1cz1hbGwvZW50cnlfZGF0ZT0yMDExLDIwMjIvc29ydD1tYXRjaC9wYWdlX3NpemU9MjAv.

- A website[6] operated by Mattey Supply Co., Ltd, showing images of a product called "NMN Water." The website and company appear to be based in China; however, the website does not contain any evidence as to when this NMN water was first marketed.
- Two patents that reference NMN. Patent No. US 7,776,326 B2[7], entitled Methods and Compositions for Treating Neuropathies, appears to discuss NMN as part of the NAD biosynthetic pathway and does not appear to contain any evidence of the marketing of NMN as a food. Patent No. US 8,075,934 B2[8], entitled Nutritional Composition with Improved Digestibility, describes NMN, along with a long list of other substances, as an optional ingredient in the composition of the invention, a nutritional formulation with many variants intended for use in infant formula, "growing-up milk," or medical foods. However, the patent does not include any evidence showing that NMN was actually marketed as a food at a specific point in time.
- Articles and videos about research on physiological effects of NMN[9], including a researcher's public statements regarding personal use of NMN. Information about NMN research or researchers taking NMN does not establish when NMN was first marketed as a food.

Although we have decided not to open a docket at this time, we will continue to review any relevant evidence submitted to us. Should you or your member companies have additional information to submit to FDA pertaining to the earliest marketing of NMN as a food or dietary supplement, please send it to NDITEAM@fda.hhs.gov and reference "NMN marketing" in the subject line.

Sincerely,

Cara Welch -S Digitally signed by Cara Welch -S
Date: 2023.01.20 17:11:32 -05'00'

Cara Welch, Ph.D.
Director
Office of Dietary Supplement Programs
Center for Food Safety and Applied Nutrition

[6] https://www.transform-water.com/en/nmn/.
[7] https://patentcenter.uspto.gov/applications/11144358.
[8] https://patentcenter.uspto.gov/applications/12371100.
[9] See, e.g., https://www.youtube.com/watch?v=UjyD_Ati9ac, https://khn.org/news/a-fountain-of-youth-pill-sure-if-youre-a-mouse/, and https://time.com/5209427/aging-nicotinamide-mononucleotide-nmn/.