PRE-IND AND SCIENTIFIC ADVICE MEETINGS

By the time a typical virtual biotech company is close to "first in human" studies there is often a web of data generated over years often at many CROs. Our consultancy has found that great value can be added when your "body of data" is organized in a format consistent with the requirements for your proposed submission be it an IND or IMPD. The simple activity of organizing your data within the format of the eCTD invariably identifies studies which may have been overlooked. We have yet to complete this task without finding gaps often resulting in a change of development strategies. In addition to uncovering omissions the resulting document can form the basis for a well-informed Pre-IND or Scientific Advice (Pre-IMPD) meeting package. So often we come upon companies and they have not taken advantage of these free and encouraged programs. Meeting types for Pre-IND include written-only answers, teleconferences, and face to face meetings. According to the FDA CMC information constitutes the most frequent cause of clinical holds. Generating the *right* content and questions for your meeting package can result in issues being identified before experiencing a clinical hold. There is a multitude of unpublished data that *only* the FDA knows thus providing even a brief summary of your NCE structure, route of manufacture, and composition, may yield information that could prevent a clinical hold. Based on our experience of filing more than 50 meeting packages over the last decade for large and small molecules including oral, injectable, dermal and ophthalmic topicals, we find the following are quality and CMC safety questions that are frequently over-looked by virtual drug development organizations prior to their 'first in human' studies.

CMC Questions for Pre-IND or Scientific Advice Meetings (Pre-IMPD)

- How to set specifications for an unstable drug substance drug product
- How to assign the regulatory starting materials in the synthesis of drug substance
- How to identify and control for potential genotoxic agents in the synthesis of drug substance
- How to set specifications for drug substance and drug product based on GLP toxicology studies
- How to plan for and select drug substance and drug product batches for GLP v. Clinical studies
- How to present and test for a novel excipient
- How to control for drug substance physical form for solid and semi-solid dosage forms
- How to design and assign a drug substance and drug product shelf-life for an IMPD filing
- How to identify and interpret the applicable Guidances that govern these questions

Even if you "think" you know the answers to these questions there is no substitute for having an official document to provide credibility to your investors in support of your proposed studies and plan. In the end, no matter how much experience you may have, no one but the FDA can know if a NCE has a clear path to an IND. But don't let me influence your decision. The following content for Pre-IND Meetings is taken verbatim directly from the FDA website.

FDA Summary of P-IND Meeting Value

Small Business and Industry Assistance: Frequently Asked Questions on the Pre-Investigational New Drug (IND) Meeting

The pre-IND meeting can be very valuable in planning a drug development program, especially if sponsors' questions are not fully answered by guidances and other information provided by FDA. Early interactions with FDA staff can help to prevent clinical hold issues from arising. A pre-IND meeting can also provide sponsors information that will assist them in preparing to submit complete investigational new drug applications. Efficient use of FDA resources can lead to more efficient drug development. These questions and answers can be especially helpful to small businesses that may have limited experience interacting with the Agency, or are unfamiliar with pre-IND meetings.

Can pre-IND meetings reduce time to market? Yes, time can be reduced by the following:

- Identifying and avoiding unnecessary studies
- Ensuring that necessary studies are designed to provide useful information
- Gaining FDA support for a proposed strategy
- Potentially minimizing potential for clinical hold
- Obtaining regulatory insight
- Minimizing costs
- Clearly defining endpoints and goals of the development program

In the process of drug development, when can a pre-IND meeting be very important?

- When the product is intended to treat a serious or life-threatening disease
- When there is a novel indication
- When there are sponsors new to drug development
- When there are questions from the sponsor
- When there are pharmacologic or toxicologic signals of concern
- When the drug is a new molecular entity

Are there recurrent problems at pre-IND meetings? Yes, the following have been identified in pre-IND meetings:

- Inadequate CMC information
- Insufficient pre-clinical support

- Unacceptable clinical trial design
- Noncompliance with Good Clinical Practices (GCPs)
- Lack of information on selection of dosage
- Present data clearly and consistently

Additional information (regulations, guidances, and websites)

- 21 CFR 312.47 (meetings) and 312.82 (early consultation)
- Guidance for Industry- Formal Meetings Between the FDA and Sponsors or Applicants – May 2009
- Guidance for Industry- M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals – January 2010
- Guidance for Industry- E6 Good Clinical Practice: Consolidated Guidance – April 1996
- CDER Small Business and Industry Assistance webpage

SUMMARY

TRIPHASE© has seasoned published authors who have Ph.D.s in complex areas of science with proven skills in summarizing hundreds of pages of tedious data into concise summary tables to identify gaps and support your proposed “first in human” studies in the form of a Pre-IND Meeting Package. Our gap analysis often results in a more concise development strategy to remove obstacles to an IND. The resulting Pre-IND packages can be easily adapted to include EU member states in the form of Scientific Advice Meetings and “Company Positions” to ensure a smooth filing in such member states.

Contact us today to discuss your program and answer your questions….

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