How to Prepare a Pre-Request for Designation (Pre-RFD)

Guidance for Industry

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Contains Nonbinding Recommendations

How to Prepare a Pre-Request for Designation (Pre-RFD) Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) 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

This guidance is intended to assist sponsors in obtaining a preliminary assessment from the U.S. Food and Drug Administration (FDA or Agency) through the Pre-Request for Designation (Pre-RFD) process. Specifically, this guidance explains the Pre-RFD process at the Office of Combination Products (OCP) and helps a sponsor understand the type of information to provide in a Pre-RFD.

The Pre-RFD process is available to provide informal, non-binding feedback regarding the regulatory identity or classification of a human medical product as a drug, device, biological product, or combination product. In addition, this informal process provides information about a non-combination or combination product's assignment to the appropriate Agency center (Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH), or Center for Biologics Evaluation and Research (CBER)) for premarket review and regulation.

Additional information on topics outside the scope of this guidance may be found on our website (at https://www.fda.gov/combination-products). These topics include the definition of a combination product, a description of a non-combination product, as well as information about the formal Request for Designation (RFD) process.

This guidance replaces the final guidance for industry with the same title issued in February 2018. This replacement is intended to enhance the transparency, consistency, and efficiency of the Pre-RFD program by clarifying the information to include in a Pre-RFD submission and providing clarifications and updates to the Pre-RFD process.

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

[1] This guidance has been prepared by the Office of Combination Products in the Office of Commissioner, in cooperation with the Center for Biologics Evaluation and Research, the Center for Drug Evaluation and Research, and the Center for Devices and Radiological Health at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2017-D-0040.

the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Since its establishment on December 24, 2002, OCP has served as a resource for sponsors at various stages of development of their product. Sponsors often seek OCP feedback on 1) whether their medical product will be regulated as a non-combination product (i.e., a drug, a device, a biologic) or a combination product,[2, 3] and 2) which FDA medical product center (CDER, CBER, or CDRH) will regulate it (if it is a non-combination product) or will have the primary jurisdiction for the premarket review and regulation of the product (if it is a combination product).

There are two ways that a sponsor can receive such feedback from OCP. One option is to submit an RFD to receive a formal, binding determination for the sponsor's product with respect to classification and/or center assignment (see section 563 of the Federal Food, Drug, and Cosmetic Act). The RFD process is codified in 21 CFR Part 3, and OCP has issued a guidance about this process.[4] A second option is for a sponsor to submit an informal inquiry to OCP to receive a preliminary jurisdictional assessment, which is not binding. This informal process is called the Pre-RFD Program, available through OCP. This guidance describes this structured process with clear recommendations for sponsors wishing to submit Pre-RFDs. It also provides the process for review of Pre-RFDs by FDA staff, the general timeframes for sponsors to receive feedback from OCP, and the process for scheduling meetings in relation to a Pre-RFD.

III. GENERAL INFORMATION REGARDING THE PRE-RFD PROCESS FOR NON-COMBINATION AND COMBINATION PRODUCTS[5]

A. What is a Pre-RFD?

A Pre-RFD is a clear and concise written submission that a sponsor may make to OCP to request FDA's preliminary, nonbinding assessment of their product's classification and/or center assignment. OCP will provide a written preliminary classification and/or jurisdictional

[2] See 21 CFR 3.2(e) for the definition of combination product.
[3] Fixed-combination prescription drugs for humans (21 CFR 300.50) are not combination products as defined in 21 CFR 3.2(e). Contact CDER's Division of Drug Information with questions on these products (druginfo@fda.hhs.gov).
[4] Guidance for industry *How to Write a Request for Designation (RFD)* (April 2011). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.
[5] For the purposes of this guidance document, parties who submit a Pre-RFD to the Agency are referred to as "sponsors," "you," or "your"; the terms "we," "us," and "our" refer to FDA staff from the Office of Combination Products.

assessment of the product based on the information provided in a specific Pre-RFD and other available information that is relevant to classification and center assignment.[6]

Please note that if you change your product significantly after receiving OCP's feedback on the Pre-RFD, such as changing its proposed use or indication; changing ingredients; and/or for a biologic, making a manufacturing change, OCP's feedback may no longer be applicable. Accordingly, if you consider making such a change to your Pre-RFD product, we recommend that you contact OCP.

