

Wayne State University Human Investigation Committee	
Subject	Principal Investigator Roles and Responsibilities
Form Date	February 2, 2009 (Rev. 03/07/11)
Approvals	Steering Committee: Rev. 12/07/06, Initial, All IRBs: 022101 Administrative: 02/27/01 General Counsel 11/20/06, Administrative Approval 12/18/06, Administrative Approval 01/30/09; Administrative Approval 09/30/10, Administrative Approval 03/07/11

Background

The Principal Investigator (PI) who accepts responsibility for conducting research with human participants must have the experience, expertise, professional qualifications and the research facilities and resources necessary to ensure that the rights and welfare of the human participants are protected. Although some sponsors recognize Co-Principal Investigators, the Wayne State University (WSU) Human Investigation Committee (HIC) and its Institutional Review Boards (IRBs) recognize **only one individual** as the Principal Investigator on any protocols that involve human participants (subjects). All other investigators on the protocol are considered “co-investigators” or “key personnel”.

Scope

This Standard Operating Procedure (SOP) applies to all persons who accept the responsibility as PI in the conduct of research with human participants at Wayne State University and any of its affiliate institutions; this includes faculty, staff, and students.

Definitions

The WSU HIC accepts all of the following definitions as appropriate, depending on the type of human research that is being conducted:

Principal Investigator:

1. The Office of Human Research Protections (OHRP) Guidebook defines Principal Investigator as “the scientist or scholar with primary responsibility for the design and conduct of a research project.”
2. The VA defines a Principal Investigator as any individual who conducts research involving human subjects including, but not limited to, the PI, Co-PI and Local Site Investigator (LSI).” [VHA Handbook 1200.05 3.ss.].

Clinical Investigator:

According to the Food and Drug Administration (FDA), a clinical investigator is defined as “an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed or used involving a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team” [21 CFR 56.102(h)].

Responsibilities of the Principal Investigator

The Study Design:

1. Develop a research plan that is: (a) scientifically valid, (b) consistent with sound research design, (c) minimizes risks to human participants, and (d) includes a data safety monitoring board when required by the National Institutes of Health, FDA, or HIC.
2. Ensure that all facilities and resources necessary to protect participants are present before conducting the research study.
3. Maintain oversight of the research protocols and research staff. The PI's signature on forms submitted to the HIC certifies that he/she has reviewed all of the submitted information and affirms that it is accurate to the best of his/her knowledge.

Laws, Regulations, Ethical Standards and Internal Policies:

1. Conduct the study in accordance with: (a) The protocol as approved by the WSU HIC, (b) Ethical standards (e.g., the Belmont Report, the Declaration of Helsinki), (c) Applicable federal regulations (45 CFR 46.160 and 164, 38 CFR 16, 21 CFR 50 and 56), (d) Applicable state and local laws (45 CFR 46.102 and 116, 38 CFR 46.118, 38 CFR 16.402, 28 CFR 50 and 56), (e) Good Clinical Practice guidelines, (f) The signed agreement/contract between the study sponsor and the PI, and (g) All WSU internal HIC policies, standard operating procedures and any conditions of approval imposed by the IRB.
2. For research sponsored by the ***Department of Defense*** (DoD), please see federal regulations 32 CFR 219 and DoD Directive 3216.02, and 45 CFR 46 subpart A.
3. For research sponsored by the Environmental Protection Agency (EPA), see 40 CFR 26 Subparts C and D.
4. For research conducted by ***VA investigators***, please see VHA Handbook 1200.05 Paragraph 9.
5. For international research, please see the HIC Policy “International Research” available on the HIC website.
6. For research sponsored by the ***Department of Energy*** (DOE), investigators are required to follow DOE requirements for the protection of personally identifiable information by completing and complying with the requirements of the “Checklist for IRBs to Use in Verifying that Human Subject Research Protocols are in Compliance with DOE Requirements.”
7. For research sponsored by the ***U.S. Department of Education***, access to instructional material used in a research or experimentation program must meet the following requirements:
 - a. All instructional material—including teachers’ manuals, films, tapes, or other supplementary instructional materials—which will be used in connection with any research or experimentation program or project must be available for inspection by the parents or guardians of the children engaged in such research.

