INVESTIGATIONAL NEW DRUG (IND)

- Investigational New Drug is defined under 21 CFR 312.3(b) as ' *a new drug or biological drug that is used in clinical investigation*'.
- The term also includes a biological product used *in vitro* for diagnostic purposes.
- After pre-clinical investigations when the new molecule has been screened for pharmacological activity and acute toxicity potential in animals the sponsor requires permission from FDA for its clinical trials in humans.

- The sponsor submits the application for conduct of human clinical trials called Investigational New Drug (IND) application to FDA or DCGI .
- Once IND application is submitted , the sponsor must wait for 30 days before initiating any clinical trial.
- Clinical trials in humans can begin only after IND is reviewed by the FDA and a local *institutional review board* (IRB).
- IRBs approve clinical trial protocol, informed consent of all participants and appropriate steps to prevent subjects from harm.

- If the FDA accepts the IND request within 30 days of submission, clinical testing of the new molecule on human may begin by the investigator.
- At this point, the molecule under the legal status of FDA becomes a new drug subject to specific requirements of drug regulatory system.
- If at any time during clinical testing, the data furnished to FDA indicate the IP to be toxic under the criterion of FDA's Benefit/Risk ratio, FDA can terminate clinical trial and its actions are not subject to any judicial review.

TYPES OF INDs

A. COMMERCIAL INDs

- These are applications that are submitted primarily by the companies to obtain marketing approval for a new product.

B. NONCOMMERCIAL (Research)INDs

- These INDs are filed for noncommercial research. These are :

1) **Investigator's IND-** It is submitted by a physician who both *initiates* and *conducts* an *investigation* and who *also administers* and dispenses the IP. A physician might submit a research IND to propose studying an unapproved drug or an approved drug for new indications or in new patient population.

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3) **Treatment IND-** Also called Expanded Access IND this IND may be submitted for experimental drugs showing promise in *clinical testing of serious and immediately life threatening conditions* while the final clinical work is conducted and the FDA review takes place (21 CFR 312.34).

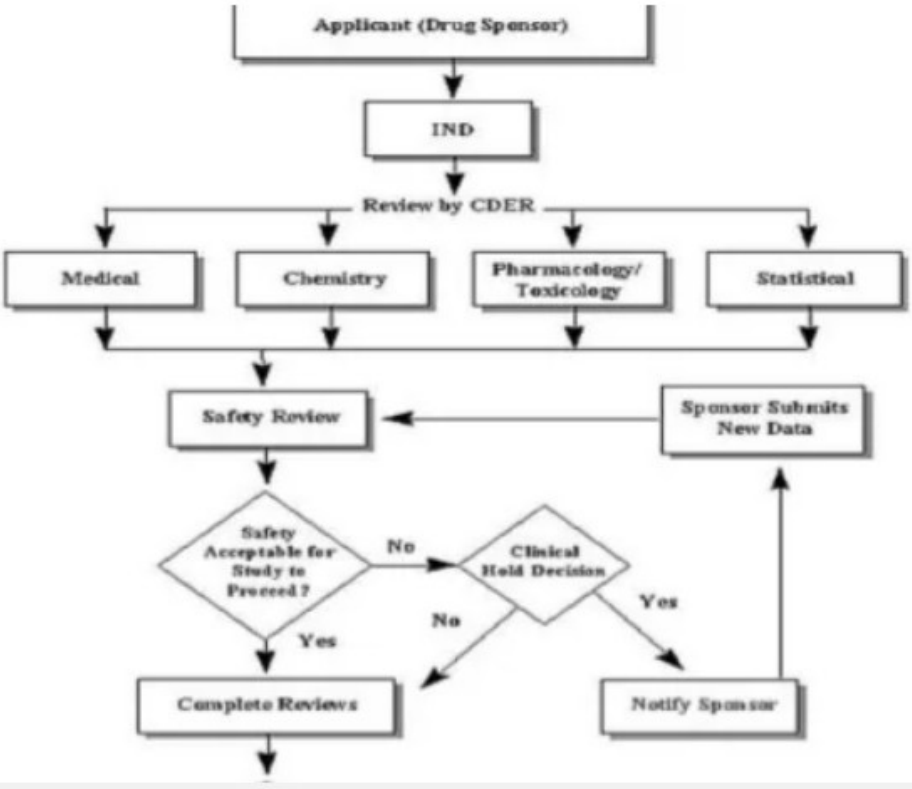
- The IND application must contain information in 3 broad areas:

i. **Animal Pharmacology and toxicology studies**- Preclinical data to assess if the product is reasonably safe for initial testing in humans. Also , included are any previous with drug in humans.
ii. **Manufacturing information**- Information pertaining to composition, manufacturer, stability and controls used for manufacturing drug product to ensure that the company can adequately produce and supply consistent batches of the drug.

iii. Clinical Protocol and Investigator information

- Detailed protocols for proposed clinical studies to make sure subjects are not exposed to undue risks. Also, information on the qualifications of the investigators (chiefly physicians) if they fulfill their clinical duties.
- Finally, commitments to obtain informed consent from all research subjects, to obtain review of the study by an IRB and to adhere to the investigational new drug regulations.
- An IND must also include *The Investigator's brochure.*