Additionally, if you have classification or center assignment questions regarding similar products that have different configurations, we recommend you contact OCP for advice on whether to submit one or more Pre-RFDs.

Though our Pre-RFD feedback is not binding on the Agency or sponsor, it is OCP's intent to provide the best advice possible based on the information relevant to classification and center assignment provided in the Pre-RFD and otherwise available to us. Our review will include involvement from the relevant Agency centers, as well as the Office of Chief Counsel when necessary. OCP's written feedback will include the rationale for our assessment of the information relevant to classification and center assignment.

Regarding similarities between the RFD and Pre-RFD processes, in both processes certain basic information is needed for FDA to provide an assessment of the classification and center assignment of a product. The basic information includes, for example, a description of the product, proposed use or indication, and a description of how the product achieves its intended purpose(s) (see IV.A, #7).[7]

B. When should I submit a Pre-RFD?

A Pre-RFD may be submitted at any point during medical product development, but OCP's ability to respond will depend on whether it has the basic information needed to develop a preliminary classification and/or jurisdictional assessment (see section IV.A for the basic information that should be included in a Pre-RFD).[8]

[continued on next page]

[6] A Pre-RFD response does not specify what type of premarket submission may be appropriate; for information on this topic see other Agency guidance (e.g., guidance for industry and FDA Staff *Principles of Premarket Pathways for Combination Products* (January 2022)).

[7] Please note that the information listed in this Pre-RFD guidance does not include all the information required for an RFD. If you wish to submit an RFD, you should consult 21 CFR 3.7 as well as the guidance about what to include in an RFD (see the guidance for industry *How to Write a Request for Designation (RFD)*).

[8] A Pre-RFD is not appropriate for a developing technology/concept that has no defined composition, proposed use, and/or indication. You may contact OCP if you have questions on such products.

A Pre-RFD is beneficial when the classification of a product and/or the Agency center to which it should be assigned is unclear or in dispute. Sponsors should consult any applicable statutory provisions and regulations and exhaust any applicable FDA resources[9] regarding product classification and center assignment when considering if classification and/or center assignment is unclear. We note that a Pre-RFD is not necessary for every product. Most products have clearly established classification and center assignment, and sponsors should work with the relevant center for these products.

C. May I request a meeting with OCP related to a Pre-RFD?

Yes, you may request a meeting. You may contact OCP with any questions before requesting a meeting. In our experience, many questions can be resolved promptly without a meeting. Meeting formats may be by teleconference, face-to-face virtually, or face-to-face in person. In OCP's experience, teleconferences and face-to-face virtual meetings are just as effective in achieving meeting objectives and are logistically more efficient than face-to-face in person meetings. The meeting types you may request with OCP related to a Pre-RFD:

- **Informational meeting:** A meeting held prior to the submission of a Pre-RFD to provide OCP with a better understanding of your product. In most cases, the Agency will be able to make its preliminary classification and center assignment assessment based on a Pre-RFD prepared following the recommendations in section IV. However, if you believe a meeting with OCP may be helpful, you can request an informational meeting. However, OCP may decline the request if OCP believes a meeting is not necessary to inform a Pre-RFD assessment. While FDA staff may ask clarifying questions during an informational meeting, they will generally be listening.

- **Explanatory meeting:** A meeting following the issuance of a Pre-RFD assessment. The purpose of an explanatory meeting is to discuss and address, if possible, any questions that a sponsor may have about the FDA's Pre-RFD assessment.

