IND Application

The United States FDA's Investigational New Drug (IND) program is the means by which a pharmaceutical companies obtains permission to ship an experimental drug across state lines (usually to clinical investigators) before a marketing application for the drug has been approved.

- The FDA reviews the IND application for safety to assure that research subjects will not be subjected to unreasonable risk.
- If the application is cleared, the candidate drug usually enters a phase 1 clinical trial.

Criteria for application:

An IND is required for a clinical study 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 (e.g paediatric) or a population at greater or increase of

risk (elderly, HIV positive; immunocompromised)
- Significant change in the promotion of an approved drug

Exemption from IND application:

The FDA or an IRB may grant an exemption from IND requirements for the clinical investigation of a drug or biologic that is lawfully marketed in the United States if all six of the following conditions are met:

1. It is not intended to be reported to FDA in support of new indication for use or to support any other significant change in the labeling for the drug.
2. The drug is lawfully marketed as a prescription drug product and its proposed use is not intended to support a significant change in the advertising for the product.
3. It does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks

associated with the use of the drug product.
4. It is conducted in compliance with the requirements for IRB review and informed consent.

-It is conducted in compliance with the requirements concerning the promotion and sale of drugs and in addition, the investigator must not intend to invoke an exception from informed consent for emergency research.

□When to use IND application:

Conditions in which IND application need to be submitted:

1. Drug intended to treat or diagnostic serious or life threatening condition;
2. No satisfactory alternative available.
3. Controlled clinical trials in progress under IND or when trials completed and FDA review of request to market is pending.
4. Sponsor activity pursuing device marketing approval with FDA

5. Need FDA authorization to use experimental drug in an emergency situation that does not allow time for submission of an IND in accordance with 21 CFR Part 312.

6. May be used for patients ineligible per existing study protocol(s), or if approved study protocol does not exist.

□ Application Categories: ← commercial / research (non-commercial)

There are two main categories of IND:

1. Investigator-initiated
2. Sponsor-initiated

Both of these types of studies require approval by an institutional review board (IRB), an independent body constituted of medical, scientific, and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial.

Three IND types:

1. (Regular) IND (investigator)

- Submitted by a physician who both initiates and conduct: an investigation, and under whose immediate direction the investigational drug is administered or dispensed.

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 an IND in accordance with 21 CFR, Sec. 312.23 or Sec. 312.34.

- 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:

- It is submitted for experimental drugs showing promise in clinical testing for serious or immedi-

ately life-threatening conditions while the final clinical work is conducted and the FDA review takes place.

•The IND application must contain in three broad areas:

1. Animal pharmacology and toxicology Studies:

Preclinical data to permit an assessment as to whether the product is reasonably safe for initial testing in humans. Also included are any previous experience with the drug in humans (often foreign use).

