

Wayne State University Human Investigation Committee	
<b>Subject:</b>	<b>Reporting Unexpected Problems, Suspensions and Terminations, Serious &amp; Continuing Non-Compliance and the Institutional Official's Responsibilities</b>
<b>Section:</b>	
<b>Form Date:</b>	11/2008
<b>Approvals</b>	Office of the General Counsel 1/08/07, Steering Committee 2/05/07, Administrative Review 02/28/07, Administrative Approval 10/29/08, Office of General Counsel 11/7/08

## Background

An Institutional Review Board (IRB) is required to promptly report: (1) unexpected problems involving risks to subjects and others; (2) serious or continuing noncompliance; and (3) suspensions and/or terminations of previously approved research to appropriate institutional officials and departmental or agency heads [Office of Human Research Protections (OHRP), The Food and Drug Administration (FDA), The Veterans Administration Office of Research Oversight (ORO)]. See 45 CFR 46.103(a), 38 CFR 16.103(a) and 21 CFR 56.103(a).

At Wayne State University (WSU), the Institutional Official has delegated authority to the Associate Vice President of Research (AVPR) for reporting these situations and is responsible for providing administrative oversight concerning all research involving human participants at WSU. The oversight duties of the AVPR include review and reporting of: (a) unexpected problems involving risks to participants or others; (b) serious or continuing noncompliance with federal regulations or the determinations of the Institutional Review Boards (IRBs); and (c) any suspension and/or termination of IRB approval to other institutional officials, supporting agencies and/or regulatory authorities.

## Scope

This HIC Policy and Standard Operating Procedure applies to all research conducted at WSU or any of its affiliate institutions.

## Definitions

*Continuing non-compliance* - repeated pattern of non-compliance (as defined below) by an individual investigator or research staff member either on a single protocol or multiple protocols.

*Non-Compliance* - is the failure to comply with regulations, requirements, or determinations of the IRB and federal regulatory agencies. Non-compliance includes, but is not limited to:

- failure to obtain IRB approval for research involving human participants;
  - inadequate or non-existent procedures for informed consent;
  - inadequate supervision in research involving drugs, devices or procedures;
  - failure to follow recommendations made by the IRB to insure the safety of participants;
  - failure to report adverse events or proposed protocol changes to the IRB;
  - failure to provide ongoing progress reports;
  - failure to provide the required HIC Continuation/Renewal documents or Closure form.
- (see HIC Policy/SOP "Identifying, Defining & Managing Non-Compliance in Human Research")

*Serious Non-Compliance* – a failure to comply with regulations, requirements, or determinations of the IRB and Federal regulatory agencies that involves or could result in one or more of the following:

- Harm to research participants;
- Exposure of research participants to a significant risk of substantive harm;
- Compromised privacy and confidentiality of the participants;
- Damage caused to scientific integrity of the data that has been collected;
- Willful or knowing non-compliance on the part of the investigator;
- An adverse impact on ethical principles.

*Suspension* – A suspension occurs when the AVPR, HIC Chair, IRB Committee or IRB Chair places a temporary hold on research that had previously been approved so that no new participants can be accrued, no research interventions may occur (unless necessary for the safety and well-being of the enrolled participants) and no follow-up can be conducted unless it is in the best interest of the participant and approved by the IRB.

*Termination of a previously approved protocol* – Termination of a previously approved protocol occurs when the IRB withdraws approval or stops all research activity permanently. No new participants may be enrolled and no additional research interventions can occur. However, future follow-up may be conducted with the approval of the IRB to monitor the well being of and any potential risk to participants enrolled prior to termination.

| *Termination of activities that have never received prior review and approval* - On the occasion when research activities have occurred that did not receive prior review and approval from the IRB, the HIC shall stop all such activities permanently. None of the data collected in this activity can be used in any future publication or presentations.

*Unexpected Problem* – An unexpected problem is an unanticipated problem associated with any aspect of the research study that may involve not only risks to the participant enrolled in a research study, but to other individuals who may or may not be directly associated with the research study. Unexpected problems may occur in non-clinical (behavioral or social science) as well as clinical research studies (see HIC Policy and Procedure "Unexpected Problems Involving Risk to Participants").