In addition to the two above meeting requests, if you would like FDA feedback on a study design to help inform classification and/or center assignment for your product (e.g., studies that inform mechanism of action of a product or the relative therapeutic/diagnostic contributions of a combination product's constituent parts), contact OCP.[10]

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[9] For example, see *Contact Us – Division of Industry and Consumer Education (DICE)* webpage (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice), *CDER Division of Drug Information* webpage (https://www.fda.gov/about-fda/cder-offices-and-divisions/office-communications-cder-division-drug-information), *Contacts in the Center for Biologics Evaluation & Research (CBER)* webpage (https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/contacts-center-biologics-evaluation-research-cber).

[10] Safety and effectiveness study design to support future product development and FDA authorization are outside OCP's purview and are reviewed by FDA's centers.

1. Meeting Request

Meeting requests should be sent via email to combination@fda.gov. The request should include suggested dates, times (see section III.C.3 for meeting timeframes), and format for the meeting, and meeting material.

2. Meeting Material

For an informational meeting request, you should include a complete explanation of the topics you would like to address and any supportive information. The meeting package should have enough information so that FDA can understand your product. At a minimum it should contain your product's basic composition and proposed use or indication. We note that it is important to provide a background package that is sufficient to enable OCP to engage in the meeting as needed. However, the submission of extraneous information can be counterproductive. Therefore, please keep your background information targeted and focused on the topics in your Pre-RFD that you would like us to consider. There is not a specific format for the meeting material.

For an explanatory meeting request, you should provide the questions to which you are seeking clarity regarding OCP's response on the Pre-RFD submission. Additional material is unnecessary.

You have the option to make a presentation at the meeting using a visual aid (e.g., via PowerPoint slide deck). Should you choose to use a visual aid that is not included in the meeting material, you should submit (via email) the visual aid no later than two weeks prior to the scheduled meeting date. Please note that new information that is not in the meeting package, should not be included in a visual aid.

3. Timeframe for Meeting

OCP generally aims to hold informational meetings within 6 weeks after receipt of a complete meeting package. This timeframe allows OCP and the necessary subject matter experts from the FDA centers adequate time to review materials prior to your meeting. If you wish to supplement your background information package with any new or modified information, we may have to reschedule the meeting or delay our feedback on discussion topics related to the new or updated information.[11]

OCP generally aims to hold explanatory meetings within 2 weeks after receipt of the meeting request, depending on the availability of the sponsor and FDA staff.

Please note that the timing to schedule meetings may vary based on factors including the number of subject matter experts to be included from interested Agency centers, the availability of conference rooms for face-to-face in person meetings, and the complexity of the issues the product raises. Meeting minutes are not provided.

[11] If the revised package changes the scope of the meeting, we may reevaluate the meeting request.

D. How do I submit a Pre-RFD for my product?

You may submit a Pre-RFD by email to combination@fda.gov in a common electronic format, such as a Portable Document Format (PDF) or a Word Document. Include "Pre-RFD" in the subject line of the email.

E. How promptly will OCP review my Pre-RFD?

OCP aims to review the Pre-RFD submission to ensure that it has adequate information for us to make our preliminary assessment within 10 business days of its receipt.[12] After such an evaluation, OCP will then either send you an email to acknowledge that our assessment will proceed, or detail the additional information needed before we can begin our assessment (i.e., provide you with an additional information request).

OCP's goal is to provide feedback on a Pre-RFD within 60 calendar days after we send you an acknowledgement that we have accepted your submission for review. However, please keep in mind that the speed of the review ultimately depends on the quality and quantity of the information submitted and its corresponding complexity. For instance, if you choose to submit a large amount of data and/or information for OCP to consider, or if the information is not concise or organized as recommended in section IV, it may be necessary for us to take longer to fully consider the information provided.

F. May I withdraw my Pre-RFD after submission?

Yes, you may withdraw your Pre-RFD by notifying OCP in writing, via email to combination@fda.gov. You may do so at any time after its submission and before OCP issues its preliminary assessment. Following receipt of your request, OCP intends to send you an email that confirms withdrawal of the submission.

G. What if I disagree with FDA's preliminary assessment?

You may request an explanatory meeting (see section III.C) if you disagree with FDA's preliminary assessment of your product and have questions about the Pre-RFD assessment.

