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Dietary Supplements: New Dietary Ingredient Notification Procedures and Timeframes: Guidance for Industry

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Dietary Supplements: New Dietary Ingredient Notification Procedures and Timeframes: Guidance for Industry¹

This guidance represents 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 of 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. This guidance is intended to help manufacturers and distributors of NDIs and dietary supplements (you) prepare and submit such premarket safety notifications, commonly referred to as New Dietary Ingredient Notifications (NDINs).

This guidance focuses on frequently asked questions about the NDIN submission and review process. We encourage you to consult this guidance when you are ready to submit your NDIN.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Background

The term "dietary supplement" is defined in section 201(ff) of the FD&C Act (21 U.S.C. 321(ff)), and the term "new dietary ingredient" in section 413 of the FD&C Act (21 U.S.C. 350b). Under section 413(a)(2) of the FD&C Act, the manufacturer or distributor of an NDI, or of the dietary supplement that contains the NDI, must 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)).

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

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As defined in section 201(ff)(1) of the FD&C Act (21 U.S.C. 321(ff)(1)), a “dietary ingredient” is any one of the following:

- A vitamin;
- A mineral;
- An herb or other botanical;
- An amino acid;
- A dietary substance for use by man to supplement the diet by increasing the total dietary intake; or
- A concentrate, metabolite, constituent, extract, or combination of any dietary ingredient from the preceding categories.

An NDI is defined in section 413(d) of the FD&C Act as a dietary ingredient that was not marketed in the United States before October 15, 1994 (21 U.S.C. 350b(d)). Thus, a substance cannot be a new dietary ingredient unless it is also a dietary ingredient. Dietary ingredients marketed in the United States before October 15, 1994 are not NDIs and, therefore, do not require an NDIN.

An NDIN must contain the information, including any citation to published articles, that provides the basis on which the manufacturer or distributor of the NDI or dietary supplement (the notifier) has concluded that the dietary supplement containing the NDI will reasonably be expected to be safe (21 U.S.C. 350b(a)(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 (21 U.S.C. 350b(a)).

To help industry comply with the FD&C Act’s premarket notification requirements for dietary supplements that contain an NDI, FDA issued an NDIN regulation (21 CFR 190.6). This regulation specifies the information the manufacturer or distributor must include in its premarket NDIN (see 21 CFR 190.6(b)):

- The name and complete address of the manufacturer or distributor that is submitting the notification.
- The name of the NDI that is the subject of the premarket notification. For botanicals, the Latin binomial name must be given, including the author citation (i.e., the name of the scientist who gave the botanical its Latin binomial name).
- A description of the dietary supplement (or dietary supplements) that contains the NDI, including:
 - the level of the NDI in the dietary supplement; and
 - the conditions of use recommended or suggested in the labeling of the dietary supplement, or if no conditions of use are recommended or suggested in the supplement’s labeling, the ordinary conditions of use of the supplement.

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- The history of use or other evidence of safety establishing that the dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe.
- The signature of a person authorized by the manufacturer or distributor to sign the notification on its behalf.

In addition to the requirements for the content of NDINs, the NDIN regulation establishes the administrative procedures for these notifications. The NDIN regulation defines the filing date of a notification as the date FDA receives it and, consistent with section 413(a)(2) of the FD&C Act, prohibits the manufacturer or distributor of the dietary supplement that contains the NDI from introducing the product into interstate commerce, or delivering it for introduction into interstate commerce, for 75 days after the filing date (see 21 CFR 190.6(c)). If the manufacturer or distributor submits additional substantive information in support of the original NDIN, the date FDA receives this supplemental submission becomes the new notification filing date, and the 75-day period restarts (see 21 CFR 190.6(d)). FDA will not disclose the existence of, or the information contained in, an NDIN for 90 days after the filing date of the notification (see 21 CFR 190.6(e)). After the 90th day, the entire notification, except trade secrets and confidential commercial information, will be placed on public display (see 21 CFR 190.6(e)). Finally, the regulation provides that FDA's failure to respond to an NDIN does not constitute a finding by us that the NDI or the dietary supplement containing the NDI is safe or is not adulterated under section 402 of the FD&C Act (21 U.S.C. 342) (see 21 CFR 190.6(f)).

