Saint Louis University

Additional Criteria for Sponsor Investigator Responsibilities

This document summarizes additional responsibilities when an investigator holds an IND or IDE and thus becomes a “sponsor” of a clinical trial. The full set of regulations for sponsor-investigators of drug studies can be found at [21 CFR 312 Subpart D](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312&showFR=1&subpartNode=21:5.0.1.1.3.4). The full set of regulations for sponsor-investigators of device studies can be found at [21 CFR 812 Subpart C](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812&showFR=1&subpartNode=21:8.0.1.1.9.3).

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4. **Drug Study Sponsor Responsibilities**

1. Selecting qualified investigators

For each site investigator and sub-investigator obtain:

* Signed FDA form 1572 (Investigator Agreement)
* CV or other statement of qualifications such as a professional license
* Written disclosure of any financial conflicts of interest
* Clinical protocol to be used and approved by the investigator’s institution

2. Ensuring that the investigator and sub-investigators:

* Understand the nature and purpose of the clinical trial and the clinical trial procedures
* Are capable of conducting or supervising the conduct of the clinical trial
* Are aware that any Investigator-recommended changes to the clinical trial protocol must be first communicated to the Sponsor, who is ultimately responsible for making such changes
* Have submitted new risk information and protocol changes to the IRB and that IRB-approval of respective research protocol/consent form modifications has been obtained

3. Ensuring proper monitoring of investigations by:

* Selecting a monitor

*All sites must have a monitoring log and maintain correspondence with the*

*Monitor. See FDA Guideline for the Monitoring of Clinical Investigations*

* Assuring that the clinical trial is being conducted in accordance with the current version of the clinical trial protocol and applicable regulations and policies
* Having a documented and adequate monitoring plan to include the review and evaluation of the data and drug safety and effectiveness

Safety data reviewers:  PI  DSMB  Medical Monitor  Other:

* Reviewing monitoring reports, protocol deviations, and other anticipated problems (e.g., medical and ethical issues that may arise during the course of the clinical trial); to include how the Sponsor will respond to identified investigator and/or study site non-compliance or other deficiencies

4. Promptly reporting to FDA and participating investigators the following:

* Current Investigator’s Brochure - *This must be provided to all participating investigators prior to starting the investigation*
* Changes to the clinical trial protocol
* Serious and unexpected adverse events (i.e., associated with the investigational drug) *Notification to FDA should be within 15 calendar days after receipt of information. For any* *unexpected fatal or life-threatening experience associated with the use of the drug, notification to FDA should be within 7 calendar days after receipt of information*
* New risk information related to the drug under investigation
* Notification (of FDA, all participating investigators, and institutional review boards) if the drug presents unreasonable and significant risk to subjects and discontinue investigation within 5 working days

5. Maintaining an effective IND with respect to the investigations

Provide FDA with the following:

* Annual reports on the progress of the investigation - *within 60 days of the anniversary date that the IND went into effect*
* Protocol amendments:
* Changes in a protocol relating to: Phase 1 protocol that significantly affects the safety of subjects, or Phase 2 or 3 protocol that significantly affects the safety of subjects, the scope of the investigation or the scientific quality of the study
* A new investigator
* A new protocol
* Information amendments containing essential information on the IND that is not within the scope of a protocol amendment, IND safety reports, or annual report, such as new toxicology, chemistry, or other technical information; or a report regarding the discontinuance of a clinical investigation
* Preparing an adequate Final Study Report following completion of the clinical trial and the submission of this report to the FDA

6. Ensuring control of the investigational new drug

* Distributing the investigational drug to the Investigator’s study site; to include, if applicable, ensuring accountability of the investigational drug at the Sponsor’s manufacturing and/or central storage location
* Maintaining adequate records showing receipt, shipment, or other disposition of IND

*Records must include name of investigator to whom drug is shipped, date, quantity,*

