Wayne State University Institutional Review Board

<table>
<thead>
<tr>
<th>Subject</th>
<th>Reporting Unexpected Problems, Suspensions and Terminations, Serious &amp; Continuing Non-Compliance and the Institutional Official’s Responsibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approvals</td>
<td>Administrative Approval: 07/2011; Office of the General Counsel 01/08/2007; Steering Committee 02/05/2007; Administrative Review 02/28/2007; Administrative Approval 10/29/2008; Office of General Counsel 11/07/2008; Administrative Approval 9/30/10, Administrative Approval 03/07/11, 07/20/11, Administrative Approval 11/30/11; Administrative Approval 03/15, Administrative Approval 03/15/16, Administrative Approval 3/19/2018</td>
</tr>
</tbody>
</table>

**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). 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 Assistant/Associate Vice President for 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 IRB’s; and (c) any suspension and/or termination of IRB approval to other institutional officials, supporting agencies and/or regulatory authorities.

Wayne State University (WSU) limited the scope of its Federalwide Assurance (FWA) to federally funded research. Research projects that present no more than minimal risk to human participants are eligible for flexible review and oversight. Federally sponsored studies, projects with FDA-regulated components, projects with prisoner participants, and projects with contractual obligations or restrictions that require adherence to federal regulations are not eligible for flexible review and oversight. Refer to the WSU IRB “Flexible Review and Oversight of Research Not Covered by Federalwide Assurance” Policy for information about flexibility in the reporting of unexpected problems, suspensions, terminations, and non-compliance.

**Scope**

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

Definitions

Administrative Hold – A voluntary interruption of research enrollments and ongoing research activities by an appropriate VA facility official, researcher, or Sponsor (including the ORD when ORD is the sponsor).
- The term “administrative hold” does not apply to interruptions of VA research related to concerns regarding the safety, rights, or welfare of human research participants, research investigators, research staff, or others.
- An administrative hold must not be used to avoid reporting deficiencies or circumstances that otherwise require reporting by federal agencies.

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.
- 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 IRB Continuation/Renewal documents or Closure form. (see IRB Policy/SOP “Identifying, Defining & Managing Non-Compliance in Human Research”)

Immediately/ Promptly – Without interval of time; without delay; promptly; instantly; at once.

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, 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 IRB 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 IRB Policy and Procedure “Unexpected Problems”).

The IRB can suspend or terminate approval of research that has been associated with unexpected serious harm to participants.

Suspensions and terminations by someone other than the convened IRB must be reported to and reviewed by the convened IRB.

Suspensions and terminations do not include:
- Interruptions in research resulting solely from the expiration of a protocol approval period.
- Administrative holds or other actions initiated voluntarily by a VA facility official, researcher, or sponsor for reasons other than those described in preceding items

**IRB Policy and Procedure**

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 IRB. These may include the following, but not necessarily in this order: the AVPR; the SD-C; the Chair of the IRB of record; the Associate Director, IRB Administration (AD_IA); 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 SD-C, AD_IA; 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 Facility Director and the VA Research and Development Committee within 24 hours.

Reporting to Sponsors

The IRB requires that research sponsors be notified of any suspension or termination of research and serious or continuing noncompliance of research. The IRB will forward a copy of any suspension/termination determination memo, and/or serious or continuing noncompliance memo 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, within two months of the suspension or termination.

Mechanisms for Informing the Organization or IRB of Non-Compliance by Staff and Employees

When the Unexpected Problem Form is submitted to the IRB, that concerns non-compliance by Staff or employees 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 would initiate this notification within 24 hours. Any unexpected problem that causes 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. A copy of the reporting letter must be maintained in the IRB file.

Unexpected Problems Causing Harm to Subjects or Others

PI Reporting Responsibilities

The PI or sponsor will notify the IRB 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 IRB 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 IRB Policy/SOP “Unexpected Problems Involving Risk to Participants”.

Once the report is received in the IRB office, it is sent to the designated IRB reviewer. The SD-C or AD-IA 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” for potential actions the IRB committee may take).

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

When the Unexpected Problem Form is submitted to the IRB, 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 would initiate this notification within 24 hours. Any unexpected problem that causes 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. A copy of the reporting letter must be maintained in the IRB file.

