WAYNE STATE UNIVERSITY

HIC Policy/Procedure

Wayne State University Human Investigation Committee	
SUBJECT	Investigator Initiated Research
Section	
Form Date	10/06
Approvals	Office of the General Counsel 12/06/06, Steering Committee 12/19/06, Administrative Approval 03/02/07

Background

The Food & Drug Administration (FDA) requires Institutional Review Board (IRB) approval of regulated clinical investigations. When a Principal Investigator (PI) initiates research using an investigational or unlicensed test article (drug or device), the PI assumes the obligations and responsibilities of a sponsor in sponsored research. The IRB must assure that the research complies with all federal, state, and local regulations. Use of an investigational drug or device in a clinical trial to obtain safety and effectiveness data must be conducted according to FDA's Investigational Device Exemption (IDE) regulations, Investigational New Drug regulations, and applicable Veteran's Health Administration (VHA) regulations [21 CFR 50, 56; 21 CFR 312, 314; 21 CFR 812, 814; 21 CFR 812-814; VHA Handbook 1200.5 3, 1200.5 4, 1200.5 14, 1200.5 15].

No drug or device study on human participants may proceed without IRB approval. This includes an off-label use of a legally marketed drug or device that is part of a research study collecting safety and effectiveness data involving human research participants.

Scope:

This Policy/Procedure covers the PI in the role of sponsor and investigator and the role of the IRB in all PI-initiated research involving human research participants.

Definitions:

IDE – An acronym for the term "investigational device exemption". An IDE is an FDA-approval of the application for an exemption that permits an unmarketed device to be shipped for the purpose of doing research on the device.

IND – An acronym for the term "investigational new drug", used to refer to an investigational new drug application that has been submitted to the FDA. IND is synonymous with the notice of claimed investigational exemption for a new drug.

Investigational New Drug - A drug or biologic that is used in clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are deemed synonymous. In VA research, this may be an approved drug that is being studied for an unapproved or approved use in a controlled, randomized or blinded clinical trial.

Investigational Device - A device, including a transitional device, that is the object of a clinical study designed to evaluate its safety or effectiveness. In VA research an investigational device may be an approved device that is being studied for an unapproved use or efficacy.

Investigational Device Exemption - Clinical trials that use unapproved medical devices on human research subjects are performed under an Investigational Device Exemption (IDE). An IDE from the FDA is required when the unapproved device poses a significant risk to subjects (21 CFR 812.30).

Non Significant Risk Device-A device that does not meet one or more of the criteria for a significant risk device. In other words, is not an implant, not used to support or sustain human life, not of substantial importance in diagnosing curing, mitigating or treating disease, or is not significantly involved in preventing impairment of human health, or does not present a potential risk for serious risk to the health, safety, or welfare of a subject [21 CFR 812.2(b)].

Significant Risk Device - A device that may present a potential for serious risk to the health, safety, or welfare of a participant, and is intended: (1) as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject" is considered a significant risk device [21 CFR 812.3(m)].

Sponsor-Investigator - An individual who both initiates and conducts an investigation and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual.

Test Article - A drug, device, or other article including a biological product used in clinical investigations involving human subjects or their specimens

HIC Policy/Procedures:

Principal Investigator Responsibilities in Drug Research:

- Assuring that the research is conducted according to the approved protocol;
- Protecting the rights, safety, and welfare of human participants under their care;
- Control of drugs under investigation;
- Assuring that there is a quality assurance and quality control plan in place and that it is being followed;
- Administering the drug only to participants under the investigator's personal supervision or under the supervision of a designee responsible to the investigator [21 CFR 312.61]; who have signed legally effective consent;
- The investigator shall not supply the investigational drug to any person not authorized to receive it;
- Obtaining the legally effective informed consent of the participant or the participant's legally authorized representative;
  (See HIC Policy/Procedure: "Informed Consent Process" and "Informed Consent Options");
- Maintaining 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 investigator shall return the unused supplies of the drug to the manufacturer, or otherwise provide for disposition of the unused supplies of the drug according to the Protocol Submission Form and Institutional policy [21 CFR 312.59, 312.62];
- Maintaining adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered by the investigational drug or employed as a control in the investigation [21 CFR 312.62];

