Council for Responsible Nutrition
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March 7, 2025

Via Electronic Submission

Division of Dockets Management
U.S. Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm 1061
Rockville, Maryland 20852

Re: Supplemental Submission to CRN's Citizen Petition Requesting FDA Reconsider Its Position with Respect to the Application of Section 201(ff)(3)(B) of the Food, Drug, and Cosmetic Act; Acknowledge That Agency Prior Statements and Actions Cannot be Reversed on Drug Preclusion Grounds; and Clarify Its Position on Rulemaking – Docket # FDA-2023-P-1867

Dear Sir or Madam:

The Council for Responsible Nutrition (CRN)[1] submits these comments to further clarify the requests in its May 9, 2023, citizen petition[2] in anticipation that FDA will respond to that petition in the coming months. In the interest of reasserting the industry's interests in this matter and bringing it to proper closure later this year, CRN files this submission to refocus the agency's attention to the issues at hand.

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[1] The Council for Responsible Nutrition (CRN), founded in 1973 and based in Washington, D.C., is the leading trade association representing dietary supplement and functional food manufacturers, marketers and ingredient suppliers. CRN companies produce a large portion of the functional food ingredients and dietary supplements marketed in the United States and globally. Our member companies manufacture popular national brands as well as the store brands marketed by major supermarkets, drug stores and discount chains. These products also include those marketed through natural food stores and mainstream direct selling companies. CRN represents more than 180 companies that manufacture dietary ingredients, dietary supplements and/or functional foods, or supply services to those suppliers and manufacturers. Our member companies are expected to comply with a host of federal and state regulations governing dietary supplements and food in the areas of manufacturing, marketing, quality control and safety. Our supplier and manufacturer member companies also agree to adhere to additional voluntary guidelines as well as to CRN's Code of Ethics. Learn more about us at www.crnusa.org.

[2] Citizen Petition Requesting FDA Reconsider Its Position with Respect to the Application of Section 201(ff)(3)(B) of the Food, Drug, and Cosmetic Act; Acknowledge That Agency Prior Statements and Actions Cannot be Reversed on Drug Preclusion Grounds; and Clarify Its Position on Rulemaking, submitted by CRN May 9, 2023, Docket # FDA-2023-P-1867

Summary of the Current Situation

CRN filed a citizen petition in May 2023 asking FDA to examine its positions with respect to Section 201(ff)(3)(B) of the Food, Drug, and Cosmetic Act (referred to as "drug preclusion" in the May 2023 citizen petition and this comment). CRN's petition also asked FDA to provide the industry with clear direction as to how the agency intends to interpret this statutory provision. Almost two years have lapsed since that filing without a substantive response from FDA.[3]

In November 2024, FDA represented to CRN that it was committed to respond to CRN's citizens petition by the end of July 2025 in conjunction with another citizen petition asking for clarity on the status of a single ingredient and that is the subject of an FDA lawsuit. The agency has acknowledged that the larger issue of how Section 201(ff)(3)(B) should be interpreted for the application of drug preclusion is inextricably intertwined with specific determinations for any particular ingredient. CRN looks forward to FDA's imminent response to our citizen's petition.

Recommendations for FDA's Response

First and foremost, FDA's forthcoming response represents an opportunity for FDA to correct the past errors in its interpretation of 201(ff)(3)(B). Rather than asking FDA to justify its previous, incorrect interpretations of the law,[4] CRN respectfully requests that FDA examine the drug preclusion provision anew and with appreciation for the current dietary supplement marketplace, the evolving scientific fields of research for nutrition and prevention, and the growing consumer interest in supplementation to promote better health and wellness. FDA should announce with its response to CRN's citizen petition an interpretation that aligns with the Congressional purpose for drug preclusion – one that properly balances the interest of pharmaceutical and dietary supplement stakeholders. Setting forth a transparent and consistent approach for applying drug preclusion in a manner that follows correct statutory interpretation principles, is supported by DSHEA's purpose, and provides predictable guidance for introducing new ingredients, will be far more useful than trying to justify FDA's previous actions with a retrospective lens.

