IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

NATURAL PRODUCTS ASSOCIATION,
400/444 North Capitol Street NW,
Ste 638
Washington, DC 20001

Plaintiff,

v.

FOOD AND DRUG ADMINISTRATION, Robert M. Califf in his official capacity as Commissioner of Food and Drug Administration,
10903 New Hampshire Ave.,
Silver Spring, MD 20993-0002

DEPARTMENT OF HEALTH AND HUMAN SERVICES and Xavier Becerra in his official capacity as Secretary of the Department of Health
200 Independence Ave., SW,
Washington, DC 20201

Defendant.

Case No.: _____

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiff, Natural Products Association ("NPA"), brings this action against the defendants, Food and Drug Administration ("FDA"), Department of Health and Human Services ("HHS"), Xavier Becerra, in his official capacity as Secretary of the Department of Health and Human Services, and Robert M. Califf, in his official capacity as Commissioner of the Food and Drug Administration (collectively referred to as the "Defendants"), for the purposes requesting this court enter a declaratory judgment holding that ß-Nicotinamide Mononucleotide ("NMN") should not be excluded from the definition of a dietary supplement and alleges as follows:

INTRODUCTION

1. This case is about FDA's improper interpretation and application of subsection (ii) of Section 321(ff)(3)(B) (the "Drug Exclusion Clause") of the Dietary Supplement Health and Education Act ("DSHEA") and how that improper interpretation and application has led to the erroneous classification of NMN.

2. As set forth in further detail below, DSHEA established a regulatory framework for dietary supplements in the United States for the purpose of ensuring consumer access to dietary supplements while also protecting the health and welfare of US citizens. This framework created a careful balance of incentives to (1) protect investments by pharmaceutical companies that develop new drugs and (2) encourage the sale of dietary supplements containing health-promoting substances that have not undergone substantial clinical trials for use as a drug.

3. But instead of following the law, FDA has ignored Congress and the plain language of the statute by applying a facially incorrect interpretation of the Drug Exclusion Clause that places a thumb on the scale in favor of pharmaceutical companies. And FDA has stubbornly refused to heed any guidance or criticism of its approach. For example, in 2011 when FDA originally issued draft new dietary ingredients ("NDI") guidance, the principal authors of DSHEA—Sens. Orrin Hatch and Tom Harkin—urged FDA to withdraw the draft NDI guidance because it undermined DSHEA in important ways. FDA ignored the request, perhaps believing it understood the law better than the elected representatives who wrote the legislation.[1] Recent attempts by elected representatives for FDA accountability have also fallen on deaf ears.

[1] As discussed below, FDA's silence on NPA's request for clarity on FDA's about-face ignores the advice given by the Reagan-Udall Foundation for the Food and Drug Administration in October 2023 that "[p]rioritizing communications and being accountable for communication efforts should permeate the Agency." "Strategies for Improving Public Understanding of FDA-Regulated Products" at 6.

Representative Jeff Duncan's request for FDA to hold a public hearing on NMN was also rejected by FDA.

4. FDA's misinterpretation of DSHEA harms NPA members who cannot sell dietary supplements, and the public, who are denied the benefits of dietary supplements. Under this misapplication of the law, FDA has created an unprecedented power for itself to reverse the status of dietary supplement ingredients that were previously reviewed by the agency. This has never happened in the thirty years of DSHEA. Reasonable attempts for clarification of FDA's policies have been, and remain, in vain. FDA's refusal to act on these requests further denies companies and trade associations from appealing the decision. In fact, recent detention of NMN by FDA shows that it has made a final decision and is engaging in enforcement efforts in accordance with that decision.

5. FDA's interpretation of subsection (ii) of the Drug Exclusion Clause threatens to severely limit dietary supplement innovation and block consumer access to dietary supplements due to FDA's actions that unfairly favor pharmaceutical companies and permit those companies to seek removal of otherwise safe dietary supplements from the market.[2] A primary motivation behind DSHEA legislation was that if FDA remained unchecked, it would begin classifying everyday vitamins, minerals, herbs and amino acids as drugs.[3]

---

[2] FDA is the administrative agency responsible for enforcing the Food, Drug, and Cosmetic Act ("FDCA"), as amended by DSHEA. The term "dietary supplement" is defined in DSHEA and authorizes FDA to determine whether certain products fall under that definition.

[3] It was noted during the congressional hearings on DSHEA that in 1973, FDA published final regulations classifying many popular vitamins and minerals as drugs and the public reaction was "so intense" that Congress amended the FDCA in 1976 to "make clear that safe vitamin and mineral products should not be regulated as if they were dangerous drugs." 139 Cong. Rec. S4561-02 (April 7, 1993), 1993 WL 102951 at *S4577. Several years later, FDA began soliciting comments on whether certain amino acids and herbs should be classified as drugs. 140 Cong. Rec. S11708-01 (Aug. 13, 1994) 1994 WL 424972 at *S11712. Based on this track record, Congressman Hatch expressed great concern that, if left unchecked, FDA would begin

6. The Drug Exclusion Clause was added as a compromise to the original DSHEA legislation specifically to assuage the fears of some members of Congress that pharmaceutical companies "could avoid the drug approval process by marketing drug products as dietary supplements."[4] FDA's interpretation of subsection (ii) of the Drug Exclusion Clause is in direct contravention of congressional intent.[5]

7. In the Senate Report recommending the passage of DSHEA, the Senate clarified that under the Drug Exclusion Clause, "a substance which has been marketed as a dietary ingredient in a dietary supplement, or otherwise as a food, does not lose its status as a food (assuming it is intended for use as a dietary supplement or other food purpose as shown by its promotional materials) just because FDA approves the substance for use as an active ingredient in a new drug, certifies a finished product containing the substance as an antibiotic, or licenses a finished product containing the substance as a biologic. Those types of products would be drugs because they would be promoted with drug claims. They would, and should, have no effect on the food status of a properly labeled dietary supplement. For example, if ever FDA should eventually

---

transforming vitamins, minerals, herbs, animo acids and other nutritional substances into prescription drugs, regardless of the substantial and reputable scientific research supporting the safety of the dietary supplement. *Id*.

[4] S. Rep. 103-410 (Oct. 8, 1994), 1994 WL 562259 at *20 (drafters of the Drug Exclusion Clause emphasized that "[a]lthough current authorities should be adequate to deal with such potential problems, the committee is sensitive to those concerns."); *see also* 140 Cong. Rec. S12104-01 (Aug. 18, 1994), 1994 WL 424972 at *S12104; *see also* 140 Cong. Rec. S11708-01 (August 13, 1994), 1994 WL 424972 at *S11709.

[5] Note that while the chief sponsors of DSHEA specifically stated that, aside from the Statement of Agreement, "it is the intent of the chief sponsors of the bill that no other reports or statements be considered as legislative history for the bill." Despite this clear instruction, FDA has repeatedly cited to prior congressional records in support of their arguments of congressional intent. *See* 140 Cong. Rec. H11173-02 (Oct. 6, 1994), 1994 WL 553639 at *H11179; *see also* FDA, *Dockets Nos. FDA-2021-P-0523 & FDA-2021-P-0938* (Mar. 31, 2022), available at https://downloads.regulations.gov/FDA-2021-P-0938-0030/attachment_1.pdf (letter written by FDA where it cites to congressional reports and statements in support of its arguments).

approve Vitamin C as a drug to treat cancer, Vitamin C properly would also continue to be available as a dietary supplement (food) product, so long as it is promoted as a dietary supplement without disease prevention claims."[6]

8. Throughout the legislative history, it is abundantly clear that the Drug Exclusion Clause was added to DSHEA for the very limited purpose of ensuring that drugs and bona fide pending drugs (i.e., products that have undergone substantial clinical trials that have been made public) would not evade appropriate testing and investigation by being marketed as a dietary supplement.[7] Yet, despite Congress' intent, FDA has instead interpreted subsection (ii) of the Drug Exclusion Clause to knock otherwise safe dietary supplements off the market simply because there was, at some point in time, a clinical trial conducted on the supplement (irrespective of whether the supplement is ever formally approved to be sold as a drug).

9. In practice, FDA's interpretation of subsection (ii) of the Drug Exclusion Clause permits pharmaceutical companies to game the system. They can secretly conduct a single basic clinical trial (that, by itself, is not enough to get formal drug approval) on a dietary ingredient, build up the public's demand for that dietary ingredient, and then, once that demand gets high enough, cut off the supply by announcing to the public and FDA that it has conducted clinical trials

---

[6] S. Rep. 103-410 (Oct. 8, 1994), 1994 WL 562259 at *20-21.

[7] S. Rep. 103-410 (Oct. 8, 1994), 1994 WL 562259 at *20 (during consideration of DSHEA, "concerns were expressed that manufacturers or importers of drugs could avoid the drug approval process by marketing drug products as dietary supplements"); *see also* 140 Cong. Rec. S12104-01 (Aug. 18, 1994), 1994 WL 424972 at *S12104 ("the [Drug Exclusion Clause] assures that prescription drugs cannot escape appropriate review and oversight by being classified as dietary supplements"); *see also* 140 Cong. Rec. S11708-01 (August 13, 1994), 1994 WL 424972 at *S11709 ("Some then believed that [the original DSHEA legislation] would allow drugs such as taxol to be marketed in the United States as dietary supplements. Senator Harkin and I worked for some time after the markup to resolve that issue, and the language we present today addresses that concern.")

on the ingredient and so the ingredient can no longer be sold as a dietary supplement. This is no mere attorney-created hypothetical, it is the exact chain of events took place with NMN.

