

IND Investigator's Responsibilities

What are the general responsibilities of the Investigators?

Investigator's responsibilities can be divided into the following general areas:

- 1. Compliance with Investigator's Statement (Form FDA-1572)** – The Investigator must ensure that the clinical study is being conducted according to the terms of the signed Investigator's Statement (FDA Form 1572), the investigational plan, and the FDA regulations governing IND applications
- 2. Control of the Investigational Product** - The Investigator can only administered the product to subjects under his or her personal supervision or under the supervision of a co-investigator. If the Investigational product is subject to the Control Substances Act, the investigator must take adequate precautions to secure the product.
- 3. Recordkeeping and Record Retention** – The Investigator must keep adequate drug accountability records, and must prepared and maintain, for each subject, adequate records of all observed and data pertinent to the investigation.
- 4. Investigator Reports** – The Investigator must provide to the sponsor: (1) reports on the progress of the study; (2) safety reports on all adverse experiences that may be reasonable be regarded as cause by, or probably caused by the investigational drug; (3) adequate reports shortly after the completion of the investigator's participation in the study.
- 5. Assurance of IRB Review** – The Investigator must assure that a qualified IRB will be responsible for the initial and continuing review and approval of the proposed clinical study. The Investigator must also report to the IRB all changes to the proposed protocol and all serious adverse events and unanticipated problems involving risk to human subjects.

What are the specific responsibilities of the Investigators?

- 1. Compliance with Investigator's Statement (Form FDA-1572)**
 - By signing this form, the investigator also pledges to: (1) to conduct the study in accordance with the clinical protocol and to take proper actions should deviations become necessary; (2) to comply with all requirements regarding the obligations of clinical investigators; (3) to personally conduct or supervise the described investigation; (4) to inform subjects that the drug is being used for investigational purposes and to ensure that the requirements related to obtaining informed consent and IRB review and approval are met; (5) to report to the sponsor adverse experiences that

occur in course of the investigations as per regulatory requirements; (6) to review and understand the information in the clinical protocol and investigators brochure, including drug's potential risks and side effects; and (7) to ensure all study staff ascertaining in the conduct of the studies are informed about their obligations.

- In addition, the investigator promises to report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects and to not implement any such changes without IRB approval, except when necessary to eliminate apparent immediate hazards to study subjects.

2. Control of the Investigational Product.

- An investigator can only administer the investigational drug to subjects under the investigator's personal supervision or under the supervision of a sub-investigator who is responsible to the investigator.
- An investigator can not supply the investigational drug to any person who is not authorized to receive the drug.
- If the investigational drug is a controlled substance listed in any schedule of the Controlled Substances Act (21 CFR Part 1308), the principal investigator is required to ensure that the drug is stored in a securely locked, substantially constructed cabinet or other enclosure, access to which is limited; so as to prevent theft or diversion of the drug into illegal channels of distribution.

3. Investigator record-keeping and record retention requirements.

- The principal investigator is required to maintain accurate records of the disposition of the investigational drug, including the date(s) and quantity (quantities) of the drug dispensed to research subjects and the date(s) and quantity (quantities) of the drug returned unused by research subjects. The investigator is required to return all unused supplies of the investigational drug to the sponsor, or properly dispose of the unused supplies of the drug in accordance with the directive(s) of the sponsor.
- Case histories - An investigator is required to prepare and maintain adequate and accurate case histories for each subject that records all observations and other data pertinent to the evaluation of the investigational drug. This includes the case report forms and supporting data; the latter including, but not limited to, signed and dated consent forms and source medical record information including physician progress notes, hospital chart(s) and nurses' notes.

- Record retention - The principal investigator is required to retain the records for a period of 2 years following the date that the FDA approves a marketing application for the drug for the clinical indication for which it is being investigated; or, if no application for marketing is to be filed or if the marketing application is not approved for the clinical indication being studied, until 2 years after the FDA has been notified that the investigation of the drug for the clinical indication is discontinued.

4. Investigator Reports

- An investigator is required to provide the sponsor of the IND application with a completed FDA Form 3455 disclosing completely and accurately any (1) Equity interest, Proprietary interest, or Financial interest that the investigator (including the spouse and each dependent child of the investigator) has or may have (i.e., for up to 1 year following conclusion of the clinical study) in the investigational drug, or, if applicable, the company that owns the drug being evaluated under the IND application; or (2) compensation received by the investigator that is explicitly greater for a favorable clinical study outcome than for an unfavorable outcome. An investigator shall promptly update this information with the sponsor if any relevant changes occur during the course of the investigator's participation in the clinical study and for 1 year following completion of the study.
- Safety reports - An investigator is required to promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by the investigational drug.
- Final report - The principal investigator is required to provide the sponsor with a final report shortly following completion of the respective site's participation in the clinical study.
- Inspection of records and reports - The principal investigator, if request from any properly authorized officer or employee of the Food and Drug Administration, permit access to, copy, and verify any required records and reports. Investigators are not required to divulge subject names unless the records of particular individuals require a more detailed study of the case histories, or unless there is reason to believe that the records do not represent actual case studies or do not represent the actual results obtained.

5. Assurance of IRB Review: Protection of the rights, safety and welfare of research subjects.

- The principal investigator is required to ensure that an Institutional Review Board (IRB) that complies with the requirements set forth at 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the proposed clinical study in which the investigator is involved.

- An investigator is required, in accordance with 21 CFR Part 50, to obtain prospectively the informed consent of each human subject to whom the investigational drug is administered.
- An investigator cannot make any changes to an IRB-approved clinical study without IRB approval, except where necessary to eliminate apparent immediate hazard(s) to human subjects.
- An investigator is required to promptly report all changes in the research activity, all serious adverse events, and all unanticipated problems involving risks to human subjects or others to the reviewing IRB.

For additional information about IND sponsor responsibilities, please review 21 CFR subpart D part 312:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=312&showFR=1&subpartNode=21:5.0.1.1.3.4>