Table of Contents

1.0 Purpose

This SOP defines the content and format of Pre-IND Information Packages for submission to the FDA.

2.0 Scope

This procedure applies to Biopharmaceutical Development Program (BDP) and Regulatory Affairs personnel who are involved in the preparation, review, and approval of Pre-IND Information Packages for the Frederick National Laboratory of Cancer Research of NCI.

3.0 Authority and Responsibility

3.1 The Director, Regulatory Compliance, or designee has the authority to define this procedure.

3.2 BDP Regulatory Affairs may be responsible for the preparation of Pre-IND information packages to aid IND Sponsors or applicants.

3.3 The sponsor or applicant is responsible for finalizing and submitting the Pre-IND Information Package to the FDA.

3.4 BQA is responsible for quality oversight of this procedure.

4.0 Definitions

4.1 **Applicant -** an applicant is a person who submits an IND, or an amendment to an IND, to the FDA to conduct clinical investigations with an investigational new drug.

4.2 **Day -** One calendar day.

4.3 **IND -** an investigational new drug application, synonymous with "Notice of Claimed Investigational Exemption for a New Drug."

4.4 **Investigational New Drug -** a new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used *In Vitro* for diagnostic purposes. The terms investigational drug and investigational new drug are deemed to be synonymous for purposes of this procedure.

4.5 **Information Package (briefing package or backgrounder) -** Information provided by an external constituent to CDER or CBER as background information for a meeting.

4.6 **Meeting -** As used in this document, a meeting is any formal, planned interaction between FDA and an external constituent that occurs face-to-face, via teleconference/ videoconference, or as written response only (WRO).

4.7 **Sponsor -** A person who takes responsibility for and initiates a clinical investigation (see 21 CFR 312.3).

4.8 **RPM –** Regulatory Project Manager.

4.9 **Form 1571 -** FDA form for IND submissions.

5.0 Purpose of the Pre-IND Meeting

A pre-IND meeting is a Type B meeting held between a sponsor and the FDA. The primary purpose of a pre-IND meeting is to discuss safety issues related to the investigational drug; issues related to pre-clinical studies, clinical trial design, and manufacturing; and to identify potential clinical hold issues. The meeting may also include a discussion of various scientific and regulatory aspects of the drug as they relate to safety and/or potential clinical hold issues. FDA encourages sponsors to request pre-IND meetings for use of drugs/biologics not previously approved or licensed.

6.0 Requesting a Pre-IND Meeting

6.1 The Sponsor makes a written request for a Pre-IND meeting following ***SOP 24401 - Preparation of Pre-IND (Type B) Meeting Request Letters***. The pre-IND Meeting Request Letter is used to obtain a date and time for the pre-IND meeting and has specific content and format described in ***SOP 24401***.

6.2 BDP Regulatory Affairs (or designees) may assist in the preparation of the letter, if requested.

6.3 If a meeting is granted, the Sponsor should receive a meeting confirmation letter from the FDA within 21 days of receipt of the meeting request letter. For face-to-face and teleconference/videoconference meetings, the FDA's letter will include the date, time, conferencing arrangements and/or location of the meeting, as well as expected FDA participants. For WRO, the FDA's letter will include the date the FDA intends to send the written responses. The meeting confirmation letter may also specify if paper copies (desk copies) are requested (CDER only). Refer to the meeting confirmation letter or contact the FDA RPM if you have any questions.

7.0 Content of Pre-IND Information Packages

7.1 Reference Content Summary (per FDA Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants of PUDFA Products).

Although the contents of the information package will vary depending on the product, indication, phase of drug development, and issues to be discussed, information packages generally include the following.

(1) Cover letter. Clearly identify the date, time, and subject of the pre-IND meeting and include the pre-assigned application number.

(2) Form 1571 (available via FDA's Website)

(3) The application number (if known).

(4) The product name.

(5) Chemical name, established name, and/or structure.

(6) Proposed regulatory pathway

(7) Proposed indication(s).

(8) Dosage form, route of administration and dosing regimen (frequency and duration).

(9) Pediatric study plans, if applicable.

(10) Human factors engineering plan (for devices), if applicable.

(11) Combination production information, if applicable

(12) A list of individuals, with their titles and affiliations, who will attend the meeting from the requestor (including consultants, etc.).

(13) A background section that includes a brief history of the development program and the relevant communications with FDA prior to the meeting, any substantive changes in the product development plans (new indication, population, or basis for combination), as well as the status of the development program (as applicable).