2. Chemistry manufacturing information:

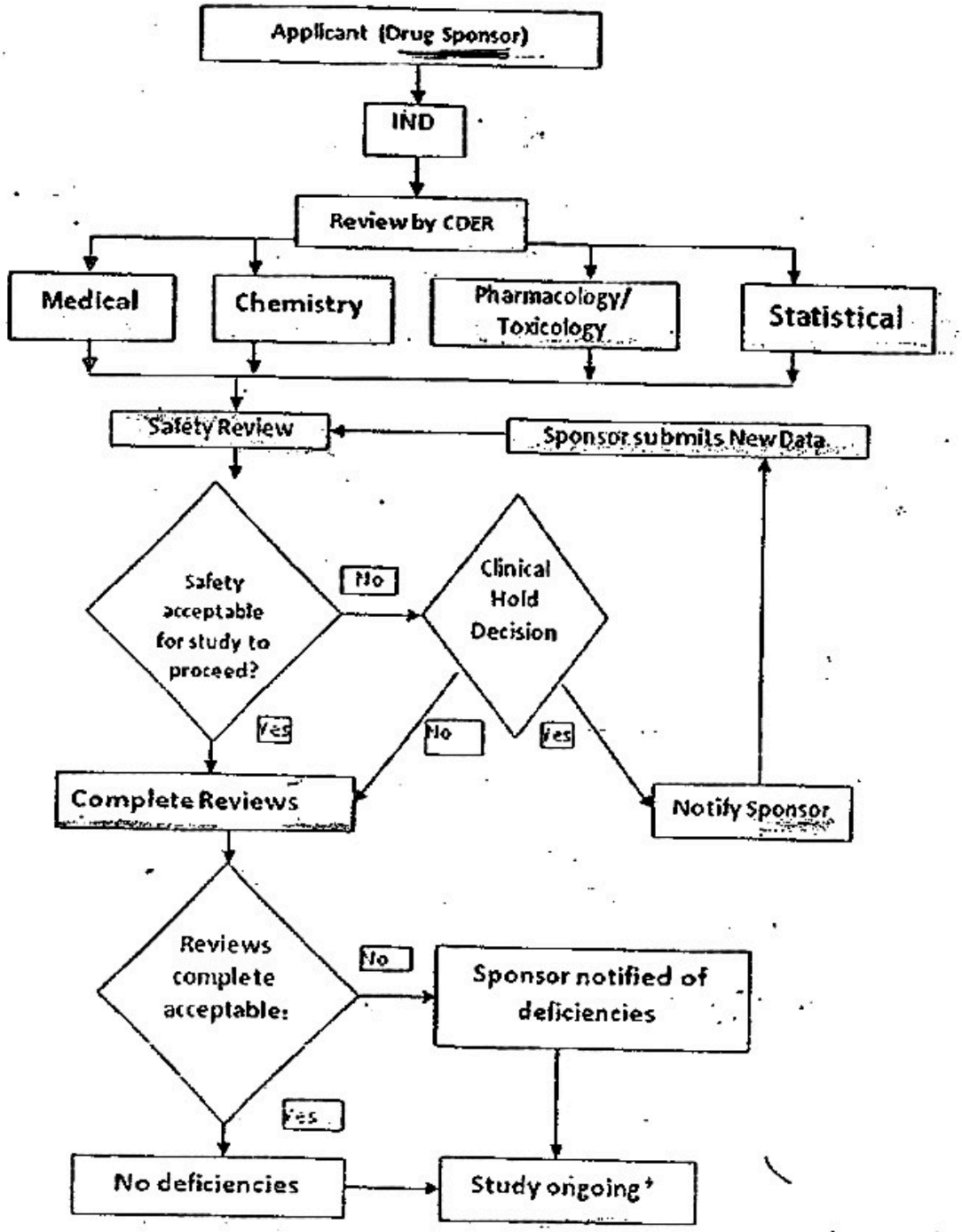
Information pertaining to the composition, manufacturer, stability and controls used for manufacturing the drug substance and the drug product.
This information is assessed to ensure that the company can adequately produce and supply consistent batches of the drug.

3. Clinical protocols and investigator information:

Detailed protocols for proposed clinical studies to assess whether the initial-phase trials will expose subjects to unnecessary risks. Also, information on the qualifications of clinical investigators-professionals (generally physicians) who oversee the administration of the experimental compound-to assess whether they are qualified to fulfill their clinical trial duties. Finally, 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 the investigational new drug regulations.

-Once the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials. During this time, FDA has an opportunity to review the IND for safety to assure that research subjects will not be subjected to unreasonable risk.

IND CHART



* While sponsor answers any deficiencies

□IND application contents:

1. Cover sheet / application form (Form FDA-1571)
2. Table of contents
3. Introductory statement
4. General investigational plan
5. Investigator brochure
6. Protocol(s)
7. Chemistry, manufacturing and control info.
8. Pharmacology and Toxicology info
9. Previous human experience with drug
10. Additional information as required by FDA:
   - Drug dependence/abuse potential
   - Radioactive drugs
   - Pediatric studies

IND application contents:

1. Application form (Form FDA-1571)

- Required for initial IND and all subsequent submissions.
- Provides basic info about sponsor and submission contents

- Must be signed and dated
- Obligates sponsor to comply with laws and regulations

2. Introductory Statement.

- Drug name, structure, pharmacological class, development history, foreign testing.

3. General investigational plan:

- Summary of studies anticipated in first year
- Study rationale.

4. Investigator brochure

- Package insert
- Early versions contain more pre-clinical data
- Later versions more heavily weighted with clinical area.

5. Protocol(s):

- Must include at least initial protocol
  - No subjects planned
  - Eligibility requirements

- Dosing
- Safety assessments
- Phase II and III - detailed protocols

6. Chemistry, manufacturing and control info:

- Manufacturing process
- Raw materials and finished product testing
- May refer to drug master file or previous application

7. Pharmacology and toxicology info:

- Non-clinical study summaries of pharmacological and toxicological effects.

8. Previous human experience with drug

- Foreign trials
- Data from other INDs, NDAs

9. Additional information as required by FDA:

- Other relevant info
- Copies of referenced materials
- Address issues are possible drug abuse,

dependence, radioactivity etc.

IND Amendments:

1. New protocol introduced
2. Changes made to protocol that may affect
   - Scientific Soundness of study
   - Rights, Safety or welfare of study subjects
3. Addition of new study investigators (FDA Form 1572)
4. New/revised information not related to protocol
   - New pharmacology, toxicology, chemistry, clinical info
   - Discontinuance of a study