

## **IND Sponsor's Responsibilities**

### **What are General Responsibilities of the Sponsor of an IND Application?**

Sponsor responsibilities can be divided into the following general areas:

- 1. Selecting Qualified Investigators and Monitors** – The sponsor must select physicians, investigators and other professionals to conduct the clinical study.
- 2. Informing Investigators** – The sponsor is responsible for keeping all investigators involved in the clinical study to be fully informed about the investigational product and research findings.
- 3. Monitoring Ongoing Investigations** – The sponsor must closely monitor conduct and progress of their clinical trial to ensure the study is conducted in compliance with the protocol, applicable federal regulations, and acceptable GCP, and whether the new drug being studied is presenting unreasonable and significant risks to the study subjects.
- 4. Record keeping and retention** – The sponsor must maintain adequate records showing receipt, shipment, or other disposition of the investigational product.
- 5. Ensuring the Return or Proper Disposal of Unused Investigational Drug Supplies** – The sponsor must ensure the return or proper disposal of all unused supplies of the drug from each investigator whose participation is discontinued or eliminated.

### **What are the Specific Responsibilities of the Sponsor of an IND Application?**

- 1. Selecting Investigators** – A sponsor shall only select investigators who are qualified, trained and experienced with the investigational drug. The sponsor is required to obtain the following information for each investigator and co-investigator prior to participating in the study.
  - A completed and signed Investigators Statement (**FDA Form 1572**).
  - A *Curriculum Vitae* or other statement of qualifications which must include the education, training and experience that qualifies the investigator as an expert to study the investigation drug for the specific use in the study
  - The sponsor is required to indentify those clinical investigators who have or may have certain equity interest, proprietary interest, or financial interest in the investigational drug. Or anyone's compensation which would be directly affected by the outcome of the clinical study.
  - Each investigator must sign a complete Form **FDA 3454** attesting to the investigator's (which includes the spouse and each dependent child of the investigator) absence of reportable financial interest. The form must

signed and dated by the investigator/sponsor or for University sponsored IND applications by a responsible official of the University.

- For any investigator who has a reportable financial interest, the sponsor is required to obtain 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.
  - The sponsor is required to describe on **FDA Form 3455** any steps taken to minimize the potential for bias resulting from the disclosure of reportable financial interests
  - **FORM FDA 3455** is required to be signed and dated by the investigator/sponsor or for University sponsored IND applications by a responsible official of the University.

**Selecting Monitors** – The sponsor is required to select a monitor who is qualified, trained and experienced to monitor the progress of the clinical study being conducted under the IND

**2. Informing Investigators** – Before a clinical study begins, a sponsor (other than an investigator/sponsor) is required to provide each clinical investigator with an Investigator’s Brochure.

- Sponsors of IND applications are required to provide each participating investigator (including sub-investigator) with a copy of the clinical protocol.
- The sponsor is required as the clinical study proceeds to keep each participating investigator informed of new observations regarding the investigational drug that are discovered or reported to the sponsor, especially adverse event and safe use of the investigational drug.
  - New drug safety information may be distributed to investigators by means of periodically revised investigator brochures, reprints of published studies, reports or letters directed to investigators, or other appropriate means.
  - IND Safety Reports are required to be sent to all participating investigators.

**3. Monitoring of Ongoing Investigations** – The sponsor is required to monitor the progress of all clinical studies being conducted under the IND. Specified FDA recommendations on proper monitoring duties and procedures are provided in the agency’s *Guidance for the Monitoring of Clinical Investigations* (January 1988). In this document the FDA identifies six different monitoring responsibilities:

