This information should not be considered to represent advice or guidance on behalf of the U.S. Department of Health and Human Services or any agency or office thereof.

Pre-IND Meetings

Refer to the **NIH OER Regulatory Knowledge Guides** for more specific guidance on the regulation of:

- Small Molecules
- Biological Products
- Cell and Gene Therapies

Context

Before submitting an Investigational New Drug (IND) application, innovators can request a pre-IND (Type B) meeting with FDA. The pre-IND meeting is a critical milestone in the regulatory process; therefore, maximizing its value is important. Sharing the results of early development work gives FDA reviewers insight into your product knowledge base and enables innovators (also called sponsors) to receive direct feedback from FDA to increase their chance of a successful IND filing.
Usually only one pre-IND meeting is accepted by FDA per investigational product/indication, so it is important to prepare properly to ensure you understand FDA's expectations for your IND. This feedback helps you estimate the program's cost, duration, and potential risks. Your goal for this meeting is to ask the right questions, in the right way, at the right time. All questions and supporting data must be in the meeting briefing package and submitted by the pre-meeting deadline.

As you prepare your meeting request, develop a message-driven, issue-oriented, data-supported agenda. Companies may rush a request for a pre-IND meeting with FDA to appease investors, but that is unadvisable if your data does not support the meeting – for instance, if you do not have sufficient data to support your questions, or if your development is lagging in a critical area (usually manufacturing).

Once your meeting request is accepted, practice your presentation, and test your questions on experts inside and outside your organization. During the meeting, carefully listen to FDA's comments and ask for clarification when needed.

Key Takeaways

- Asking well-defined, targeted questions (not open-ended questions) results in more actionable responses from FDA.

- Thoroughly research the regulatory process and similar products. Focus your questions on IND-enabling issues not already covered in FDA guidance or from previous submissions of related products.
- Have a nearly complete draft of the briefing package before submitting a pre-IND meeting request. Questions and company positions generally should not change. This early planning helps you prepare for the meeting and may prevent delays.
- Stay focused on the agenda and do not add to it without FDA's approval.
- Do not hide concerns; instead put them "on the table" to stimulate debate and identify potential solutions.
- It is strongly recommended that new innovators work with a regulatory expert who can help prepare the pre-IND meeting request (and IND), the briefing package, and help coordinate and "unpack" the meeting itself.

How to Prepare

Submitting a Pre-IND Meeting Request

Before submitting a request for a pre-IND meeting, determine which FDA division to send the formal pre-IND meeting request letter (MRL) and check for any division-specific guidance. The MRL tells FDA the proposed agenda and scope of the meeting. It should include information about the product, specific objectives for the discussion, and a preliminary list of questions as well as proposed attendees from both the company and FDA. It may be more productive to identify subject areas where you are seeking insight, such as agreement upon a proposed animal model, and allow FDA to find the right reviewer to contribute to the meeting.

The pre-IND meeting is helpful because it is typically your first interaction with FDA. You are likely at a point in development where many decisions are not yet final, so facilitating a productive discussion with FDA and ensuring that you understand FDA's feedback is critical.
Asking appropriate questions in the pre-IND request is key because FDA uses this information to determine:

- If a face-to-face or teleconference meeting or written response only (WRO) should be granted or denied
- Which reviewers should be at the meeting to facilitate a productive discussion

FDA will also assign a review division Regulatory Project Manager (RPM) as the primary point of contact for the IND. All future communication with FDA will be facilitated through the RPM. You can also work with the RPM to understand preferences and expectations about meetings.

Consider All Aspects of Drug Development

Do not limit questions in the pre-IND meeting to only the early stages of a program. Include a brief description of the overall development plan, indication, and clinical trial approach. The pre-IND meeting is an opportunity to receive feedback on IND-enabling studies and first-in-human clinical trial design. Giving FDA reviewers a chance to understand your overall plan for developing a product helps

ensure studies are designed to provide the most beneficial information, which could minimize a development program's costs and potential risks.
Some common pre-IND questions are:

- Does FDA agree the proposed non-clinical studies are sufficient to enable the anticipated clinical development program?
- Does FDA agree that the current control strategy based on the outlined drug substance and drug product quality attributes will be sufficient for the first-in-human studies??