In July 2011, we published a draft guidance entitled "Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues," in compliance with our statutory requirements under section 113(b) of the FDA Food Safety Modernization Act (Pub. L. 111-353). This draft guidance discussed FDA's views and recommendations on when an ingredient intended for use in a dietary supplement is an NDI, when the requirement to submit an NDIN to FDA applies, the types of data and information that manufacturers and distributors should consider when they evaluate the safety of a dietary supplement containing an NDI, what to include in an NDIN (including recommendations about identity and safety information), and the procedures for submitting an NDIN. In 2016, we replaced the 2011 draft guidance with a revised draft guidance, a portion of which is being finalized in this document. We understand the importance of finalizing other parts of the 2016 revised draft guidance, and we plan to finalize other individual sections as we complete our review and analysis of those sections.

III. NDIN Procedures and Timeframes

A. Who must submit an NDIN?

Either the manufacturer or distributor of a dietary supplement that contains an NDI, or the manufacturer or distributor of the NDI, must notify FDA at least 75 days before marketing the article in the United States, 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 CFR 190.6(a)). Although FDA does review NDINs from manufacturers and distributors of NDIs, notifications from ingredient manufacturers do not eliminate the requirement for a NDIN from the manufacturer

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or distributor of the dietary supplement in which the NDI will be used unless the prior notification for the NDI included information about the dietary supplement, specifically: (1) a description of the dietary supplement that contains the information required by 21 CFR 190.6(b)(3); and (2) the history of use or other evidence of safety that formed the basis of the notifier's conclusion that the dietary supplement would reasonably be expected to be safe under its labeled conditions of use. (For more information, see the response to question B in this section.)

B. Can you submit a single NDIN that contains safety data for a range of conditions of use and covers multiple products?

Yes. We accept NDINs that cover multiple dietary supplements and include safety data for a range of doses, daily intake levels, or other variations in conditions of use (e.g., serving size, duration of use, frequency of intake, target population, dosage form). We recommend you submit safety data up to and including the highest dose and daily intake level at which the NDI may be marketed, indicate any lower daily intake levels at which the NDI may be marketed, and include research that evaluates statistically relevant data points, such as a range of daily intake levels, to strengthen the safety analysis. FDA has received a number of NDINs that cover a range of doses and daily intake levels. These NDINs are publicly available in the NDIN docket on www.regulations.gov (see question IV.D. in this guidance for more information on this docket).² Contact FDA's Office of Dietary Supplement Programs by email at NDIN@fda.hhs.gov for more information.

C. How should the information in an NDIN be organized and presented?

The NDIN should be well organized to facilitate an efficient and timely FDA review. If you file electronically, the system organizes the NDIN for you. We encourage electronic submission to help ensure that you submit a complete NDIN and to enhance FDA's ability to process and review your NDIN efficiently (see the responses to questions I and J in this section for more information on electronic submission).

Instead of electronic submission, you may submit a paper NDIN for us to review. We recommend that the paper NDIN be organized by sections, with continuous and consecutive pagination throughout the notification. The page number should appear in the same location on every page. In addition, each subject area should begin with a new page to facilitate division of the NDIN among reviewers. FDA encourages those who wish to submit NDINs on paper to consult Appendix A of this guidance, which contains a recommended template for organizing a paper NDIN.

D. How should the NDIN describe the NDI?

Your NDIN should: (1) specify which of the dietary ingredient categories in section 201(ff)(1) of the FD&C Act the NDI belongs to and explain the basis for your conclusion; (2) describe the manufacturing process used to make the NDI, including process controls; (3) describe the physical properties and chemical or molecular composition and structure of the NDI; and (4) include a

² Information on how to access redacted copies of FDA's response letters to NDINs is available at <https://www.fda.gov/food/new-dietary-ingredients-ndi-notification-process/submitted-75-day-premarket-notifications-new-dietary-ingredients>.