- Maintaining records for two 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;.
- The investigator must submit annual reports to the FDA on the progress of the clinical investigations;
- Promptly reporting to the IRB any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse event is serious, the investigator must report the adverse reaction immediately;
- Promptly reporting unanticipated problems involving risk to human participants or others;
- An investigator shall, upon request, from any properly authorized officer or employee of the 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. [21 CFR 312.62; 21 CFR 312.68]
- Adhering to all VA polices concerning investigational drugs in VA research [VHA Handbook 1200.5 4.d; 1200.5 3.y]
- If the drug has an IND number the investigator must provide to the Institutional Review Board (IRB) supporting evidence of the number. (e.g. FDA letter, sponsor letter, commercial protocol with corresponding number);
- If the drug does not have an IND number the principal investigator must provide to the IRB the category of research allowing an exemption form an IND number and justification that the research meets the appropriate criteria. [21 CFR 312.2(b)].

Principal Investigator Responsibilities in Device Research:

- Ensuring that the study is conducted according to the approved protocol and all applicable federal, state, and local regulations and Institutional policy;
- A PI shall permit an investigational device to be used only with participants under the investigator's supervision. An investigator shall not supply an investigational device to any person not authorized to receive it;
- Upon completion or termination of a clinical study, an investigator shall return to the manufacturer any remaining supply of the device or otherwise disposition of the unused supplies of the device according to the Protocol Submission form and institutional policy;
- If a device is approved for marketing and does not have an IDE number, the investigator must provide to the IRB the exemption category [21 CFR 812.2 ©] and justification that the research meets the criteria in that category, or;
- Provide justification to the IRB that the abbreviated requirements for an IDE are met. [21 CFR 812.2(b) or (c)(1-7);
- The investigator shall maintain accurate, complete, and current records as required in 21 CFR 812.140(a) and maintain those record for 2 years after either: The date in which the study is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol. [21 CFR 812.140(d);
- An investigator who has authority to grant access shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held;
- An investigator shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation [21 CFR 812.145(b)];

- An investigator shall permit authorized FDA employees to inspect and copy records that identify participants, upon notice that FDA ahs reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted to the IRB have not been submitted or are incomplete, inaccurate, false, or misleading. [21 CFR 812/145©;
- An investigator must prepare and submit the following complete, accurate, and timely reports [21 CFR 812.150(a):
    - A report to the IRB of any unanticipated adverse device effect occurring during a study as soon as possible, but in no event later than 10 working days after the investigator first learns of the event.
    - A report to the manufacturer, within 5 working days, a withdrawal of approval by the reviewing IRB.
    - A report to the IRB of any deviation from the investigational plan to protect the life or physical well-being of a participant in an emergency as soon as possible, but no late than 5 days after the emergency occurred. Except in cases of emergency, prior approval by the IRB is required.
    - A final report to the IRB within 3 months after termination or completion of the study.

Institutional Review Board Responsibilities in Investigator Initiated Research:

- The IRB must determine if the investigator has the medical expertise, qualifications, training and support, and the facilities necessary to conduct the study in a way that protects the human participants, fulfills the scientific purpose of the protocol and meets federal, state and local laws and regulations. If necessary, additional staff or an outside consultant may be required;
- The IRB must determine if there is an adequate and effective data and safety monitoring plan. An outside data safety and monitoring board or IRB review conducted more frequently than the yearly standard may be required;
- The IRB must determine if the device meets the FDA definition of significant risk (See definitions). They will consider the proposed use of the device as well as any protocol related procedures and tests in making their determination;
- If the FDA has already made a risk determination and the IRB does not agree, they must notify the investigator that the study involves a significant risk device [21 CFR 812.66].