## HIC Policy/Procedures

In general, when there are unexpected problems, serious or fatal adverse events, serious or continuing non-compliance or any for-cause suspension or termination of a protocol, the person who receives the initial report notifies all appropriate members of the HIC. These may include the following but not necessarily in this order: the AVPR; the HIC Chair; the Chair of the IRB of record; or the IRB Committee as a whole. The AVPR notifies appropriate institutional officials and regulatory officials when appropriate as a part of the reporting process.

Anytime there are critical issues needing immediate attention and when there is an immediate threat to or risks to the safety or welfare of research participants, the AVPR is notified immediately and the succession of appropriate notification follows.

### Suspensions/Terminations

#### *Reporting to the Principal Investigator (PI)*

If a protocol is suspended or terminated, the PI must be notified in writing immediately by the AVPR, the HIC Chair, or Chair of the IRB that originally approved the protocol. This is done the day the notification letter is prepared. The information in the notice/letter must specify the reason(s) for the suspension and/or termination, any required corrective action plan, any required notification of the participants already enrolled in the research and the mechanism available to the PI to address the actions taken and respond to the decision.

#### *Reporting to Institutional Officials, Department Chairpersons, Deans, or Appropriate Research Team Members*

Copies of the above-referenced notice are sent to the Vice President for Research, appropriate Department Chairs, Deans, and/or Directors within the Institution, and members of the research team as deemed appropriate. All suspensions and terminations of Veteran's Administration (VA) protocols must be reported to the VA Research and Development Committee within 24 hours.

#### *Reporting to Sponsors*

The HIC requires that research sponsors be notified of any suspension or termination of research. The HIC will forward a copy of the suspension/termination notice directly to the sponsor.

#### *Reporting to Appropriate Regulatory Agencies or Departments*

Any suspension or termination must be reported to the OHRP, the FDA, if applicable, and the Veterans Administration ORO, if applicable, within two months of the suspension or termination.

## Unexpected Problems Causing Harm to Subjects or Others

### *PI Reporting Responsibilities*

The PI or sponsor will notify the HIC whenever there is an unanticipated event that involves risks or potential risks to the participants or others. For John D. Dingell Veterans Administration Medical Center (JDD VAMC) research studies, a duplicate report must be submitted to their Research and Development Committee at the same time the report is being sent to the HIC office. This Unexpected Problem Form must contain the causes of the event, if known, and actions taken to protect the rights and safety of participants, and planned follow-up. The timeline for submitting this form is specified in the HIC Policy/SOP "Unexpected Problems Involving Risk to Participants" "

Once the report is received in the HIC office, it is sent to the designated HIC reviewer. The HIC reviewer forwards the report to the IRB Reviewer, the IRB Chair and the Committee members. After review the PI is notified in writing of further actions required on the event. If needed, an audit can be requested by the IRB (see "Unexpected Problems Involving Risk to Participants" for potential actions the IRB committee may take).

### *Reporting to Institutional Officials/Chairs/Deans*

When the Unexpected Problem Form is submitted to the HIC, a decision may be made at that time as to whether or not immediate notification of WSU Institutional Officials, Department Chairs and/or Deans is required. If required, the AVPR or HIC Chair would initiate this notification. Any unexpected problem that cause harm or risk of harm to individual or groups of human participants must be reported to the John D. Dingell VAMC Research and Development Committee [VA 1200.5,7.d.(5)(6)(7)]. A copy of the reporting letter must be maintained in the IRB file.

### *Reporting to Regulatory Agencies or Federal Departments*

The OHRP, FDA and ORO will be notified in writing of any unexpected event that resulted in harm to participants or others within 60 days of any official action taken by the HIC/IRB. When deemed appropriate, a preliminary report may be sent to these agencies prior to the completion of a formal investigation with a follow-up report sent after the final audit report has been completed and presented to the IRB Committee for final decision.

