FDA/CDER
SMALL BUSINESS CHRONICLES

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The IND justifies that the product will not expose humans to unreasonable risks when used in limited, early-stage clinical studies

IND 101

You have just realized that you need to submit an IND but do not know where to start, or even what the term IND means. We often receive anxious calls and emails from small businesses in this same situation. Stop, breathe, read, and let us guide you.

IND Basics The IND, or investigational new drug application, is a compilation of preclinical scientific information and plans for clinical development, supporting that a drug is reasonably safe for initial use in humans. This information shows that the compound exhibits pharmacological activity that supports commercial development. Overall, the IND justifies that the product will not expose humans to unreasonable risks when used in limited, early-stage clinical studies.

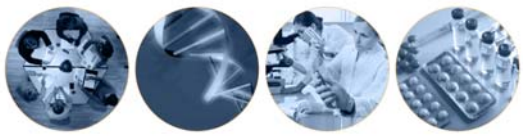
Current Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor may import or ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the means through which the sponsor technically obtains this exemption from the FDA.

Many INDs are sponsored by pharmaceutical companies or the federal government. However, most INDs are research-based (sponsored by individual investigators or academia).

To start, make sure that you need an IND. With certain exceptions, clinical investigations in which a drug is given to human subjects must be conducted under an IND per 21 CFR part 312. The FDA draft guidance document, "Investigational New Drug Applications (INDs) - Determining Whether Human Research Studies Can Be Conducted Without an IND" clearly describes when FDA requires an IND, specific situations where FDA does not require an IND, and issues that have been the source of confusion about the application of the IND regulations.

An exception is the investigational use of approved, marketed products. When the principal intent of the investigational use of a drug is to support safety or efficacy, FDA may require an IND submission. However, according to 21 CFR 312.2, the clinical investigation of a marketed drug or biologic does not require submission of an IND if all five of the following conditions are met:

(i) it is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;
(ii) it is not intended to support a significant change in the advertising for the product;
(iii) it does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
(iv) it is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]; and
(v) it is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7].



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IND Content 21 CFR 312.23 outlines the content and format of the IND. An IND should include:

- **Cover Letter/ Form FDA 1571**: Investigational New Drug Application (Instructions)
- **Form FDA 3674**: Certification of Compliance with Requirements of ClinicalTrials.gov
- **FDA Forms 3454/3455** for Financial Interests and Arrangements of Clinical Investigators
- **Table of Contents**
- **Introductory Statement/General Investigational Plan**
- **Investigator's Brochure**
- **Clinical Protocols & Investigator Information**: Detailed protocols for proposed clinical studies to assess whether the initial-phase trials will expose subjects to unnecessary risks; Information on the qualifications of clinical investigators; Commitments to obtain informed consent from the research subjects, to obtain review of the study by an institutional review board (IRB), and to adhere to IND regulations
- **Chemistry, Manufacturing, & Control Information**: Information on the composition, manufacturer, stability, and controls used for manufacturing the drug substance and the drug product
- **Pharmacology & Toxicology Information/Previous Human Experience with the Investigational Drug**: Preclinical data to allow an assessment whether the product is reasonably safe for initial testing in humans; Any previous experience with the drug in humans (often foreign use)

Many sponsors also submit FDA Form 1572 to provide the information required by 21 CFR 312.23(a)(6)(iii). FDA does not require the form itself, but does require the information that the form gathers.

IND Submission Before you submit your IND, you may wish to request a pre-IND meeting with FDA. 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. Please review the guidance document, "Formal Meetings With Sponsors and Applicants for PDUFA Products," for details.

Although CDER still accepts paper IND submissions, we strongly encourage sponsors to present INDs in the electronic common technical document (eCTD) format. Our website contains information to help you with this. We are also developing a CDERLearn course to guide you through the eCTD process, which we anticipate delivering by year's end.

There is no FDA fee to submit an IND.

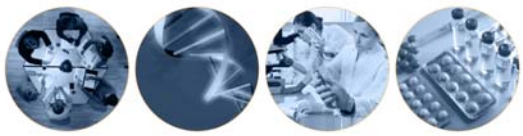
Once the IND is submitted, you must wait 30 calendar days before starting any clinical trials. This gives FDA the opportunity to review the IND for safety, to assure that it will not expose study subjects to unreasonable risk (21 CFR 312.40).

Once your IND becomes active you will need to maintain it… but this is a topic for another time. We hope that we have been able to simplify the process for you! As always, please email us with any topics of interest.

Cheers!

The CDER Small Business Assistance Team

Issues of this newsletter are archived at http://www.fda.gov/cdersmallbusinesschronicles



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