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FDA Pre-IND Meetings: Setting Yourself up For Successful 505(b)(2) NDA Submissions

Successfully navigating FDA's 505(b)(2) New Drug Application (NDA) pathway requires more than just innovative science–it demands strategic regulatory planning from the earliest stages of development. One of the most critical early milestones for Sponsors is their Pre-Investigational New Drug (Pre-IND) meeting with FDA.

While optional, this meeting provides an invaluable opportunity to engage Agency on your proposed product, development approach, and plans to leverage existing data. By taking advantage of a Pre-IND meeting, Sponsors have the opportunity to maximize regulatory clarity, streamline development timelines, and increase the likelihood of approval. In order to be successful at this stage, there are a number of key considerations unique to 505(b)(2) submissions, including how to establish an effective bridging strategy, formulate precise FDA-facing questions, and avoid common missteps that can lead to costly delays.

Whether you're reformulating an existing drug, introducing a new dosage form, or developing a combination product, early and well-executed FDA engagement—supported by experienced regulatory professionals—can provide the insight and alignment needed to position your product for long-term success.

How to Maximize Early FDA Engagement and Streamline Drug Development

For drug developers pursuing the 505(b)(2) New Drug Application (NDA) pathway, the FDA Pre-Investigational New Drug (Pre-IND) meeting is a crucial milestone. This early interaction with the FDA offers a strategic opportunity to introduce FDA to your product and its intended use, clarify regulatory expectations, address potential roadblocks, and align development plans to avoid costly delays. A successful Pre-IND meeting can significantly improve the chances of a streamlined and successful 505(b)(2) NDA submission.

To be successful, it is critical for Sponsors to know how to effectively plan, prepare for, and conduct a Pre-IND meeting, which is critical to set your 505(b)(2) program on a solid regulatory path.

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Understanding the 505(b)(2) Pathway

The 505(b)(2) pathway is a hybrid NDA route that allows drug developers to rely in part on existing data (e.g., published literature or FDA's previous findings of safety and efficacy for an approved drug) to support approval. This can dramatically reduce the time and cost associated with bringing a product to market, especially for reformulations, new dosage forms, combination products, alternative routes of administration, or new indications/patient populations.

This pathway utilizes a unique blend of original and referenced data; because of this, early FDA engagement is critical to clarify expectations and establish a viable development strategy.

What is a Pre-IND Meeting?

A Pre-IND meeting is a formal, voluntary meeting with the FDA to discuss your proposed development program before submitting an IND (Investigational New Drug) application. For 505(b)(2) submissions, this meeting helps determine:

- What existing data and/or prior FDA determinations can be leveraged
- How the new product will establish a bridge to the information that will be referenced
- What additional studies are required (nonclinical and clinical)
- CMC (Chemistry, Manufacturing, and Controls) considerations
- Regulatory and approval requirements

Benefits of Pre-IND Meetings for 505(b)(2) Submissions

Conducting a Pre-IND meeting is actually not required by FDA before an IND submission can be sent to the Agency. However, submitting an IND without meeting with FDA is highly discouraged by the Agency. The pre-IND meeting is a critical milestone; engaging with FDA at this point for a pre-IND meeting allows the Sponsor to introduce the FDA to important features of the product and the company itself, if the company is new to the review Division. Furthermore, it offers several strategic advantages that can shape the success of your 505(b)(2) development program. Some of these benefits include:

Regulatory Clarity

Gain early feedback on your development plan, including the use of existing data, proposed studies, and overall regulatory pathway (including applicable expedited development/review programs).

De-Risking Development

Identify potential roadblocks early—such as missing data, an insufficient bridging approach, or clinical trial design issues—before investing significant time, capital, and resources.

Validation of the 505(b)(2) Approach

Confirm that your product qualifies for the 505(b)(2) pathway and ensure FDA agrees with your strategy for leveraging prior findings of safety and efficacy.

Streamlined IND Preparation

Receive guidance on what data are necessary for a complete and acceptable IND submission, which helps avoid clinical holds or the need to provide additional information during IND review, potentially delaying initiation of your clinical study.

CMC Alignment

Discuss manufacturing and quality expectations early, especially when changes from a reference product or novel formulations are involved.

Strengthened FDA Relationship

Establish an early, collaborative rapport with the Agency, which can facilitate smoother communications throughout development

By leveraging these benefits, Sponsors can proactively shape their regulatory roadmap and increase the likelihood of a successful, efficient NDA submission.