10. Moreover, FDA's interpretation of subsection (ii) of the Drug Exclusion Clause is also erroneous for the following reasons:

(1) Basic canons of statutory interpretation require that the operative date for subsection (ii) of the Drug Exclusion Clause to be the date the substantial clinical trial is made public[8], not the date the IND is "authorized" by FDA.[9] Yet FDA has interpreted the operative date for subsection (ii) of the Drug Exclusion Clause to be a date FDA is prohibited from disclosing to the public pursuant to FDA's later promulgated regulation, 21 C.F.R. 312.130(a). This misinterpretation of the statute means that dietary supplement makers are in the dark about when clinical studies allegedly began, and this regulation—established by FDA itself—contradicts the statutes intent regarding publication of the clinical trial. *See Section VII(A) infra.*

(2) FDA's interpretation of the phrase "substantial clinical investigations" fails to define (or provide context) to the term "substantial". Thus, in effect, FDA improperly treats *any* clinical trial as one that is "substantial." *See Section VII(C) infra.*

(3) FDA has interpreted the phrase "marketed as a dietary supplement or food" to mean lawful marketing in the United States, however, the plain language of the statute does not make this distinction—and FDA does not require proof of "lawful" marketing when approving a new dietary ingredient.[10] *See Section VII(F) infra.*

11. In addition to the reasons outlined above, FDA's interpretation of subsection (ii) of the Drug Exclusion Clause in respect to NMN specifically is erroneous for the following reasons:

---

[8] *I.e.*, the last required element and the date that necessarily occurs last.

[9] *I.e.*, the middle element and a date that cannot logically occur after the date the clinical trial is made public.

[10] DSHEA's definition of a dietary supplement uses the terms "article," "dietary ingredient," and "dietary supplement" in a manner where those terms can, at times, be used interchangeably. This is discussed further herein, but those terms should be treated as synonymous in this complaint, unless the context in which they are used confers a difference amongst them.

(1) FDA permits companies to certify that its products are Generally Regarded as Safe (GRAS). NMN has self-GRAS[11] status and, according to FDA's own guidelines, does not require a New Dietary Ingredient Notification ("NDIN") to be sold as a dietary supplement. *See* Section V(B) *infra.*

(2) It is indisputable that (a) NMN is naturally present in foods and the human body and (b) NMN is a naturally occurring derivative of vitamin B3 and a precursor of nicotinamide adenine dinucleotide ("NAD+"), both of which are dietary supplements. *See* Section V(A) *infra*.

(3) The clinical trials cited by FDA do not mention NMN.

(4) The clinical trials cited by FDA cannot, at this phase, be considered "substantial" because they are not adequate to support drug approval.

I. FINAL AGENCY ACTION

12. On multiple occasions, FDA has stated its conclusion that NMN is excluded from the definition of a dietary supplement under subsection (ii) of the Drug Exclusion Clause. This has been demonstrated by FDA's revocation of Acknowledgement Letters of NDIN notifications, refusal to respond to NPA's Citizen's Petition, and most recently detaining shipments of NMN.

13. In 2022, FDA approved NMN as a new dietary ingredient that could be marketed as or in a dietary supplement.[12] Later that same year, however, FDA revoked[13] its approval of

[11] Self-GRAS refers to the self-determination process for effectuating ingredients as GRAS using the same scientific procedure used by FDA.

[12] *See* Letter from FDA to SyncoZymes Co., Ltd, Regarding NDIN 1247 (May 16, 2022), attached hereto as **Exhibit A**.

[13] To NPA's knowledge, the reversal of an Acknowledgement Letter has only occurred in one other instance. In 2016, FDA indicated its intent to withdraw its acknowledgement of the dietary supplement vinpocetine (which had received five prior acknowledgements) due to new information that came to light. When attempting to withdraw its acknowledgment, FDA conceded it was aware that "by not objecting to the NDI notifications, FDA allowed the development of a market for dietary supplements containing vinpocetine, and we are cognizant of the fact that numerous firms did their best to comply with the law in reliance on our apparent regulatory posture. We assure you that FDA will be mindful of the need to treat responsible companies fairly as we move forward and that we will comply with all relevant statutes and regulations as we determine what next steps are appropriate." *See* Letter from FDA to Senator Orrin G. Hatch, Regarding the Request for Comment on the Status of Vinpocetine (Dec. 16, 2016), attached hereto as **Exhibit B**.

NMN due to "new information that came to light." This "new information" allegedly demonstrated "NMN is an article authorized for investigation as a new drug *by the FDA*" and, as such, "may not be marketed as or in a dietary supplement" because NMN is excluded from the definition of a dietary supplement pursuant to subsection (ii) of the Drug Exclusion Clause.[14]

14. On December 1, 2022, NPA requested FDA to open a public docket to receive information regarding the earliest marketing of NMN in a food or dietary supplement, which FDA summarily denied, stating that it had already "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."[15]

15. On March 9, 2023, NPA along with Alliance for Natural Health USA, filed a Citizen's Petition challenging FDA's determination that NMN is excluded from the definition of a dietary supplement.[16]

16. Under 21 C.F.R. 10.30(e)(2)—a regulation promulgated by FDA—FDA is required to respond to all Citizen's Petitions within one hundred and eighty (180) days.

17. The 180-day deadline for NPA's Citizen's Petition fell on September 5, 2023.

18. On August 30, 2023, just before the expiration of the 180-day deadline, FDA sent NPA a letter stating that "in accordance with 21 CFR 10.30(e)(2), [FDA has] not reached a decision

[14] *See* Letter from FDA to SyncoZymes Co., Ltd., Regarding NDIN 1247 (November 4, 2022); *see also* Letter from FDA to Mongolia Kingdomway Pharmaceutical Limited, Regarding NDIN 1259 (October 11, 2022); *see also* Letter from FDA to Mongolia Kingdomway Pharmaceutical Limited, Regarding NDIN 1259 (November 4, 2022); Letter from FDA to CellMark, Regarding NDIN 1265 (January 18, 2023). All letters are attached hereto as **Exhibit C**.

[15] *See* Letter from FDA to NPA, Response to Request to Open a Docket for NMN (January 20, 2023), attached hereto as **Exhibit D**.

[16] *See* Citizen's Petition, Regarding NMN (March 9, 2023), attached hereto as **Exhibit E**.

on your petition within the first 180 days due to competing agency priorities. However, be advised that our staff is evaluating your petition."[17]

19. As of the date of this lawsuit, which is filed almost a year after the expiration of the 180-day deadline and almost a year and half after the filing of the Citizen's Petition, FDA has still not substantively responded to the Citizen's Petition.[18]

20. On August 13, 2024, FDA issued a "Notice of FDA Action" to one of NPA member's.[19] The Notice states that the NMN it sought to import was detained "subject to refusal pursuant to the Federal Food Drug and Cosmetic Act (FD&CA)" because "it appears to be a new drug within the meaning of Section 201(p) without an approved New Drug Application (NDA)."[20]

21. FDA's ongoing refusal to respond to NPA's Citizen's Petition combined with FDA's recent detention of a member of NPA's NMN has placed NPA and its members in an untenable position. FDA has shown it will seek to enforce its conclusion on NMN and improperly detain NMN while intentionally refusing to respond to NPA's Citizen's Petition.

22. This is not an issue that will resolve itself absent judicial intervention. This is supported by the fact that FDA's delay in responding to NPA's Citizen Petition is not unique to this case.

---

[17] *See* Letter from FDA to NPA, Regarding Citizen's Petition (August 30, 2023), attached hereto as **Exhibit F**.

[18] The only response NPA has received regarding its Citizen's Petition is the August 30, 2023 letter discussed in paragraph 18 above.

[19] *See* **Exhibit I**.

[20] *Id.* at 2.

23. According to a study[21] done by Epstein, Becker and Green, a national law firm, FDA routinely sits on Citizen's Petitions well past the 180-day deadline. The Epstein, Becker and Green study shows a significant number of Citizen's Petitions still open 4,000 days—more than *20 times* longer than permitted by the 180-day deadline.[22]

24. FDA's routine (and often indefinite) delay in responding to Citizen's Petitions prejudices stakeholders like NPA and its members. FDA's actions plainly demonstrate that it will not timely or substantively address these Petitions, and its failure to act prevents organizations like NPA from seeking judicial redress if a court were to sanction FDA's inaction as a final agency action under the APA. This is especially true where NPA has actively requested FDA to substantively respond to the Petition, or at least formally acknowledge FDA's stated conclusion NMN is excluded from the definition of dietary supplement.[23]

25. FDA's (1) refusal to open a public docket to gather information regarding the earliest marketing of NMN, (2) its public "conclusion that NMN is excluded from the definition of dietary supplement,"[24] (3) its determination to permit NPA's Citizen's Petition to sit in limbo for the past year and a half with no substantive response or resolution, and (4) its detention of NMN imported by an NPA member, amounts to a final agency action because FDA's actions and

---

[21] *See* Bradley Merill Thompson, *Unpacking Averages: FDA's Extraordinary Delay in Resolving Citizen Petitions*, Epstein, Becker and Green – Health Law Advisor (October 3, 2023), attached hereto as **Exhibit G**.

[22] In fact, the status of the dietary supplement vinpocetine, referenced in footnote 12 above, is still pending before FDA today, nearly eight (8) years later.

[23] *See* Letter from Congressman Duncan to FDA, Regarding NMN (April 27, 2023); *see also* Letter from Congressman Duncan to FDA, Regarding NMN (August 21, 2023). Both letters are attached hereto as **Exhibit H**.

[24] *See* Letter from FDA to NPA, Responding to Request to Open a Docket for NMN (January 20, 2023), attached hereto as **Exhibit D**.

inactions foreclose any further agency review of FDA's position regarding the status of NMN as a dietary supplement.

26. However, if the foregoing circumstances are not deemed a final agency action, in the alternative, NPA alleges that FDA's actions and inactions show that FDA has no intention of changing its position on the status of NMN as a dietary supplement, as evidenced at least by the detention of imported NMN. As a result, any contention by FDA that administrative remedies have not been exhausted should be rejected because any additional administrative review would be futile. *See Etelson v. Off. of Pers. Mgmt.*, 684 F.2d 918, 923 (D.C. Cir. 1982); *Cutler v. Hayes*, 818 F.2d 879 (D.C. Cir. 1987) ("It is now beyond dispute that the exhaustion doctrine is to be applied flexibly, with an eye toward its underlying purposes); *Cutler v. Hayes*, 818 F.2d 879 (D.C. Cir. 1987) (quoting *Etelson* stating where an agency has committed itself to not change its rule, it has made known that its general views are contrary to those of the complainant and the doctrine of exhaustion need not be applied).