*and batch or code mark of each shipment*

* Ensuring the return of all unused supplies/IND from each investigator and maintaining adequate records of all returns/disposal of IND
* Complying with the Controlled Substances Act
* Ensuring the immediate packaging of the IND intended for human use bears a label with the statement, ***Caution: New Drug-Limited by Federal (or United States) law to investigational use***, and the drug label does not bear any statement that is false or misleading and does not represent that the IND is safe or effective for the purposes for which it is under investigation
* Must not represent the IND in a promotional context that it is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
* Current Good Manufacturing Practices (cGMPs): Ensure the minimum current good manufacturing practice for preparation of drug products for administration to humans or animals in compliance with the requirements of §501(a)(2)(B) of the FD&C Act

Other Requirements:

* If any responsibilities will be transferred to a contract research organization (CRO), such transfers must be detailed in writing
* Maintaining all regulatory documentation including original IND application, FDA form 1571, FDA letter of no objection, IND safety reports, amendments, annual reports, and any other correspondence with the FDA, participating site investigators, and CRO (if applicable)
* Allowing the FDA, at reasonable times, to and copy and verify any records or reports relating to the clinical investigation

1. **Device Study Sponsor Responsibilities**

1. Selecting qualified investigators

For each site investigator obtain the following:

* Signed Investigator Agreement
* CV or other statement of qualifications such as a professional license
* Written disclosure of any financial conflicts of interest
* Clinical protocol to be used and approved by the investigator’s institution

2. Ensuring that the investigator and sub-investigators:

* + Understand the nature and purpose of the clinical trial and the clinical trial procedures
  + Are capable of conducting or supervising the conduct of the clinical trial
  + Are aware that any Investigator-recommended changes to the clinical trial protocol must be first communicated to the Sponsor, who is ultimately responsible for making such changes

2. Ensuring proper monitoring of the investigation by:

* Selecting a monitor

*All sites must have a monitoring log and maintain correspondence with the monitor. See FDA Guideline for the Monitoring of Clinical Investigations*

* Assuring that the clinical trial is being conducted in accordance with the current version of the clinical trial protocol and applicable regulations and policies
* Reviewing monitoring reports, protocol deviations, and other anticipated problems (e.g., medical and ethical issues that may arise during the course of the clinical trial); to include how the Sponsor will respond to identified investigator and/or study site non-compliance or other deficiencies
* Securing compliance from all participating investigators with the signed agreement, investigational plan, applicable FDA regulations, or with condition of IRB or FDA approval
* Having a documented and adequate monitoring plan to include the review and evaluation of the data and drug safety and effectiveness

Safety data reviewers:  PI  DSMB  Medical Monitor  Other:

3. Promptly informing and reporting to FDA, IRB, and participating investigators:

* Submitting the IDE application to the FDA
* Obtaining FDA & IRB approval for the application or supplemental application before beginning an investigation or part of an investigation
* Submitting to the FDA, at 6 month intervals, a current list of the names and addresses of all investigators participating in the investigation
* Providing the FDA, investigators, and IRB with the investigational plan and report of prior investigations of the device
* Notifying FDA and all reviewing IRBs and participating investigators of any withdrawal of approval of an investigation or a part of an investigation by a reviewing IRB within 5 working days after receipt of the withdrawal of approval
* Notifying all reviewing IRBs and participating investigators of any withdrawal of FDA approval of the investigation within 5 working days after receipt of notice
* Conducting an evaluation of any unanticipated adverse device effect(s) and submitting to FDA, all reviewing IRBs, and participating investigators a report with the results from any evaluations conducted for an unanticipated adverse device effect within 10 working days after the sponsor is first notified
* Verifying that the Investigator has submitted new risk information and protocol changes to the IRB and that IRB-approval of respective research protocol/consent form modifications has been obtained
* Terminating all or parts of the investigation immediately if the device presents unreasonable and significant risk to subjects (within 5 working days after sponsor makes risk determination, and within 15 days after sponsor is first notified of device effect). The investigation may not resume without IRB and FDA approval.
* Submitting to FDA a copy of any report by an investigator who uses a device without obtaining informed consent within 5 working days of receipt of notice
* The Sponsor’s reporting, to the Investigator, of changes to the clinical trial protocol; to include the requisite time frame for the prompt dissemination of this information.
* Preparing Supplemental IDE Applications and Investigator Lists and Progress Reports
* IDE Supplements:
* Changes in a protocol relating to: Phase 1 protocol that significantly affects the safety of subjects, or Phase 2 or 3 protocol that significantly affects the safety of subjects, the scope of the investigation or the scientific quality of the study
* A new investigator
* A new protocol
* Submitting annual progress reports to all reviewing IRBs
* Submitting a final report to all reviewing IRBs, to the FDA, and to participating investigators