NIH Program Officer Attendance at the Pre-IND Meeting

Keep your NIH Program Officer (PO) informed about any interactions you have with FDA. Though not a requirement in most cases, you may choose to invite your Program Officer to attend your pre-IND meeting; however, they are not obligated to attend. POs may request a copy of the official meeting minutes, including essential discussion points, decisions, recommendations, agreements/disagreements, issues for further discussion, and action items.

Preparing a Meeting Package

Once a pre-IND meeting or WRO is scheduled, a full meeting package must be submitted at least 30 days prior to the meeting. The meeting package is much more detailed than the meeting request letter. It provides summary information relevant to the product and should be organized according to the proposed agenda. It should describe the principal areas of interest and provide concise information about the discussion topics. Each section of the planned IND should be described and summarized. It should also include a summary of information relevant to the product and all the necessary supplementary information for FDA to answer your questions. Any additional information that supports the product can be included as supplementary information with short summaries clearly stating decisions, results, and specific data.

The meeting package allows FDA to prepare for the meeting. It also helps narrow the focus on the areas of greatest interest. While writing the meeting request, consider the time constraints and focus the pre-IND meeting package on issues not already addressed by current guidance documents or information available on FDA's website. In addition, the specific FDA reviewing division may request you limit the number of questions (e.g., to ten critical inquiries). Do not embed multiple questions into one question. It is not advisable to revise or add questions between the meeting request and the meeting package, as that may result in a delay of the scheduled meeting. Contact the RPM for instructions on sending the meeting package to the appropriate personnel at CBER or CDER.

Preparing for the Meeting

A day or two before a scheduled meeting, FDA sends initial pre-meeting comments. At that time, you should gather your team and hold an internal meeting with the key participants (including your regulatory expert) to review FDA's comments. The team should determine which responses are straightforward and require no further clarification and which responses need further discussion during the meeting. Let the RPM know if any of the questions require additional discussion. If the

responses from FDA are sufficient and there are no questions, you can cancel the meeting by contacting the RPM.

It is also helpful to hold a preparatory session to develop a strategy for the meeting based on the initial pre-meeting comments, including identifying who will serve as the primary representative and which subject matter experts will speak about each point. For those unfamiliar with FDA meetings or for products with specific regulatory challenges, it is good to have someone experienced with FDA interactions assist in the meeting preparation. It may also be helpful to have someone play "devil's advocate" to explore what would be done if FDA says "no" to a proposal or suggests an alternative approach that would require a costly or time-consuming change. Commitments made during the meeting are recorded in the meeting minutes, so innovators should be cautious about making commitments. If you cannot formally commit to a change, it is acceptable to tell FDA during the meeting that you will consider their advice.

Regulatory Resources

Innovators should use the extensive publicly available sources of product development information before seeking a meeting. It is likely that many of your questions can be answered by online resources. FDA develops and maintains web pages, portals, and databases and participates in interactive media to advise on matters outside of established guidance, policy, or practices.

- Guidance documents and FDA resources
    - Biologics Procedures (SOPPs) – overview of CBER's standard operating procedures and policies
        - SOPP 8101.1: Regulatory Meetings with Sponsors and Applicants for Drugs and Biological Products – CBER staff guidelines for scheduling and conducting regulatory meetings
    - Guidance for Formal Meetings Between FDA and Sponsors or Applicants of PDUFA Products – recommendations on formal meetings relating to the development and review of drug or biological products
    - Best Practices for Communication Between IND Sponsors and FDA During Drug Development Guidance for Industry and Review Staff – recommendations for innovators on conducting timely, transparent, and effective communications with FDA
    - CGMP for Phase 1 Investigational Drugs – guidelines for using current good manufacturing practices when manufacturing new INDs
    - Drug Development Process: Clinical Research – overview for innovators as they develop a clinical research plan
    - Small Business and Industry Assistance: Frequently Asked Questions on the Pre-Investigational New Drug (IND) Meeting – resources for innovators planning an pre-IND meeting with FDA
- NIH network
    - Work with program officers to obtain feedback within NIH
    - NIH awardees can request a meeting with the NIH Small Business Education and Entrepreneurial Development (SEED) Innovator Support Team to ask questions about this process and request they review the draft cover letter and overall approach. However, the SEED office does not review or comment upon the scientific validity or data elements of the submission.

What to Expect

Steps and Timelines

Below are some general steps and timelines for formal pre-IND meetings with FDA. Check the specific reviewing division's website for any division-specific timelines.

