What Is an IND and Why Do I Need One?

WHY DO I NEED TO SUBMIT AN INVESTIGATIONAL NEW DRUG APPLICATION (IND) TO THE FDA?

Drug developers looking to bring their therapies into human clinical testing in the United States are required to file an Investigational New Drug Application (IND) with the United States Food & Drug Administration (FDA). Let us explore the purpose of the IND, their types, the format, what the FDA really cares about, and how the applications are approved by the FDA.

Purpose of an IND

Legal Purpose

- Current federal law in the United States requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. An IND is the mechanism that allows an investigational drug to be exempt from this federal law and to be transported across state lines.

Practical Purpose

- The primary purpose of an IND is to allow initiation of clinical testing within the United States.

Additional Reasons for Submitting an IND

- Allows importation of an investigational drug into the US
- Allows exportation of an investigational drug from the US to a non-listed country (i.e., not listed in 21 CFR 312.110)
- Enables submission of certain expedited program applications (e.g., Fast Track, Breakthrough Designation, etc.)

IND Categories and Types

An IND can fall into one of two broad types: commercial and research. A commercial IND is for a product intended to be marketed at a later date in the US. Any other IND is considered a research IND.

Under each type, there are three categories of IND:

1. **A traditional IND**
   Usually to propose studying an unapproved drug, or an approved product for a new indication, new formulation or in a new patient population.
2. **Emergency Use IND**
   Allows the FDA to authorize use of an experimental drug in an emergency situation that does not allow time for submission of a traditional IND in accordance with 21 CFR, Sec. 312.20 or Sec. 312.23. It is also used for patients who do not meet the criteria of an existing study protocol, or if an approved study protocol does not exist.
3. **Treatment IND**
   Submitted for experimental drugs showing promise in clinical testing for serious or immediately life-threatening conditions while the final clinical work is conducted and the FDA review takes place.

An IND can be sponsored by companies, institutions, or individuals (“Sponsor-Investigators”).

Source: https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application#FDA%20Guidances%20for%20Investigational%20New%20Drugs

Key Components of an IND

An IND is submitted to the FDA in the Common Technical Document (CTD) format, which is a consistent format used by the United States, Europe, Japan and other Regulatory Authorities. The CTD was originally developed to organize documents for inclusion in a full marketing application such as an NDA or MAA. While the CTD has also been adopted for use for clinical trials applications, such as INDs, not all components of the CTD will be complete in the IND. The CTD contains five modules as outlined below with some key elements highlighted (not comprehensive):

Module 1: Administrative information

- 1.1 Forms (1571 and 3674)
- 1.2 Cover Letter
- 1.12.14 Environmental Analysis Waiver
- 1.14.4.1 Investigator’s Brochure
- 1.14.4.2 Investigational Drug Label
- 1.20 General Investigational Plan

Module 2: Summary Documents

- 2.2 Introduction
- 2.3 Quality Overall Summary
- 2.4 Nonclinical Overview
- 2.5 Clinical Overview
- 2.6 Nonclinical Written and Tabulated Summaries
- 2.7 Clinical Summary (not usually needed for IND)

The Module 2 summary documents are not all strictly required at the IND stage; however, certain ones can be very helpful in guiding reviewers to the high level information contained within the application. Veristat typically recommends including 2.2, 2.4 and 2.5. Module 2.6 tabulated summaries can also be quite helpful at the IND stage.

Module 3: Quality (CMC)

- 3.2.S Drug Substance
- 3.2.P Drug Product
- 3.2.A.1 Facilities & Equipment

Module 4: Nonclinical Study Reports

- 4.2.1 Pharmacology
- 4.2.2 Pharmacokinetics
- 4.2.3 Toxicology
- 4.3 Literature References

Module 5: Clinical Study Reports

- [Completed clinical study reports or summaries – if available]
- Protocol for initial clinical study
- CV – for at least one Investigator
- Signed 1572 Form
- Literature References

FDA Focus in Reviewing an IND

As you prepare your IND, remember that the FDA will primarily focus their review on four critical areas, including:

1 Scientific Data (safety assessment)	• Animal Toxicology and Safety Pharmacology Studies • Previous Human Experience (if any) • Manufacturing Information
2 Clinical Protocol	• Safety monitoring is appropriate and adequate • Dose selection/dose escalation • Patient population selection is appropriate • Endpoints • Credentials of investigator(s)
3 Investigator’s Brochure	• Information provided to investigators is transparent • Explains all known risks • Class or mechanistic risks
4 General Investigational Plan	• Does the plan support the development program?

FDA Submission and Review of IND

IND is published and dispatched to FDA electronically

All commercial INDs submitted to the FDA must be published in eCTD format and dispatched through the Electronic Submissions Gateway (ESG).

30-day passive approval process

An IND is effective in 30 days unless FDA finds fault with application (places it on “Clinical Hold”). Some Divisions of FDA will issue a formal “study may proceed” letter, while other Divisions do not.

Meet Veristat – Getting It Right, the First Time

We understand that the stakes are high, and submitting your IND is the next critical milestone in your clinical development program. To give you an advantage, Veristat has assembled a team of scientific-minded experts that is adept at planning, writing, and publishing your IND. Get introduced to Veristat today.

www.veristat.com