

IND Content and Format Requirements for an IND

According to the current IND application form (Form FDA 1571), and IND will consist of as many as 9 principal sections:

1. **Cover Sheet (Form FDA 1571):** The form and instructions are located on the FDA website here: <http://www.fda.gov/cder/forms/1571-1572-help.html>
 - Person responsible for monitoring the conduct and progress of the investigation.
 - Person responsible for review and evaluation of safety information
2. **Table of Contents:** There is no standard format for the table but the FDA requires that the format be “in the interest of fostering an efficient review of the application.”
3. **Introductory Statement and General Investigational Plan:** These sections should be brief; generally two pages per section should suffice.

Introductory Statement should cover the follow:

- Name of investigational drug and, if applicable, all other active ingredients in the drug product
- Investigational drug’s pharmacological class
- Investigational drug’s structural formula, if known
- Formulation of dosage form(s) to be used
- Proposed route of administration of investigational drug product
- Summary of broad objectives and planned duration of proposed clinical investigation(s)
- Previous human experience with investigational drug
- If the drug has ever been withdrawal from investigation or marketing

General Investigational Plan should cover the follow:

- Rationale for the investigational drug or research study
- Indication(s) to be studied
- Evaluation approach
- Briefly describe the general approach to be followed in evaluating the investigational drug
- Trials to be conducted
- Number of research subjects
- Anticipated risks

4. **Investigational Brochure** (*Not required for single investigator, single site, Phase I - IND*): is an information package providing each participating clinical investigator with available information on the drug:
- Brief description of the drug substance and the formulation, including structural formula, if known.
 - Summary of the pharmacological and toxicological disposition of the drug in animals and, to the extent known, in human.
 - Summary of information relating to safety and effectiveness in humans obtained from prior clinical studies.
 - A description of possible risks and side effects to be anticipated on the basis of prior experience with the drug under investigation or with related drugs, and of precautions or special monitoring to be done as part of the investigations use of the drug.
5. **Protocol:** The regulations require submission of a copy of the protocol for the conduct of each proposed clinical trial. In general, protocols for phase 1 studies may be less detailed and more flexible than protocols for Phase 2 and 3 studies.
- Phase 1 studies should be directed primarily at providing an outline of the investigation, an estimate of the number of subject to be involved, safety exclusions, and a description of the dosing plan including duration, dose, or method to determine dose, and necessary monitoring of vital signs and blood chemistries.
 - Phase 2 and 3 studies are detailed protocols describing all aspects of the study. A protocol should be designed in such a way that, if the sponsor anticipates the some deviation from the study design may become necessary as the investigation progresses, alternative should be provides for such a deviation are built into the protocol.
6. **Chemistry, Manufacturing, and Control Information:** The purpose of the IND's chemistry, manufacturing and control (CMC) section is to establish that the methods used to manufacturing and assay the investigational product are adequate to ensure the products safety. Although in each phase of the investigation sufficient information is required to be submitted to assure the proper identification, quality, purity, and strength of the investigational drug, the amount of information needed to make that assurance will vary with the phase of the investigation, duration, dosage form, an amount of information available.
7. **Pharmacological and Toxicology Information:** Adequate information about pharmacological and toxicological studies of the drug involving laboratory animals or in vitro, on the basis of which the sponsor has concluded that is reasonably safe to conduct the proposed clinical investigations.

PLEASE NOTE: Letter of Authorization - A letter of authorization is an authorization that the manufacturer is allowing FDA to refer to their IND/IDE or marketing application in providing the technical information supporting the proposed clinical investigation. A sponsor-investigator submitting an IND/IDE not subject to a manufacturer's IND, IDE or

marketing application is ordinarily required to submit all technical information, unless such information may be referenced from the scientific literature. (312.22 (d)) In this case, the letter of authorization including the file identification (IND/DMF/NDA number) must be: 1) submitted to the authorizer's application and, 2) included in the initial submission of the new sponsor's IND. The sole exception to this requirement is when a marketed drug is used in the study, without modification to its approved packaging, in which case the marketed drug product must be identified by trade name, established name, dosage form, strength, and lot number.

8. **Previous Human Experience with the Investigational Drug:** If the investigational drug, or any of its active ingredients, has been marketed or tested in humans previously, the sponsor must provide specific information that might be useful in the FDA's evaluation. If there has been no previous human experience, the submission must state so.
9. **Additional Information:** Any other information that would aid in the evaluation of the proposed clinical study should be included in this section.

For additional information about the IND content and formation please review the following sources:

- 1) Guidance for Industry - *Content and Format of INDs for Phase 1 Studies of Drugs, Including Well-Characterized, Therapeutic, Biotechnology-Derived Products*: <http://www.fda.gov/cder/guidance/clin2.pdf>
- 2) 21 CFR Part 312.32 – IND content and format regulations: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.23>
- 3) FDA Guidance for Industry - *Content and format for INDs for Phase I Studies of Drugs, Including Well-Characterized, Therapeutic, Biotechnology-derived Products*: <http://www.fda.gov/cder/guidance/phase1.pdf>
- 4) Center for Drug Evaluation and Research (CDER) – Investigational New Drug (IND) Application Process: http://www.fda.gov/cder/regulatory/applications/ind_page_1.htm
- 5) Center for Biologics Evaluation and Research (CBER) – IND Guidance's: <http://www.fda.gov/cber/ind/indpubs.htm>