**Reporting to Regulatory Agencies or Federal Departments**

The OHRP, FDA and will be notified in writing of any unexpected event that resulted in harm to participants or others within 30 business days of any official action taken by the 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.

**IRB’s reporting requirements for the VA**

- If the convened IRB or the IRB reviewer determines that the problem or event was serious, unanticipated, and related to the research, the IRB Chair must report in writing the unanticipated problem or event within five business days after the determination to:
  - Medical center director.
  - Associate chief of staff for research.
  - The Research and Development Committee.
- The medical center director must report the problem or event to the appropriate Office of Research Oversight research officer within five business days after receiving such notification.
- If the convened IRB or the IRB Chair determines that the problem or event was serious, unanticipated, and related to the research, a simultaneous determination is required regarding the need for any action (e.g., suspension of activities; notification of participants) necessary to prevent an immediate hazard to participants in accordance with VA regulations.
- All determinations of the IRB reviewer/Chair (regardless of outcome) must be reported to the IRB at its next convened meeting.
- If it was determined that the problem or event is serious, unanticipated, and related to the research, the convened IRB must determine and document whether a protocol or consent document modification is warranted.
- If the convened IRB determines that a protocol or consent document modification is warranted, the IRB must also determine and document:
  - Whether previously enrolled participants must be notified of the modification.
When such notification must take place and how such notification must be documented.

Serious or Continuing Non-Compliance

**PI Reporting Responsibilities**: When serious or continuing non-compliance comes to the attention of the 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 IRB 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, IRB 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 IRB, 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 IRB Chair initiates this notification (the Chair must do this if it is a VA study). Any serious or continuing noncompliance must be reported to the John D. Dingell VAMC facility director no later than 5 business days [VHA Handbook 1058.01].

**IRB's reporting requirements for the VA**
Determination that non-compliance is “serious” or “continuing” rests with the IRB.

IRB review of apparent serious or continuing non-compliance.
- The IRB must review a report of apparent serious or continuing non-compliance at its next convened meeting.
- Should the IRB determine that the reported incident constitutes serious non-compliance or continuing non-compliance, within five business days after the determination, the IRB chair must provide a written report of the determination directly to:
  - Medical center director.
  - Associate chief of staff for research.
  - Research and Development Committee
  - Other relevant research review committee.
- Unless the non-compliance has already been reported, within five business days after receiving such notification, the medical center director must report the determination to:
  - The appropriate Office of Research Oversight research officer.
  - The VISN director.
  - Office of Research Development.
- An initial report of an IRB determination that serious non-compliance or continuing non-compliance occurred is required, even where the determination is preliminary or disposition of the matter has not been resolved at the time of the report.
- The IRB must reach a determination that serious or continuing non-compliance did (or did not) occur within 30-45 days after receiving a report of apparent non-compliance.
- Remedial actions involving a specific study or research team must be completed within 90-120 days after the IRB’s determination.
- Remedial actions involving programmatic non-compliance must be completed within 120-180 days after the IRB’s determination, unless remediation requires substantial renovation, fiscal expenditure, hiring, or legal negotiations.
- The Privacy Office, when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information.
- The Information Security Officer when the report involves violations of information security requirements.
When following Department of Defense Regulations

Determination of “serious” or “continuing” non-compliance of DoD-supported research must be promptly (no longer than within 30 days) reported to the Department of Defense Human Research Protection Officer.

**Reporting to Regulatory Agencies or Federal Departments:** The OHRP, FDA, and will be notified in writing of any serious or continuing noncompliance that result in harm to participants or others within 30 business days of any official action taken by the 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.

For **Department of Energy** (DOE)-regulated research, investigators must promptly report the following to the human subject research program manager:

- Any significant adverse events, unanticipated risks; and complaints about the research, with a description of any corrective actions taken or to be taken.
- Any suspension or termination of IRB approval of research
- Any significant non-compliance with human research protection program procedures or other requirements.
- The time-frame for “promptly” is defined.
- Any compromise of personally identifiable information must be reported immediately.
- The time-frame for “immediately” is defined.

**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, and FDA.

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; VA Medical Center Director; and
- Appropriate supporting and/or regulatory agencies. (OHRP, FDA).

**Timing of the Notification**

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 IRB 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 IRB’s; 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.