

## **IND FAQ**

### **What is an IND?**

The Investigational New Drug (IND) application fulfills two regulatory requirements. First, the application is through which a drug sponsor alters the FDA of its intentions to conduct clinical studies with an investigational drug. The second purpose is a request for an exemption from the federal statute that prohibits an unapproved drug from being shipped in interstate commerce. In many ways, the IND application is the result of a successful preclinical development program, and the vehicle the sponsor uses to advance to the next stage.

### **What is the purpose of an IND?**

- It affirms a body of knowledge about the manufacturing, pharmacology, and toxicology of the drug to support its use in human testing
- Requires that the clinical investigation be performed in accordance with Good Clinical Practice (GCP)
- Provides an additional level of protection through FDA oversight. The FDA's review focuses on safety of human subjects and ensuring that the studies will produce useful information to assess safety and efficacy of the test product.

### **What is a drug?**

Any substance that achieves its primary intended purpose through chemical action within or on the body of man or other animal and is dependent upon being metabolized to achieve its primary intended purpose.

The term "drug" means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C). A food or dietary supplement for which a claim, subject to sections 403(r)(1)(B) and 403(r)(3) or sections 403(r)(1)(B) and 403(r)(5)(D), is made in accordance with the requirements of section 403(r) is not a drug solely because the label or the labeling contains such a claim. A food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made in accordance with section 403(r)(6) is not a drug under clause (C) solely because the label or the labeling contains such a statement.

### **Who is the Sponsor?**

Sponsor means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or a pharmaceutical company, government agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator.

### **Who is a Sponsor-Investigator?**

Sponsor-Investigator means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. A Sponsor-Investigator is required to fulfill the responsibilities of both the Investigator and Sponsor.

### **Who is an Investigator?**

An individual who actually conducts a clinical investigation, they are responsible for how the test article is administered and/or dispensed to and in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

### **What is FDA Form 1571?**

The cover sheet for the Investigational New Drug Application - It is the responsibility of a sponsor to complete the form FDA 1571. However, if the investigator is the IND holder, she/he would have to assume the sponsor's responsibility, and therefore complete the form.

### **What is FDA Form 1572?**

Statement of Investigator - is a form that is completed by each investigator prior to participating in an investigational new drug study. This form should be updated during the course of an investigation if any information on the form changes.

### **Types of INDs**

**Investigator IND:** an application submitted by a physician who both initiates and conducts the investigation, and under whose immediate direction the investigational drug is administered or dispensed.

**Emergency Use IND:** is a vehicle through which the FDA can authorize the immediate shipment of an experimental drug for a desperate medical situation. Emergency use INDs generally are reserved for life-threatening situations in which no standard acceptable treatment is available and there is not sufficient time to obtain institutional review

board (IRB) approval. Emergency use INDs are also sometimes called “compassionate use” or “single-patient” INDs.

**Treatment IND:** experimental drugs showing promise in clinical testing for serious or life-threatening conditions are made widely available while the final clinical work is performed and the FDA review takes place.

**Screening INDs:** this type is a subcategory of a commercial IND. In early phases of drug development, before the development path is clear, exploratory studies may be conducted on a number of closely related drugs to choose the preferred compound or formulation. Usually the FDA requires a separate IND for each compound, but at this stage this type of studies may be best and most efficiently conducted under a single IND.

### **What is a Phase I study?**

Are studies which initially introduce an investigation new drug into humans. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with use of the drug, and if possible gain early evidence on the effectiveness of the drug.

### **What is a Phase II study?**

Are controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication(s) in subjects with the condition under study and to determine the common short-term side effects and risk associated with use of the drug.

### **What is a Phase III study?**

These are expanded studies which are performed after preliminary evidence suggesting effectiveness of the drug has been obtained. There intended to gather the additional information about effectiveness and safety that is needed that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling.

### **When can I start a clinical trial on my IND application?**

The FDA is required by the Modernization Act to respond to an IND sponsor within 30 calendar days of receipt of a complete IND application. Unless you are contacted, you may begin your study thirty days after FDA receives your IND application. The FDA may grant approval, an exemption or place a Complete or Partial Clinical Hold to delay the proposed clinical investigation. Holds may require modifications to the protocol and resubmission. When a proposed study has been placed on hold, the investigational drug may not be administered to research subjects.

No News = Good News

### **What if there is an amendment to your protocol?**

Protocol amendments are necessary when a sponsor wants to change a previously submitted protocol or to add a study protocol not submitted in the original IND.

For protocol amendments that introduce a new protocol should contain the protocol itself along with a brief description of the most clinically significant differences between the new and previous protocols.

Amendments that specify changes to previously submitted protocols are required when a sponsor seeks: (1) Phase 1 modified in a manner that significant affects the safety of the clinical subjects; or (2) a Phase 2 or 3 protocol modified in a manner that significant affects the safety of the subjects; the scope of the investigation, or scientific quality of the study.

**PLEASE NOTE: All amendments still need to be submitted, reviewed and approved by the IRB.**

For additional information about IND protocol amendments please review the following regulation on this topic (21 CFR Part 312.30):

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=312.30>

### **What are IND Safety Reports?**

Sponsors must submit IND safety reports to inform the FDA and all participating investigators of any adverse event experience (AE) that is associated with the use of a product and that is both serious and unexpected. The goal of this requirement is to ensure the timely communication of the most important new information about experiences with the investigational drug.

For additional information about IND safety reports please review the FDA regulation 21 CFR part 312.32:

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=312.32>

### **What are the FDA requirements for pre-clinical studies?**

Under FDA requirements, a sponsor must first submit data showing that the drug is reasonably safe for use in initial, small-scale clinical studies. Depending on whether the compound has been studied or marketed previously, the sponsor may have several options for fulfilling this requirement: (1) compiling existing nonclinical data from past in vitro laboratory or animal studies on the compound; (2) compiling data from previous clinical testing or marketing of the drug in the United States or another country whose population is relevant to the U.S. population; or (3) undertaking new preclinical studies

designed to provide the evidence necessary to support the safety of administering the compound to humans.

During preclinical drug development, a sponsor evaluates the drug's toxic and pharmacologic effects through in vitro and in vivo laboratory animal testing. Genotoxicity screening is performed, as well as investigations on drug absorption and metabolism, the toxicity of the drug's metabolites, and the speed with which the drug and its metabolites are excreted from the body. At the preclinical stage, the FDA will generally ask, at a minimum, that sponsors: (1) develop a pharmacological profile of the drug; (2) determine the acute toxicity of the drug in at least two species of animals, and (3) conduct short-term toxicity studies ranging from 2 weeks to 3 months, depending on the proposed duration of use of the substance in the proposed clinical studies.