

17.0 Institutional Responsibilities

17.1 Investigating Reports of Non-compliance

I. Definitions

A. Non-compliance

1. Failure on the part of a PI or any member of a research team to adhere to the terms of HSC approval, or
2. Failure to abide by applicable laws or regulations or KUMC policies, including failure to submit research for HSC review and approval prior to implementing the research.

B. Minor non-compliance is non-compliance that does not impact subjects' rights and welfare, safety of subjects, the willingness of subjects to participate in the study, or the integrity of the study data. Examples of minor non-compliance include, but are not limited to, isolated incidences of the following:

1. Missing original signed and dated consent form (only a photocopy is available)
2. Failure to follow the approved study procedure that, in the opinion of the IRB, does not affect subject safety or data integrity:
 - a. Study procedure conducted out of sequence
 - b. Omitting an approved portion of the protocol
 - c. Study visit conducted outside the required timeframe, if no risk to the subject is incurred
 - d. Failure of the subject to return study medication

C. Serious non-compliance is a failure to comply with laws or regulations, KUMC policies, or the requirements or determinations of the HSC when that failure increases risk of harm to participants, or adversely affects the rights and welfare of the participants. A single instance of non-compliance may be serious. Any failure to comply is serious if it either actually, or potentially, increases risk of harm or adversely affects the rights and welfare of the participants.

D. Continuing non-compliance is a pattern of reports of minor non-compliance that, if unaddressed, may compromise the integrity of the research or may result in harm to participants. The pattern may reflect a lack of knowledge on the part of the investigator or a lack of commitment by the investigator and study team to human subjects protection. .

E. Report of non-compliance is a notification to the HSC Office, HSC members, the HRPP Director or the Institutional Official (IO). Reports of non-compliance may come from a variety of sources, including:

1. Self report from the research team, through a Problem Report filed with HSC.
2. Discovery by the HSC during ongoing review (e.g., reviews of adverse events or continuing review)
3. Discovery during an internal audit
4. Discovery during monitoring or audit by an external entity

5. Allegation from a professional colleague
6. Complaint from a research subject, subjects' family or member of public

II. Initial Evaluation

- A. When a report or allegation of non-compliance is received, the HSC Office is notified. The IRB Administrator, or experienced staff member evaluates the report. An experienced staff member is one who (a) has worked with the HSC for at least two years, or (b) has worked with the HSC for one year and has designation as a Certified IRB Professional. The IRB Administrator or experienced staff member evaluates whether the report represents an imminent threat of harm to subjects or others.
 1. If there is an indication of imminent threat of harm, the IRB Administrator notifies the HSC Chair. The Chair determines whether immediate suspension is warranted. The Chair may consult with the IO and HRPP Director. In the Chair's absence, the IO or HRPP Director can suspend a study on an urgent basis.
 2. When a study is suspended, the Chair or HRPP Director notifies the IO. The Chair or HRPP Director notifies the investigator by phone call and in writing.
 3. The IO notifies federal authorities of the suspension. The IO files a preliminary report within five working days. The report is filed as described below in section IV.B.
 4. The Chair works with investigator to provide for continued safety and welfare for subjects. Depending on the nature of the non-compliance and the subjects' best interests, they may be continued on an investigational drug, transferred to clinical care, placed under additional safety monitoring, or provided with other protective measures.
 5. When a study is suspended, the HRPP Director coordinates an investigation to gather further information, at the direction of the Chair and the IO.
 6. The HSC is notified of and reviews the suspension at its next meeting.
- B. If the initial evaluation does not indicate imminent threat of harm, the IRB Administrator or an experienced staff member evaluates the report to determine whether it is minor non-compliance.
 1. If the report meets the definition of minor non-compliance, the report is evaluated by the HSC staff. If it is minor, HSC staff examines past reports to see if there is a pattern of behavior that may indicate continuing non-compliance. If the staff determines that a continuing non-compliance investigation is not warranted, the staff develops a corrective action plan that is communicated to the investigator to prevent similar cases of non-compliance from occurring in the future. If a corrective action plan is not warranted,

the report is placed in the file with no further action. The report is marked with a yellow tab to easily identify similar reports in the file.