- Selection of a Monitor – A sponsor may designate one or more appropriate trained and qualified individuals to monitor the progress of a clinical investigation.
- Written Monitoring Procedures – A sponsor should establish procedures for monitoring clinical investigations to ensure the quality of the study and ensure each person involved in the process carries out their duties.
- Pre-Investigation Visits – A sponsor must ensure that the investigator clearly understands and accepts the obligations involved in undertaking, have appropriate facilities to conduct the investigation, and has sufficient time to honor their responsibilities in this study.
- Periodic Visits – The sponsor must ensure that throughout the clinical investigation that the investigator’s obligations are fulfilled and that the facilities used in the investigation are acceptable.
- Review of Subject Records - The sponsor must ensure that safety and effectiveness data submitted to the FDA is accurate and complete. The FDA recommends that the monitor review individual subject records and other supporting documentation and compare these records with the reports prepared by the investigator for submission to the sponsor.
- Record of On-Site Visit – The monitor should maintain a record of the findings, conclusions, and actions taken to correct deficiencies for each on-site visit.

The sponsor is required to review and evaluate evidence relating to the safety and effectiveness of the investigational drug.

- The sponsor is required to submit written IND Safety Reports to the FDA and participating investigators.
- The sponsor is required to submit Annual Reports to the FDA.

If it is determined that the investigational present an unreasonable and significant risk to the human subject, the sponsor is required to (1) discontinue the clinical studies that present the risk; and (2) notify the FDA; (3) notify all involved IRBs; and (4) notify all investigators who at anytime participated in clinical study of the drug.

- The sponsor is required to discontinue the clinical study of the drug as soon as possible, and no later than 5 days after making the determination that the clinical study should be discontinued. (Please note the FDA will confer with the sponsor regarding the need to discontinue the clinical study.)

- If the clinical study is discontinued, the sponsor is required to ensure that the investigator properly disposes or returns the unused investigational drug to the sponsor.

If a sponsor discovers that an investigator is not complying with the obligations addressed under the signed Statement of Investigator (**FDA Form 1572**), the general investigation plan, or applicable FDA regulations is required to promptly secure compliance or discontinue supplying the investigational drug.

- The sponsor would be required to discontinue from supplying the investigational drug to any investigator who has failed to maintain records or reports of the clinical study or declines to make these reports available to the FDA.
- If the investigator's participation in a clinical study is terminated, the sponsor is required to have the investigator return the investigational drug or ensure it is disposed of properly.

**4. Record-Keeping and Record Retention Requirements** – The sponsor is required to retain records and reports for IND applications for up to 2 years after a marketing application is approved for the drug or the sponsor has discontinued the IND and notified the FDA. The FDA must be allowed access to these records.

- **Investigational drug accountability** – The sponsor is required to maintain adequate records showing the receipt, shipment, or other disposition of the investigational drug. Investigational drug accountability records are required to include, as appropriate, the name of the investigator to whom the drug is shipped or otherwise provided and the date, quantity, and batch or lot number of each such shipment.
- The sponsor is required to ensure that investigators have adequate investigational drug accountability records and that the drug is stored in a secured manner in accordance with the sponsor's established storage parameters (e.g., temperature, humidity, light exposure, etc.) for stability of the drug. If the investigational drug is a controlled substance listed in any schedule of the Controlled Substances Act (21 CFR Part 1308), the sponsor is required to ensure that the drug is stored in a securely locked, substantially constructed cabinet or other enclosure, for which access is limited; so as to prevent theft or diversion of the drug into illegal channels of distribution.

**5. Return or Disposition of Unused Investigational Drug Supplies** - The sponsor is required to ensure that all unused supplies of the investigational drug from each investigator who participated in the study is either returned or disposed of properly.

**Can a Sponsor transfer IND responsibilities to a contract research organization (CRO)?**

A sponsor may transfer any or all of their responsibilities to a CRO. This must be described in detail in the IND Application. If only certain of the sponsor's responsibilities are being transferred to the CRO, the written statement must describe specifically each of the obligations being assumed by the CRO. Any obligations not covered in the written statement shall be deemed by the FDA to remain the responsibility of the sponsor. A CRO that assumes responsibility for any obligations of the sponsor must comply with all FDA requirements to those obligations. They will be subjected to the same regulatory action as a sponsor for failure to comply with the respective FDA requirements.

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>