27. FDA cannot be permitted to use its failure to perform its congressionally mandated duties as both a sword and a shield. On the one hand, FDA has publicly concluded that NMN is excluded from the definition of a dietary supplement and refused requests from members of Congress and industry members to undertake any further review of this decision by refusing to open a public docket on the matter. On the other hand, FDA may attempt to sidestep judicial scrutiny by contending that NPA's citizens petition remains open, and is therefore not finally concluded, even though FDA has had over a year and a half to affirm or revise its prior conclusion that NMN is excluded from the definition of a dietary supplement (approximately three times longer than the 180-day deadline). Any attempt by FDA to insulate itself from this judicial

proceeding by manufacturing an alleged lack of standing defense based on the *appearance* of a lack of final agency action while taking a *de facto* agency action must be rejected.

28. Accordingly, NPA respectfully requests that this Court find that FDA has rendered a final agency action that prevents the manufacturing, distributing, supplying or selling NMN as a dietary supplement and grant the relief requested in NPA's Prayer for Relief.

29. Alternatively, if this Court finds that FDA actions are not final, NPA respectfully requests this Court to (a) hold the Defendant's delay in responding to the Citizen's Petition is unreasonable and compel FDA to respond to NPA's Citizen's Petition forthwith pursuant to the Administrative Procedure Act, or (b) determine that NPA has standing because any further attempts to resolve the issue at FDA would be futile.

II. DEFENDANTS AND JURISDICTION

30. Defendant FDA is an agency of the United States government tasked with administering and enforcing the FDCA, as amended by DSHEA.

31. Defendant HHS is an executive department of the United States Government and is tasked with overseeing the actions of FDA.

32. Defendant Xavier Becerra is the Secretary of HHS and, as such, is responsible for overseeing the actions of FDA.

33. Defendant Robert M. Califf is the Commissioner of FDA and, as such, is responsible for overseeing the activities of FDA.

34. Defendant Xavier Becerra and Defendant Robert M. Califf, are being sued in their official capacities under the doctrine of *Ex Parte Young*, 209 U.S. 123 (1908).

35. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331, 1346, and 5 U.S.C. §§ 701-06.

36. An actual controversy exists between the parties within the meaning of 28 U.S.C. § 2201(a) and this Court may grant declaratory relief, injunctive relief, and other relief pursuant to 28 U.S.C. §§ 2201-02 and 5 U.S.C. §§ 705-06.

37. More particularly, jurisdiction under 5 U.S.C. §§ 701-06 is proper due to FDA's conclusion that NMN does not fall under the definition of a dietary supplement pursuant to 21 U.S.C. § 321(ff)(3)(B)(ii) or, in the alternative, due to FDA's unreasonable delay in responding to NPA's Citizen's Petition.

38. This Court has personal jurisdiction over Defendant pursuant to Fed. R. Civ. P. 4(k)(1), because the Defendants either reside in and/or conduct a substantial proportion of their official business in the District of Columbia.

39. Venue is proper in the District of Columbia under 28 U.S.C. § 1391(b) because the Defendants either reside in and/or conduct a substantial proportion of their official duties within the District of Columbia and events giving rise to this action occurred in the District of Columbia.

III. NPA'S STANDING

40. NPA is a Delaware non-profit corporation having its principal place of business in Washington, DC.

41. NPA advocates before Congress, FDA, HHS, the Federal Trade Commission and other federal and state agencies, legislatures, state attorneys general and courts across the country on behalf of its members.[25]

42. NPA is the nation's largest and oldest nonprofit trade association dedicated to the natural products industry. The term "natural products" includes a wide array of consumer goods,

[25] Additional information regarding NPA and its work can be found on its website at News Room, https://www.npanational.org/news-room/.

including natural and organic foods, dietary supplements, health, wellness and beauty products, functional foods, "green" cleaning supplies, and more.

43. Many of NPA's members[26] are manufacturers, distributers, suppliers or sellers of dietary supplements and, more specifically, NMN. Therefore, as a direct result of FDA's conclusion that NMN is excluded from the definition of dietary supplement and cannot be sold or marketed as or in a dietary supplement, NPA's members are prohibited from manufacturing, distributing, supplying, or selling NMN as a dietary supplement to consumers.

44. One or more NPA members either (a) previously manufactured, distributed, supplied or sold NMN prior to FDA revoking NMN's status as a dietary supplement and have been forced to cease such activity to their detriment, (b) are dietary supplement manufactures, suppliers, distributors or retailers who are ready, willing and able to manufacture, distribute, supply or sell NMN pending the outcome of this action and who would otherwise manufacture, distribute, supply or sell NMN but for FDA's posture, and/or (c) had its NMN detained upon importation into the United States.

45. **Exhibit I** attached hereto includes affidavits from NPA members who have suffered economic harm due to FDA's revocation of NMN's status as a dietary supplement.

46. As set forth in the attached affidavits, at least three of NPA's members, iHerb, LLC, Cellmark USA, LLC, and Galaxy Nutrition LLC, were directly harmed by FDA's conclusion that NMN does not fall under the definition of a dietary supplement as each company manufactured, distributed, supplied and/or sold NMN and have suffered verifiable lost revenue or seizure of

[26] NPA's Board of Directors, several of which are directly involved in the dietary supplement industry, are listed on NPA's website, Board of Directors, https://www.npanational.org/about/board-of-directors/.

goods directly attributable to NMN sales as a direct consequence of FDA's conclusion that NMN does not fall under the definition of a dietary supplement.

47. The relief requested herein will redress the harms suffered by iHerb, LLC, Cellmark USA, LLC, Galaxy Nutrition LLC, and other harmed NPA members.

48. Based on the above, one or more NPA members have individual standing to sue the Defendants.

49. However, because this action involves a facial challenge to the legality of FDA's actions, NPA's members' individual participation in this action is unnecessary.

50. By challenging FDA's conclusion that NMN is excluded from the definition of a dietary supplement (and as a result cannot be sold to consumers as a dietary supplement), NPA is carrying out its stated mission to "advocate for the rights of consumers to have access to products that will maintain and improve their health, and for the rights of retailers and suppliers to sell these products."[27]

51. Accordingly, NPA has standing to bring this action on behalf of its members under the theory of associational standing. *See Window Covering Mfrs. Assoc. v. Consumer Product Safety Comm'n*, 82 F.4th 1273, 1282 (D.C. Cir. 2023) (holding that trade organization has standing to pursue APA claim on behalf of its members).

IV. DSHEA AND THE UNDERLYING DEFINITION FOR DIETARY SUPPLEMENTS

52. DSHEA was enacted to strike a balance between the need for consumers to have access to dietary supplements while also preserving the government's interest in protecting the

[27] NPA's bio, as well as their mission and vision statements can be found on their website, About Natural Products Association, https://www.npanational.org/about/ and, Mission and Values, https://www.npanational.org/about/mission-and-vision/.

public from products that make false and misleading claims and from unsafe or adulterated products.[28]

53. DSHEA's expansive language was intended to cast a wide net around what constitutes a dietary supplement by classifying products as dietary supplements by default unless they cause harm to the public or are mislabeled. This intention is embodied in the Congressional findings supporting the passage of DSHEA which states that while "the Federal Government should take swift action against products that are unsafe or adulterated, the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products and accurate information to consumers."[29]

54. Under DSHEA, a dietary supplement is defined as an article that:

(a) contains at least one dietary ingredient,

(b) is swallowed,

(c) is not intended to replace a meal,

(d) is labeled as a dietary supplement and

(e) does not contain an ingredient found to be excluded under 21 U.S.C. § 321(ff)(3)(B) of DSHEA.

See 21 U.S.C. § 321(ff).

55. A "dietary ingredient" is defined as a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance used by man to supplement the diet by increasing the total dietary intake or a concentrate, metabolite, constituent, extract, or combination of any ingredient described above. 21 U.S.C. § 321(ff)(1).

---

[28] 103rd United States Congress, S.784 – Dietary Supplement Health and Education Act of 1994, Public Law 103-417; October 25, 1994, available at https://ods.od.nih.gov/About/dshea_Wording.aspx (original text PDF).

[29] *Id*.

56. As noted in paragraph 54(e) above, a product will not be considered a dietary supplement if it contains an ingredient excluded under 21 U.S.C. § 321(ff)(3)(B).

57. An ingredient is excluded under 21 U.S.C. § 321(ff)(3)(B), if it contains:

***

> (ii) an article authorized for investigation as a new drug, antibiotic or biological 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, certification, licensing 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 Act.

21 U.S.C. § 321(ff)(3)(B).

58. Pursuant to 21 U.S.C. § 350b(d) of DSHEA, any dietary ingredient which was *not* marketed in the United States prior to October 15, 1994[30] will be considered an NDI. Any company wishing to market a dietary supplement containing an NDI must submit a premarket safety notification (also known as an "NDI notification" or "NDIN") to FDA at least 75 days prior to introducing the product to the market, unless the NDI has "been present in the food supply as an article used for food in a form in which the food has not been chemically altered." *See* 21 U.S.C. § 350b(a)(1).

59. An NDIN must include information, including any citation(s) to published articles, which forms the basis for the company's conclusion that the dietary supplement containing the NDI will "reasonably be expected to be safe."[31]

---

[30] There is no authoritative list of dietary ingredients that were marketed prior to October 15, 1994.

[31] U.S. Department of Health and Human Services, Food and Drug Administration and Center for Food and Safety and Applied Nutrition, *Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry, Draft Guidance*, p. 61 & 82, available at https://www.fda.gov/media/99538/download (April 2024 version, replaces draft guidance issued in August 2016 and March 2024)(still open for comment). This draft guidance shall be referred to herein as "April 2024 Draft Guidance."

60. FDA reviews NDINs to determine if they provide an adequate basis to support the company's conclusion that the dietary supplement can be reasonably expected to be safe.[32]

61. After FDA finishes its review of the NDIN, FDA will respond by sending one of the following letters: (a) a letter of acknowledgment without objection (an "Acknowledgement Letter"), (b) a letter listing deficiencies that make the NDIN incomplete under 21 CFR 190.6[33], (c) an objection letter raising concerns with the adequacy of the identity information or safety information (e.g., identifying gaps in the history of use or that the safety information on the NDI does not support the conditions of use), or (d) a letter raising other regulatory issues with the ingredient or product (e.g., the ingredient is not a dietary ingredient under 21 U.S.C. 321(ff)(1) or the product does not satisfy all parts of the dietary supplement definition under 21 U.S.C. 321(ff)).[34]

62. Receiving an Acknowledgment Letter without objection means FDA did not find any reason to object to the notifier's basis for concluding that the NDI and the dietary supplement containing the NDI will reasonably be expected to be safe.[35]

---

[32] *See id* at 10-11.