Tips for Conducting a Successful Pre-IND Meeting for a 505(b)(2) Product

Navigating the Pre-IND process requires more than just regulatory knowledge—it demands strategic foresight, meticulous planning, and clear communication. The goal of this meeting is not only to gain FDA feedback, but to build a collaborative foundation that guides your development pathway efficiently. By treating the Pre-IND meeting as a strategic engagement rather than a regulatory formality, Sponsors can align expectations, reduce development risks, and ensure their 505(b)(2) NDA submission is built on a sound regulatory framework.

1. Define Optimal Timing and Plan Strategically

The timing of a Pre-IND meeting, for a 505(b)(2) NDA product, largely depends on the key questions that a Sponsor wishes to ask the FDA. Ideally, the Pre-IND meeting can be held after key elements of your product concept, target indication, and development approach are defined, and at least some preliminary data are available to allow FDA to respond to a Sponsor's questions. The Pre-IND meeting is generally not the appropriate meeting for input from the FDA on very early proof-of-concept or pilot toxicity study designs. Those topics, if FDA input is needed, can be discussed at an INTERACT or a Type D meeting.

2. Submit a Well-Prepared Pre-IND Meeting Request

Your request is not just a formality required to obtain a meeting with the FDA, it provides the FDA with critical information about the product and the status of development, which allows them to determine whether a meeting is, in fact, necessary and what subject matter expertise within the FDA needs to be involved in providing feedback to the Sponsor. As such, in addition to informing the FDA of the desire to have a Pre-IND meeting, it is important to succinctly present:

Product Description

- Product identifiers (e.g., name, structure, molecular wt.)
- Product class (does the product belong to a recognized pharmacological or biological class; is it a drug-device, drug-biologic, or biologic-device combination product; is the intent for the product to be marketed over-the-counter, etc.)
    - For drugs, also include route of administration; formulation or formulation critical attributes; and dosing schedule (if known)
    - If the product is a drug-device or biologic-device combination product, the device portion should also be described (e.g., constituent parts, use parameters, whether human factors testing has or will be conducted)

Proposed Indication(s)

A simple statement is generally sufficient. The meeting request letter is not the place to expand on the nature or severity of the disease or need in the marketplace for your intended product

Background and Purpose of the Meeting

This information is key. Sponsors request Pre-IND meetings at all stages of product development and likely FDA familiarity with the product. For example, the intended product for a Pre-IND meeting for a 505(b)(2) product may be early in development, relying on early published work to establish proof of concept with only minimal IND-enabling safety data available to discuss at a meeting. At the other end of the spectrum, the product may be an incremental improvement (e.g., new dosing schedule) for a product previously approved by the FDA or may have undergone a full development program outside the United States but has not yet been reviewed for marketing by the FDA. It is important to provide the FDA with enough information on the status of development so that they can obtain a quick picture of the breadth of work that has been completed. If prior meetings or advice from the FDA on the specific product have been received, their existence can also be noted.

The other essential piece of the background and purpose section is to give the FDA a high-level summary of the essential issues for which the Sponsor wishes to obtain agreement. Simply stating that the Sponsor hopes to obtain "agreement on the CMC, nonclinical, and clinical studies needed to initiate clinical testing under an IND" squanders the opportunity to reinforce the issues that are most important that agreement be reached on in the questions that follow.

Specific Questions for FDA Feedback

This is the most important part of the meeting request letter. FDA meetings are structured around responses to questions asked of the Agency. Therefore, successful meetings depend on the quality of the questions that are asked. Although the questions posed by a Sponsor are also presented in the briefing package and there is the opportunity to edit or omit questions when the briefing package is submitted following the granting of an FDA Pre-IND meeting, it is essential that the questions that are presented in the meeting request letter are well thought-out and clearly identify the Sponsor's position and the input requested from the FDA. Ideally, enough of the briefing package has been prepared prior to submission of the meeting request letter so that questions are fully refined and require little editing for the briefing package. Introduction of a new question at the time of the briefing package may derail a future meeting, resulting in the need for rescheduling if individuals within the FDA with different subject matter expertise need to participate.