- b. Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.
- c. Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.

Training:

1. Successful completion of the HIC's responsible conduct in research on-line training program - the Collaborative Instructional Training Initiative (CITI).
2. Ensure that all members of the research team are adequately trained and have successfully completed the HIC training modules in human research protection, health information privacy and responsible conduct in research.
3. Understand that the PI maintains ultimate responsibility for conducting interviews and obtaining consent from participants. Delegation of these duties can only be given to an individual(s) (i.e., co-investigator or key personnel) appropriately trained for this activity – including mandatory on-line training.

Conduct of the Study:

1. The PI will conduct the study according to the signed protocol, the investigational plan and all pertinent regulations.
2. Obtain legally effective informed consent from participants or their legally authorized representative.
3. Ensure that the currently approved version of the consent form is being used for all participants, and that it is appropriately documented.
4. Recruit participants in a fair and equitable manner, weighing the potential risks and vulnerability of the participants with the potential benefits of the research.
5. Ensure that the availability of medical care for research-related injuries is clearly defined in the contract/agreement for sponsored research. Information regarding available medical care and whom to contact for further information must be clearly stated in the informed consent document.
6. In VA studies the PI is responsible for informing Pharmacy Service that the IRB and Research and Development Committee approval has been obtained.
7. Maintain complete records and documentation appropriate to the type of research and the study population per Good Clinical Practice guidelines.
8. Ensure that response to participant complaints or requests for information are addressed in a timely manner.
9. Monitor the safety and well-being of all research participants and remain current on literature related to the research study.
10. Submit a Closure Form at completion of the study (see HIC Policy on Continuation/Renewal of a Research Protocol and Closure).
11. For VA studies the PI must inform the Chief, Pharmacy Service, and the Research and Development Committee when a study involving investigational drugs has been terminated.
12. A qualified physician (or dentist, when appropriate), who is an investigator or co-investigator for the clinical trial, is responsible for all clinical trial-related medical (or dental) decisions.

13. During and following a participant's participation in a clinical trial, the investigator ensures that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the clinical trial.
14. The investigators must inform participants when medical care is needed for other illnesses of which the investigator(s) become aware
15. The investigator must follow the clinical trial's randomization procedures, if any, and ensure that the code is broken only in accordance with the protocol. If the clinical trial is blinded, the investigator must promptly document and explain to the Sponsor any premature unblinding.

Reporting Responsibilities:

1. Submit all protocol modifications or amendments to the HIC. No changes can be initiated by the PI prior to receiving IRB approval **unless** immediate changes are required in order to prevent harm to the participants or others.
2. Submit a protocol amendment upon notification of a change to the protocol. If these changes involve a change in risks or benefits to participants this should be reported to the IRB as soon as possible. Examples include: (a) An interim analysis indicates that participants have a lower rate of response to treatment than initially expected, (b) Safety monitoring indicates that a particular side effect is more severe or more frequent than initially expected, (c) A breach of confidentiality, (d) A change in FDA labeling or withdrawal from marketing of a drug, device or biologic used in a research protocol, (e) Incarceration of a participant in a protocol not approved to enroll prisoners, (f) An event that requires prompt reporting to the sponsor, (g) A protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) caused harm to participants or others or indicates that participants or others are at increased risk or harm, and (h) Sponsored imposed suspension for unacceptable risk.
3. Promptly report to the HIC any unanticipated events or adverse reactions involving risks to participants or others in accordance with the HIC Policy and SOP (see HIC Policies "Reporting Unexpected Problems, Suspensions, and Terminations, Serious and Continuing Non-Compliance and the Institutional Official's Responsibilities" and "Unexpected Problems" for examples and reporting time frames). Because full board review and approval of an amendment that alters the risk/benefit ratio of a protocol involves a time lag between submission, review, and final approval, any added risks must be communicated to existing participants and to any new enrollees **prior** to IRB approval of the change. In this case, documentation must be placed in the research record that each participant was notified about the change in risk and the exact information that was given to each (see the HIC SOP "Amendments to the Research Protocol and Informed Consent Documents" for examples of when a participant must be made aware of changes).
4. Report progress of the research at intervals as determined by the IRB, **but not less than once per year**.
5. Report any (COI) involving the PI, co-investigators or key personnel to the Conflict of Interest Coordinator (see HIC Policy/Procedure, "Conflict of Interest Policy and Procedure").

