

Non-compliance with Human Subjects Research Regulations

J. Bruce Smith, MD, CIP

November 2014 Continuing Education for IRB
Members

Definitions

(1) Allegation of non-compliance is an unproven assertion or report

(2) Non-compliance is a violation of any federal, state, or local regulation or any university or IRB policy that governs human research – may be relatively inconsequential or

(a) Serious

Non-compliance that may affect subject safety, increase risks to subjects, affect the integrity of the data, violate the rights and welfare of research participants, or affect a subjects' willingness to continue in a research study.

(b) Continuing

A pattern of non-compliance that indicates a lack of understanding of the regulations or ethical requirements that may affect the rights and welfare of participants. Pattern and frequency of non-compliance are assessed by the number of incidents occurring during the course of a protocol and whether the same noncompliant action was repeated or many different events occurred.

Examples of non-compliance with human subjects regulations

Investigator non-compliance

- Performing human subject research without first obtaining IRB approval or an IRB declaration of exemption
- Deviating from or violating the provisions of an IRB-approved protocol
- Enrollment of participants in a lapsed study
- A publication about human subjects research for which there is not an IRB approval
- Audit report indicating non-compliance

IRB non-compliance

- Failure of the IRB to document in its meeting minutes or supporting documents protocol-specific findings supporting the IRB's determinations for waiver or alteration of the consent process
- Failure of the IRB to document that the study is consistent with regulations specific to research involving pregnant women, fetuses and neonates, prisoners, or children
- Discrepancy between the sponsor contract and the consent document regarding payment for study participation and payment in the event of a research-related injury

Who can submit an allegation of IRB non-compliance?

- A research subject
 - By calling the DHSP using the number provided in the consent form
 - Via the TJU compliance hotline
- A TJU employee
 - By calling the DHSP
 - By calling the TJU Hotline
 - By calling the University Ombudsman
- The IRB - based on findings at continuing review, information provided by the sponsor, or an internal, federal, or sponsor audit
- An investigator may also self-report

IRB response to allegations of IRB non-compliance

- Not serious or continuing
 - usually reported via OHR-20, or
 - found during DHSP QA/QI audit
- Director and Associate Director meet with investigator and research team to discuss corrective action plan (CAP)
- Report and CAP are kept on file in the DHSP

Serious or continuing non-compliance

- Allegation reviewed by a “screening committee” within 24 hours of receipt of allegation (Director, Associate Director, chair of IRB that provided initial review of study)
- Screening Committee determines
 - if immediate suspension of study enrollment is necessary
 - whether other studies with same PI should be suspended
 - any other action that may be required to eliminate possible risk to subjects

If study enrollment is suspended

- Letter of suspension sent to PI with copies to DHSP Director and Associate Director, Co-investigators, PI's Department Chair, ORA (if sponsored study), the relevant IRB chair, Associate Vice Provost for Research Support
 - If federally funded, OHRP must be notified
 - Relevant IRB notified at next convened meeting
- Letter states requirement for enrollment suspension and that PI must notify enrolled subjects of any increased risk (using IRB approved telephone script) followed by an IRB-approved letter.

Criteria for further investigation

- Screening Committee determines if allegation requires formal investigation
- If the incident appears to be non-serious and/or not of a continuing nature, the Screening Committee will resolve the issue. Screening Committee decisions will be communicated to all relevant personnel and agencies
- Screening Committee findings are communicated to the next convened meeting of the relevant IRB which votes to approve or not approve the recommendations, or asks for further information or investigation

Investigation of serious and continuing non-compliance

- Director of DHSP appoints a Non-Compliance Sub-Committee
 - Chair of IRB that originally approved study
 - A member of that IRB
 - Director and/or Associate Director, DHSP
 - Member of the Office of University Counsel
- A QI/QA audit of the study file will be performed by the DHSP
- Subcommittee may interview the PI or other relevant study personnel (they may have an attorney or advisor present but that person may not participate in the proceedings)
- Subcommittee makes determination within 60 days and reports recommendations to the IRB

Possible recommendations may include

- Dismissal if allegation is determined to be unjustified or unsubstantiated
- Due diligence where violation is administrative in nature (record keeping issues, etc.)
- Corrective actions of various sorts
- Notification of current participants if information may affect their willingness to continue in study or if re-consent is required
- Referral to Vice Provost for Research if investigation finds possible research misconduct (falsifying data, plagiarism, fabrication of data)

Dissemination of findings

- When decision becomes final, the IRB will release written findings to
 - Appropriate University Officials including the President of the University, the Dean of the individuals' College, University Counsel, Vice Provost for Research, individuals' Department Chair
 - OHRP - if federally funded study
 - FDA - if FDA-regulated study and sponsor and FDA have not been notified via other channels