As we detailed in our May 2023 citizen petition, the drug preclusion provision was added to DSHEA to help assuage fears from some members of Congress that "manufacturers or importers of drugs could avoid the drug approval process by marketing drug products as dietary

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[3] FDA notified CRN on November 2, 2023 that the agency had "not reached a decision on your petition within the first 180 days due to competing agency priorities. However, be advised that our staff is evaluating your petition." Letter from C. Welch, FDA to CRN, November 2, 2023, Docket Number FDA-2023-P-1867. No further response has been provided by the agency.

[4] Another petitioner in this matter has requested FDA respond to its petition by providing "a legal basis" for its various prior statements with respect to drug preclusion. Rooting FDA's response to the current issues in legal justification for past statements does not serve the industry or American consumers; it would simply seek to justify FDA's past posturing in legal precedent that fails to consider the current dynamic climate and provide a roadmap for growth in the industry.

supplements."[5] It was not intended to permit pharmaceutical manufacturers to obtain perpetual monopolies over substances that would otherwise meet the FDCA definition of a dietary supplement in order to stifle supplement innovation. DSHEA was enacted in 1994 to allow consumers more access to products that promote and advance their health, not to broadly establish limitations on their access to enrich drug companies.

To help frame and crystalize FDA's anticipated response, in its original petition, CRN requested that FDA reconsider its positions with respect to section 201(ff)(3)(B), specifically asking FDA:

- To determine that the preclusion date referenced in the statute (i.e., the date on which the "race to market" between a drug and a supplement is adjudicated) is the date the existence of substantial clinical trials are made public, not the non-public date on which an investigational new drug (IND) application goes into effect;
- To determine that "marketing" as used in section 201(ff)(3)(B) is not limited to marketing in the United States, nor does it require "legal" marketing of the ingredient;
- To determine that evidence of marketing as a food or dietary supplement should be dispositive, unless FDA has met its statutory burden of demonstrating that the marketing was unlawful;
- To determine that "substantial clinical investigations" as used in section 201(ff)(3)(B) refers only to clinical trials that are adequately designed and powered to support approval of a drug, and does not refer to Phase I clinical trials; and
- To determine that the agency's prior affirmative statements recognizing the legal status of a particular article as a legal dietary ingredient prevents FDA from subsequently reversing that decision on the grounds of drug preclusion.

Each of these aspects of the drug preclusion issue deserve express response from FDA.

Further, CRN requested that FDA issue guidance indicating how it will utilize the discretion conferred upon the agency in section 201(ff)(3)(B) to create regulatory exceptions to drug preclusion that may arise under the statute through notice and comment rulemaking. Such guidance should provide clear criteria by which the Agency would determine that an article "would be lawful under this [Act]"and provide a framework for companies to petition for such rulemaking. When Congress included this express language of the statute setting forth this pathway for exceptions, it clearly intended that FDA would effectualize this process and allow for marketing of certain ingredients as dietary supplements even when they might otherwise be prohibited by the express reading of the section. After 31 years, FDA should make that a reality.

Lastly, FDA should not consider an announcement of enforcement discretion with respect to NMN as a satisfactory resolution of the drug preclusion interpretation issue. That false remedy

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[5] S. Rep. 103-410 (1994), at V § 3.

did not solve the interpretation issues raised by FDA's drug preclusion determination for NAC, and it will not resolve the critical issues raised with respect to NMN. Most critically, however, enforcement discretion will not provide any predictability for other ingredients that may come under FDA's scrutiny in the future. Indeed, over two years after FDA committed in August 2022 to introducing a rulemaking that would have granted a regulatory exemption to drug preclusion for NAC, no such rulemaking has been promulgated or even initiated. A cloud of uncertainty still hangs over the legal status of NAC with FDA observing a period of enforcement discretion related to NAC but offering no clear direction. The drug preclusion matter will be solved only with a clear roadmap from FDA on how it interprets section 201(ff)(3)(B) going forward—or a legislative solution to amend the law if FDA fails to provide that clarity.

We look forward to hearing from FDA and appreciate this opportunity to further our effort to provide clarity to our members.

Sincerely,

Steve Mister
President & CEO

Megan Olsen
Senior Vice President & General Counsel