[33] 21 C.F. R. 109.6 establishes the requirements for premarket notification.

[34] *See* U.S. Department of Health and Human Services, Food and Drug Administration and Center for Food and Safety and Applied Nutrition, *Dietary Supplements: New Dietary Ingredient Notification Procedures and Timeframes: Guidance for Industry*, p. 12-13, available at https://www.fda.gov/media/176512/download (March 2024)(this guidance finalizes Section V ("NDI Notification Procedures and Timeframes") of the 2016 revised draft guidance (Draft Guidance for Industry: New Dietary Ingredient Notifications and Related Issues) in addition to several related questions from other sections of the draft guidance). This final guidance shall be referred to herein as "Final March 2024 Timeline Guidance"

[35] *Id* at 5.

63. Once a party receives an Acknowledgment Letter it may begin marketing the dietary supplement containing the NDI seventy-five (75) days after the date it filed its NDIN.[36]

64. The caveat is that FDA may, even after sending an Acknowledgment Letter, later determine that the NDI and the dietary supplement that contains the NDI is, e.g., adulterated due to safety concerns (i.e., significant or unreasonable risk of illness or injury).[37]

65. FDA bears the burden of demonstrating that an NDI is adulterated due to safety concerns.[38] However, even a finding of adulteration does not provide a basis to withdraw the Acknowledgment Letter for the NDI but rather presents an opportunity for the NDIN holder to address FDA's safety concerns.[39]

66. Notwithstanding the foregoing, an NDIN is not required when the NDI has been "present in the food supply as an article used for food in a form that has not been chemically altered."[40] FDA interprets the phrase "present in the food supply" to refer to the conventional food supply.[41]

67. An NDIN is also not required for an NDI that has Self-GRAS (defined in paragraph 11(1) above) so long as the substance (a) has been used in the food supply (i.e., in conventional foods) and (b) is to be used as a dietary ingredient without chemical alteration.[42]

---

[36] *Id*.

[37] *Id*.

[38] 21 U.S.C. § 342(f)(1)(D).

[39] Final March 2024 Timelines Guidance at 13.

[40] April 2024 Draft Guidance at 23.

[41] *Id*.

[42] *Id*; *see also* Letter from FDA to Attorney Kevin Bell, Regarding beta-alanine (April 28, 2021) (public letter form the director of FDA noting that because beta-alanine could be found in energy drinks, it was present in the food supply and did not require an NDIN). This letter attached hereto as **Exhibit J**.

V. NMN DOES NOT REQUIRE AN NDIN TO BE SOLD AS A DIETARY SUPPLEMENT FOR TWO (2) REASONS

68. As a preliminary matter, a search of FDA's adverse event reporting system identifies no instances of adverse events arising from the usage of NMN, even though NMN has been on the market as a dietary supplement across the world for years, including the United States.[43] Research suggests that supplementing diets with NMN may have anti-aging and metabolic benefits.[44]

69. NMN does not require an NDIN for at least two reasons.

A. ***Reason 1****: NMN is "present in the food supply as an article used for food in a form that has not been chemically altered."*

70. Scientific studies demonstrate that NMN is naturally present in foods such as cow milk, mushrooms, tomatoes, edamame, avocados, broccoli, cabbage, cucumbers, beef, shrimp and many other foods.[45]

71. NMN is also naturally present in human breast milk, meaning infants have been ingesting NMN for as long as humans have been around.[46]

---

[43] NMN has been sold as a dietary supplement in Japan, Canada and the UK since at least 2015. *See* **Exhibit E**, p. 7.

[44] Shade, Christopher, *The Science Behind NMN–A Stable, Reliable NAD+Activator and Anti-Aging Molecule*, Integr Med, Feb. 2020, vol. 19, issue 1, p. 12-14, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7238909/#:~:text=It%20is%20well%20known%20that,and%20extracellular%20form%20(eNAMPT).

[45] Mills, Kathryn, et. al., *Long-term administration of nicotinamide mononucleotide mitigates age-associated physiological decline in mice*, Cell Metabolism, Oct. 27, 2016, Vol. 1, Issue 6, p. 795-806, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5668137/; Trammell, Samuel, et al., *Nicotinamide Riboside Is a Major NAD+ Precursor Vitamin in Cow Milk*, Journal of Nutrition, May 2016, Vol 146, Issue 5, p. 957-963, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6879052/.

[46] Saito, Yoshie, *Effect of Nicotinamide Mononucleotide Concentration in Human Milk on Neurodevelopmental Outcome: The Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study*, Nutrients, Dec. 16, 2023, Vol. 16, Issue 1, available at

72. Accordingly, the NMN dietary supplement NPA's members want to sell (as compared to the chemically altered and patented MIB-626 sold by Metro International Biotech ("Metrobiotech")), is in a non-chemically altered form and has existed in food for many years (and before the submission of any clinical study), is not subject to the NDIN requirement and *cannot*, under FDA's own interpretation of DSHEA, be excluded from the definition of a dietary supplement.

73. NMN also meets the definition of a dietary supplement under Section 321(ff)(1) because it (a) is "a dietary substance for use by man to supplement the diet by increasing the total dietary intake" and (b) is a metabolite of other lawfully sold dietary ingredients. *See* 21 U.S.C. § 321(ff)(1).

74. A product is considered a dietary supplement if it contains "a concentrate, metabolite, constituent, extract, or combination of any [vitamin, mineral, herb, botanical or amino acid]."

75. NMN is a type of molecule know as a nucleotide. Nucleotides are the building blocks of DNA.[47]

76. NR and NMN are both precursors to NAD+.

77. The human body naturally converts NR to NMN and then converts NMN into NAD+.[48]

---

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10780616/#:~:text=The%20median%20amount%20of%20NMN,in%20infants%20at%2024%20months.

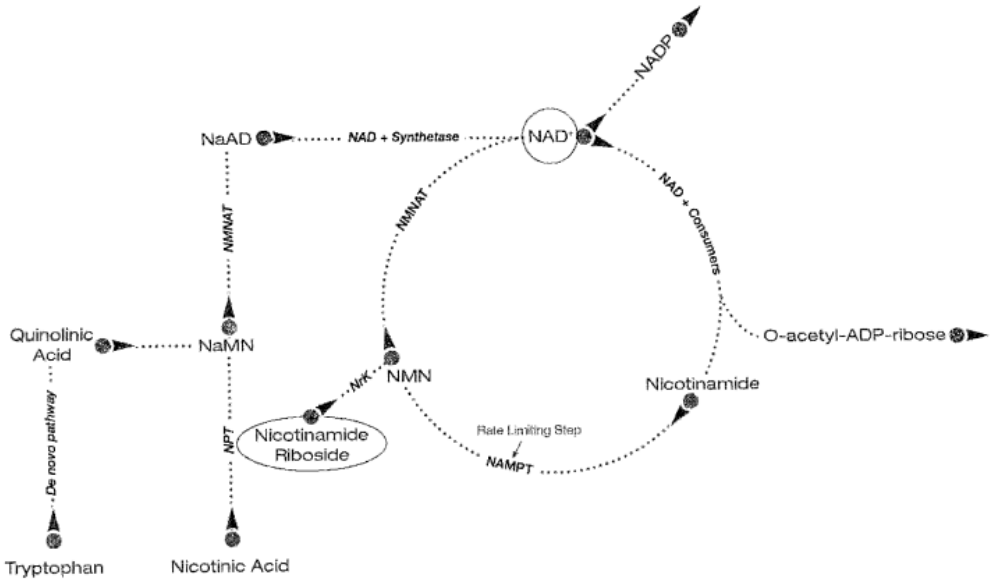
[47] Meissner, Morgan, *NMN (NicotinamideMononucleotide): Benefits, Side Effects and Dosage*, Healthline, Aug. 10, 2022, available at https://www.healthline.com/health/nmn-nicotinamide-mononucleotide-benefits-side-effects-and-dosage.

[48] Raman, Ryan, *Nicotinamide Riboside: Benefits, Side Effects and Dosage*, Healthline, July 13, 2023, available at https://www.healthline.com/nutrition/nicotinamide-riboside; Elysium Health, *NMN and NR: How These NAD+ Precursors Measure Up*, Elysium, available at https://www.elysiumhealth.com/blogs/aging101/nmn-and-nr-how-these-nad-precursors-measure-

78. NMN supplementation is also believed to increase the NAD+ in the body.

79. NAD+ is a critical coenzyme that is found in every cell of the human body. It is essential for many cellular processes, including converting food into energy, repairing damaged DNA, and energy metabolism.[49]

80. The metabolic pathway in humans is depicted below:



81. It is uncontroverted that NMN is a naturally occurring derivative of vitamin B3 (e.g. nicotinamide riboside or "NR") and a precursor to NAD+, which is an essential coenzyme involved in the numerous biological processes.

---

up#:~:text=Like%20NR%2C%20NMN%20is%20a,%2C%20as%20a%20result%E2%80%94crucial; Yang, Yue, et al., *NAD+ metabolism: Bioenergetics, signaling and manipulation for therapy*, Biochimica et Biophysica Acta (BBA) – Protiens and Proteomics, vol. 1864, no. 12, December 2016, p. 1787-1800, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5521000/.

[49] *Id*.

82. In the pathway shown above, NR is converted to NMN in the human body, thereby establishing NMN's status of a metabolite of NR.

83. NR has been sold as a dietary supplement or dietary ingredient prior to any of the published clinical trials related to NMN.

84. Accordingly, NMN, was and remains a lawful dietary supplement due to (a) its ability to increase the total dietary intake of NAD+ and (b) its existence as a metabolite of NR, which was lawfully marketed and sold as a dietary ingredient long before the date of any alleged IND.

B. ***Reason 2****: NMN has Self-GRAS status.*

85. As outlined above, according to FDA an NDIN is not required for an NDI that has Self-GRAS status as long as the substance (a) has been used in the food supply (i.e., in conventional foods) and (b) is to be used as a dietary ingredient without chemical alteration.[50]

86. On December 19, 2018, Nutraland (also known as AceOneRS) and GeneHarbor received a Self-GRAS for their NMN product.[51]

87. Approximately two (2) years later, on September 25, 2020, CellMark USA, LLC and SyncoZymes (Shanghai) Co. Ltd ("SyncoZymes") also received Self-GRAS status for their product containing NMN.[52]

88. NMN, therefore, has Self-GRAS status.

---

[50] *See also* Letter from FDA to Attorney Kevin Bell, Regarding beta-alanine (April 28, 2021) (public letter form the director of FDA noting that because beta-alanine could be found in energy drinks, it was present in the food supply and did not require an NDIN). This letter attached hereto as **Exhibit J**.