(14) A brief statement of the purpose/objectives of the meeting. Identify the milestone type of meeting (Type B pre-IND Meeting). This statement could include a discussion of the types of completed or planned studies or data that the sponsor or applicant intends to discuss at the meeting, and the general nature of the critical questions to be asked.

(15) A proposed agenda, including estimated amounts of time needed for each agenda item.

(16) A list of final specific questions for discussion grouped by discipline (usually in the order of chemistry, manufacturing, and controls, then preclinical, and then clinical questions), with a brief summary for each question to explain the need or context for the question.

(17) Data to support discussion organized by discipline and question. This should include at least a draft clinical protocol synopsis or clinical study design (as appropriate), nonclinical protocol or data summary (as appropriate), and chemistry, manufacturing and controls information (as appropriate) to support discussion of the list of questions.

NOTE: Refer to Attachment 1 for an example of a Table of Contents for a Pre-IND Information Package.

7.2 It is critical that the meeting Information Package content support the intended objectives of the meeting. The Information Package should contain information that the FDA would need to respond to the questions proposed for the meeting.

7.3 The Pre-IND Information Package should contain the most current and accurate information available to the Sponsor to address the items outlined in Step 7.1. The contents of the Pre-IND Meeting Request Letter may be used as a starting point for preparation of the Pre-IND Information Package.

7.4 If specific guidance regarding the contents of the information package is desired, contact the FDA review division, or if known the regulatory project manager (RPM) assigned to the submission. Normally, the RPM is identified in the Pre-IND meeting confirmation letter as the meeting leader. If the product is in the early stages of development and no RPM has been assigned, contact the appropriate CDER or CBER review office to which the pre-IND meeting request letter was sent.

7.5 Sponsors should coordinate the agenda and the content of the information package to expedite review of the material and discussion at the meeting. The FDA will lead the pre-IND meeting and typically does not wish to hear a presentation of the information package. The FDA has already reviewed the information in the package and prefers to address the questions raised by the applicant as listed in the information package and provide additional comments based on their review.

7.6 A sequentially paginated document with a table of contents differentiating sections is recommended. Individual sections can be numbered separately as long as there is overall pagination for the entire submission. Indices, appendices, and cross references may be included as needed. The document should be bookmarked to enhance the reviewer's navigation across the different sections.

7.7 Electronic submissions in the Common Technical Document (CTD) format should be submitted via the FDA Electronic Submissions Gateway (ESG). Meeting packages are filed in CTD format under Module 1, Section 1.6.2 Meeting background materials.

8.0 Submission of Pre-IND Information Packages

8.1 It is the responsibility of the sponsor or applicant to submit the information package to the appropriate Division Director in CDER or CBER with product review responsibility.

8.2 The FDA generally schedules Type B meetings to occur within 60 calendar days from the receipt of the meeting request letter. The information package must arrive at the FDA no later than 30 days before the scheduled meeting date. Careful planning is required to assure that the information package will be available in a timely manner.

8.3 The FDA may postpone or cancel a meeting if supporting documentation essential for a productive meeting has not been received within the prescribed time frames. Depending on the circumstances a meeting may be rescheduled. Contact the FDA RPM to determine if a meeting maybe rescheduled and what is required.

8.4 A few days prior to a Pre-IND meeting, the requestor can expect to receive preliminary written responses to their questions from the FDA with the option to cancel the meeting if the written responses are sufficient. The requester will let the FDA know if they accept the responses with no meeting, or if a meeting is still requested.

9.0 References

For assistance in preparing Pre-IND Information Packages, the following references and FDA Guidance Documents may prove helpful and can be obtained by visiting the BQA/Regulatory Group, or the FDA website (http://www.fda.gov).

