

Policy Regarding Certain New Dietary Ingredients and Dietary Supplements Subject to the Requirement for Pre-market Notification: Guidance for Industry

Draft Guidance

This guidance document is being distributed for comment purposes only.

Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that FDA considers your comment on this draft guidance before we begin work on the final version of the guidance, submit either electronic or written comments on the draft guidance within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <https://www.regulations.gov>. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number FDA-2022-D-0281 listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact the Center for Food Safety and Applied Nutrition (CFSAN), Office of Dietary Supplement Programs at 855-543-3784 or 240-402-2375.

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Food Safety and Applied Nutrition**

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Policy Regarding Certain New Dietary Ingredients and Dietary Supplements Subject to the Requirement for Pre-market Notification: Guidance for Industry¹

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or we) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. Introduction

Under section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 350b(a)(2)), the manufacturer or distributor of a new dietary ingredient (NDI) that has not been present in the food supply as an article used for food, or a dietary supplement that contains the NDI, must submit a premarket safety notification to FDA at least 75 days before introducing the product into interstate commerce. If the required premarket notification is not submitted to FDA, section 413(a) of the FD&C Act (21 U.S.C. 350b(a)) provides that the dietary supplement containing the NDI is deemed to be adulterated under section 402(f) of the FD&C Act (21 U.S.C. 342(f)).

FDA is aware that some manufacturers and distributors have marketed products for which a premarket NDI notification under section 413(a)(2) of the FD&C Act was required, but never submitted. To increase the amount of safety information we have about NDI-containing dietary supplements in the marketplace and to promote risk-based regulation, we are informing manufacturers, distributors, and other interested persons of our intent to exercise enforcement discretion, for a limited time and in limited circumstances, to encourage firms to correct past failures to submit an NDI notification.

¹ This guidance has been prepared by the Office of Dietary Supplement Programs and the Office of Regulations and Policy, both in the Center for Food Safety and Applied Nutrition (CFSAN) at the Food and Drug Administration.

Contains Nonbinding Recommendations

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The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA guidances means that something is suggested or recommended, but not required.

II. Background

On October 25, 1994, the Dietary Supplement Health and Education Act of 1994 (DSHEA) (Pub. L. 103-417) was signed into law. DSHEA amended the FD&C Act by adding, among other provisions, section 413 (21 U.S.C. 350b), which defines the term “new dietary ingredient.”

Section 413 of the FD&C Act also requires the manufacturer or distributor of an NDI, or of the dietary supplement that contains the NDI, to submit a premarket notification to FDA at least 75 days before introducing the product into interstate commerce or delivering it for introduction into interstate commerce, unless the NDI and any other dietary ingredients in the dietary supplement “have been present in the food supply as an article used for food in a form in which the food has not been chemically altered” (21 U.S.C. 350b(a)(1)). Under section 413(a)(2) of the FD&C Act (21 U.S.C. 350b(a)(2)), the notification must contain the information, including any citation to published articles, which provides the basis on which the manufacturer or distributor of the NDI or dietary supplement has concluded that the dietary supplement containing the NDI will reasonably be expected to be safe.²

If the required premarket notification is not submitted to FDA, section 413(a) of the FD&C Act (21 U.S.C. 350b(a)) provides that the dietary supplement containing the NDI is deemed to be adulterated under section 402(f) of the FD&C Act (21 U.S.C. 342(f)). Even if the notification is submitted as required, the dietary supplement containing the NDI is adulterated under section 402(f) of the FD&C Act unless there is a history of use or other evidence of safety establishing that the NDI, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe.

A robust NDI notification process represents FDA’s only opportunity to evaluate the safety of NDIs in dietary supplements before they become available to consumers. Since DSHEA’s enactment, the dietary supplement market has grown significantly. In 1994, there were about 4,000 products on the market; according to recent estimates, there are over 50,000--and possibly as many as 80,000 or more--products available to consumers. Although not every dietary supplement requires an NDI notification, we estimate that more than 4,600 notifications should have been submitted and were not.³ Despite the expanded marketplace, however, we have received only about 1,200 NDI notifications since DSHEA’s enactment.

² Our NDI notification regulation (21 CFR 190.6), which implements section 413(a)(2) of the FD&C Act, specifies the procedure for submitting a premarket NDI notification and the information the manufacturer or distributor must include in the notification.

³ See Transcript, FDA Public Meeting on Responsible Innovation in Dietary Supplements (May 16, 2019), available at <https://www.fda.gov/media/127746/download>, at 180:19 – 183:4.

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FDA recognizes that not every dietary supplement containing an NDI is subject to the notification requirement in section 413(a)(2) of the FD&C Act. However, we are aware that some manufacturers and distributors have marketed ingredients and products that are subject to this requirement without having submitted the required notification. A number of firms have told us informally that they realize they should have previously submitted notifications and have the information ready to be submitted, but they are afraid of drawing attention to themselves with a late submission. As part of our ongoing efforts to manage safety risks and to promote risk-based regulation and transparency, we are informing manufacturers, distributors, and other interested persons that we intend to implement a limited enforcement discretion policy regarding the requirement to file an NDI notification, as described in section III of this document.