Alternatively, you may submit a new Pre-RFD if you wish to present additional information or new data that was not presented in the original Pre-RFD. Once you submit a new Pre-RFD to us, OCP will consider this Pre-RFD a new submission and provide it with a new review and thorough assessment.

[12] In some cases, OCP may take longer than 10 business days to assess whether a Pre-RFD has adequate information for FDA to make a preliminary assessment. For example, if you submit a Pre-RFD that contains a large amount of data and/or information, we may need longer to assess if it has adequate information. Similarly, if you submit a Pre-RFD that is not concise and/or organized in a manner we recommend, such as in section IV of this guidance, we may require additional time to assess the adequacy of your submission.

Finally, you can submit an RFD for our consideration (see 21 CFR Part 3 and the guidance for industry *How to Write a Request for Designation (RFD)* for additional information on the necessary information, format, and page limit for an RFD).

H. How may a Pre-RFD response impact my future interaction with FDA for the product?

A Pre-RFD response includes FDA's preliminary classification and/or center assignment assessment (as requested by the sponsor). A sponsor should use that information regarding which FDA center to interact with going forward. We recommend including the Pre-RFD response in your communication with the appropriate FDA center.

I. How can I contact OCP?

You may contact OCP by email at combination@fda.gov.

J. Where can I find more information?

More information about product classification and center assignment, as well as the regulation of combination products, is available on the OCP website at https://www.fda.gov/combination-products.

IV. WHAT SHOULD I CONSIDER WHEN I SUBMIT A PRE-RFD?

A. What is the basic information that I should include in my Pre-RFD?[13, 14]

1. Sponsor's name and address and contact information for the official correspondent, including a contact name, a single email address, and telephone number.
    a. If the sponsor has an authorized representative who is serving as the official correspondent, the authorized representative's name, company, a single email address, and telephone number.[15]

2. A complete description of the product, which includes the following information:
    a. Name of the product.

    b. The 510(k), Premarket Approval Application (PMA), De Novo Request, New Drug Approval (NDA), Abbreviated New Drug Approval (ANDA), Biologics License Application (BLA), or any other FDA regulatory submission number (e.g., investigational) associated with the product, as applicable.

[13] We note that to the extent any information a sponsor provides in a Pre-RFD is trade secret or confidential commercial information, such information is protected by the same confidentiality laws as those that protect such information provided in an RFD.
[14] Please note that any information submitted should be contained within the Pre-RFD itself rather than referencing other FDA submissions.
[15] OCP will send correspondence to the single email address.

c. Detailed information on all the components of the product that includes the name(s) and source(s) of the component(s) and any regulatory and marketing history of the components, e.g.:

- Any FDA regulatory submission number associated with the components
- Whether any component is marketed as not being subject to premarket authorization or has received an investigational exemption or is under FDA review.

This information can be provided as a list or table. See also item numbers 5 and 7 in this section for additional component information OCP recommends to include.

d. A photo/diagram of the product.

3. Proposed use/intended use[16]/indication for use statement, including any additional claims you have made or plan to make about your product. To facilitate OCP's assessment, a Pre-RFD should focus on a single intended use.

4. Instructions for use/conditions of use.

5. A listing of all components, such as ingredients, including the following:

   a. Clear description of all the components (active and inactive) and their material composition (e.g., plastics, metals, chemicals, etc.).

   b. Detailed explanation of the reason/purpose for inclusion of each component.

   c. The specific amount/concentration for each ingredient (e.g., mass/volume, ingredient percentage).[17]

6. For products that include biologically-derived materials, provide a detailed description of how the material is processed (e.g., manufactured), source of each material, and characterization, including identity (e.g., analysis of the materials) of the final product.

7. An explanation of how the product, including how each component, works (i.e., the mechanism(s) of action) in achieving its intended purpose and the basis for the explanation. If the explanation is based on studies, include the study data and information. For information on product classification considerations, including the Agency's thinking with regard to the classification of drugs or devices, see, e.g., the guidance for industry and FDA staff *Classification of Products as Drugs and Devices and Additional Product Classification Issues* (September 2017). The guidance explains FDA's classification evaluation is based on the statutory definitions of drug and device. That guidance recommends that a sponsor

[16] 21 CFR 201.128 and 801.4.