## Serious or Continuing Non-Compliance

### *PI Reporting Responsibilities*

When serious or continuing non-compliance comes to the attention of the HIC/IRB, the PI will be required to submit a formal Unexpected Problem Report within the time frame specified by the IRB. When the IRB reviewer and/or IRB committee members require

additional information from the PI, the PI's response must be received in the HIC office by the date listed on the memo.

#### *Reporting to the IRB*

Once the report from the PI is received, the Unexpected Problem Report is then sent to the IRB reviewer, IRB Chair and the IRB committee members. The IRB Committee Members may request additional information and/or corrective action(s) from the PI. The AVPR, the HIC Chair, or the IRB Committee Members may request a for-cause audit at anytime during the process.

#### *Reporting to Institutional Officials/Chairs/Deans*

When the Unexpected Problem Report concerning serious or continuing non-compliance is submitted to the HIC, a decision will be made at that time whether or not immediate notification of WSU Institutional Officials, Department Chairs and/or Deans is required. If required, then the AVPR or HIC/IRB Chair initiates this notification. Any serious or continuing noncompliance must be reported to the John D. Dingell VAMC Research and Development Committee. A copy of the report must be maintained in the IRB file. [VA 12000.5, 7d]

#### *Reporting to Regulatory Agencies or Federal Departments*

The OHRP, FDA, and ORO will be notified in writing of any serious or continuing non-compliance that result in harm to participants or others within 60 days of any official action taken by the HIC/IRB. When deemed appropriate, a preliminary report may be sent to these agencies prior to the completion of a formal investigation with a follow-up report sent after the final audit report has been completed and presented to the IRB of record for a final decision.

### **Preparation of the Final Report**

When the IRB Committee has received the results of the investigation and has approved its contents and recommendations, the AVPR must send the final report to other institutional officials, supporting agencies, and/or regulatory agencies such as OHRP, FDA and/or ORO.

The contents of the report will include: the OHRP Registration Number of the IRB that originally approved the protocol, the Federal Wide Assurance (FWA) number for WSU, the name of the PI, the title of the study, the sponsor of the study and its code number, the date(s) of the events, the nature of the event(s), the findings of the institution, actions taken by the IRB, including the required corrective action plan, the rationale for the actions, and any plans for continued investigation and/or action.

### **Distribution of the Final Report**

A copy of the final report will be provided to:

- The IRB that originally approved the research protocol;

- Appropriate Institutional Officials such as the Dean, Chairs, and other officials within the Office of the Vice President for Research or University administration; and
- Appropriate supporting and/or regulatory agencies. (OHRP, FDA, VA).

### **The Timing of the Notification**

The timing of the notification to appropriate federal agencies is dependent on the nature of the risk. Issues may be discussed informally with relevant representatives and a formal notification may be postponed until sufficient information is known and an internal investigation on the matter is completed. Please refer to the HIC Policy/SOP on "Suspension and Termination of a Research Protocol", "Unexpected Problems Involving Risk to Participants", "Identifying, Defining, and Managing Non-compliance in Human Research", and "For Cause Audits" for specific time requirements that ensure prompt reporting of these occurrences to appropriate agencies and institutional officials.

### **Requirements for Notification of Institutional Official**

The types of protocols requiring AVPR oversight at the time of IRB review include, but are not limited to, the following:

- Protocols that involve prisoners;
- Protocols that involve the need for community consensus;
- Research projects that place the research team at additional risk;
- Research that places the institution at additional risk;
- Research of a sensitive nature; and
- Research that requires review by the Secretary of the Department of Health and Human Services (DHHS).

The AVPR must be notified if any of the following occur after a protocol has been approved:

- Unexpected Problems involving risks to participants or others;
- Serious or continuing noncompliance with federal regulations or requirements of the IRBs; and
- Any suspension or termination of IRB approval.

Decisions made by WSU's AVPR may not overrule an IRB's decision to disapprove a research protocol (45 CFR 46.112). However, he/she may ask the IRB to reconsider its decision after the Principal Investigator (PI) has made appropriate changes to the design of the research protocol. The AVPR, in consultation with the Institutional Official, may disapprove research that was previously approved by an IRB.