WAYNE STATE UNIVERSITY

HIC Policy/Procedure

Wayne State University Human Investigation Committee	
Subject	Identifying, Defining, and Managing Non-Compliance in Human Research
Form Date	June, 2008 (Rev. 03/07/11)
Approvals	Office of General Counsel 02/12/2007; Steering Committee 03/12/2007; Administrative Approval 03/26/2007; General Counsel 02/29/2008, Administrative Approval 9/30/10, Administrative Approval 03/07/11

Background

Investigators, research team members, the Institutional Review Board (IRB) members and/or Wayne State University (WSU) administrative staff are required to conduct research ethically and in accordance with federal regulations and WSU and/or IRB policies. Non-compliance occurs when research involving human participants is conducted in a manner that disregards or violates federal regulations, ethical standards, and WSU and/or IRB policies and procedures governing research and human research protection. Non-compliance with respect to human research participant protection requirements violates WSU's Federal Wide Assurance (FWA 00002460). Regardless of intent, any unapproved and non-compliant research activity may place a research participant at unnecessary risk. (See [38 CFR 16.103(b)(5)(i); 38 CFR 16.116(b)(5); 45 CFR 46.103(b)(5)(i); 21 CFR 50.25(b)(5).25(b)(5); 21 CFR 56.108(b)(2).

Non-compliance applies to investigators, research team members, the IRB members and/or WSU HIC administrative staff.

Authority

WSU has granted the IRB the authority to approve, require modifications (to secure approval), disapprove, and suspend or terminate approval of research activities not being conducted in accordance with IRB requirements; and to observe or have a third party observe the informed consent process and the conduct of the research. The Vice President for Research has delegated the authority for research compliance activities to the Associate Vice President for Research.

Definitions

Allegation – An assertion of non-compliance, made by a party, which must be supported with evidence.

Confirmed Non-Compliance – Non-compliance that has been verified as a result of a for-cause audit or investigation.

Continuing Non-Compliance – A repeated pattern of non-compliance with all federal regulations, including veteran's regulations and guidance, by an individual investigator or research staff member either on a single protocol or multiple protocols. Examples of non-compliant activities include:

- Conducting research without IRB approval (i.e., either before IRB approval is obtained, or after an approved research protocol expires);
- Non-use or misuse of consent forms (i.e., consent/assent not obtained, wrong consent document used, missing signatures, failure to document consent process);
- Failure to follow approved protocol;
- Modifying or changing protocol without prior IRB approval;
- Failure to report unexpected problems, unanticipated events or adverse reactions or not reporting in a timely fashion;
- Failure to maintain adequate records;
- Inadequate training of investigators or research staff;
- Other failure to follow University policies and federal regulations;
- Failure to comply with an IRB request

Non-Compliance – The failure to comply with all federal regulations, including Veteran's Administration regulations and guidance, state and local requirements, WSU Policy and determinations of the IRB.

Serious Non-Compliance – The failure to comply with all federal regulations, including Veteran's Administration regulations and guidance, state, and local requirements, WSU Policy and determinations of the IRB that involve one or more of the following:

- Harm to research participants;
- Exposing research participants to a significant risk of substantive harm;
- Compromising the privacy and confidentiality of research participants;
- Damage caused to scientific integrity of the research data that has been collected;
- Willful or knowing non-compliance on the part of the investigator;
- Adversely impacting ethical principles

HIC Policy

Reporting Allegations to the HIC

Non-compliance may be reported to the HIC by any person, including the researcher or his/her designee. The HIC will accept anonymous allegations, and will make every effort to protect the confidentiality of the complainant if necessary. Allegations are routed to the Sr. Research Compliance Specialist (RCS); in his/her absence it may be reported to the Education Coordinator. Allegations/reports of non-compliance may be reported to:

- HIC Sr. Research Compliance Specialist (313-577-2901).
- Education Coordinator (313 577-9534)
- HIC Chair (313-577-1628)
- Associate Vice President for Research Compliance (313-577-9064)
- Vice President for Research (313-577-9600)

Non-compliance or potential non-compliance may also be discovered by the IRB through audits or other routine review or quality control activities. Allegations of potential non-compliance may also be reported to the IRB by non-investigators or investigators who are not involved with the research in question.

