

Wayne State University Human Investigation Committee	
SUBJECT	Identifying, Defining, and Managing Non-compliance in Human Research
Section	
Form Date	09-06-06
Approvals	Office of General Counsel 2/12/07, Steering Committee 03/12/07, Administrative Approval 03/26/07

Background

Non-compliance occurs when research involving human participants is conducted in a manner that disregards or violates federal regulations, ethical standards, and Wayne State University (WSU) and/or Institutional Review Board (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); VHA Handbook 1200.5 7]).

Non-compliance applies to investigators, research team members, the Institutional Review Board (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 Assistant Vice President for Research.

Definitions

Allegation - An assertion made by a party that must be proved or 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 - repeated pattern of non-compliance by an individual investigator or research staff member either on a single protocol or multiple protocols

Non-compliance - The failure to comply with regulations, requirements, or determinations of the IRB and federal regulations.

Serious non-compliance – is non-compliance that involves 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

Examples of noncompliant 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 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

Human Investigation Committee (HIC) Policy

Reporting Allegations to the IRB

Non-compliance may be reported to the IRB by an investigator or his/her designee. Non compliance or potential non-compliance may 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.

Allegations of non-compliance may be reported to the HIC Process Improvement/Compliance Coordinator (313-577-2901) or the Assistant Vice President for Research (AVPR) (313-577-9064).

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 3 days** of the investigator becoming aware. (See HIC Policy/Procedure: "Adverse Reactions/Unexpected Events.").

- 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 initial 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

HIC Procedures

Allegations

The allegation is received by the HIC Office or the Assistant Vice President for Research. A request is made, to the person making the allegations, to submit the report in writing on an Adverse Reaction/Unexpected Events (AR/UE) form to the Process Improvement/Compliance Coordinator.

- **Take Immediate action, if necessary, to protect participants** (e.g. suspension, termination) and an initial report is sent to the appropriate University officials, sponsor(s) and agencies.
- If no immediate risk is confirmed, the HIC Chair, IRB Chair, or AVPR will initiate an evaluation. If, in the opinion of the HIC Chair, AVPR, or IRB Committee the allegation is not credible, the inquiry ends.

Substantiated Non-compliance

If it is determined that non-compliance has occurred, an audit by the Process Improvement/Compliance Coordinator is conducted. (See HIC Policy/Procedure: "For-Cause Audit.") In issues of scientific misconduct, an inquiry is conducted by the AVPR, this process is separate from the IRB actions.

If non-compliance is determined to be neither serious nor continuing, a corrective action plan is initiated which usually involves required remedial education program with the HIC Education Coordinator or immediate remediation (i.e., signature of PI on submissions, missing documentation in submissions).

If serious or continuing non-compliance is determined, a for-cause audit is conducted, and a report is generated and distributed to the PI, HIC Chair, AVPR, and Steering Committee.

The convened HIC Steering Committee makes the determination regarding the seriousness of the non-compliance and if any further actions are required. (e.g., suspension, termination, continued administrative suspension, and/or a corrective action plan).

The PI may submit a response to the audit report in writing or may request to speak to the HIC Steering Committee. He/she may be accompanied by a representative from the faculty, legal counsel, or his/her department.

Any written response from the PI is presented to the AVPR, HIC Chair, and the HIC Steering Committee for their review and adjudication.

Reporting of Non-compliance:

The final non-compliance report is written by the HIC Process Improvement/Compliance Coordinator or his/her designee and approved by the convened HIC Steering Committee and the AVPR. (See HIC Policy/Procedure: Reporting of Unanticipated Problems, Terminations, Suspensions, and Serious and Continuing Non-compliance.)

The final report is distributed to the following:

- AVPR
- Appropriate institutional officials (Chairs, Deans, Directors)
- OHRP or other regulatory officials
- VAMC Research and Development Office (for VA research protocols)
- Privacy Officer at all involved institutions
- Sponsor, if appropriate

.Possible Range of Actions

The actions taken to remedy non-compliance vary and depend on the nature and seriousness of the non-compliance. The IRB or AVPR may do any of the following: take no action; request a protocol and/or consent form modification; require that all participants be re-consented; require that previously enrolled participants be informed of any changes; require more frequent review of the research conduct; require observation of the informed consent process; require additional training of the research team; place an administrative hold on the protocol until review by the HIC Steering Committee has been completed; suspend or terminate the research; and/or refer to other organizational entities (e.g., dean, legal counsel, etc).

There are additional requirements when a protocol is suspended and/or terminated. Please see HIC Policy/Procedure: "Suspension and Termination of Research Protocols".

Roles and Responsibilities

Vice President for Research (VPR)

The Vice President for Research is the Institutional 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, especially if the issues concern misconduct on the part of the IRB. The VPR will then determine the appropriate venue for an investigation of assertions of misconduct.

Assistant 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, then the AVPR, in conjunction with the HIC Chair or designee and, possibly the HIC Steering Committee, 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 Process Improvement/Compliance Coordinator. 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 determine 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.

HIC Steering Committee

Any of the IRB committees may initiate or review allegations of non-compliance. The HIC Steering Committee 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. The HIC Steering Committee also reviews and approves the final report of the investigative findings and the corrective action plan before distribution to the appropriate Institutional officials, agencies and sponsor.

Process Improvement/Compliance Coordinator

It is the responsibility of the Process Improvement /Compliance Coordinator to accept allegations/reports of non-compliance, make a determination on the validity of the claim; and if serious or continuing non-compliance is suspected, transfers the allegation/report to either the HIC Chair or AVPR. The Process Improvement/Compliance Coordinator also conducts for-cause audits and in conjunction with the AVPR, drafts the fact finding report or corrective action plan which is then distributed to the Steering Committee.

Education Coordinator

The Education Coordinator also accepts allegations/reports of non-compliance, and refers them to the Process Improvement/Compliance Coordinator. The Education Coordinator works with the Process Improvement/Compliance Coordinator to develop and administer required or optional educational programs as specified in the correction action plan.

Contact Numbers:

Allegations/reports of non-compliance may be reported to:

- Process Improvement and Compliance Coordinator- (313-577-2901)
- Education Coordinator-(313-577-9534)
- Assistant Vice President for Research Compliance-(313-577-9064)
- Vice President for Research- (313-577-9600)