2. If the report is not minor non-compliance, or if the report may indicate a pattern of continuing non-compliance, it is referred to the HSC Chair before review by the convened HSC.
- C. The Chair evaluates the report to determine whether additional information is needed prior to HSC review. If additional information is needed, the HRPP Director coordinates the investigation. Otherwise, the report is placed on the agenda of the next HSC meeting.

III. Evaluation by the Convened Human Subjects Committee

- A. All HSC members receive documentation associated with the initial report, any additional documentation generated by the investigation, and a copy of the current consent form. A primary reviewer is assigned as described in SOP 16.5. Primary reviewers may request copies of the study protocol or any other relevant materials in the HSC files. All members have access to the complete file, which is maintained in the HSC office. During the meeting, the primary reviewer presents the report to the committee, makes an initial recommendation and begins the discussion.
- B. After discussion, the HSC may defer the review in order to obtain more information from the investigator or additional investigation by the HRPP director.
- C. If the review is not deferred, the HSC determines whether non-compliance is serious or continuing. The determination is documented in the meeting minutes. Upon finding that the event represents serious or continuing non-compliance, the HSC takes one or more of the following actions:
1. Require additional training of the investigator or research team;
 2. Require additional supervision of the investigator;
 3. Require modifications to the study protocol;
 4. Require modifications to the informed consent document;
 5. Require additional information be provided to past subjects;
 6. Require notification of current subjects;
 7. Require that current subjects re-consent to participation;
 8. Increase the frequency of continuing review;
 9. Monitor the conduct of the research;
 10. Monitor the consent process;
 11. Suspend the study pending further information;
 12. Terminate the study.
- D. If the convened HSC suspends or terminated the study, the HSC will work with investigator to provide for continued safety and welfare for subjects. Depending on the nature of the non-compliance and the subjects' best interests, they may be continued on an investigational drug, transferred to clinical care, placed under additional safety monitoring, or provided with other protective measures.

- E. If the HSC directs more than minor modifications to the protocol or consent form to address the non-compliance, the changes are reviewed by the convened committee. Minor changes may be reviewed by the HSC Chair or experienced member, as described in SOP 5.2
 - F. If the HSC determines the event is neither serious nor continuing non-compliance, the report is accepted with no further action.
- IV. Action by the IO
- A. When the HSC suspends or terminates a study, the IO may take additional actions, in consultation with the department chair and university leadership. Additional actions may include:
 - 1. Limiting the research of the investigator (by number of active protocols or number of active participants)
 - 2. Withdraw or limit the privileges of the investigator to conduct human research
 - 3. Refer the matter to other organizational entities (such as General Counsel, Risk Management, Academic Affairs)
 - B. When the HSC determines serious or continuing non-compliance, suspends or terminates a study, the IO files a letter of notification to federal authorities and others. The letter is drafted by the HRPP Director, with final approval by the IO. The letter of notification will include
 - 1. Name of the institution
 - 2. Title of the research project and/or grant proposal in which the noncompliance occurred;
 - 3. Name of the principal investigator on the protocol;
 - 4. The HSC number assigned to the protocol;
 - 5. A detailed description of the noncompliance; and
 - 6. Actions the institution is taking or plans to take to address the noncompliance (including those actions described above in III.C.)
 - C. The notification will be sent, as applicable, to:
 - 1. OHRP
 - 2. FDA, if the study is subject to FDA regulations
 - 3. Other federal agencies (if applicable) that are conducting or funding the study
 - 4. Sponsor, if the study is sponsored
 - 5. Principal investigator
 - 6. Department Chair, Center Director or Dean
 - 7. The HSC \
 - D. A copy of the letter is placed in the HSC file.