[51] *See* **Exhibit K**.

[52] *See* **Exhibit I**, Affidavit of CellMark USA, LLC.

89. As early as September of 2015, Fractal Health began marketing and selling "Nicotinamide Mononucleotide 120mg NMN" as a capsule on their website for purchase within the United States.[53]

90. As early as July 2018, Alive by Nature began marketing and selling "NMN PURE Powder" which was a sublingual powder that could be absorbed under the tongue as well as "Sublingual/Chewable Tablets" which could be chewed like a mint or left under the tongue to dissolve.[54]

91. As early as October 13, 2019, Nutraland began advertising and marketing their Self-GRAS NMN product on their website for purchase within the United States.[55]

92. On November 8, 2019, BIOM Pharmaceuticals, began marketing and selling "Longiva Sublingual Powder Pure NMN" as a food additive for beverages or yogurt.[56]

93. In June of 2020, AceOneRS (a.k.a. Nutraland) began selling NMN coffee on Amazon.[57]

---

[53] *See* Wayback Machine, Nicotinamide Mononucleotide 120mg NMN, Fractal Health (September 21, 2015) available at https://web.archive.org/web/20150921065456/http://www.fractalhealth.com/product/nicotinamide-mononucleotide/. /

[54] *See* Wayback Machine, NMN Purse Powder, Alive by Nature (March 27, 2018), avalible at https://web.archive.org/web/20180327125140/http://alivebynature.com/product/nmn-pure-12-gram-jar-certified-strength-and-purity-nicotinamide-mononucleotide/ ; *see* also Wayback Machine, Sublingual/Chewable Tablets, Alive by Nature (July 13, 2018), available at https://web.archive.org/web/20180713050844/https://alivebynature.com/.

[55] *See* **Exhibit E, p. 7**.

[56] *See* **Exhibit L**, p. 4. While the referenced Exhibit cites to an Amazon link that is no longer active, the product can be found on BIOM Pharmaceuticals website at https://biomprobiotics.com/product/biom-nmn-sublingual-powder/ (last visited June 17, 2024). The product description states it "can be easily mixed with water or milk—or sprinkled in yogurt."

[57] *See* **Exhibit L**, p. 13; *see also* **Exhibit M**.

94. As early as July of 2021, ProHealth began selling its NMN Pro™ Powder in the United States.[58] ProHealth's NMN Pro™ Powder is in powder form and ingested by mixing it in water or other beverages.

95. On November 8, 2021, Doctor's Best began marketing and selling "Instant Whey Protein Concentrate plus NMN" as a food additive for smoothies, beverages or as a baking ingredient.[59]

96. Other publicly available documents identify nutritional compositions containing NMN as a vitamin at least as early as February of 2009.[60]

97. NMN has therefore been present in the food supply since at least 2019, if not earlier.[61]

98. As evidenced above, NMN was acknowledged as being a vitamin in the food supply at least as early as 2009.

99. As outlined in more detail above, NMN is a naturally occurring substance that has not been chemically altered.

---

[58] *See* Prohealth Longevity, NMN Pro™ Powder - Uthever® NMN, 100 grams, available at https://www.prohealth.com/products/prohealth-nmn-pro-powder-100-grams-ph529?selling_plan=3936387172 (last visited on July 8, 2024) (earliest review for product was "three years ago" – i.e., 2021). iHerb began selling ProHealth's product as early as July of 2022 on its website. *See* iHerb, ProHealth Longevity, NMN Pro, Pure NMN Powder, 250 mg, 15 g, available at https://gr.iherb.com/pr/prohealth-longevity-nmn-pro-pure-nmn-powder-250-mg-15-g/114174 (last visited on July 8, 2024) (earliest review for product is July 2022).

[59] *See* **Exhibit L**, p.10-11.

[60] U.S. Patent No. 8,075,934, Col. 7, ll. 18-27 (filed Feb. 13, 2009) (available at https://patentimages.storage.googleapis.com/b8/32/3a/c01943e4cdf321/US8075934.pdf).

[61] Since FDA refuses to open a public docket to gather information regarding the earliest dates of marketing NMN in the United States, NPA is unable at this time to definitively determine when NMN was first introduced in the food supply.

100. Accordingly, because NMN has Self-GRAS status and has been present in the food supply, it is exempt from the NDIN requirement and can be sold as a dietary supplement. *C.f.* **Exhibit J** (public letter from the director of FDA noting that because beta-alanine had Self-GRAS and could be found in energy drinks, it was present in the food supply and did not require an NDIN).

101. FDA bears the burden of proving that the NDIN requirements apply to NMN. *See* **Exhibit J** ("While the NDIN process . . . provides a powerful tool to FDA to be able to evaluate the safety of certain new dietary ingredients contained in dietary supplements . . . [the] FDA bears the burden of establishing that the requirement to submit an NDIN applies.").

102. Here, FDA has failed to carry this burden. FDA's position in its reversal letter neither mentions NMN's Self-GRAS status or states why NMN is subject to the NDIN requirement. This violates FDA's own guidelines regarding Self-GRAS status and, as such, is arbitrary and capricious.

VI. FDA'S REVERSAL LETTER AND ITS INTERPRETATION OF THE DRUG EXCLUSION CLAUSE

103. Even in situations where NDINs are not required, many companies continue to voluntarily submit NDINs for NDIs. This practice is recommended by FDA.[62]

104. On December 27, 2021, SyncoZymes[63] filed a NDIN with FDA for its dietary supplement containing NMN.

105. FDA responded to SyncoZymes's NDIN on February 24, 2022, stating that it was unable to establish the safety of SyncoZymes's NMN, because (a) the proposed NMN serving

[62] *See* April 2024 Draft Guidance at 23-25.

[63]Cellmark USA, LLC is a distributor for SnycoZymes. *See* **Exhibit I**, Affidavit of Cellmark USA, LLC.

level of 300 mg/day exceeded the amount of NMN found in various foods, (b) the sale of NMN in Japan at the same serving levels of 300 mg/day was insufficient to establish safety because the duration of NMN was less than two years which was an inadequate amount of time to establish the absence of adverse events and (c) the studies provided by the company were conducted on other forms of NMN (such as nicotinamide riboside ("NR")).[64]

106. On March 2, 2022, FDA and SyncoZymes met to discuss FDA's February 24th letter.

107. During that meeting Dr. Tyna Dao of FDA informed SyncoZymes that if they could provide FDA with evidence regarding NMN's history of use in other countries, FDA would consider that evidence when determining the expectation of safety for NMN.

108. After its meeting with FDA, SyncoZymes filed an updated NDIN for NMN which addressed FDA's concerns as discussed in the March 2, 2022 meeting, including additional information regarding the history of use in other countries.

109. On May 16, 2022, FDA sent SyncoZymes' an Acknowledgment Letter and stated SyncoZymes could begin marketing NMN as an NDI in dietary supplements as early as June 4, 2022.[65]

110. In June of 2022, FDA publicly designated SyncoZymes' NMN as an approved NDI on Regulations.gov.[66]

---

[64] *See* Letter from FDA to SyncoZymes, Regarding NDIN 1240 (February 24, 2022), attached hereto as **Exhibit N**.

[65] *See* **Exhibit A**.

[66] Regulations.gov; "NDI 1247 – beta-nicotinamide mononucleotide (B-NMN) from SyncoZymes (Shanghai) Co., Ltd."; July 28, 2022; https://www.regulations.gov/document/FDA-2022-S-0023-0027 (last visited, June 17, 2024).

111. Nearly six months later, on November 4, 2022, FDA withdrew its approval of NMN by withdrawing the Acknowledgment Letter it sent to SyncoZymes.[67]

112. Notably, FDA did not withdraw its approval of NMN as a dietary supplement due to any safety concerns related to NMN.

113. Rather in its November 4, 2022 letter (the "Reversal Letter"), FDA explained that "[b]ased on new information that came to light when we were reviewing another notification," FDA discovered that NMN was "an article authorized for investigation as a new drug by FDA" and, as such, was excluded from the definition of a dietary supplement under subsection (ii) of the Drug Exclusion Clause.[68]

114. Considering FDA is solely responsible for overseeing filed investigational new drug applications ("IND"), it is confounding that during the four (4) months FDA evaluated SyncoZymes' NDIN, it apparently did not identify the three (3) separate INDs (contained in its own internal database) that it now cites as the only reason why NMN may not be marketed or sold as or in a dietary supplement, and if it did, it clearly did not deem those INDs capable of precluding the issuance of the Acknowledgement Letter.[69]

115. In a footnote of the Reversal Letter, FDA cited to three (3) clinical trials for which it based its conclusion that NMN was an article authorized for investigation as a new drug and as

---

[67] *See* **Exhibit C**, p. 3-4.

[68] *See* **Exhibit C**, p. 3.

[69] While FDA can, by regulation, create an exception to the exclusions set forth in 21 U.S.C. § 321(ff)(3)(B) where a company files a citizen petition requesting such relief under 21 C.F.R. 10.30, according to FDA, as of March 2024, no such regulation has ever been granted by FDA. *See* 21 CFR 190.6; *see also* FDA, *Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry, Draft Guidance*, at 43.

such was ineligible to be considered a dietary supplement under subsection (ii) of the Drug Exclusion Clause. Each of the trials were conducted by Metrobiotech.

116. Under subsection (ii) of the Drug Exclusion Clause, depending on the date "an article [is] authorized for investigation as a new drug . . . for which substantial clinical investigations have [begun] . . . and . . . the existence of such investigations [has] been made public" a product that would otherwise be defined as a dietary supplement may be excluded from the definition of a dietary supplement.

117. FDA has interpreted subsection (ii) of the Drug Exclusion Clause to mean that, regardless of the date the clinical investigations have been made public, the date the article was authorized for investigation in a clinical trial under an IND is the critical date.