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specification sheet (preferably in table form) that describes the critical identity and safety attributes of the NDI, including the purity and strength of the NDI and the identities and levels of any impurities and contaminants.

NDIs should be described in a way that accurately communicates their basic nature and characterizing ingredients or components, as appropriate. For example, bacteria should be described by Latin binomial name and strain designation.

If your NDI is an herb or other botanical, the name must include the Latin binomial name, including the author citation (21 CFR 190.6(b)(2)). Because different parts of the same botanical often have different chemical and physical properties, an NDIN for a botanical or botanically derived ingredient should also specify the part of the botanical that is the source of the NDI (e.g., leaf, bark, root). Unusual forms of botanicals should be identified (e.g., immature apples or malted barley). In addition, botanicals grown under controlled, specific conditions to concentrate or increase specific constituents should be identified.

If the NDI was the subject of a previous NDIN submitted by you or your supplier (the manufacturer or distributor from which you obtain the NDI), please include the NDIN number, which you can find in your FDA response letter or in the NDIN's docket file at www.regulations.gov.

E. How should the NDIN describe the dietary supplement in which the NDI will be used?

The NDIN should contain a description of the dietary supplement in which the NDI will be used, including: (1) the level of the NDI in the dietary supplement per serving; (2) the identity and level of any other dietary ingredients and non-dietary ingredients (e.g., binders and fillers) in the dietary supplement per serving; (3) a description of the manufacturing process of the dietary supplement, including process controls; (4) a specification sheet for the dietary supplement that describes its critical safety attributes; and (5) the conditions of use recommended or suggested in the labeling of the dietary supplement, or if no conditions of use are recommended or suggested in the labeling of the dietary supplement, a discussion of the ordinary conditions of use of the dietary supplement.

The conditions of use include the serving form (e.g., tablet, capsule, powder, liquid), serving size (e.g., weight or volumetric measure per serving), frequency of use (e.g., number of servings per day and interval between servings), duration of use, instructions for use, target population, excluded populations (if any), and any other restrictions on use. For purposes of FDA's review, daily lifetime use by all age groups and other populations at the highest described serving size and number of servings will be assumed, unless the notification specifies that the labeling will contain restrictions on conditions of use.

F. Should you explain how the information in the NDIN provides a basis to conclude that the dietary supplement in which the NDI will be used will reasonably be expected to be safe?

Yes. Your NDIN should include a dietary supplement safety narrative containing your objective evaluation of the history of use or other evidence of safety cited in the notification, along with an

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explanation of how the evidence of safety provides a basis to conclude that the dietary supplement containing the NDI, when used under the conditions described in the NDIN, will reasonably be expected to be safe.

G. What information should not be in the NDIN?

Your NDIN should contain only data or information that identifies your NDI or the dietary supplement containing the NDI, or that helps provide a basis for the safety of the NDI or the dietary supplement. An NDIN should not contain general or extraneous information. For example, data or information that is used primarily to substantiate a claim about the efficacy of the ingredient or supplement is not useful unless it also contains information that pertains to identity or safety. An NDIN should not include published review articles about other products, or publications and websites that promote other products, unless the information in the articles or websites can be specifically linked to the NDI or dietary supplement that is the subject of the notification. An NDIN also should not include data or information intended to satisfy other regulatory requirements. For example, the requirement to notify FDA within 30 days after marketing a dietary supplement with a labeling claim described in section 403(r)(6) of the FD&C Act cannot be met by submitting the required information in a premarket NDIN.³

H. When must an NDIN be submitted?

You must submit your NDIN at least 75 days before the dietary supplement containing the NDI is introduced into interstate commerce or delivered for introduction into interstate commerce. (21 U.S.C. 350b(a); 21 CFR 190.6(a)).

