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Navigating the Pre-IND: An Introduction and Best Practices

What is analytical method validation?

The FDA Pre-IND review serves as a crucial checkpoint for sponsors to receive valuable binding feedback on their proposed development plans, providing critical guidance that charts the course for their path to investigational new drug (IND) filing. The Pre-IND meeting ensures that sponsors are aligned with FDA expectations and recommendations ahead of completing the remaining studies to submit an IND application including the design of preclinical studies, product manufacturing and quality controls needed to initiate human studies (CMC), and the design of the planned first-in-human clinical trial. Utilizing the pre-IND process at the appropriate point in development can lead to more efficient drug development, increasing capital and timeline efficiencies, and potentially accelerating the IND and eventual approval processes by reducing the risk of delays or clinical holds later in development.

When is the right time to have a Pre-IND meeting?

A Pre-IND meeting should be requested early in the drug development process, typically after completing foundational preclinical studies (demonstrating safety and efficacy) and designing a first-in-human study but before initiating pivotal toxicology studies and/or studies supporting key aspects of the sponsor's intended clinical trial (e.g. exact dosing levels). By holding a meeting at this stage and presenting a comprehensive plan for remaining studies to be performed, sponsors can address potential concerns early on in a binding and efficient fashion.

How should you prepare for a Pre-IND meeting?

The first step is to submit a formal meeting request to the relevant FDA division. The request will include information such as the meeting objectives and specific questions grouped by discipline and a list of requested division participants from CDER/CBER, depending on the areas of guidance needed.
The next step is to file a Pre-IND briefing packet within 30 days of submitting the meeting request. The briefing packet is a comprehensive document that gives the FDA information needed to review the sponsor's development plan and address the proposed questions. The briefing packet should include the following information:

- Overall program summary
    - Key data collected to date that demonstrate safety and efficacy of the product
    - Studies that are still planned before submitting an IND application
- Rationale for safety, based on toxicological profile and safety margins
    - Results from ex vivo and in vivo nonclinical studies or planned studies that support in-human investigation
- Description of the manufacturing process for GMP drug product

- Descriptions of the drug product release strategy and analytical assays
- Summary of planned first-in-human clinical study including inclusion, exclusion, and endpoints
- Articulation of how the completed and planned preclinical studies support proposed design
- Specific questions the sponsor would like agency feedback on

Best practices CatalystBio recommends for preparing:

1. Clearly define your objectives and your comprehensive plan to IND filing.
2. Ask clear, actionable questions. Avoid open-ended requests for advice.
3. Articulate why the current approach is applicable to the stage of development and what changes are planned prior to Phase 3/commercial.
4. Consult with a team of product development experts prior to submitting a meeting request and/or filing a briefing packet.

What should you NOT do?

In a Pre-IND meeting, it is important to strike a balance between providing enough detail of the comprehensive information to be included in the IND, both executed and planned, and having already executed critical IND-enabling studies that may in fact need re-design after FDA feedback. While the sponsor should have a clear and comprehensive phase-appropriate development plan, leveraging the FDA's feedback is warranted for the Pre-IND to be useful. Being open to the FDA's suggestions, maintaining flexibility, and seeking feedback early will allow the sponsor to improve the development plan in the most efficient way possible and focus on those activities that are on the critical path.

While INTERACT meetings have recently been viewed as a critical milestone even before a Pre-IND, they are less impactful. Unlike a Pre-IND meeting, where formal guidance is provided by the FDA, the feedback in an INTERACT meeting is non-binding, offering less certainty for decision-making. Since the time needed to plan for and be granted an INTERACT meeting is often comparable to, if not longer than, that of a Pre-IND meeting, we generally do not recommend this approach, as binding feedback from a Pre-IND is far more valuable.

CatalystBio provides expert guidance to biotech companies at every stage of the product development process, from early-stage discovery through regulatory approval. Whether you are just starting to think about requesting a Pre-IND meeting, wondering if it is the right time to request one, or are actively preparing for one, our team can help you navigate this critical process. For more information, contact us at info@catalystbio.co.