VII. FDA'S INTERPRETATION OF SUBSECTION (ii) OF THE DRUG EXCLUSION CLAUSE IS ERRONOUS FOR AT LEAST SEVEN (7) REASONS [70]

A. ***Reason 1****: Basic canons of statutory interpretation require the operative date for subsection (ii) of the Drug Exclusion Clause to be the date the substantial clinical trial is made public.*

118. The plain language of subsection (ii) of the Drug Exclusion Clause statute contains three elements: the article must be (1) authorized for investigation, (2) subject to substantial clinical investigations ***and*** (3) these investigations are made public. ("an article [is] authorized for investigation as a new drug . . . for which substantial clinical investigations have [begun] . . . and . . . the existence of such investigations [has] been made public").

[70] In the recent Supreme Court Case, *Loper Bright Enterprises v. Raimondo*, 144 S. Ct. 2244, 2247 (2024), the Court in overruling *Chevron, U.S.A., Inc. v. Nat. Res. Def. Council, Inc*., 467 U.S. 837 (1984), held that the Administrative Procedure Act requires courts to exercise their own independent judgment in deciding whether an agency has acted within its statutory authority. The APA "makes clear that agency interpretation of statutes—like agency interpretations of the Constitution—are *not* entitled to deference. Under the APA, it thus remains the responsibility of the court to decide whether the law means what the agency says." *Id* at 2261 (emphasis in original).

119. Yet, under FDA's arbitrary and capricious interpretation of subsection (ii) of the Drug Exclusion Clause, the only operative date that matters for purposes of excluding the NDI from the definition of a dietary supplement is the date the IND was authorized for investigation.

120. In this scenario, Company A can receive an Acknowledgment Letter from FDA and begin legally marketing a dietary supplement containing ingredient X, while, unbeknownst to Company A, FDA, prior to sending it an Acknowledgment Letter to Company A, also authorized Company B's IND for ingredient X. However, the moment that Company B makes its purportedly "substantial" (which FDA will not define) clinical trials "public," (based on FDA's arbitrary and capricious misinterpretation of statutory language) FDA can, by using the date it authorized the IND for ingredient X (regardless of the date the clinical trial started or how long Company A has been publicly marketing ingredient X) rescind Company A's ability to market its dietary supplement containing ingredient X.

121. In other words, FDA's interpretation of the statute sets up a situation where the second and third elements of the exclusionary clause are effectively written out of the statute. Under FDA's arbitrary and capricious interpretation, an approved dietary supplement can be suddenly and retroactively excluded from the definition of a dietary supplement.

122. This interpretation is contrary to the statute's plain text and defies common sense. Congress could not have logically intended this result.

123. FDA's interpretation of subsection (ii) of the Drug Exclusion Clause can lead to situations where companies manufacture, distribute, supply or sell dietary supplements containing NDIs and then FDA later withdraws Acknowledgment Letters (for which it has no authority) when a clinical trial becomes public months (or even years) after a company has been manufacturing, distributing, supplying or selling the NDI on the market without any safety concerns.

124. FDA's interpretation of subsection (ii) of the Drug Exclusion Clause is arbitrary and capricious because not only does this interpretation lead to illogical and retroactive application of Drug Exclusion Clause, but it ignores the fact that Congress, when drafting subsection (ii) of the Drug Exclusion Clause specifically included three separate elements in chronological order: (1) the article must be authorized for investigation, (2) undergoing substantial clinical investigations (i.e. clinical trials) ***and*** (3) ***the existence of these investigations must have been made public***. The third element cannot be satisfied with satisfaction of the first two elements, and the second cannot be satisfied without the first. Moreover, the use of the term "and" means that the relevant date is the date when all three (3) elements are satisfied.

125. If Congress wanted the IND authorization date to be the critical date, it would have simply left the third element out of the statute. But it did not. It specifically included a third element which requires the existence of the clinical trials be made public.

126. And the reason for this additional element makes sense, as it serves to put companies on notice of the potential disqualification of their proposed NDI and prevents the retroactive application of the statute.

127. Moreover, unlike the date the article is "authorized for investigation," the date the clinical trials have been made public is a date everyone can access and determine.

128. FDA's interpretation of subsection (ii) of the Drug Exclusion Clause creates a one-sided regulatory race-to-market between those wishing to use and market certain articles as dietary ingredients/supplements and those wishing to use and market those same articles as drugs, except only the IND-submitter and FDA has access to the relevant data (i.e., the authorization date of the IND that triggers the drug exclusion provision) necessary to determine the marketability of an ingredient.

129. As a result, an IND-submitter can leverage FDA's arbitrary and capricious interpretation of the law to establish an exclusive (and perpetual) quasi-property right to preclude others from entering the market while also retaining the ability to market the ingredient as a dietary supplement, regardless of the likelihood of eventual final approval of the ingredient subject to the IND.[71]

130. In other words, FDA is propagating a scheme whereby market participants can tactically exclude others from fairly entering the market to sell a product as a dietary ingredient by leveraging FDA's arbitrary and capricious regulation of DSHEA.

131. Indeed, this is almost exactly what happened with NMN.

132. As early as 2015, David Sinclair, one of the founders of Metrobiotech,[72] the entity that submitted the IND relied upon by FDA here, was using and creating dietary supplements containing the ingredient NMN.[73]

---

[71] Anywhere from 80 to 90 percent of all clinical trials fail, meaning the article is never approved as a drug. From 2014 to 2023, an average of 4,894 clinical trials were instituted; yet according to FDA from 2013 to 2022, FDA approved an average of 43 drugs per year. *See* New Drug Therapy Approvals 2022, https://www.fda.gov/drugs/novel-drug-approvals-fda/new-drug-therapy-approvals-2022#:~:text=From%202013%20through%202022%2C%20CDER,novel%20drug%20approvals%20per%20year (last visited, June 18, 2024); *See* Global Trends in R&D 2024: Activity Productivity, and Enablers, https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2024-activity-productivity-and-enablers (last visited, June 18, 2024). This creates a very concerning scenario where pharmaceutical companies can indefinitely knock perfectly safe dietary supplements (such as NMN) off the market, yet never request approval of the product to be formally approved as a drug (or, in the alternative, request approval and get denied).

[72] Although David Sinclair is no longer on the Metrobiotech website, he was one of its founders and was involved with the company during the relevant period. *See* Wayback Machine, About Us, Metrobiotech (February 12, 2024) available at https://web.archive.org/web/20240212234057/https://www.metrobiotech.com/aboutus; *compare* Metrobiotech's current website, available at https://www.metrobiotech.com/aboutus.

[73] Anne-Marie Guarnieri, *The Future of Anti-Aging*, HARPER'S BAZAAR, https://www.harpersbazaar.com/beauty/skin-care/a12776110/future-of-anti-aging/ (last visited, June 17, 2024) (David Sinclair states that he had been taking his own custom NMN supplements

133. In fact, in David Sinclair's book titled *Lifespan: Why We Age And Why We Don't Have To*, he states "NMN isn't a regulated substance, it's available as a supplement . . .. I take 1 gram (1,000 mg) of NMN every morning along with 1 gram of resveratrol (shaken into my homemade yogurt) and 1 gram of metformin. . .. My father follows almost the same regimen as I do."[74]

134. Now, David Sinclair, through the company he co-founded, Metrobiotech, is attempting to preclude dietary supplement manufacturers from selling NMN stating that their IND date "clearly predate[s] any lawful dietary supplement marketing."[75]

135. David Sinclair helped fuel the demand for NMN as a dietary supplement during the time that it was lawfully sold as a dietary supplement but is now leveraging FDA's arbitrary and capricious interpretation of the drug exclusion provision of DSHEA to wrongfully exclude others from the NMN market.

136. Indeed, FDA's arbitrary and capricious interpretation of subsection (ii) of the Drug Exclusion Clause permits and encourages entities like Metrobiotech to exclude others from the supplement market in a manner contrary to Congress's intent and the plain languge of DSHEA.

---

for almost two (2) years prior to the writing of the article in 2017); Alice Park, *The Compound Can Reverse Aging in Mice. Will it Work in People?*, TIME, https://time.com/5209427/aging-nicotinamide-mononucleotide-nmn/ (last visited, June 17, 2024) (David Sinclair states that he takes NMN supplements and the same are available for purchase online); Joe Rogan, *Episode 1234, Joe Rogan Experience*, David Sinclair, January 29, 2019, and https://www.youtube.com/watch?v=75doh5hJVRI (at 2 minutes 24 seconds into the video, David Sinclair stated "so I take NMN every morning").

[74] David Sinclair, LIFESPAN: WHY WE AGE—AND WHY WE DON'T HAVE TO (2019). Sinclair mentions NMN over 150 times in his book. This book predates the earliest publicly available study conducted by Metrobiotech.

[75] *See Letter from Metrobiotech regarding Citizen's Petition from Natural Products Association and Alliance for Natural Health USA / Citizen Petition from the Council for Responsible Nutrition*, REGULATIONS.GOV (November 20, 2023).

137. FDA's own regulations make its interpretation of the Drug Exclusion Clause untenable. FDA has interpreted subsection (ii) of the Drug Exclusion Clause to exclude NDIs from the definition of dietary supplements based upon the date an IND is "authorized" by FDA.[76]

138. Under 21 C.F.R. 312.130(a) (a regulation promulgated and adopted by FDA) FDA is prohibited from disclosing not only the date an IND is authorized for investigation, but the mere existence of an IND. Under this interpretation, there is no way for anyone, other than the IND holder and someone at FDA with clearance to access the IND records, to know the date an IND has been authorized until either (a) a clinical study identifying the active ingredient has begun, which would be posted on clinicaltrials.gov, or (b) there is a press release or publication written about the upcoming clinical trials by the IND holder.

139. But FDA's interpretation is wrong because it conflicts with the statutory Drug Exclusion Clause. To the extent the rule is not improper in all applications at FDA, it is improper as it is applied to DSHEA which requires public notice of the operative date. Because the rule conflicts with DSHEA, it is unlawful, arbitrary and capricious.

