

# **FDA-Regulated Clinical Investigations Principal Investigator's Acknowledgment of Responsibilities:**

## **Clinical Investigations**

FDA regulations at 21 CFR 50.3(c), 21 CFR 56.102(c), 21 CFR 312.3(b), and 21 CFR 812.3(h) define a clinical investigation to be:

- any study in which a test article (i.e., drug) is administered, dispensed to, or used, involving one or more human subjects.
- OR
- Research involving “one or more subjects to determine the safety and/or effectiveness of a device.”

Clinical Investigations are considered to be “FDA regulated” research regardless of whether the study requires an IND or IDE, or the study is exempt from IND or IDE regulations.

## **Investigator's Responsibilities**

The Principal Investigator is responsible for ensuring that an investigation is conducted according to:

- That an investigation is conducted according to the signed investigator statement, the investigational plan, applicable regulations, and applicable institutional policies;
- For protecting the rights, safety, and welfare of subjects under the investigator's care; and
- For the control of the drug(s) and/or device(s) used as part of the investigation.

The following list has been developed as a reminder of the responsibilities of the principal investigator in a clinical investigation.

***The PI attests to responsibility by electronically signing the HSERA application.***

## **Investigator's Qualifications and Agreements**

1. The investigator must be aware of, and must comply with, GCP and the applicable regulatory requirements.
2. The Investigator must review and understand the University of Pennsylvania's SOPs and policies.
3. The investigator must have thorough knowledge of the protocol, and personally conduct or supervise the investigation.
4. The investigator(s) must be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, and must provide evidence of such qualifications.
5. The investigator must be thoroughly familiar with the appropriate use of the

investigational product(s).

6. The investigator must permit monitoring and auditing of the study.
7. The investigator must maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties

### **Adequate Resources**

8. The investigator must have sufficient time to properly conduct and complete the trial within the agreed trial period.
9. The investigator must have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
10. The investigator must ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.

### **Medical Care of Trial Subjects**

11. A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, must be responsible for all trial-related medical (or dental) decisions.
12. Although a subject is not obliged to give his/her reason(s) for withdrawing prematurely from a trial, the investigator must make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights.

### **Communication with IRB**

13. Before initiating a trial, the investigator must have written and dated approval from the IRB for the trial protocol, informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.
14. If the Investigator's Brochure is updated during the trial, the investigator must supply a copy of the updated Investigator's Brochure to the IRB.

### **Compliance with Protocol**

15. The investigator must conduct the trial in compliance with the approved protocol. The investigator and the sponsor must sign the protocol, or an alternative contract, to confirm their agreement.
16. The investigator must not implement any deviation from, or changes of, the protocol without agreement by the sponsor, and prior review and documented approval from the IRB of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects.
17. The investigator, or person designated by the investigator, must document and explain any deviation from the approved protocol.
18. The investigator may implement a deviation from, or a change in, the protocol to eliminate an immediate hazard(s) to trial subjects without prior IRB approval/favorable opinion. As soon as possible, but always within 10 working days, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) must be submitted to the IRB. The sponsor must

be informed as soon as possible.

**Financial Conflicts of Interest**

19. The investigator must report to the IRB and to the Penn-Faculty Sponsor whether they or any other person responsible for the design, conduct, or reporting of the research (including staff and family members as defined in the COI policies) has any economic interest in, or acts as an officer or a director of any outside entity whose financial interests would reasonably appear to be affected by, the research
20. The Investigator also shall disclose to the IRB and to the Penn-Faculty Sponsor any changes in these financial interests or relationships.
21. The disclosure must consider a full assessment of relationships with outside entities associated with a research study, including commitments of financial support unrelated to the study in question, financial incentives, serving as a paid consultant or speaker on behalf of a commercial funding sponsor, and less obvious situations, such as non-monetary inducements or rewards.

**Investigational Product(s)**

22. Responsibility for investigational product(s) accountability at the trial site(s) rests with the investigator.
23. The investigator must maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product(s).
24. The investigational product(s) must be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s).
25. The investigator must ensure that the investigational product(s) are used only in accordance with the approved protocol.

**Informed Consent of Trial Subjects**

26. In obtaining and documenting informed consent, the investigator must comply with the applicable regulatory requirements.
27. The written informed consent form and any other written information to be provided to subjects must be revised whenever important new information becomes available that may be relevant to the subject's consent. Any revised document must receive the IRB's approval opinion in advance of use.
28. Neither the investigator, nor the trial staff, must coerce or unduly influence a subject to participate or to continue to participate in a trial.
29. Before informed consent may be obtained, the investigator, or a person designated by the investigator, must provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial must be answered to the satisfaction of the subject or the subject's legally acceptable representative.
30. Prior to a subject's participation in the trial, the written informed consent form must be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.
31. Prior to participation in the trial, the subject must receive a copy of the signed and

dated written informed consent form, any other written information provided to the subjects, and any update of those.

**Records**

- 32. The investigator must ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- 33. Essential documents must be retained as specified by the sponsor or the applicable regulation, wherever period is longer.
- 34. Upon request of the monitor, auditor, IRB, or regulatory authority, the investigator must make available for direct access all requested trial related records.

**Progress Reports**

- 35. The investigator must submit written summaries of the status of the trial to the IRB annually, or more frequently, if requested by the IRB.
- 36. The investigator must promptly provide written reports to the sponsor, and the IRB on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.

**Safety Reporting**

- 37. All serious adverse events must be reported to the sponsor as outlined in the protocol.
- 38. It is the Investigator's responsibility to keep the IRB informed of unexpected, protocol-related (probably or definitely), non-serious and serious adverse events, as well as unanticipated problems that pose risk to participants or others.
- 39. The investigator must report to the IRB within 10 working days any reportable events and unanticipated problems posing risk to the study subjects or to others. The exception to this rule is if the event involved an unexpected, protocol-related (probably or definitely) death. In this situation, the report to the IRB must be submitted within 3 working days of having notice of the event.
- 40. An investigator is responsible for the accurate documentation, investigation, and follow-up of all possible study-related adverse events.
- 41. Investigators are also responsible for informing government funding agencies and other sponsors of any unanticipated serious events, as appropriate.

**Premature Termination or Suspension of a Trial**

- 42. If the trial is terminated prematurely or suspended for any reason, the investigator must promptly inform the IRB.

**Final Report(s) by Investigator**

- 43. Upon completion of the trial, the investigator must, the IRB with a summary of the trial's outcome, and the regulatory authority(ies) with any report(s) they require of the investigator.

**Financial Compliance**

- 44. The principal investigator must have a thorough knowledge of the financial aspects of the study, and personally conduct or supervise the study billing.

45. The investigator must have available an adequate number of qualified staff and adequate tools for the foreseen duration of the trial to conduct and appropriately bill the study procedures
46. The investigator must ensure that all persons responsible for scheduling visits, placing orders and reviewing charges/bills are trained in the Research Billing procedures and tools.
47. The investigator must ensure that all persons assisting with scheduling visits, placing orders and reviewing charges/bills are adequately informed about the Prospective Reimbursement Analysis of the study.