INVESTIGATOR RESPONSIBILITIES FOR DRUG STUDIES

Federal Research Regulations

The FDA is responsible for regulating drugs for human use. Investigators conducting clinical trials involving drugs have specific responsibilities outlined in 21 CFR 312, Subpart D – Responsibilities of Sponsors and Investigators.

The University of Utah applies the principles of the International Conference on Harmonization's Good Clinical Practices (ICH-GCP) to clinical investigations, as adopted by the FDA and insofar as the standards and requirements are consistent with 21 CFR. This document describes the ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve human subjects.

Description

Investigators are responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation. Additional responsibilities are found in the FDA regulations (see Appendix A of this document) and Good Clinical Practice.

Except when an exemption is granted, investigators must obtain the informed consent of each human subject to whom the drug is administered. *Exceptions to the informed consent requirements found in 21 CFR 50 are not described in this document. For more information regarding exceptions please refer to the IRB website or contact the IRB office.*

For studies that require an IND from the FDA, investigators may not commence with the study until a valid IND and IRB approval is in place. Within 30 days, sponsors/investigators typically receive a letter from the FDA issuing an IND number. If this letter is not received within 30 days, the sponsor/investigator should follow-up with the FDA. For FDA-regulated studies conducted outside of the United States, an IND is not required provided the research is conducted under the Declaration of Helsinki and Good Clinical Practice guidelines.

Additional Considerations

All related documentation relating to the dispensing of investigational drugs must be completed as required. The IRB requires that the investigational drug go through an investigational pharmacy Any exceptions must be approved by the IRB with the concurrence of the investigational pharmacy. Depending on safety issues, the IRB may determine that the drug will need to be given in a specific setting (e.g., GCRC setting).

Investigators must be familiar with the respective pharmacy policies (e.g. University of Utah, Primary Children's Medical Center, etc.) and may be contacted at the phone numbers listed below:

University of Utah Health ~~Center~~ and Huntsman Cancer Institute Investigational Drug Service, (801) ~~585-2185 Huntsman Cancer Hospital,~~ 585-0272
Primary Children's Hospital, (801) 662-2655
VA Salt Lake City Health Care System (VASLCHSC), (801) 582-1565 ext. 1454

Points to Address

Application:	1. **HIPAA and the Covered Entity Page:** There will be a question about whether the study involves the investigational use of a drug. Mark "yes". Marking "yes" will prompt additional pages to complete in the ERICA system.

	2. **Investigational Use of a Drug Page:** Complete the page as directed. Attach the additional documentation as requested. Read "Statement of Compliance" and indicate your agreement by checking the appropriate box. 3. **Investigational Drug Data Form (IDDF):** Add and complete the page as directed for each drug.
Consent Document:	1. **Background:** State that the drug used in the study is or is not investigational and whether or not it has been approved by the FDA. 2. **Confidentiality:** If the research is subject to FDA regulation, a statement must be included that notes the possibility that the FDA may inspect the records. 3. **Authorization for Use of Protected Health Information:** If the research is subject to FDA regulation, the FDA should be listed as an agency that will have access to protected health information. 4. **Signature Block:** Signature and date of the participant and the person obtaining consent must be included.
Documents and Attachments:	**If an investigational new drug (IND) number is required:** 1. **Verification of the IND:** Attach a document which verifies the IND (e.g. FDA letter, IND number printed in protocol, letter from Sponsor or other Sponsor-generated document). 2. **Investigator Brochure:** The Investigator Brochure (IB) or product insert must be attached to the application. **If an investigational new drug (IND) number is NOT required:** 1. **Product Insert:** The product insert must be attached to the application.

References & Links

IRB SOP 502: Clinical Research Involving Investigational Drugs and Devices	*http://irb.utah.edu/guidelines/irb-sops.php*
ICH E6: Good Clinical Practice: Consolidated Guidance ~~(see page 13 for the list of Investigator Responsibilities)~~	*~~http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf~~ https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e6r2-good-clinical-practice-integrated-addendum-ich-e6r1*

Appendix A: Selections from 21 CFR §312 (Subpart D – Responsibilities of Sponsors and Investigators)

An investigator is responsible for the following:

1. Ensuring that an investigation is conducted according to the signed investigator statement of assurance, the investigational plan, and applicable regulations. [21 CFR §312.60~~0~~]

2. Protecting the rights, safety, and welfare of participants under the investigator's care. [21 CFR §312.60]

3. The control of drugs under investigation.
   a. An investigator shall administer drug only to participants under the investigator's personal supervision or under the supervision of a co-investigator responsible to the investigator. [21 CFR §312.61]
   b. The investigator shall not supply the investigational drug to any person not authorized under this part to receive it. [21 CFR §312.61]
   c. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by participants. [21 CFR §312.62]
   d. If the investigation is terminated, suspended, discontinued, or completed, the investigator shall return the unused supplies of the drug to the sponsor, or otherwise provide for the disposition of the unused supplies of the drug under 21 CFR §312.59. [21 CFR §312.62]
   e. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. [21 CFR §312.62]
      i. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes.
      ii. The case history for each individual shall document that informed consent was obtained prior to participation in the study.
   f. An investigator shall retain records required to be maintained under this part for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified. [21 CFR §312.62]
   g. The investigator shall furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained. The sponsor is required under §312.33 to submit annual reports to the FDA on the progress of the clinical investigations. [21 CFR §312.64]
   h. An investigator shall promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator shall report the adverse effect immediately. [21 CFR §312.64]

4. An investigator shall provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation. [21 CFR §312.64]

5. The clinical investigator shall provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under part 54 of this chapter. The clinical investigator shall promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study. [21 CFR §312.64]

6. An investigator shall assure that an IRB that complies with the requirements set forth in part 56 will responsible for the initial and continuing review and approval of the proposed clinical study. [21 CFR §312.64]
   a. The investigator shall also assure that he or she will promptly report to the IRB all changes in research activity and all unanticipated problems involving risk to human participants or others, and that he or she

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will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human participants.

7. An investigator shall upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 21 CFR §312.62. [21 CFR §312.68]
    a. The investigator is not required to divulge participant names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.

8. If the investigational drug is subject to the Controlled Substances Act, the investigator shall take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution. [21 CFR §312.69]

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