B. ***Reason 2****: FDA's interpretation of subsection (ii) of the Drug Exclusion Clause is contrary to Congress' intent.*

[76] For the avoidance of doubt, with certain very limited exceptions, an IND is required *prior* to conducting a clinical investigation (i.e., a clinical trial). However, unlike an NDI application, an IND application will be automatically approved within thirty (30) days of its submission unless FDA notifies the IND applicant otherwise. *See* U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, Center of Biologics Evaluation and Research and Center for Food and Safety and Applied Nutrition, *Guidance for Clinical Investigators, Sponsors, and IRBs Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without and IND*, p. 2, available at https://www.fda.gov/files/drugs/published/Investigational-New-Drug-Applications-%28INDs%29-Determining-Whether-Human-Research-Studies-Can-Be-Conducted-Without-an-IND.pdf (Sept. 2013).

140. As outlined in further detail (*see* paragraph 5, FN 3), the legislative history indicates that Congress enacted the Drug Exclusion Clause specifically for the purposes of ensuring that drugs and bona fide pending drugs (i.e., products that have undergone substantial clinical trials that have been made public) would not evade appropriate testing and investigation by being unsafely sold as a dietary supplement.

141. The overall purpose of DSHEA was to "improve the health status of the people of the United States and help constrain runaway health care spending by ensuring that the Federal Government erects no regulatory barriers that impede the ability of consumers to improve their nutrition through the free choice of safe dietary supplements . . . [and] clarify that . . . dietary supplements should not be regulated as drugs."[77]

142. Yet, contrary to Congress' intent, FDA has continuously used the Drug Exclusion Clause in a way that restricts consumer access to otherwise perfectly safe dietary supplements to the detriment of consumers and to the advantage of pharmaceutical companies.

C. Reason 3*: FDA fails to define (or provide context) to the term "substantial."*

143. The plain language of subsection (ii) of the Drug Exclusion Clause requires that the article under investigation be undergoing "substantial clinical investigation**s**," (i.e. more than one) (emphasis added).

144. As such, any attempt by FDA to rely on the IND date for the *first* clinical study conducted by Metrobiotech is insufficient to meet the elements of the drug exclusion provision because as of that date there were not multiple clinical investigations, which is required by the statute's use of the plural "investigation**s**."[78]

---

[77] 140 Cong. Rec. H11173-02, at H11173 (October 6, 1994), 1994 WL 553639.

[78] Note that since FDA will not disclose the date it is relying on, Plaintiff is unsure if FDA is relying on the IND date of the first, second or third clinical trial.

145. FDA has also failed to provide any definition or context to the word "substantial" as it is used to modify "clinical investigations," nor has it explained why it considers the three clinical investigations it relied upon were "substantial." *See Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999) (the APA's prohibition that an agency not engage in arbitrary and capricious action requires FDA to explain why it has made a certain decision, which includes giving definitional context to operative terms).

146. In its letters revoking NMN's approval as a dietary supplement, FDA conclusorily stated that "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. Accordingly, we conclude that NMN is excluded from the dietary supplement definition under 21 U.S.C. § 32l(ff)(3)(B)(ii) and may not be marketed as or in a dietary supplement." In a footnote, FDA cited to three (3) clinical trials, all of which were conducted by Metrobiotech.

147. In these letters, FDA offers no explanation regarding why it believes Metrobiotech's three (3) clinical trials should be considered "substantial," nor can it, given that the studies contain a very limited number of participants, are for very short durations, lack sufficient clinical endpoints or remain ongoing and incomplete. Its determination, without evidence or justification, is arbitrary and capricious.

D. ***Reason 4****: The clinical trials cited by FDA do not mention NMN.*

148. Notably, all of Metrobiotech's clinical trials posted on clinicaltrials.gov only refer to the administration of "MIB-626."

149. MIB-626 is Metrobiotech's patented microcrystalline form of β-NMN, for which it has at least (3) patents: U.S. Patent Nos. 10,233,208, 10,392,416, and 11,059,847. Pursuant to 35 U.S.C. § 101 and other provisions of the Patent Act, to obtain a patent on a chemical compound, that compound must be different from that which naturally exists in nature.

150. Accordingly, Metrobiotech's *patented* MIB-626 must be a distinct article (as that term is used in the FDCA) from the naturally occurring NMN present in the dietary supplement sought to be marketed by NPA's members pursuant to the Acknowledgment Letter and cannot form the basis for FDA's invocation of the drug exclusion provision of DSHEA.

151. Moreover, not a single one of Metrobiotech's clinical trials available on clinicaltrials.gov mention the administration of NMN and, as such, are incapable of reasonably putting anyone on notice that NMN was the article being investigated as a new drug.

E. Reason 5*: The clinical trials cited by FDA cannot, at this point, be considered "substantial" because they are not adequate to support drug approval.*

152. FDA has not provided a definition of the word "substantial," but has instead, apparently treated *any* clinical trial as being substantial thereby reading the term out of the statute. Nevertheless, the first two (2) studies cited by FDA cannot be considered "substantial" in these circumstances.

153. Metrobiotech's first clinical study (NCT04817111) cited by FDA, purportedly began on May 17, 2021 and was first posted on clinicaltrials.gov on March 25, 2021. This trial consisted of only seven (7) participants where Metrobiotech purportedly administered two (2) 500 mg tablets daily of its proprietary drug MIB-626 product.

154. Metrobiotech's second clinical study (NCT05038488) cited by FDA, purportedly began on October 26, 2021 and was first posted on clinicaltrials.gov on September 7, 2021. This

trial lasted only fourteen (14) days, had forty-two (42) participants and purportedly sought to assess declines in kidney function in individuals with Covid-19.

155. Other studies were conducted but, because FDA will not provide a definition of "substantial," it is impossible to determine if any of these additional studies constitute "substantial clinical trials." Moreover, clinical trials consisting of only seven participants, for example, should not be assumed to be "substantial" without some basis for categorizing it as such.

156. In addition to failing to meet any reasonable interpretation of the word "substantial", the first two (2) clinical trials cited by FDA do not even mention NMN as the article being administered or tested.[79] Accordingly, these two (2) clinical trials cannot reasonably support FDA's position that "NMN is an article for which substantial clinical investigations have been instituted."

157. The third clinical trial cited by FDA (NCT05759468) lists Brigham and Women's Hospital as the sponsor but also administered Metrobiotech's patented "MIB-626." This study purportedly began on April 13, 2023 and was first posted on March 3, 2023. It seeks to "determine whether NMN administration improves DKD [diabetes kidney disease], as indicated by a significantly greater reduction in UACR [urine albumin-creatinine ratio] compared with placebo administration." Participants are to be given 1000 mg of MIB-626 or placebo twice daily.

158. Given that Metrobiotech's third clinical study contained the first mention of NMN, this is arguably the very first entry that could trigger DSHEA's drug exclusion provision. However, this 2023 submission is over four (4) years after NMN had obtained Self-GRAS status (December 19, 2018), approximately two (2) years after the submission of NDINs on NMN (December 27,

[79] The studies list the patented MIB-626, which under the Patent Act cannot be the same as the naturally occurring NMN that is sold as a dietary supplement. *See* 35 U.S.C. § 101.

2021), and for a patented article identified as MIB-626. Consequently, Metrobiotech's third clinical trial cannot serve the basis for FDA to invoke the drug exclusion provision because its publication was long-after NMN had obtained its status as a dietary supplement.

159. A fourth Metrobiotech clinical study (NCT05878119) purportedly began on October, 25 2023 and was first posted on May 17, 2023. It seeks to determine the "Effects of MIB-626 With and Without A High-Intensity Multi-Dimensional Exercise Training Program." In other words, this clinical study is akin to a sports nutrition study and should therefore not be immediately assumed to be a drug study. Certain participants are to be given 1000 mg of MIB-626 twice daily and others will receive placebo.

160. Like Metrobiotech's third clinical study, Metrobiotech's fourth clinical study cannot trigger DSHEA's drug exclusion provision. This 2023 submission was years after NMN had been sold as a dietary supplement, over four (4) years after NMN had obtained Self-GRAS status, approximately two (2) years after the submission of NDINs on NMN, and for a proprietary article identified as MIB-626. Consequently, Metrobiotech's fourth clinical trial cannot serve the basis for FDA to invoke the drug exclusion provision because its publication was long-after NMN had obtained its status as a dietary supplement.

161. The mere existence of a clinical trial, without more, is not enough to conclude that a study on an article (e.g., a supplement or ingredient thereof) is substantial and triggers the drug exclusion provision.

162. For example, the Institutional Review Board (IRB), an entity tasked with providing ethical and regulatory oversight of research involving human subjects, will often require clinical trials for the purpose of studying the effects of a dietary supplement when transitioning from administration in animal models (e.g., in mice) to humans. Dietary supplements are also subjected

to clinical investigations for the manufacturer to prove claim substantiation of label claims on dietary supplements or to satisfy the requirements of the NDIN process. These studies obviously do not trigger the drug exclusion clause, nor could they without causing the implosion of DSHEA and the exclusion of all NDIs.

163. In fact, a simple search on www.clinicaltrials.gov for "nicotinamide mononucleotide" reveals nineteen (19) instances of clinical trials where NMN was administered to participants. In each of those trials, NMN was administered in various amounts (e.g., 300 mg and 400 mg) and of those trials, eleven (11) define NMN as a dietary supplement and three (3) refer to "supplementation" with NMN.

164. Accordingly, even in the event FDA subsequently attempts to define the word "substantial" or why it considered the clinical investigations "substantial," the studies that predate NMN's Self-GRAS status and NDIN submissions cannot under any reasonable definition be considered "substantial." And even if the later-instituted clinical trials are deemed substantial (which NPA does not concede), they were submitted after NMN was sold as a dietary supplement, as evidenced by the repeated reference to NMN as a supplement in those trials, along with the sales of NMN discussed above.

F. ***Reason 6****: FDA has interpreted the phrase "marketed as a dietary supplement or food" to mean lawful marketing in the United States, however, the plain language of the statute does not make such distinction.*

165. FDA has interpreted the phrase "marketed as a dietary supplement or as a food" in Section. § 321(ff)(3)(B)(ii) to mean lawful marketing in the United States only. But the plain language of the statute does not distinguish between marketing in the United States or marketing abroad.

166. Basic statutory interpretation instructs that where Congress, within the same statute, has previously delineated when something only applies to the United States market, the absence

of this limitation in other sections, implies that Congress did not intend to import this limitation to those sections.