Researcher Responsibility for Reporting to the HIC

Investigators must report the following circumstances to the HIC Office within 10 days of the investigator's knowledge of the circumstance unless it is a serious adverse reaction or unexpected event (AR/UE) which must be reported within 5 days of the investigator becoming aware. (See HIC Policy/Procedure: "Unexpected Problems").

- Information that indicates a potentially detrimental change to the risks or potential benefits of the research. For example:
  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 paper is published from another study that shows that an arm of the research study is of no therapeutic value
- A breach of confidentiality
- Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol
- Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant
- Incarceration of a participant in a protocol not approved to enroll prisoners
- Event that requires prompt reporting to the sponsor
- Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team
- Protocol deviation or violation (meaning an accidental or unintentional change to the IRB approved protocol if it presents potential or actual harm to the participant or the data)
- Sponsor imposed suspension for risk

For VA research:

In accordance with VHA Handbook 1058.01, Research Compliance Reporting Requirements, members of the VA research community are required to ensure that apparent serious or continuing noncompliance has been reported in writing to the HIC within 5 business days of becoming aware. In addition to non-compliant activities previously listed in this policy, examples include:

- Any finding of noncompliance with human research requirements by any VA office (other than ORO) or any other Federal or state entity (e.g., FDA);
- Initiation of VA human subject research without written notification from the ACOS for Research that the project may begin;
- Participation by one or more members of the research team in the conduct of an active protocol without the required credentialing, privileging, or scope of practice, or engaging in activities outside the approved scope of practice.
- Involvement of prisoners or children in VA research, or conduct of international VA research, without the required approval by the VHA Chief Research and Development Officer (CRADO).

HIC Procedures

The Human Investigation Committee (HIC) receives reports of possible non-compliance with federal, state, local regulations, VA regulations or University or HIC policies related to protections of human research subjects through various means of communication. Individuals making such reports are referred to the HIC Chair or the Sr. Research Compliance Specialist (RCS) for initial review. If after a review of all relevant materials (e.g. IRB file, communications with PI, research materials, past audits) the HIC Chair or RCS determines that the report may meet the criteria for serious or continuing non-compliance and has a basis in fact, they will consult with the AVPR. If the AVPR concurs with this initial determination, further processing of the report proceeds as described below and according to HIC policy.

When reports of non-compliance are determined by the IRB Chair or RCS not to meet the definition of serious or continuing non-compliance by a review of the materials listed above, and the remedial actions, if any, are determined to be appropriate for the reported incident(s), this must be documented on the report form and included in the research file.

If the IRB Chair, RCS, or the AVPR determine that immediate actions are required to protect the safety and well-being of research participants (see HIC website, "Unexpected Problem Checklist for PI's"), the HIC Chair is notified. Depending on the initial availability of information and the immediacy of the reported event, the AVPR or HIC Chair may place an administrative hold on the protocol or specific research activities or initiate other corrective steps such as requesting an interview with the investigator, an audit, a focused review, educational remediation, notification of currently enrolled participants, etc. The HIC Policy and Procedure "Suspension and Termination of Research Protocols" outlines the steps to take for those actions.

If the HIC Chair, RCS, or AVPR determine that the problem does not require immediate action, an internal review of the protocol, a focused review with phone or in-person interviews with the research staff and/or PI, or a for-cause audit is conducted to gather more information on the problem. Depending on the initial availability of information, the AVPR or IRB Chair may place an administrative hold on the protocol or

specific research activities until the IRB has reviewed the issue and placed further sanctions. (See HIC Policy/Procedure, "Suspension and Termination of Research Protocols").

The initial report and the supporting data will be presented at the next convened meeting of the appropriate IRB (i.e., the IRB of record). Information provided to the IRB members in order to review non-compliance will include (as applicable): An audit report to include findings based upon review of the protocol, informed consent document(s), eligibility criteria, AR/UE's, data collection tools, protocol adherence, documentation, data collection, drug/device review and oversight (including storage and accountability records), and a description of the event(s) that precipitated the audit including dates.

