

Wayne State University Human Investigation Committee	
SUBJECT	Continuation/Renewal of a Protocol
Section	
Form Date	06/08
Approvals	General Counsel 11/20/06, Steering Committee 02/14/07, Administrative Approval 03/26/07, General Counsel 2/29/08

Background

Under federal regulations the Institutional Review Board (IRB) is responsible for a continuing review of research at intervals appropriate to the degree of risk, but at least once each year [45 CFR 46.109(e)]. A Continuation Review must be completed as long as the collection of private identifiable information of human participants is being collected through interaction or intervention with those participants or as long as there is analysis of private identifiable information. When all collection of private identifiable information has been completed for all study participants the Principal Investigator (PI) must send in a Closure form (See Closure of a Research Protocol Policy/Procedure) Continuing review of research must be substantive and meaningful and follow written institutional procedures [46.103(b) (4)]. Regulations require review by a convened IRB, with a recorded vote on each study [45 CFR 46.108(b) and 46.115(a) (2)], unless the research is otherwise appropriate for expedited review under Section 46.110(b) (1). 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). The minutes of IRB meetings must document separate deliberations, actions, and votes for each protocol undergoing continuation review by the convened IRB.

In accordance with federal regulations, Wayne State University (WSU) uses a primary reviewer system to conduct continuing reviews.

Scope

This Policy/Procedure applies to all research protocols that have previously been approved at Wayne State University and its affiliate institutions.

Definitions

Expiration Date – The date on which an approved research protocol terminates unless a request for continuation or renewal has been submitted to the HIC. A previously approved research protocol terminates at midnight on the date of expiration.

Protocol Approval Period - Renewal of protocols through the IRB occurs at intervals specified by the IRB and no less than annually. Federal regulations stipulate research approval can be no longer than 365 days. (See Below)

Institutional Review Board (IRB) – a specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research.

Minimal Risk – 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.

Significant Risk – the probability and magnitude of harm or discomfort anticipated in the research that are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Risk – the probability of harm, injury, or loss (physical, psychological, social, legal 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 – the probability of bodily harm, injury or loss that may arise from the use of test agents such as chemicals or therapeutic drugs, devices, physical agents (including radiation), and clinical procedures.

Psychological Risks – the probability of mental or emotional harm, injury or loss that 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 – the probability of harm, injury or loss that may arise from actual or potential breaches of confidentiality and/or anonymity such as harm to interpersonal relationships, damage to reputation or social standing, or exposure to legal sanctions.

Economic Risks – the probability of harm, injury or loss that may affect an individual's financial status, employability or insurability.

Legal Risks – may arise from the utilization of behavioral questionnaires or surveys, interview interactions, or the collection of sensitive data.

HIC Policy/Procedures

The IRB will conduct 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 (See HIC Policy/Procedure "Criteria for Determining Frequency of Review" and "Determining Projects that Require Additional Verification").

The level of review for continuation of an approved protocol will generally maintain the level of review that was required for initial approval. Thus, a full board initial approval will likely warrant a full board continuation. Full board approved studies may be eligible for expedited approval if they meet the criteria outlined in 45 CFR 46.110(b) (1) (See HIC Policy/Procedure "Expedited Review Procedures"). For Full Board reviews, each IRB Committee has a designated member who is responsible for conducting primary review for all continuations. If the IRB Chairperson determines that additional scientific or scholarly expertise is required for continuation review of a particular protocol, another member of the IRB Committee may be selected for that review, or the IRB chair will obtain a consultant who is knowledgeable about, or experienced in, the research area or vulnerable population in question.

A protocol that initially met the criteria for expedited review will usually be eligible for an expedited continuation review unless the risk to participants has increased. (See HIC Policy/Procedure "Expedited Review Procedures"). In that instance the protocol would require revision and a resubmission for full board review (45 CFR 46.108).