Responsibilities of the PI in Drug and Device Studies:

1. Ensure that the investigation is conducted according to the signed investigator agreement, the investigational plan, and applicable regulations [per FDA regulations 21 CFR 312.60 (drugs) and 21 CFR 812.100 (devices)].

2. Retain records required for an investigational **drug** study in accordance with 21 CFR 312.62, and for an investigational **device** study in accordance with 21 CFR 812.140(d) (Refer to SOP's on "Investigational Drug Studies/Investigational Device Studies").
3. Prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each participant who receives an investigational drug or device (including those employed as a control in the research study). For example, the case history should include: (a) Signed and dated consent forms **and** documentation that the informed consent was obtained **prior** to beginning any study activities, (b) All history and physical exam results, (c) Laboratory and other diagnostic exams, (d) Progress notes, (e) Nursing notes and (f) Other appropriate documents.

Drugs:

1. The PI shall supply the investigational drug only to participants enrolled in the study, or those research personnel who are designated to supply the investigational drug to the participants (21 CFR 312.61 and 62). The PI must ensure that the study drug will be administered only to participants enrolled in the study and under the PI's supervision or by research personnel responsible to the PI.
2. Maintain records of (a) drug disposition – including dates, quantity, and use by participants, (b) who dispensed the drug, (c) where the drugs are stored and (d) if the drug is to be returned to the sponsor or destroyed [as well as the methods and timing for doing so (21 CFR 312.62)].
3. Report all adverse events and unexpected problems to the IRB in accordance with the HIC Policy and SOP "Reporting Unexpected Problems, Suspensions and Terminations, Serious and Continuing Non-Compliance and the Institutional Official's Responsibilities".
4. When the Investigator holds the IND or IDE, the PI assumes the functions of the Sponsor. The PI is knowledgeable about the additional regulatory requirements of sponsors and follows them (see HIC Policy "Investigator Initiated Research").

Devices:

1. The PI shall permit an investigational device to be used only with participants under the investigator's supervision. A PI shall not supply an investigational device to any person not authorized to receive it (per FDA, OHRP, VA, and sponsor contract).
2. Record the: (a) receipt, use, or disposition of the device, (b) type and quantity of the device, (c) date of receipt, and (d) batch number or code mark for the device.
3. Record the: (a) names of all participants who receive the device, (b) the names of all persons (i.e., co-investigators or other key personnel) who used, or disposed of each device, (c) the number and reasons for returning the device to a sponsor (e.g., repair), and (d) The method of disposal (21 CFR 812.140).
4. Report all unexpected problems and adverse events relative to the investigational device. This would include: (a) Any serious effect on health or safety, (b) Any life-threatening problem or death caused by or associated with the investigational device (i.e., if that effect, problem, or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application).
5. Report any other unanticipated serious problem associated with the investigational device that relates to the rights, safety, or welfare of participants in accordance with the HIC Policy and SOP "Reporting Unexpected Problems, Suspensions and Terminations, Serious and Continuing Non-Compliance and the Institutional Official's Responsibilities".
6. Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as directed by the sponsor [21 CFR 812.110(e)].