I. Does FDA accept NDINs electronically?

Yes. We encourage you to submit your NDIN electronically through FDA's CFSAN Online Submission Module (COSM). COSM's data validation helps prevent incomplete notifications by ensuring that all required fields are completed before the NDIN is submitted. For more information about how to submit electronic NDINs, see the New Dietary Ingredients Notification Process page on the FDA website.⁴

Firms that prefer to submit a paper NDINs still have the option to do so. Please see the recommended template for the format and content of a paper NDIN in Appendix A. To avoid delays, we recommend using the template in Appendix A to ensure the notification is complete before submission.

J. How many copies of an NDIN should be submitted?

If you are submitting on paper, you must submit an original and two copies of your NDIN (see 21 CFR 190.6(a)). If the NDIN is submitted through COSM, you need not submit any duplicate

³ The regulation governing these notifications is 21 CFR 101.93. Please refer to 21 CFR 101.93(a)-(e) for instructions on how to submit a notification of a dietary supplement labeling claim under 21 U.S.C. 343(r)(6). Notifications for labeling claims are not reviewed by the same staff who review NDINs.

⁴ FDA's New Dietary Ingredients Notification Process page may be accessed at <https://www.fda.gov/food/new-dietary-ingredients-ndi-notification-process/how-submit-notifications-new-dietary-ingredient>.

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copies.

K. Where should an NDIN be submitted?

If you are submitting your NDIN electronically, you may do so via COSM at <https://cfsan-onlinesubmissions.fda.gov>. FDA's website provides details on how to use COSM.⁵

If you are submitting a paper NDIN, send it to:

Office of Dietary Supplement Programs (HFS-810)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740-3835

L. How should published literature and other scientific information cited in the NDIN be listed?

If you are submitting your NDIN electronically, COSM provides instructions for listing your references. For paper NDINs, we recommend listing your references in a reference section at the end of the notification (see suggested format in Appendix A to this guidance). The list of references for both paper and electronic NDINs should include full citations to all published and unpublished sources cited or relied upon in the notification. Furthermore, the list of references should include the reference number or short descriptor used to cite to each study or publication in the body of the NDIN.

M. Do you have to provide copies of publications cited in the NDIN to FDA?

Yes. Whether submitting electronically or on paper, all references to published information offered in support of the NDIN must be accompanied by reprints or photocopies of such references (see 21 CFR 190.6(b)(4)). That means submitting a photocopy or reprint of the full text of each reference. Submitting only the abstract or bibliographic citation of a publication is not sufficient for FDA to evaluate whether the study supports the assertions in your NDIN. In addition, we do not recommend submitting abstracts that are the only published report of a scholarly or scientific work. Because abstracts do not contain sufficient information to judge the reliability of the scientific conclusions drawn in the study and generally do not undergo the rigorous review and editing used to evaluate full-length publications, they do not provide data that are useful in evaluating the safety of an NDI.

N. Can you use material published in languages other than English to support the safe use of an NDI?

Yes. Material written in a foreign language may be used as part of the basis for a conclusion that the NDI will reasonably be expected to be safe under the conditions of its intended use in the dietary supplement; however, the material must be accompanied by an accurate and complete

⁵ FDA's New Dietary Ingredients Notification Process page may be accessed at <https://www.fda.gov/food/new-dietary-ingredients-ndi-notification-process/how-submit-notifications-new-dietary-ingredient>.

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English translation (21 CFR 190.6(b)(4)).

O. How should unpublished scientific work be described in an NDIN?

In your NDIN, you should provide a complete description of the data and methods used in an unpublished scientific work. Without such a description, FDA reviewers may not be able to evaluate whether the data and methods support the safe use of the dietary supplement containing the NDI. Abstracts or summaries of data (e.g., “a 90-day study in five rats failed to show any toxicity”) do not provide enough detail to make a safety determination.