167. The Drug Exclusion Clause does not include the words "United States." Other sections of DSHEA, however, do.[80]

168. In fact, Congress's chosen silence about the geographic scope of marketing implicated by Subsection (ii) of the Drug Exclusion Clause demonstrates that Congress expressly intended *not* to limit such marketing to the United States.

169. Moreover, FDA (in contravention of its own position regarding the interpretation of Drug Exclusion Clause) considers marketing outside of the United States when reviewing NDIs. Here, as noted in Paragraphs 105-07 above, during a meeting discussing the prior marketing of NMN, FDA informed SyncoZymes that if they could provide FDA with evidence regarding NMN's history of use in other countries, FDA would consider that when determining the expectation of safety for NMN.

170. The lack of consistency and notice to regulated entities is another example of FDA's arbitrary and capricious interpretation and application of DSHEA.

171. There is also no reference to "lawful" marketing of a dietary supplement in the Drug Exclusion Clause, and this requirement is nothing more than FDA improperly amending the statute by adding additional requirements. To be clear, DSHEA allows for the marketing of supplements without formal "approval" that arises in the drug context. The problem with FDA's

[80] *See* 21 U.S.C. 343(r) ("a statement for a dietary supplement may be made if . . . the statement claims a benefit related to a classical nutrient deficiency disease and discloses the prevalence of such disease in the *United States*")(emphasis added); *see also* 21 U.S.C. 350b ("For purposes of this section, the term 'new dietary ingredient' means a dietary ingredient that was not marketed in the *United States* before October 15, 1994 and does not include any dietary ingredient which was marketed in the *United States* before October 15, 1994)(emphasis added).

interpretation arises by virtue of its unsubstantiated conclusions that a product was not lawfully marketed and its imposition of a requirement that does not exist in the statute.

HARM TO NPA'S MEMBERS

172. Members of NPA were directly harmed as result of FDA's conclusion that NMN does not fall under the definition of a dietary supplement.[81]

173. As a result of FDA's Reversal Letter, Amazon.com, Inc. announced on February 16, 2023 that it would no longer allow dietary supplements containing NMN to be sold on its platform.[82]

174. Because of Amazon's announcement, members of NPA that were selling and marketing NMN could no longer do so through Amazon.com.

175. Similarly, Shopify and PayPal payment processors stopped processing sales for NMN.[83]

176. LegitScript, an internet compliance company that offers brand monitoring for companies like Google, Facebook, and Amazon among other major internet regimes and FDA itself, classified NMN as a pseudo-pharmaceutical based on FDA's public statements that NMN is excluded from the definition of a dietary supplement. NPA's members reasonably believe LegitScript's classification will lead other organizations to cease sales and/or payment processing for NMN.

[81] *See* **Exhibit I** (Affidavits from members of NPA)

[82] *See* **Exhibit O**.

[83] *See* **Exhibit P**.

177. Indeed, to the extent that any ambiguity exists as to FDA's position on NMN, major e-commerce and internet gatekeepers like Amazon and Legitscript (and the companies that rely on Legitscript's classifications) foreclose the possibility of meaningfully marketing NMN.

COUNT ONE

(Violation of the Administrative Procedure Act)

178. Plaintiff incorporates by reference, as if fully set forth herein, all of the above allegations.

179. Pursuant to 5 U.S.C. §706(2)(A) and (D) of the APA, a court must hold unlawful and set aside agency action found to be arbitrary, capricious, an abuse of discretion or otherwise not in accordance with the law or without observance of procedure required by law.

180. FDA's decision to exclude NMN from the definition of a dietary supplement is arbitrary, capricious, not in accordance with law for at least the following reasons.

181. NMN categorically falls under DSHEA's definition of a dietary supplement, and this status predates any potential IND at issue. NMN qualifies as a dietary ingredient under 21 U.S.C. § 321(ff)(1) as naturally occurring in foods and in the human body, and as a metabolite of other products sold as a dietary supplements (e.g., Vitamin B3 or NR). NMN is a dietary ingredient under DSHEA that cannot be excluded from the definition of dietary supplement by 21 U.S.C. § 321(ff)(3)(B)(ii) because NMN was a metabolite of a dietary ingredient that itself was marketed as a dietary supplement or food prior to the date of any alleged IND.

182. By failing to consider NMN's Self-GRAS status, in direct contravention of the established FDA statutory interpretation and practice, FDA has engaged in arbitrary and capricious action.

183. By interpreting 21 U.S.C. § 321(ff)(3)(B)(ii) in such a way that is inconsistent with the plain text of the statute, FDA has engaged in arbitrary and capricious action that is not in

accordance with plain language of the statute and the general presumption against retroactive statutes.

184. By informing companies applying for an NDIN that marketing in other countries would be considered in the approval of the NDIN on the one hand, but stating that such marketing is irrelevant to show marketing prior to the filing of any alleged IND on the other hand, FDA has arbitrarily and capriciously acted by taking inconsistent positions without any basis in the law or fact.

185. By failing to articulate a definition for the term "substantial" and/or by failing to articulate any explanation as to why it failed to consider any exclusion-triggering studies, including the three Metrobiotech studies at the time of acknowledging NDINs which it later cited in its unprecedented Reversal Letter, as being "substantial" clinical investigations, FDA has engaged in arbitrary and capricious action.

186. Moreover, there is no indication that any of the alleged clinical studies constitute "substantial clinical investigations" as used in the statute. Or, in the case of Metrobiotech, there has been no finding that the patented MIB-626 used in Metrobiotech's clinical trials is the same article as the NMN previously sold and sought to be sold by NPA's members.

187. FDA's reliance on, and interpretation of, 21 U.S.C. § 321(ff)(3)(B)(ii) is arbitrary and capricious because the interpretation is in contravention to DSHEA, which is a statute requiring public notice of INDs to trigger the drug exclusion provision. FDA has interpreted 21 U.S.C. § 321(ff)(3)(B)(ii) to improperly exclude NDIs from the definition of dietary supplements based upon the authorization date of the IND rather than the statutorily prescribed publication date.

188. NPA's members have been harmed by FDA's arbitrary and capricious interpretation and enforcement because they have been improperly foreclosed from selling a lawful dietary supplement, NMN, which has caused financial harm due at least to lost sales of NMN.

COUNT TWO

(Violation of the Due Process Clause)

189. Plaintiff incorporates by reference, as if fully set forth herein, all of the above allegations.

190. A court must "hold unlawful and set aside agency action … found to be … contrary to constitutional right, power, privilege, or immunity." 5 U.S.C. § 706(2)(B).

191. The Fifth Amendment's Due Process Clause states: "No person shall … be deprived of life, liberty, or property, without due process of law." U.S. Const. Amend. V. Where a government action deprives an individual of a protected life, liberty, or property interest, the Due Process Clause requires, at minimum, fair notice and an opportunity to be heard. *Mathews v. Eldridge*, 424 U.S. 319, 333 (1976).

192. FDA has denied NPA's members of their due process rights by arbitrarily and capriciously interpreting and enforcing the FDCA because its illogical and contradictory interpretations of the law have deprived NPA's members of selling NMN, which would otherwise be lawful but for FDA's actions set forth herein.

193. FDA has misinterpreted and misapplied the law, without just and fair consideration of the facts and law, and been derelict in its duties by, among other things, failing to timely and substantively responding to NPA's Citizens' Petition, and refusing to open a public docket on the matter in the face of requests from industry members (like NPA) and both branches of Congress.

194. NPA and others have diligently and continuously sought redress from FDA via the submission of Citizen's Petitions and repeated requests for updates and a hearing, but FDA has failed to respond to NPA's Citizen's Petition during its more than year and a half pendency and denied any requests to address the issues set forth herein.

195. Throughout the relevant time period, NPA's members have been and continue to suffer harm due to FDA's arbitrary and capricious conclusion that NMN does not fall under the definition of a dietary supplement.

REQUEST FOR RELIEF

NPA requests the following relief:

a. judgment in its favor on all claims against Defendants;

b. a declaratory judgment pursuant to 28 U.S.C. § 2201(a) in favor of NPA and against Defendants declaring that the drug exclusion in 21 U.S.C. § 321(ff)(3)(B)(ii) does not apply to the dietary ingredient NMN and that FDA's actions are contrary to law, and arbitrary and capricious;

c. to the extent necessary, a declaratory judgment pursuant to 28 U.S.C. § 2201(a) in favor of NPA and against Defendants declaring that the Drug Exclusion Clause in 21 U.S.C.§ 321(ff)(3)(B) does not preclude from marketing, distributing, supplying, or selling NMN as a dietary supplement;

d. recission or revision of 21 C.F.R. 312.130(a) that, as passed and imposed by FDA, precludes the publication in contravention of 21 U.S.C. § 321(ff)(3)(B)(ii);

e. a preliminary and permanent injunction prohibiting Defendants from taking any regulatory action against manufacturers, distributors, suppliers, and sellers, or distributors of NMN-containing dietary supplements based on the claim that the

product is excluded from the definition of a dietary supplement under 21 U.S.C. § 321(ff)(3)(B)(ii) or any actions by FDA that are contrary to law, and arbitrary and capricious;

f. reasonable attorneys' fees as allowed by law;

g. costs pursuant to Fed. R. Civ. P. 54(d) or otherwise provided by law; and

h. such other relief as the Court deems just and appropriate under the circumstances.

ALTERNATIVE REQUEST FOR RELIEF

In the event the Court concludes that NPA lacks standing arising from FDA's failure to reach final agency action in the more than year and half that has passed since the filing of NPA's Citizen's Petition, NPA requests the following relief:

a. a ruling mandating FDA to issue a final decision on NPA's Citizens' Petition within 21 days of a finding of no final agency action.

Dated: August 28, 2024

Respectfully submitted,

/s/ Jeremy Ritter-Wiseman
Jeremy Ritter-Wiseman (Bar No. 90020480)
Matthew D. Zapadka (*pro hac vice forthcoming*)
Kevin M. Bell (*pro hac vice forthcoming*)
Andrew K. Beverina (*pro hac vice forthcoming*)
April Meeks (*pro hac vice forthcoming*)
ARNALL GOLDEN GREGORY LLP
2100 Pennsylvania Avenue NW, Suite 350S
Washington, DC 20037
Tel: (202) 677-4930
Email: jeremy.ritter-wiseman@agg.com

Attorneys for Plaintiff Natural Products Association