III. Discussion

A. Scope of Enforcement Discretion Policy Regarding Certain NDIs and Dietary Supplements for Which a Notification Was Not Timely Filed

To encourage manufacturers, distributors, and other affected parties (collectively, “you”) to correct any past failure to submit a required NDI notification, we intend to exercise enforcement discretion with regard to the premarket notification requirement in section 413(a)(2) of the FD&C Act for a limited time and under limited circumstances. In general, FDA intends to exercise enforcement discretion if you submit to us the NDI notification required by 21 CFR 190.6 and the other information recommended in section III.B. (referred to collectively as a “notification package”) within 180 days following the publication of a notice in the *Federal Register* announcing that the final version of this guidance document is available, and if you can show that the dietary supplement that is the subject of your notification was marketed in the United States as of May 20, 2022.

This enforcement discretion policy relates solely to the timing of the requirement to file an NDI notification under section 413(a)(2) of the FD&C Act. In other words, we generally do not intend to take enforcement action based on a failure to comply with the requirement to file an NDI notification in a timely fashion against firms marketing products within the scope of this enforcement discretion policy. This enforcement discretion policy does not extend to NDIs and NDI-containing dietary supplements that would be adulterated under section 402(f) of the FD&C Act (21 U.S.C. 342(f)) even if an NDI notification had been submitted, nor to any other regulatory requirements that pertain to dietary supplements.

B. What Information Should You Provide to FDA and What Will We Do With the Information?

If you submit a late notification consistent with this enforcement discretion policy, you must include the information required under section 413(a)(2) of the FD&C Act and 21 CFR 190.6. In addition to the notification, we recommend that you provide us with: (1) documentation that the NDI-containing dietary supplement described in your notification was marketed in the United States as of the date described in section III.A., above; and (2) a copy of the current label for the dietary supplement.

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With respect to what information you should provide to support your conclusion that your product is reasonably expected to be safe, we note that you are not limited in what evidence you may rely on. In general, we suggest including a history of safe use, safety studies, or both. Additional information on this topic may be found at <https://www.fda.gov/food/guidance-documents-regulatory-information-topic-food-and-dietary-supplements/dietary-supplements-guidance-documents-regulatory-information>.

Since your product is already on the market, we suggest that you also include any evidence related to the history of your product's use since it has been on the market, including any customer complaints and adverse events⁴ (whether serious⁵ or non-serious) associated with the product. If you conclude that the product's history of use does not raise safety concerns, you should explain how you reached that conclusion.

One goal of this guidance is to help ensure that consumers have access to safe dietary ingredients and dietary supplements, while addressing and controlling the risks that are presented by failure to file an NDI notification. When a manufacturer fails to file a required NDI notification, we do not have the opportunity to assess the manufacturer's evidence of safety.⁶ Therefore, to protect consumers from possibly unsafe NDI-containing dietary supplements, it is important that we receive this safety information. Moreover, once we have more evidence about the identity and safety of NDI-containing dietary supplements in the marketplace, we will be able to better prioritize our enforcement efforts and protect consumers against products that do not satisfy the applicable safety standards.

C. How to Submit Your Notification Package and What to Expect

You may submit your notification and the other information discussed in section III.B. (dietary supplement label and documentation showing that the dietary supplement was marketed in the United States as of May 20, 2022, electronically via the CFSAN Online Submission Module (COSM)).⁷ Although we encourage electronic submission, physical media and paper submissions may be sent via U.S. Mail or courier using the address on our Web site.⁸ We intend to consider physical media and paper submissions as submitted on the date they are postmarked or on the date of delivery if delivered in person during regular business hours.

⁴ As defined in section 761(a)(1) of the FD&C Act (21 U.S.C. 379aa-1(a)(1)), the term "adverse event" means any health-related event associated with the use of a dietary supplement that is adverse.

⁵ As defined in section 761(a)(2) of the FD&C Act (21 U.S.C. 379aa-1(a)(2)), the term "serious adverse event" means an adverse event that results in death, a life-threatening experience, inpatient hospitalization, a persistent or significant disability or incapacity, or a congenital anomaly or birth defect, or that requires, based on reasonable medical judgment, medical or surgical intervention to prevent one of the above outcomes.

⁶ As stated in section I of this document, if a required premarket notification is not submitted to FDA, section 413(a) of the FD&C Act (21 U.S.C. 350b(a)) provides that the dietary supplement containing the NDI is deemed to be adulterated under section 402(f) of the FD&C Act (21 U.S.C. 342(f)).

⁷ FDA has provided details as to how to use COSM on our Web site. For more information, go to: <https://www.fda.gov/food/dietary-supplements/new-dietary-ingredients-ndi-notification-process>.

⁸ For information, go to: <https://www.fda.gov/food/new-dietary-ingredients-ndi-notification-process/how-submit-notifications-new-dietary-ingredient>

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Because of our focus on safety, we intend to make our review of these submissions a priority. However, although we expect to confirm receipt of your submission within 75 days after we receive it, we do not anticipate being able to complete our scientific evaluation and provide a response within 75 days after receipt.⁹

We encourage early communication and discussion so that you can obtain initial feedback on the kind of information to provide and how to provide it. Furthermore, if you are uncertain as to the regulatory status of your product, you may contact us within the first 90 days of the enforcement discretion period with questions about whether your product is subject to the requirement for premarket notification or other questions you may have regarding your product's status.

⁹ For more information on the types of response letters FDA commonly sends, see the response to question 3 (*What type of response may I expect to receive from FDA, and when?*) in section V.B. of FDA's draft guidance entitled "Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Draft Guidance for Industry (81 FR 53486; Aug. 12, 2016) (the 2016 Draft Guidance) (available at <https://www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/UCM515733.pdf>).