Guidance -
Special Considerations for the Oversight of Research Protocols in FDA-regulated Drug or Device Studies

This provides an overview of the FDA regulations and guidance for sponsors and investigators when using FDA test articles. A test article includes drugs (including botanicals, biologicals, and gene therapy, and genetically derived products that meet the definition of a "drug"), and medical devices for human use. The FDA has statutory authority to regulate the development and marketing of these products.

In ***sponsor-investigator research***, the PI assumes all of the responsibilities in overseeing the research normally assumed by sponsors in industry-sponsored projects.

INVESTIGATIONAL DRUG STUDIES

1. **Before beginning participation in an investigation**, the PI must commit to the sponsor that he or she: [21 CFR §312.53(c)(1)]
   - will conduct the studies in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, the rights, or welfare of participants.
   - will comply with all requirements regarding the obligations of clinical PIs and all other pertinent requirements in this part.
   - will personally conduct or supervise the described investigation(s).
   - will inform any potential participants that the test article(s) (i.e., drugs or devices) are being used for investigational purposes and will ensure that the requirements relating to obtaining informed consent and IRB review and approval are met.
   - will report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with §312.64; (f) has read and understands the information in the investigator's brochure, including the potential risks and side effects of the drug.
   - will ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

2. A **PI is responsible for**: [21 CFR §312.60]
   - ensuring that an investigation is conducted according to the signed statement, the investigational plan, and applicable regulations.
   - protecting the rights, safety, and welfare of participants under the PI's care.
   - the control of drugs under investigation.

3. **The following regulations apply to control of the investigational drug**:
   - The PI will administer the drug only to participants under the PI's personal supervision or under the supervision of a sub-investigator responsible to the PI. [21 CFR §312.61]
   - The PI will not supply the investigational drug to any person not authorized under this part to receive it. [21 CFR §312.61]
   - The PI is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by participants. [21 CFR §312.62]

- If the investigation is terminated, suspended, discontinued, or completed, the PI must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.

4. The PI is required to adhere to the following **regulations for documentation** of their investigational drug research studies:
   - A PI 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]
   - Case histories include the case report forms and supporting data (e.g., 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). The case history for each individual will document that informed consent was obtained prior to participation in the study.

   PI must 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]

INVESTIGATIONAL MEDICAL DEVICE STUDIES

1. For medical device studies, **each participating PI must sign an agreement with the sponsor** that includes a statement of the PI's commitment to: [21 CFR §812.43(c)(4)]
   - conduct the investigation in accordance with the agreement, the investigational plan, this part and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA
   - supervise all testing of the device involving human participants
   - ensure that the requirements for obtaining informed consent are met

2. A **PI is responsible for**: [21 CFR §812.100]
   - ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations
   - protecting the rights, safety, and welfare of participants under the PI's care
   - the control of devices under investigation

3. **The PI must maintain the following accurate, complete, and current records** relating to the PI's participation in an investigation: [21 CFR §812.140]
   - All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
   - Records of receipt, use or disposition of a device that relate to:
     (1) The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
     (2) The names of all persons who received, used, or disposed of each device.
     (3) Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
   - Records of each participant's case history and exposure to the device.

Case histories include the case report forms and supporting data (e.g., signed and dated consent forms and medical records, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes). Such records will include:

(1) Documents evidencing informed consent and, for any use of a device by the PI without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual will document that informed consent was obtained prior to participation in the study.

(2) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each participant upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.

(3) A record of the exposure of each participant to the investigational device, including the date and time of each use, and any other therapy.

(4) The protocol, with documents showing the dates of and reasons for each deviation from the protocol.

(5) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.