IND chart



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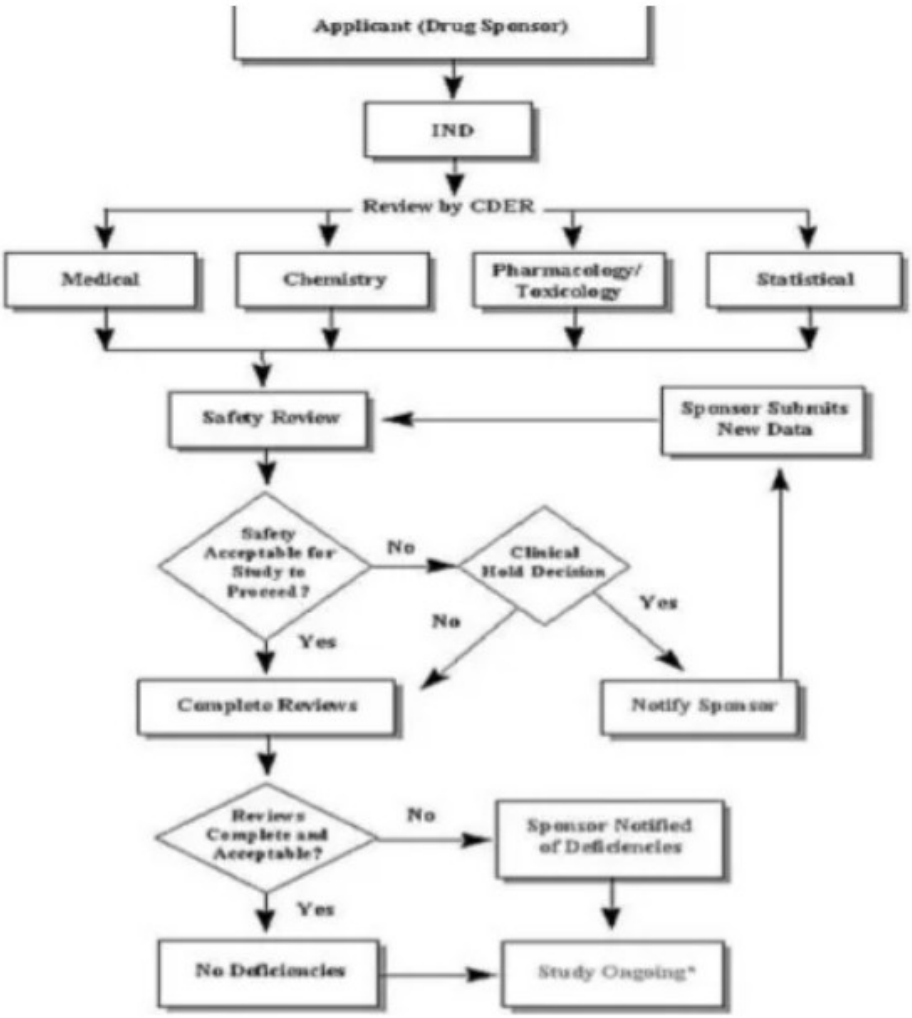

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Criteria for IND application

A clinical study is required for an IND if it is intended to support :

- A new indication
- Change in the approved route of administration or dosage level.
- Change in the approved patient population (vulnerable subjects e.g. pediatrics, elderly, HIV +ve, immunocompromised)
- Significant change in the promotion of an approved drug.

Code of federal regulations (cfr)

21CFR PART 312	• Investigational new drug application.
21CFR PART 314	• INDA and NDA for FDA approval to market a new drug.
21CFR PART 316	• Orphan drugs
21CFR PART 58	• Good lab practice for Nonclinical laboratory (animal) studies.
21CFR PART 50	• Protection of human subjects.
21CFR PART 56	• Institutional review boards.
21CFR PART 201	• Drug labeling.
21CFR PART 54	• Financial disclosure by clinical investigator.

Format and content of IND

1. Cover sheet (Form FDA 1571).
2. A table of contents.
3. Introductory statement and General Investigational Plan.
4. Investigator's Brochure.
5. Protocols.
6. Chemistry, Manufacturing and Control information.
7. Pharmacology and Toxicology Information.
8. Previous human experience with IP.
9. Additional Information.

WITHDRAWAL OF an IND

- At any time a sponsor can withdraw an effective IND . In such a case, FDA and IRB shall be so notified with reasons for withdrawal, all clinical studies ended, all current investigators and subjects notified, all stocks of drug returned to the sponsor or otherwise disposed off on request of sponsor in accordance with 312.59.

IND PROCESS IN INDIA

- IND has been defined under Rule 122-DA (3) of Drugs and Cosmetics Rules 1945 as a chemical entity having therapeutic indication but which have never been earlier tested on humans.
- No clinical trial for new drug for any purpose be conducted without permission , in writing, of the Licensing Authority (DCGI).
- Application for conducting clinical trials in India require submission by the sponsor on Form 44 along with requisite fee (Rs 50k) and documents as provided under Schedule Y to Drugs and Cosmetics Act 1940.

- Data to be submitted along with the application on Form44 to conduct clinical trials (2 hard copies and 2 soft copies i.e., CDs in PDF format)

1. Application on Form 44
2. Introduction of the drug
3. Fee Rs 50K through challan form
4. Chemical and Pharmaceutical information as per Appendix I of Schedule Y
5. Animal Pharmacology as per Appendix IV
6. Animal Toxicology as per Appendix III
7. Human/Clinical Pharmacology data as per Appendix I
8. Regulatory status in other countries as per Appendix I.