The formatting of questions for the FDA is not strictly defined, but the FDA does not answer open-ended questions. The most effective questions for eliciting useful responses from the FDA include:

- A brief statement of facts pertaining to the question
- The Sponsor's position on the issue
- The feedback requested of the FDA

Posing a concluding statement of the question after providing the Sponsor's position and asking, "Does the FDA agree?" allows FDA to clearly state their opinion on the Sponsor's position on the question and justify their response. The length of questions is also not proscribed, but Sponsor's should aim to keep questions concise (approximately half a page – or less - in length). It is perfectly reasonable to refer the FDA to information to be provided in the briefing package if more detailed information than can be presented in the body of the question is necessary for the FDA to respond. While the formatting of each question is not proscribed, the FDA prefers that Sponsors limit the number of questions to 10-12 per meeting. Separating questions into multiple subparts is not an effective strategy for complying with this limit as the FDA counts each sub-question as an individual question. If Sponsors submit too many questions, the FDA may request that some be omitted or that a separate Pre-IND meeting be requested to cover a circumscribed category of questions. It is not unusual for separate CMC/nonclinical and clinical Pre-IND meetings to be conducted for products with multiple complex issues to discuss.

Successful development programs rely on the understandings and agreements reached at these meetings. Therefore, it is important to obtain FDA feedback on all of the critical issues for which FDA guidances do not provide sufficient information. Fear of receiving an unfavorable response from the FDA is not a reason to not ask a question. It is better to know early in development what a requirement may be than to find this out after considerable resources have been expended on a futile approach. Not asking and assuming that the absence of unsolicited comments by the FDA indicates their agreement with the overall development plans may cost a company in the long run.

Finally, the Facilitate Scheduling

Suggested times for the meeting as well as times for which the Sponsor is unavailable should be included in the meeting request. Submit this request at least **60 days** before your desired meeting date. FDA will review the request and determine whether a formal meeting or written response only is appropriate.

3. Prepare a Comprehensive Briefing Package

A strong briefing document is key to a successful Pre-IND meeting. It expands on information presented in the meeting request letter in a number of important ways. In addition to information provided in the meeting request letter (see Item 2, above), it should include:

- **Expanded background information.** For 505(b)(2) products, it is important to include information on the Sponsor's plans for relying on prior approved products or published literature and a high-level description of how the Sponsor intends to bridge the results obtained with the referenced products to their own product. The background section of the briefing package should also provide more detail on the development plans for CMC and the nonclinical and clinical programs (e.g., lists of studies conducted and those planned to be conducted) intended to supplement information being relied on from the reference product. In addition, it can include more detail on prior advice from the FDA pertaining to their product as well as implications (if any) of FDA requirements for similar products. A data section (which follows the presentation of questions for the FDA) that provides greater breadth and detail than is present in the individual questions for the FDA is almost always included in briefing packages. The data section includes (as is appropriate for the questions that have been asked) relevant details on the CMC, nonclinical, and clinical data that has been collected for the proposed product. Exhaustive detail and/or study reports are not appropriate, but the sponsor should provide sufficient detail and analysis so that the FDA understands what has been done, what has been observed, and how the Sponsor is interpreting that information. Though not required, it is helpful for the FDA in locating information in the data section if it is presented within each discipline according to the order in which information is presented in Module 2 summary sections of the Common Technical Document. If the Sponsor is requesting feedback on study design, protocol synopses rather than full study protocols are the preferred means of conveying plans for a study.

- To facilitate the conduct of the meeting, the Sponsor should also include **a comprehensive list of all individuals who will attend the meeting from the Sponsor's side** (with titles and affiliations) as well as a **proposed agenda**. The agenda is considered tentative because the FDA provides preliminary responses no later than 2 days prior to a scheduled meeting and Sponsors find that not all of the responses by the FDA merit discussion at the meeting. Generally, the Sponsor is given the opportunity the day before the meeting to submit a list of questions and responses that they would like to focus on at the meeting.

Submit this at **least 30 days prior** to the meeting.

4. Ask the Right Questions

Your questions should be clear, concise, and focused on obtaining FDA feedback that will guide development. It is critical that questions are complete and formatted/worded appropriately, as FDA will not answer open ended questions during the meeting. This is where experience comes into play – having someone on your team who has conducted successful FDA meetings in the past is extremely beneficial to achieve successful interactions.