17.2 Quality Assurance and Quality Improvement for the HRPP

- I. The Institutional Official (IO) directs the HRPP Director and HRPP staff to ensure continuous improvement of the HRPP. Activities include both quality assurance and quality improvement.
- II. Quality assurance activities are designed to assess whether the HRPP policies and procedures are followed by HRPP staff, investigators and organizational units. Activities include:
 - A. Regular meetings of HSC office staff to discuss efficient workflow, accurate administrative review and collaboration with other units.
 - B. Brief presentations at HSC meetings on federal requirements, KUMC policies or current topics in human research protections.
 - C. Routine internal audits of HSC files by staff members, to ensure that all submissions were reviewed, all reviews were documented, and HSC requirements were fulfilled.
 - D. Survey of selected studies at the time of continuing review, to secure copies of consent forms and confirm that informed consent was obtained and documented as required.
 - E. Requirement that investigators notify the HSC if the sponsor's clinical trial monitoring report indicates findings that could impact the safety and welfare of subjects or alter the HSC's approval of the study.
 - F. Collaboration with the KUMC Research Institute to obtain a review of regulatory documents and case report forms for greater-than-minimal-risk studies that are not otherwise being monitored
 - G. For-cause audits as directed by the HSC or the IO.
 - H. Promotion of investigator's self-assessment activities, through the use of tools developed by the KUMC Research Institute.
- III. Quality improvement activities are designed to evaluate whether the institution is adequately protecting human subjects. These activities aim to enhance investigators' understanding of regulatory requirements, improve the efficiency and effectiveness of HSC reviews, ensure compliance with regulations and provide information about the HRPP to research volunteers and the public. On an ongoing basis, the HRPP Director keeps the IO apprised of:
 - A. Adequacy of resources to support the HRPP. Analysis includes the scope, volume and nature of research proposals. Resources may include physical, financial and staff resources, expertise of HSC members and adequacy of the number of IRBs.
 - B. Coordination between the components of the HRPP, to harmonize requirements and review processes
 - C. Continual assessment of the adequacy of HRPP policies, forms and review processes to meet current and pending regulatory requirements
 - D. Analysis of common compliance and review problems
 - E. Provision of the Research Compliance Hotline for investigators and other KUMC personnel to report concerns, ask questions and make suggestions

- F. Individual and group consultations, educational programs and web resources for investigators
 - G. Periodic survey of investigators on ways to improve the HRPP
 - H. Analysis of timeframes from submission to final approval.
 - I. Tracking of improvements made to the HRPP and analysis of their impact
 - J. Development and improvement of educational materials about the HRPP for research volunteers and the public.
- IV. At least annually, the IO, HRPP Director and IRB Administrator review the performance of HSC members. The evaluation is based upon the duties outlined in SOP 1.6. The evaluation is augmented by a periodic survey of HSC members related to needs for continuing education, committee functioning, committee support, adequate expertise, and a general self-assessment.
- A. Based upon performance evaluations, adjustments are made to the HSC membership and education of HSC members, to meet regulatory and organizational requirements.
 - B. The performance of HSC Chairs is evaluated collaboratively, between the IO, the Chairs, and the Research Advisory Council, as needed.

17.3 Responding to Concerns and Suggestions from Investigators

- I. Investigators and other research personnel may obtain answers to questions, express concerns, or convey suggestions regarding the HRPP by utilizing: the HRPP website, Compliance Helpline, consultation with the IO and consultation with HRPP staff.
- II. Any request for reconsideration of an HSC decision is handled in accordance with SOP 17.4

17.4 Request for Re-consideration of an HSC Decision

- I. When the HSC disapproves a proposed study, suspends or terminates an ongoing study for cause, the written notification to the investigator is accompanied by reasons for the decision.
- II. If an investigator disagrees with an HSC decision, he/she may request a re-consideration. The request must be accompanied by a written summary, outlining in detail the rationale for re-consideration.
- III. The summary will be distributed to all HSC members, and the protocol will be scheduled for re-consideration at the next available meeting. The investigator may attend the meeting.

- IV. After discussion of the protocol and rationale for re-consideration, the HSC will formally re-vote. A majority vote of the members present will determine the decision.
- V. If the original decision is upheld, the protocol will not be reviewed again unless significant changes are made.
- VI. Decisions by the HSC to disapprove, suspend or terminate a project may not be overruled by another entity or institutional official.

References:

45 CFR 46.112

21 CFR 56.112