P. Should raw data be provided in an NDIN?

In some cases, yes. It depends on how important the data in question are to the notifier’s conclusion of safety and whether the data suggest a safety problem. Although data summaries (e.g., a table containing the average value and range or standard deviation for each parameter measured in a safety study or the peaks in a spectrum or chromatogram) are often sufficient, raw data are sometimes necessary for a thorough safety review. The more critical the data are to the overall safety evaluation, the more likely it is that more detail is needed.

During review of the NDIN, FDA may request submission of raw data or other additional information. If the additional information is a substantive amendment, FDA will reset the filing date and start a new 75-day review period (see 21 CFR 190.6(d); see also question IV.C in this guidance, which discusses when FDA expects to contact the notifier during NDIN review).

Q. How should you identify information in an NDIN that you believe is trade secret or confidential commercial information (CCI)?

For the first 90 days after the filing date of an NDIN, FDA will not disclose the existence or content of the notification. After the 90th day, all information in the NDIN will be placed on public display, except for any information that is trade secret or CCI (see 21 U.S.C. 350b(a); 21 CFR 190.6(e)).

We recommend that you clearly identify any information in the NDIN that you believe is trade secret or CCI—either by marking the information where it appears in the notification or by identifying this information in a separate document that accompanies the notification—and that you explain the basis for this belief. Likewise, if you believe there are no trade secrets or CCI contained in the NDIN, we request that you state this in your notification.

Trade secret information may consist of any commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort (21 CFR 20.61(a)). There must be a direct relationship between the trade secret and the productive process; for example, information relating to the manufacturing process (see 21 CFR 20.61(a)). Examples of trade secret information might include manufacturing methods and product composition (if different from what is declared on the label), product specifications needed to protect proprietary composition information (including proprietary analytical methods used to evaluate the product), and certificates of analysis.

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CCI covers information that is confidential⁶ and used in a business (21 CFR 20.61(b)). Examples of CCI might include sales statistics, dollar volume, amount or source of income (e.g., a company's list of customers), profits or losses, expenditures (of any person, firm, partnership, corporation, or association), names of suppliers or subcontractors, or brand of equipment.

The following data and information contained in or related to a notification are generally not trade secrets or CCI and, therefore, would be available for public disclosure after the 90th day after the NDIN's filing date:

- Information about history of use or other safety information related to the NDI or the dietary supplement, which is generally based on published studies⁷; and
- Correspondence and written summaries of oral discussions relating to the notification, except specific information that is exempt from disclosure under 21 CFR 20.61.

R. What signature and contact information should you provide in an NDIN?

FDA regulations require an NDIN to be signed by the person designated by the manufacturer or distributor of the dietary supplement that contains the NDI (see 21 CFR 190.6(b)(5)). This person should be the primary contact, who represents the notifier in any discussions with FDA about the NDIN and who designates any additional contact persons in the notification or in subsequent correspondence. Based on our experience, FDA has found that it is helpful for the notifier to designate additional contact persons to help ensure a timely response to FDA's questions. Contact persons can be agents, employees, officers, consultants, or attorneys for the notifier.

If you are submitting your NDIN on paper, the typed or printed name, title, address, telephone number and, if available, email address of the primary contact person should be listed at the end of the cover letter that accompanies the notification (see suggested notification format in Appendix A of this guidance) so that FDA can reach them when necessary. The typed or printed names, titles, addresses, telephone numbers and, if available, email addresses of additional contact persons for the NDIN should be listed after the contact information for the primary contact.

IV. What Happens After an NDIN Is Submitted?

A. When is an NDIN considered to be filed?

The date when FDA receives a complete NDIN is the date of that notification's filing. A complete NDIN is a notification that contains all the information required by 21 CFR 190.6. The date of filing is the start of the 75-day premarket review period during which the manufacturer or distributor of a dietary supplement containing an NDI may not market the dietary supplement (21 U.S.C. 350b(a)(2); 21 CFR 190.6(c)).

⁶ *Food Marketing Institute v. Argus Leader Media*, 139 S. Ct. 2356 (2019).

⁷ On occasion, FDA gets questions regarding the posting of unpublished and published studies on www.regulations.gov. As a general matter, FDA does not post these studies in the NDIN docket on www.regulations.gov.