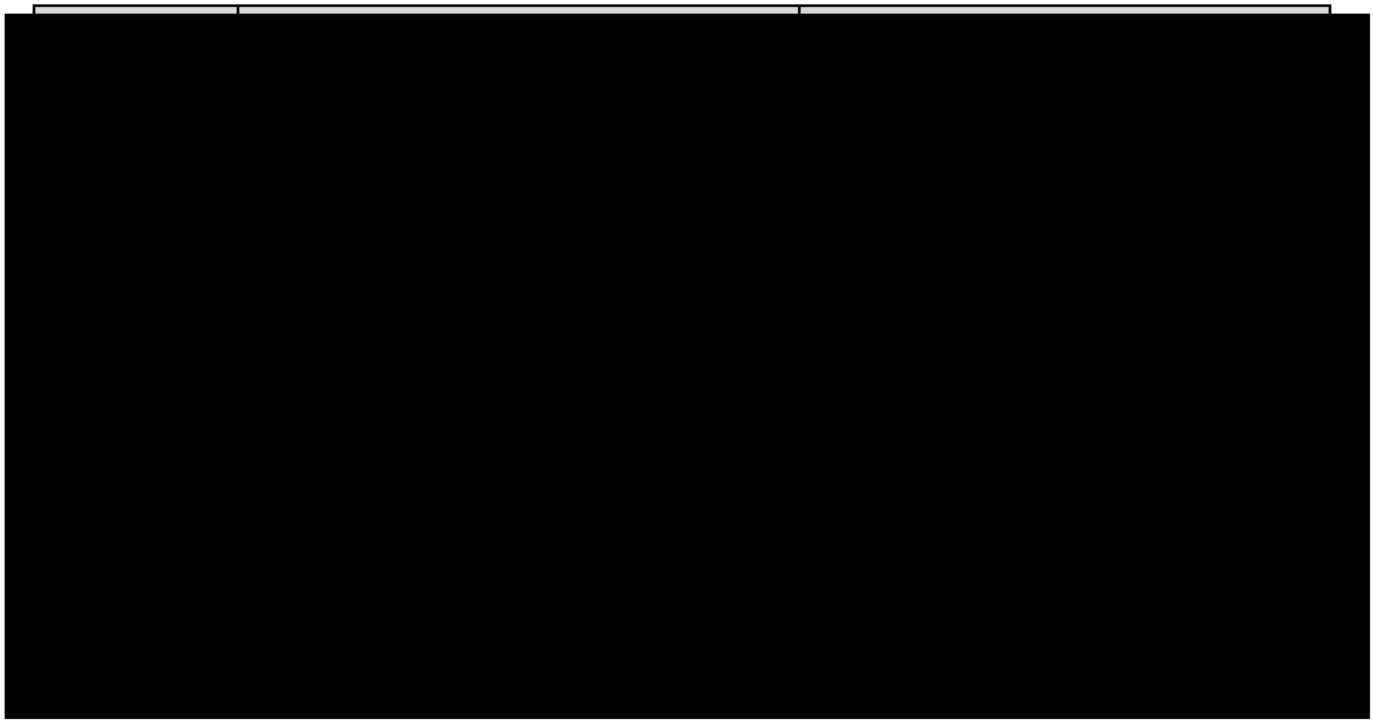
- Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products, December 2017
- Guidance for Industry: IND Meetings for Human Drugs and Biologics Chemistry, Manufacturing, and Controls Information, May 2001
- Guidance for Industry on Content and Format of Investigational New Drug Applications (INDs) for Phase I Studies of Drugs, Including Well-Characterized, Therapeutic, Biotechnology-Derived Products, November 1995
- FDA Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics, May 2014

- FDA Standard Operating Policy and Procedure (SOPP) 8101.1 Regulatory Meetings with Sponsors and Applicants for Drugs and Biological Products
- **SOP 24401** *Preparation of Pre-IND (Type B) Meeting Request Letters*

10.0 Attachments

10.1 **Attachment 1** Sample Pre-IND Information Package Table of Contents

11.0 Change Summary



Attachment 1

Sample Pre-IND Information Package Table of Contents

Cover Letter
Form FDA 1571
1.0 The Application Number (If known)
2.0 The Product Name
3.0 The Chemical Name and/or Structure
4.0 The Proposed Regulatory Pathway
5.0 The Proposed Indication(s)
6.0 The Dosage Form, Route of Administration, and Dosing Regimen
7.0 Pediatric Study Plans, if applicable
8.0 Human Factors Engineering Plan, if applicable
9.0 Combination Product Information, if applicable
10.0 A List of All Attendees
11.0 Introduction/Background Information
12.0 The Purpose of the Meeting /Type of Meeting
13.0 A Proposed Agenda
14.0 List of Questions
    14.1 CMC Questions
    14.2 Preclinical Questions
    14.3 Clinical Questions
15.0 Chemistry, Manufacturing, and Control Information
16.0 Summary of Preclinical Studies
17.0 Clinical Study Synopsis or Clinical Study Design (as appropriate)