

Wayne State University Human Investigation Committee	
SUBJECT	Initial Protocol Submission Requirements
Form Date	9/06
Approvals	General Counsel 11/17/06, Steering Committee 12/07/06, Administrative Approval 03/06/07

Background:

In accordance with The Department of Health and Human Services (HHS) regulations at 45 CFR 46.108(b), the Veteran's Administration (VA) regulations at 38 CFR 16.108(b), and the Food and Drug Administration (FDA) regulations at 21 CFR 56.108(b), all research that involves human participants must be reviewed and approved by the Wayne State University (WSU) Institutional Review Board (IRB) prior to the implementation of research. The Wayne State University Institutional Review Board uses the primary and secondary reviewer system [OHRP Guidance 71] and conducts continuing review of approved research at intervals appropriate to the degree of risk, but not less than once a year. Based on the determination of level of risk, the IRB may require additional review at more frequent intervals. The date for continuing review will be based on the date of IRB approval. [VHA 12005 7(b)]. The IRB criteria for review are based on the type of protocol being submitted.

Scope:

This Policy/Procedure applies to all human subject research activities, behavioral or biomedical, by WSU employees, faculty, and students or by individuals who are members of affiliate institutions.

Definitions:

Human participant (subject)

1. Under DHHS regulations "human subject" means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been

provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

2. Under FDA regulations “human subject” means an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used.

Note: Investigators conducting human participant research must satisfy HHS regulations [45 CFR 46], FDA regulations [21 CFR 50 and 56], and VA regulations [38 CFR 16] regarding the protection of human subjects [participants] in research, as applicable. HHS regulations [45 CFR 46.102(f)] and VA regulations [38 CFR 16.102(f)] define a **human subject** as a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual; or (2) identifiable private information.

Intervention includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the participant or their environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and participant.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the participant is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human participants.

A clinical investigation is defined by FDA regulations [21 CFR 56.102(c)] as any experiment that involves a *test article* and one or more *human subjects [participants]* and that either is subject to requirements for prior submission to the FDA, or is not subject to requirements for prior submission to the FDA under the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Research

1. Under DHHS regulations, “research” means a systematic investigation, including development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
2. Under FDA regulations research means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under

section 505(i) or 520(g) of the Food, Drugs, and Cosmetics Act, or need not meet the requirements for prior submission to the FDA under these sections of the Food, Drug, and Cosmetics Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. For research involving drugs, an experiment is any use of a drug, except for the use of a marketed drug in the course of medical practice, and is defined as a systematic investigation designed to develop or contribute to generalizable knowledge.

Note: If the research activity does not qualify under any of the above circumstances, then the activity would not need to be submitted and reviewed by the HIC. If a PI has questions about whether or not a research activity requires IRB review, consultation with the Human Investigation Committee Office (HIC) is strongly recommended.

Risk – the probability of harm, injury, or loss (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant.

- *Physical* risks may arise from the use of test agents such as chemicals or therapeutic drugs, devices, physical agents (including radiation), and clinical procedures.
- *Psychological* risks may arise from the utilization of behavioral questionnaires or surveys, interview interactions, the collection of sensitive data, or the emotional stress of study participation.
- *Social* risks may arise from actual or potential breaches of confidentiality or anonymity such as harm to interpersonal relationships, damage to reputation or social standing, or exposure to legal sanctions.
- *Economic* risks may affect an individual's financial status, employability or insurability.

A *Test article* [56 CFR 21.102(i)] is defined as any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act.

Types of Review

The types of IRB review include: 1) exemption from review, 2) expedited review, and 3) full board review. In addition, IRB notification is required for the 4) emergency single-time use of a non-approved investigational drug or biologic [21 CFR 312.34(b), 21 CFR 312.36], a non-approved investigational device [21 CFR 812.62] or a Humanitarian Use Device [21 CFR 814.124(a)]. (See HIC Policy/Procedure "Emergency and Single Time Use of a Test Article, Humanitarian Use Device")

- **Exempt Review:** Exempt review can be requested for research where the **entire** project falls within one or more of the six specific regulatory categories set forth in 45 CFR 46.101(b) and satisfies all Institutional policies and procedures. An investigator cannot exempt his/her research project from HIC review and concurrence. Instead, the HIC chairperson or his/her designee must determine that a project is eligible for exemption. (See HIC Policy/Procedure "Exempt Procedures") Any study that the HIC chairperson or his/her designee believes is not exempt must be reviewed

by either an **expedited** or **full board** review process. A research project meeting the criteria for exemption cannot start until after the HIC chairperson or his/her designee has given "concurrence" of exemption. Retroactive "concurrence" or review cannot occur. Approval of research under an exemption is given for an indefinite time period. Re-review is not required unless the investigator proposes changes to the exempt research project.