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B. What are examples of omissions that cause an NDIN to be incomplete?

An incomplete NDIN is one that does not contain all the information required by 21 CFR 190.6. If we find that your NDIN is incomplete, we will inform you via COSM or in writing by U.S. mail or a courier service. FDA does not evaluate safety or identity information in incomplete NDINs.

Examples of omissions that can cause an NDIN to be incomplete include:

- Material in a language other than English that is either not translated or is translated inaccurately or incompletely.
- Citations to published literature for which a full copy of the publication is not provided.
- An NDIN that is not signed, or contact information that is inaccurate and does not permit FDA to establish contact with the notifier.
- Failure to provide the Latin binomial name, including the author citation, for any ingredient that is a botanical or derived from a botanical.

An incomplete NDIN does not satisfy the notification requirement found in section 413(a)(2) of the FD&C Act (21 U.S.C. 350b(a)(2)). Therefore, if the dietary supplement containing the NDI is marketed in reliance on an incomplete NDIN, it is deemed to be adulterated under section 402(f) of the FD&C Act (21 U.S.C. 342(f)).

C. Will you hear from FDA during the NDIN review period?

If we have questions during the NDIN review process, we will contact you. For example, we may request that you submit more information. Note that after reviewing a submission of additional information, FDA may determine that the submission is a substantive amendment and reset the filing date (see 21 CFR 190.6(d)). Should we make this determination, we will notify you that the 75-day review period is being reset and provide the new filing date, which will be the date of receipt by FDA of the information that constitutes the substantive amendment (see 21 CFR 190.6(d)).

D. What type of response may you expect to receive from FDA, and when?

After receiving an NDIN, FDA sends an acknowledgement of receipt to the notifier stating the date of receipt of the notification (see 21 CFR 190.6(c)) and provides the NDIN number assigned to the notification. The date of the NDIN's receipt is also the filing date on which the 75-day prohibition on introducing the NDI-containing dietary supplement into interstate commerce begins (21 CFR 190.6(c)). We may use electronic communication to send the acknowledgement of receipt. In this communication, we will also state that we intend to send a detailed response letter within 75 days of the filing date.

After finishing our review, FDA will send the response letter to the notifier. Examples of the types of response FDA commonly sends include:

- Letter of acknowledgement without objection;
- Letter listing deficiencies that make the NDIN incomplete under 21 CFR 190.6;

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- 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); and
- 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)).

Note that receiving an acknowledgement letter without objection means that FDA’s review of the NDIN 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. However, such a letter does not constitute an independent finding by FDA that the NDI and the dietary supplement that contains the NDI are safe, or that they are not adulterated under section 402(f) of the FD&C Act. FDA is not precluded from taking action in the future against a dietary supplement containing your NDI if it is adulterated, misbranded, or if its distribution in interstate commerce otherwise violates the FD&C Act.

The NDIN and the response letter sent at the end of FDA’s review will be kept confidential for 90 days after the filing date, as required by our regulation at 21 CFR 190.6(e). After the 90-day date, the NDIN and the response letter will be placed on public display at www.regulations.gov, except for any information that is trade secret or CCI (see 21 CFR 190.6(e)).⁸ We recommend that you clearly identify any information in the notification that you believe is trade secret or CCI—either by marking the information where it appears in the notification or by identifying this information in a separate document that accompanies the NDIN—and that you explain the basis for this belief. Likewise, if you believe there are no trade secrets or CCI contained in the NDIN, we request that you state this in the notification.