[17] The specific targeted amount/concentration for each ingredient should be provided (e.g., 1% w/v). A range amount/concentration (e.g., 10-20% w/v) is not considered to be a specific target amount.

seeking to classify its proposed product as a device, should provide data that demonstrate that its product meets the definition of device (i.e., information that demonstrates the product does not achieve its primary intended purpose(s) through chemical action within or on the body or by being metabolized).

Please do not include the following information in your Pre-RFD because it typically does not help OCP understand how the product works: information that relates to the overall safety and effectiveness of a product (e.g., biocompatibility testing, human factors testing, electrical safety testing) or disease/condition prevalence and impact.

8. For products that might be combination products, any available information to support the relative contribution of different components to the overall intended therapeutic/diagnostic effects of the combination product (e.g., primary mode of action).[18] You may provide a detailed description of any supporting tests/studies if such information is available and you would like OCP to consider the information.

9. An explanation of how the product will be marketed. For instance, will the product have separately marketed constituent parts that are to be labeled for use together, or will it have components that either will be physically or chemically combined to make a single entity, or will it have constituent parts that are co-packaged?

OCP will use the information provided in making an assessment. Therefore, the information should be succinct and sufficient (e.g., if information is provided regarding a study to explain how a product works, include details describing the study). For studies that cannot be cited to a publicly available source (e.g., a scientific journal article), you should provide a description of how the study was conducted, the conditions of testing, the identity of all test articles and controls, a summary of results, and your conclusions as they pertain to your product's classification and center assignment. To facilitate FDA's review, we also recommend that:

- Statements are clearly written and not contradictory within the submission
- Assertions are supported (e.g., to support the proposed use, indication, and/or mechanism(s) of action)
- Assumptions are explained

If the information is not sufficient, OCP intends to send you an additional information request. OCP is always available as a resource to you. We strongly encourage you to contact OCP before submitting your Pre-RFD if you have any questions, or if you are uncertain about the type of information to include.

B. What format should I follow for my Pre-RFD?

We recommend that you concisely provide the information identified in section IV.A. It would be helpful if you include for each section of the Pre-RFD a separate heading that corresponds to the headings listed in section IV.A followed by your response.

[18] 70 FR 49848 (August 25, 2005).

If OCP provides you with an additional information request, please respond to that request with the following three documents:

- A document with OCP's questions/requests and your answers to those requests,
- A track changes version of your Pre-RFD clearly identifying the changes made from the most recent version, and
- A clean version of the revised Pre-RFD.

The track changes and clean versions should align with any revisions described in the question and answer document, as the revised Pre-RFD will be the document referred to during subsequent OCP review. If the questions/requests and your answers (first bullet in this subsection) contain substantive detail that is not in the revised Pre-RFD, we intend to ask you to align the documents and resubmit. Please include the clean version as a separate file.

We also recommend you use a standard typeface (e.g., Times New Roman), which should be in an easily readable font size (e.g., 12) and paginate the documents.

C. What is the recommended length for Pre-RFDs?

We encourage you to limit your Pre- RFD to a succinct summary of information relevant for OCP to evaluate your product's classification and center assignment.[19] In our experience, this information can typically be effectively conveyed in 15-20 pages, not including any courtesy copies of published literature.

V. PAPERWORK REDUCTION ACT OF 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520).

The time required to complete this information collection is estimated to average 24 hours per response, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate to:
Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

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 0910-0523 (expires January 31, 2027).

[19] See section III.E.

Guidance History	Date	Description
Level 2 Final Guidance	November 2025	See Introduction section of this document
Level 1 Final Guidance	February 2018	See Notice of Availability for more information*
Level 1 Draft Guidance	January 2017	See Notice of Availability for more information*

*The Notice of Availability is accessible via the Search for FDA Guidance Documents webpage.