All protocol continuations are normally submitted to the IRB that provided the initial review and/or the review of the last continuation. There may be occasions when the HIC may redirect a protocol to another IRB.

The minutes of IRB meetings document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB (45 CFR 46.115).

Approval Period

Renewal of protocols through the IRB occurs at intervals specified by the IRB and no less than annually. Federal regulations stipulate research approval can be no longer than 365 days. **The WSU approval period for research begins from the initial date of IRB approval and ends at midnight on the day of expiration.** Both dates are specified on the approval memo sent to the PI.

Approval periods will vary based on the type of review and whether or not modifications are requested. For example:

- Expedited review of a continuation that does not require additional information or modification would be approved from the date of review and would expire one year later less one day.
- Full board review of a continuation that does not require additional information or modification would be approved from the date of the convened meeting and would expire one year later less one day.
- Full board review of a continuation that requires additional information or modification would be approved from the date that approval is given and would expire one year later less one day from the date of the convened meeting. For example, a continuation that was reviewed at a

convened IRB meeting on February 2, 2006, where modifications were requested and appropriately addressed and approved by the IRB reviewer on March 3, 2006, would be approved for the period of March 3, 2006 to February 1, 2007 (one year less one day before the convened meeting). In this instance, the approval period is only for 11 months.

Timelines and Deadlines Associated with the Continuation Process

Continuation/renewal applications of approved protocols should be submitted to the HIC for review well in advance of the protocol expiration date; approximately six weeks before expiration. It is the responsibility of the Principal Investigator (PI) to assure that protocol continuation submissions are in the HIC office far enough in advance of the expiration date and at least six (6) weeks prior to protocol expiration to allow adequate time for processing and review prior to the expiration date. that the expiration date is noted and highlighted on the initial protocol approval letter or the current continuation approval memo. However, as a courtesy, a "Continuation Renewal Reminder" *may* be sent to the PI approximately six weeks prior to the date of expiration.

Protocol Expiration

The IRB and investigators must plan ahead to meet required continuation review dates. If an investigator has failed to provide continuing review information to the IRB in a timely manner and the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research must stop.

During any period when there is no IRB approval for research studies, no enrollment of new participants can take place nor can any data be collected until the protocol has received full approval for renewal of research activities.

Data that is collected during a period of non-IRB approval can never be used for research purposes. Relevant study data may be sent to data and safety monitoring committees and appropriate federal regulatory agencies as required.

Upon protocol expiration, the PI will be informed that they must immediately provide to the IRB Chair a list of participants for whom stopping research activities will cause harm and he/she must submit a participant withdrawal plan to the IRB Chair. The IRB Chair or the full committee will determine whether or not it is in the best interests of individual participants to continue receiving the research interventions or interactions research activities can continue after expiration. For all research being conducted at the John D. Dingell Veterans Administration Medical Center (JDD VAMC) the decision regarding withdrawal for VAMC patients must be made in consultation with the Chief of Staff (VHA Handbook 1200.5.12.a.p 21-22.)

When continuation review of a research protocol does not occur prior to the expiration of the approval period specified by the IRB, then IRB approval expires automatically on the expiration date (See Definitions). It is not necessary to report the expiration of an IRB approval to the Office of Human Research Protection (OHRP) as a suspension of IRB approval under HHS regulations, unless it meets the definition of continuing non-compliance (See HIC Policy/Procedure Identifying, Defining, and Managing Non-

Compliance in Human Research). However, the VAMC Research and Development Office and the Sponsor will receive a copy of the expiration memo.

Upon expiration of a protocol the following apply:

- Accrual of study participants must cease.
- Data collected from the time the protocol has expired (including the expiration date) cannot be used by the PI, and, if applicable, by the study sponsor.
- If the period of expiration exceeds the 60 days, the research must be submitted to the IRB as a new protocol.

Continuation Submission Material

The PI is responsible for the accurate completion of the Medical/Behavioral Continuation Form and is also responsible for the accuracy of all of the information provided to the HIC.