V. Meetings Between FDA and Notifiers

Some firms request meetings with FDA to ask questions and get preliminary and non-binding feedback from FDA regarding planned or potential NDINs. For example, some notifiers find it useful to obtain information regarding identity, safety, or how to submit before submitting an NDIN. Others have questions on submitting a new NDIN that is related to a previously reviewed submission. For example, they may wish to obtain clarification about what information could be useful to address concerns raised in a prior related FDA response letter. It is entirely voluntary to request feedback on a potential or planned NDIN. However, should you wish to do so, you may email FDA at NDITEAM@fda.hhs.gov, using the subject line “[Firm Name]– Pre-NDIN Meeting Request.” Note that a request for a meeting may be denied, although this is a rare occurrence. For example, we may deny a meeting request if a previous meeting for the same purpose has already been held and no significantly new information has become available, or if the subject matter is not appropriate for a meeting with FDA.

Meeting requesters should be aware that meeting materials, like other agency records, may be

⁸ Redacted copies of FDA’s response letters are publicly available on www.regulations.gov. Information on how to access them is available at <https://www.fda.gov/food/new-dietary-ingredients-ndi-notification-process/submitted-75-day-premarket-notifications-new-dietary-ingredients>.

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requested under the Freedom of Information Act⁹ (FOIA) and, unless the information being requested is classified as trade secret, CCI, or is otherwise exempt from disclosure under the FOIA, it will be released to requesters.

VI. Paperwork Reduction Act of 1995

This guidance contains information collections that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521).

The time required to complete this information collection is estimated to average one (1) hour per submission, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to:

Office of Dietary Supplement Products (HFS-810)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0330 (To find the current expiration date, search for this OMB control no. available at <https://www.reginfo.gov/public/do/PRAMain>).

Document History

- July 2011 – Original version of the draft guidance was issued.
- August 2016 – 2016 Revised Draft Guidance was issued.
- March 2024 – Final guidance issued.

⁹ 5 U.S.C. 552.

Appendix: Recommended Template for Organizing an NDIN that is Submitted on Paper

Note: Parenthetical references to question numbers in this template refer to questions in the body of the guidance.

I. Cover Letter

Consumer Safety Officer
Office of Dietary Supplement Programs (HFS-810)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740

DEAR [Name]:

The undersigned, _____, (*Name of the primary contact person designated by the manufacturer or distributor that is submitting the notification*) submits this NDIN under section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act with respect to _____ (*Name of the dietary supplement containing the NDI*), which contains the following new dietary ingredient: _____.

(*Signature of the contact person designated by the manufacturer or distributor*)

Primary Contact: (see question III.R)
(*Typed or printed name, title, address, telephone number and, if available, email address of the primary contact person.*)

Additional Contacts: (see question III.R)
(*Typed or printed name, title, address, telephone number and, if available, email address of each additional contact person.*)

II. Table of Contents

The table of contents should consist of a listing of the sections of the NDIN in the order in which they appear, along with the beginning page number of each section. Each section of the notification should begin on a new page (see question III.C).

III. Body of the Notification

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A. Administrative

1. Description of the NDI, the dietary supplement containing the NDI, and the conditions of use of the dietary supplement (see questions III.D – III.E).
2. Identification of information believed to be trade secret or confidential commercial information, including the basis for identifying the information as such (see question III.Q).
3. Safety narrative for the dietary supplement.

B. Attachments used to establish identity

[Provide only the information that identifies your NDI and dietary supplement (see question III.G).]

1. Detailed description of the identity of the NDI and the dietary supplement.
2. Manufacturing methods and practices to establish identity and safety.
3. Specifications to identify dietary ingredients, other ingredients, and contaminants, including the analytical methods used to determine each.
4. Identity References
[This subsection should contain reprints or photocopies of the full text of all published and unpublished identity references that have not already been included in other subsections of the Identity section.]

C. Safety and Toxicology Attachments

[Provide only the information that formed the basis for your conclusion that the dietary supplement containing the new dietary ingredient is reasonably expected to be safe (see question III.G).]

1. Safety Narrative for the NDI
2. Toxicology Studies
3. Human Studies
4. Other Studies
5. History of Use
6. Other Evidence of Safety
7. Other Safety and Toxicology References
[This subsection should contain reprints or photocopies of the full text of all published and unpublished safety and toxicology references that have not already been included in other subsections of the Safety and Toxicology section.]

IV. Complete List of References