- **Expedited Review:** *Expedited* review can be requested for project activities that: (1) present no more than minimal risk to human participants, and (2) involve only procedures listed in one or more of the regulatory categories set forth in 45 CFR 46.110 and satisfies all Institutional policies and procedures. (See HIC Policy/Procedure "Expedited Review Procedures")
- **Full Board Review:** A research proposal that does not meet the criteria for review by exempt or expedited process, must be reviewed by a WSU IRB. The HIC currently has four IRB's that review initial submissions; they include:
 - M1 which reviews adult medical protocols,
 - MP2 and MP4 review adult and pediatric medical protocols, and
 - B3 which reviews behavioral research only.
 - HIC Steering Committee a fully constituted IRB that reviews protocols referred from another IRB Committee

Criteria for initial IRB review and approval of research protocols are set forth by HHS regulations at 45 CFR 46.111, 38 CFR 18.111, and FDA regulations at 21 CFR 56.111 and include: determining the level of risk to the participant, potential benefits, informed consent process and documentation, and safeguarding the participant's rights and welfare (i.e., safety monitoring, equitable selection, protection of privacy and confidentiality and special protections for vulnerable populations)

Possible IRB Actions

After an in-depth review of the range of the research study, possible actions by the Institutional Review Board include: (See HIC Policy/Procedure "Outcome of Proposal Reviews by the IRB")

- Approved
- Specific minor revisions required
- Tabled
- Disapproved

Scientific Review:

Before the HIC can review a protocol involving the use of human participants in research, the protocol must be reviewed for scientific merit by the Principal Investigator's (PI) department. Various departments conduct this scientific review in different ways and the IRB will accept any of these methods as long as the Chair and/or his/her designee certifies on the Protocol Summary Form that the scientific review has been completed and that the research has scientific merit and ensures that appropriate support and resources will be provided to conduct the study. Research initiated by an investigator without a designated department must obtain certification from a department with the expertise to determine the scientific merit of the study. (See HIC Policy/Procedure "Investigator Initiated Research")

All research involving **cancer** and human participants must be reviewed by the Protocol Review Committee of the Karmanos Cancer Institute (PRMC). The approval letter must accompany the protocol submission.

All research involving human participants at the **John D. Dingell VA Medical Center (JDD VAMC)**, must be reviewed by the JDD VAMC Clinical Investigation Committee (CIC) before the protocol can be reviewed by the HIC. If the VA research involves cancer, an approval from the PRMC (see above) should be obtained before submission for review by the CIC. The approval letter(s) must accompany the protocol submission.

All research involving human participants whose Principal Investigator is a faculty member in the **Department of Psychiatry and Behavioral Neuroscience**, must first be reviewed by the Department Review Board. That approval must accompany the protocol submission.

HIC Procedures:

The IRB must review research at intervals appropriate to the degree of risk, but not less than once per year. Upon careful review of the submitted material, the IRB Committee will determine if the research project requires review more often than annually. [45 CRR 46.103(b)(4)(ii); 21 CFR 56.108(a)(1); VHA 1200.5 7.d(2)] (See HIC Policy/Procedure "Criteria for Determining Frequency of Review")

The IRB Chair will assign reviewers with appropriate scientific or scholarly expertise as appropriate to the risk of the protocol, if that expertise is not available on the committee a qualified alternate, or consultant will be obtained. (See HIC Policy/Procedure "Expectations of IRB Membership")

Consultants:

If deemed necessary, an IRB chair, in consultation with the HIC chair and/or Assistant Vice President for Research, will determine if additional scientific expertise or experience dealing with vulnerable populations is need to conduct a research review. If a consultant is used to review a protocol the following criteria apply:

- The consultant must either attend the meeting in which the protocol discussion takes place or submit the information in writing
- Any written information provided by the consultant will be maintained in the protocol file
- The minutes will document the key information provided by the consultant
- The consultant must meet the HIC Conflict of Interest policy requirements and will not participate in the review of protocols in which they have a conflict of interest, except to provide information requested by the IRB
- The consultant may participate in the IRB committee discussion but may not vote or be present when the voting takes place.