4. Ensuring control and appropriate representation of the investigational device:

* Maintaining adequate records of shipment and disposition of devices
  + Records must include name and address of the consignee, type and quantity of device, date of shipment, and batch number or code mark. Records of disposition shall describe the batch number or code marks of any devices returned to the sponsor, repaired, or disposed of in other ways by the investigator or another person, and the reasons for and method of disposal.
* Ensuring the investigational device bears a label with the following:
  + Name and place of business of the manufacturer, packer or distributor in accordance with 21 CFR 801.1 General Labeling Provisions
  + Quantity of contents, if appropriate
  + The statement: ***Caution: Investigational device. Limited by Federal (or United States) law to investigational use***
  + A description of all relevant contraindications, adverse effect, hazards, interfering substances or devices, warnings and precautions
  + Must not include any statements that may be false or misleading, and should not represent the device as safe or effective for the purposes for which it is under investigation
* Notifying FDA and all reviewing IRBs of any request that an investigator return, repair, or otherwise dispose of any units of a device within 30 days of request.
* Current Good Manufacturing Practices (cGMPs): Ensure the minimum current good manufacturing practice of devices in compliance with 21 CFR 820, Quality System Regulation

Other Requirements:

* Maintaining records concerning adverse device effects (whether anticipated or unanticipated) and complaints
* Maintaining all regulatory documentation including original IDE application, required reports, and any other correspondence with another sponsor, monitor, investigator, IRB, or FDA
* Allowing the FDA, at reasonable times, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records or results from use of devices are kept), and inspect and copy all records relating to an investigation.

1. **Device Study Sponsor Abbreviated Requirements (Nonsignificant Risk)**

Sponsors of studies involving nonsignificant risk devices are not required to submit an IDE application to the FDA for approval. Submissions for nonsignificant device investigations are made directly to the IRB of each participating institution. Sponsors should present to the reviewing IRB an explanation why the device does not pose a significant risk. If the IRB disagrees and determines that the device poses a significant risk, the sponsor must report this finding to the FDA within five working days [§812.150(b)(9)]. The FDA considers an investigation of a nonsignificant risk device to have an approved IDE when the IRB concurs with the nonsignificant risk determination and approves the study.

The sponsor also must comply with the abbreviated IDE requirements under [§812.2 (b)](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?FR=812.2):

* The device must be labeled in accordance with the labeling provisions of the IDE regulations ([§812.5](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?FR=812.5)) and must bear the statement "CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use."
* The sponsor must obtain and maintain Investigational Review Board (IRB) approval throughout the investigation as a nonsignificant risk device study.
* The sponsor must assure that investigators obtain and document informed consent from each subject according to [21 CFR 50](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=50), Protection of Human Subjects, unless documentation is waived by an IRB in accordance with §56.109(c).
* All investigations must be properly monitored to protect the human subjects and assure compliance with approved protocols (§812.46). Guidance on monitoring investigations can be found in Guideline for the Monitoring of Clinical Investigations.
* Sponsors are required to maintain specific records and make certain reports as required by the IDE regulations.
* The sponsor must assure that participating investigators maintain records and make reports as required (see Responsibilities of Investigators).
* Commercialization, promotion, test marketing, misrepresentation of an investigational device, and prolongation of the study are prohibited ([§812.7](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?FR=812.7)).