For reports determined to have a basis in fact and that meet the definition of serious or continuing non-compliance, the convened IRB will make a final determination of whether the report meets the definition of serious or continuing non-compliance (see HIC website, "Unexpected Problem Checklist for PI's"). If the reported activity or non-activity is determined to be serious or continuing, the convened IRB will consider the following possible actions

- Suspension or termination of the research;
- Notification and/or re-consenting of current participants if such information could affect the participants' willingness to continue in the research;
- Modifications of the protocol or consent document;
- Provision of information to past participants;
- Early continuation review;
- Re-auditing to monitor the research at a specified interval, and
- Required educational sessions for the PI and research team members.

For distribution of the findings, see "Reporting of Unexpected Problems, Suspensions and Terminations, Serious and Continuing Non-Compliance and the Institutional Official's Reporting Responsibilities".

If a decision is made to terminate a protocol then the PI may appeal either in person or in writing to the IRB Committee of record. The Committee of record will review the appeal at the next convened meeting, and inform the PI of their decision, in writing, within 30 days.

Reporting of Non-Compliance

The final non-compliance report is written by the RCS or his/her designee and approved by the AVPR and/or the convened IRB Committee. (See HIC Policy/Procedure: "Reporting of Unexpected Problems, Suspensions and Terminations, Serious and Continuing Non-Compliance and the Institutional Official's Reporting Responsibilities". The final report is distributed to the following:

- IRB of Record
- AVPR
- HIC Chair
- Relevant institutional officials (Chairs, Deans, Directors) as appropriate
- OHRP, VA, FDA as appropriate and/or other regulatory officials
- Information Security Officer
- Privacy Officer at all involved institutions
- Sponsor, if appropriate

For VA Research, should the IRB determine that the reported incident constitutes serious noncompliance or continuing noncompliance, the IRB Chair, or designee will report the determination in writing directly (without intermediaries) to the VA Medical Center Director within 5 business days after the determination with a simultaneous copy to the ACOS for Research, and the VA R&D Committee. An initial report of the IRB determination that serious noncompliance or continuing noncompliance occurred is required by the VA, even where the determination is preliminary or disposition of the matter has not been resolved at the time of the report.

Roles and Responsibilities

Vice President for Research (VPR): The Vice President for Research is the Institutional (WSU) Official responsible for ensuring that human participant research is conducted in compliance with all state and local laws, federal regulations and University policies. Allegations of non-compliance may be reported to the VPR.

Associate Vice President for Research (AVPR): The AVPR, as the official charged with oversight of the research compliance program, is responsible for reviewing serious and continuing allegations of non-compliance. If the alleged non-compliance is determined to pose an immediate risk to the well-being of participants, the AVPR, in conjunction with the HIC Chair or designee, will take immediate action to protect participants. Possible actions include, but are not limited to, suspension and termination of the research. If it is determined that the possibility of serious or continuing non-compliance exists, the AVPR will request an audit be conducted by the RCS. The AVPR will also review the final non-compliance report and ensure that all reporting responsibilities have been satisfied. The AVPR will also keep track of non-compliance cases to determine if there is a pattern that may require process improvement or more education and training of the research community.

HIC Chair: The HIC Chair will review allegations of non-compliance and make a preliminary determine about whether they meet the criteria of serious or continuing non-compliance. If it is determined that there is an immediate risk to the well-being of participants, the HIC Chair or designee, in conjunction with the AVPR, will take immediate action to protect participants. Possible actions include, but are not limited to, suspension and termination of the research.

IRB Committee: Any of the IRB committees may initiate or review allegations of non-compliance. The IRB of record makes the final determination on whether the evidence supports a finding of serious or continuing non-compliance and prescribes any corrective action plan(s) that may be required.

Sr. Research Compliance Specialist: It is the responsibility of the RCS to accept allegations/reports of non-compliance to make an assessment of the validity of the claim. If serious or continuing non-compliance is suspected, the RCS will transfer the allegation/report to either the HIC Chair or AVPR. The RCS also conducts for-cause audits and in conjunction with the AVPR drafts the fact finding report or corrective action plan.

Education Coordinator: The Education Coordinator also accepts allegations/reports of non-compliance, and refers them to the Sr. RCS. The Education Coordinator works with the RCS to develop and administer required or optional educational programs as specified in the Corrective Action Plan.