Before approving research that involves human participants, the IRB must determine that the following criteria are met:

- Risks to participants are minimized
- Risks to participants are reasonable in relation to anticipated benefits

- Selection of participants is equitable or justified for the center aims
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative
- Informed consent will be appropriately documented
- When appropriate, there are adequate provisions to protect the privacy interests of participants (an individual's interests in being left alone and free of physical or psychological intrusions or intrusions on information)
- When appropriate, there are adequate provisions to protect and maintain the confidentiality of participant data

The factors that are reviewed to determine if the above criteria have been met include but are not limited to:

- The scientific merit of the research
- The level risk to the participants includes the determination that:
 - Risks to participants are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose participants to risk
 - Risks to participants are minimized , when appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes
 - Risks to participants are reasonable in relationship to the potential benefits, if any, to participants, and the importance of the knowledge that might be expected to result
- If the research involves treatments or interventions, the research plan makes adequate provisions for monitoring the data to ensure the safety of participants
- The purpose of the research
- The setting in which the research will be conducted
- Whether prospective participants are vulnerable to coercion or under influence
- The inclusion/exclusion criteria
- Participant recruitment and enrollment procedures
- The influence of payments to participants

Expedited Review

When reviewing research under an expedited review procedure, the HIC Chair or designee receive and review a Medical/Behavioral Protocol Submission Form, and all consent documents, notices/flyers, and advertisements. See HIC Policy/Procedure, "Expedited Review Procedures"). The reviewer will first determine that the proposal meets federal requirements for expedited review [45 CFR 46.110] and then will conduct an in-depth review of the submitted materials to determine whether the research meets the criteria for approval (see above)

When needed, the HIC Chair or designee may request a consultant to provide additional expertise.

Full Board Review

The Committee Chair assigns a primary and secondary reviewer to each protocol based upon their expertise. If additional scientific or scholarly expertise or a reviewer knowledgeable about or experienced in working with prisoners or a vulnerable population is determined to be necessary by the IRB chair, either an alternate reviewer or consultant will be part of the review process.

The primary and secondary reviewer receives the required documentation at least one week prior to the regularly scheduled IRB meeting. The primary reviewer is provided with all of the documents required for submission (see below).

All IRB members receive a Medical/Behavioral Protocol Summary Form, a Narrative Summary, and all consent documents, notices/flyers, and advertisements. All information is available upon request, to any IRB member for use prior to or during the course of a discussion at a convened meeting. The additional information may be requested from the Research Compliance Administrator.

The IRB committee will conduct an in-depth review of the completed Medical/Behavioral Protocol Summary Form and all pertinent documents to determine whether the research meets the criteria for approval. The criteria that must be satisfied in order for the IRB to approve research include, among other things, determinations by the IRB regarding risks, potential benefits, informed consent, and safeguards for human subjects (45 CFR 46.111). (See HIC Policy/Procedure "Expectations of IRB Membership")

The Principal Investigator will be informed of the IRB committee's decision and any specific requirements via e-mail or fax and also by mail (See HIC Policy/Procedure "Outcome of Proposal Reviews by IRB").

All of the proceedings regarding review of the research will be documented in the IRB minutes for the convened meeting. This includes full discussion of controverted issues and protocol specific examples to justify the decisions that are made.

Submission Requirements

The primary and secondary reviewers receive a copy of the Protocol Summary Form and all accompanying documents (see below) as submitted by the principal investigator approximately one week in advance of the meeting. The IRB members at large will receive a copy of the Protocol Summary Form and accompanying documents. A copy of the full application is available, upon request, to any IRB member for use during the course of a discussion at a convened meeting. These documents may be requested from the Research Compliance Administrator.

Materials for submission of a new protocol to the HIC must include:

- A completed Medical Exemption Form or a Medical/Behavioral Protocol Summary Form and required Appendices (as applicable)
- A full research protocol/grant proposal
- The following items, as applicable:
 - If accessing WSU medical records, a completed HIPAA Summary Form and, if applicable, a HIPAA Authorization Form
 - Informed Consent/ Assent /Information Sheet documents
 - An Investigator's Drug Brochure
 - Surveys, questionnaires, data collection instruments or other measurement tools
 - Advertisements, notices, flyers
 - Recruitment Material
 - Educational materials that will be distributed to participants

- Data and Safety Monitoring plan if applicable

When a protocol submission is received, it is date stamped by HIC staff, checked for appropriate original signatures, logged into the Coeus database, and assigned an HIC Protocol tracking number.

Deadlines and directions for submission are available on the applicable HIC form and can be found on the HIC website (www.hic.wayne.edu).