- The FDA review division will respond within 21 days of receipt of the meeting request to inform you if the meeting has been granted or denied.
  - If the meeting has been granted, this communication will include the meeting date and type.
  - If the reviewing division plans to provide a WRO in place of a face-to-face meeting or teleconference, this will be specified in the response letter along with the date comments will be provided.
  - The RPM will schedule the meeting within 60 days of FDA's receipt of the meeting request. Coordinate with the assigned RPM on suitable dates.
- Confirm the timing for the pre-IND meeting and attendees with FDA. (This information should be included in both the meeting request and meeting package.)
- Submit the pre-IND (Type B) meeting package at least 30 days before the scheduled meeting. (Note: The FDA reviewing office will most likely either postpone or cancel the meeting if it does not receive the meeting package by the deadline.)
  - Due to this strict meeting package submission deadline, it is best to have a well-developed working draft of the meeting package ready before submitting the meeting request.
- FDA usually provides initial written comments on the meeting briefing package 24 to 48 hours before the meeting. If you feel these comments have sufficiently addressed all your pre-IND questions, you can contact FDA and cancel the meeting.
- If a WRO is provided, the WRO serves as the final piece of communication related to the meeting.
- If a meeting is held, FDA issues official minutes to all FDA attendees and the innovator within 30 calendar days of the formal meeting.

Rescheduling

Meetings may be rescheduled under certain circumstances, such as:

- You experience a minor delay in completing the meeting package and contact the RPM to explain why you cannot meet the deadline for submission and specify the date when the meeting package will be submitted. Note: This should be avoided unless you have a compelling reason based on new data that needs to be analyzed and that provides strong evidence about the product.
- The FDA review team determines that the meeting package is inadequate or additional information is needed to address the questions or other important issues.
- The meeting submission package is voluminous and FDA reviewers have insufficient time to review beforehand.

The Meeting

During the meeting you should ask for agreement on the data/content presented in the briefing package and its suitability and potential limitations for the planned IND submission. Expect that, while FDA will answer some questions, others may receive a generic response such as "*The plan presented appears to be sufficient; however, a final determination of the appropriateness of the plan will be provided during review of the IND submission*."

FDA's responses should help clarify if you are on the right developmental path. They can also help address gaps and provide input on matters related to chemistry manufacturing controls, quality, analytical testing, non-clinical studies, and design of clinical studies. You can then integrate the feedback, make appropriate adjustments in the project plan, and develop the relevant data for inclusion in your IND submission.

Some FDA divisions record live minutes during face-to-face meetings and teleconferences. This means the minutes are typed in real-time and are shown on a screen during the session. This is beneficial because the official minutes can be finalized quickly, and you can offer input regarding the wording. However, time spent wordsmithing the minutes takes time away from the pre-IND discussions. You should also take your own meeting notes and ensure they are aligned with FDA's meeting minutes. If you would like to provide FDA with your version of the meeting minutes, you should ask FDA if it would like a copy. FDA may or may not accept them.

Pre-IND Meeting Minutes

Innovator Responsibilities Following a Meeting with FDA

Once you have the formal written pre-IND responses and the official meeting minutes, FDA expects all commitments agreed upon to be met. If FDA has requested additional information or periodic updates, you should provide the RPM with the requested information at the agreed upon time.

To ensure all pre-IND comments have been addressed and those with submission deadlines are met on time, work with your subject matter experts, clinicians, and regulatory experts. Devise plans for reaching a resolution for each comment and determine the best mechanism for submitting the required information to FDA. In addition, a project manager familiar with FDA interactions can help with program oversight and management and facilitate communications with FDA.
You should regularly assess the product development status and timelines against progress made toward addressing each of the commitments. Certain areas may need immediate attention, while others may not need to be finalized by the time of IND submission. To this end, it may be helpful to provide periodic updates to determine if FDA agrees with the proposed approach to resolving an issue.

In Module 1 of the IND, include a pre-IND response document with the questions from the meeting package and FDA's responses from the meeting minutes or written responses, followed by your response and a link to the relevant information is in the electronic IND. This will confirm to FDA that its remarks were taken seriously and help it find the requested information quickly.
It is also possible that unforeseen development issues occur during product development before or after IND submission. It may be helpful to obtain FDA's input on such matters while attempting to comply with FDA's recommendations.

Following IND submission, information may be submitted as amendments to the IND. FDA is not under obligation to review these amendments within a specified timeframe, although it does target 60 days.