Common topics include:

- The planned approach to using the 505(b)(2) pathway
- The adequacy of published literature or reference product data to support the proposed product
- Adequacy of the proposed bridging strategy
- The requirements for or design of nonclinical or clinical studies intended to fill gaps in information necessary for approval
- Requirements for CMC and device development and testing (if applicable)

5. Engage a Cross-Functional Team and Conduct the Meeting Professionally

Your internal or external team should include regulatory, clinical, CMC, and nonclinical experts who understand the product and can respond to FDA feedback. If a meeting is granted, it is important to rehearse your discussion points beforehand. Individuals who can speak to the science behind each question should be assigned to address each topic. The FDA speakers at meetings are typically the discipline leaders on the review teams and expect to discuss their responses with their counterparts from the Sponsor's team. These types of interactions are generally the most productive. It may be desirable to have a separate meeting leader from the Sponsor's side that handles any introductory statements from the Sponsor, manages transitions between questions, and provides concluding summaries of agreement and action items arising from the discussions. A dedicated note taker can be essential in refreshing the team's recall of specific discussion points after the meeting, though having multiple participants taking notes can also be helpful. Recording devices are not allowed for either teleconferences or face-to-face meetings.

6. Follow-up with a Meeting Summary

Prepare internal meeting minutes immediately and submit these to the FDA project manager as soon after the meeting as possible. Though the wording from the Sponsor's meeting minutes is unlikely to make it into the official FDA meeting minutes, the submission can provide important information to the FDA. The Sponsor meeting minutes can remind the FDA of what the take-aways from the meeting were from the Sponsor's perspective, allowing the FDA to provide additional clarification (if they deem it necessary). The Sponsor's meeting minutes are also a reminder of action items, as these usually involve follow on activities by the FDA. The FDA's official meeting minutes are typically issued within 30 days. Once received by the Sponsor, it is important to ensure alignment between your understanding and FDA's written summary. These minutes will be referred to by the FDA throughout the development program and again when the NDA is reviewed. Therefore, it is important that they are as accurate as possible. If a meeting is not granted, the Sponsor retains the ability to submit follow-up correspondence to obtain clarification of points made in the FDA's written responses.

Common Pitfalls to Avoid

While Pre-IND meetings offer valuable opportunities, they can also become missed opportunities if not approached thoughtfully. Many Sponsors underestimate the level of preparation required or fail to ask the right questions, resulting in vague or unhelpful feedback. Others may overlook critical development components—such as CMC or bridging strategies—until later in the process, leading to delays or rework. Understanding and avoiding these common missteps can help ensure that your pre-IND meeting delivers actionable guidance and sets your 505(b)(2) program on a clear, efficient path forward.

Some common pitfalls to ensure you avoid at this stage, include:

- **Submitting a poorly organized or incomplete briefing package**. Although it may not be fair, the Pre-IND briefing package may be the first glimpse by the FDA of the competence of the Sponsor and first impressions are difficult to dispel.
- **Asking vague or overly broad questions**. The most helpful responses from the FDA come when they can respond to a specific concern of the Sponsor. Vague questions lead to vague responses.
- **Failure to have a third party review the planned development program prior to finalizing questions for the FDA**. A fresh set of eyes may identify additional questions or more effective ways of framing questions to elicit helpful responses by the FDA.

- **Failing to explain reliance on existing data** or the plan for bridging to that data.
- **Asking questions that the FDA cannot answer without a thorough review of the data**. The FDA will not commit to read study reports or thoroughly evaluate study analyses for a Pre-IND meeting. Asking if a study is acceptable or if the product is approvable based on information provided in a Pre-IND briefing package is a sure way to obtain "That will be a review issue" in response.
- **Forgetting that the FDA does not have unlimited time to review your briefing package**. Simplifying the presentation of information and presenting it in a well-organized fashion allows the FDA more time to spend considering how to respond to your questions.

Your Partner in Conducting Successful Interactions with FDA

A successful Pre-IND meeting can significantly de-risk your 505(b)(2) development program, clarify data requirements, and ensure alignment with FDA expectations. By investing the time to prepare a thoughtful strategy and engage the FDA early, you lay the groundwork for an efficient and successful NDA submission.

If you're navigating the 505(b)(2) pathway or preparing for a Pre-IND meeting, regulatory consultants or experienced drug development professionals can provide valuable support to strengthen your strategy and documentation. ProPharma's team of expert regulatory affairs consultants have an expansive breadth and depth of experience with both the science leading your submission as well as the regulations you must comply with to get it on the market in the US. Our expertise is unparalleled, which is why we have such a long-standing relationship with the FDA, built on a history of successful interactions with the Agency.

ProPharma: The World's Leading Regulatory Consultancy

For more than 40 years, we have been helping clients conduct successful Pre-IND meetings with FDA, enabling them to effectively reach the next regulatory milestone. Contact us today to learn how we can help you achieve successful interactions with FDA.