Information and Materials Required for Submission:

- Continuation/Renewal Form (Including, but not limited to, the number of subjects/data/specimens accrued, racial and ethnic characteristics of participants, withdrawals of participants from the study, holds, audits, significant changes to risk/benefit ratio, etc.)
- Current copy of the consent form,
- Initial Protocol Summary Submission Form
- Approved advertisements, recruitment material,
- A brief summary of research methodology and procedures [VHA 1200.5 7.g(1)],
- Multi-center trial reports (if applicable),
- The number of vulnerable participants enrolled (VHA 1200.5)
- A summary of Adverse Reactions /Unexpected Events involving risks to subjects or others and any withdrawal of subjects from the research or complaints about the research since the last IRB review,
- A summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review, and
- Any other relevant information, especially information about risks associated with the research.

Expedited Continuation Review

When reviewing research under an expedited review procedure, the HIC Chair or designated IRB member(s) receive and review the Initial Protocol Summary Submission Form, Medical/Behavioral Continuation Form, Narrative Summary, and all currently approved informed consent documents, notices/flyers, and advertisements along with the HIC file which contains the complete history, appropriate documentation of the course of the protocol and all complete protocols, including the most up-to-date version (See HIC Policy/Procedure, "Expedited Review Procedures".)

Full Board Continuation Review

Each IRB has an appointed Continuation Reviewer (a primary reviewer). An alternate to the primary reviewer may also be identified to serve in the absence of the primary reviewer. 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 provided.

The primary reviewer conducts his/her review at the HIC Office approximately one week prior to the regularly scheduled IRB meeting. The primary reviewer is provided with a copy of the initial protocol summary form, Medical/Behavioral Continuation Form submission, a Narrative Summary, and all currently approved consent documents, notices/flyers, and advertisements (as applicable). In addition, the HIC file is pulled containing the entire protocol, and a Reviewer's Form is generated for use by the reviewer. When the review is completed, a copy of the Reviewer's Form containing his/her comments and recommendations is printed and provided to each IRB member at the convened meeting. (See also HIC Policy/Procedure "IRB Review of Initial Research Proposal") All IRB members receive the Initial Protocol Summary form, Medical/Behavioral Continuation Form, a Narrative Summary, and all currently approved consent documents, notices/flyers, and advertisements. A copy of the full application which contains the complete history, appropriate documentation of the course of this protocol, and the most up-to-date version of the entire protocol is available, upon request, to any IRB member for use prior to or during the course of a discussion at a convened meeting.

The IRB committee will conduct an in-depth review of the Initial Protocol Summary Form, completed Medical/Behavioral Continuation Form and all pertinent documents to determine whether the research continues to meet 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). The factors that are reviewed to determine if the above criteria have been met include but are not limited to:

- Has the risk level changed?
- Has there been a high number of Adverse Reactions/Unexpected Events (AR/UE)?
- Is the data monitoring process adequate?
- Is the consent form still adequate?
- Are there significant new findings that may affect a participants' willingness to continue in the study? If so, have those findings been provided to the participant?
- How many participants have been accrued?
- A summary of adverse events and any unanticipated problems involving risks to subjects or others and any withdrawal of subjects from the research or complaints about the research since the last IRB review,
- A summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review,
- Any relevant multi-center trial reports,
- Any other relevant information, especially information about risks associated with the research, and
- A copy of the current informed consent document and any newly proposed consent document.

No official action can be taken at a meeting of an IRB in the absence of a quorum (50% plus 1 of the total voting membership). Issues may be discussed, but an official vote cannot be taken until a quorum is present.

- 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").
- If a protocol is suspended or terminated the PI has the opportunity to appeal that decision to the IRB Committee of record, either in person or in writing. The Committee will review the appeal at the next convened meeting, and inform the PI of their decision, in writing, within 30 days.

All of the proceedings regarding review of the continuations for 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.