



GUIDELINE FOR RSRB REVIEW OF ALLEGATIONS OF NON-COMPLIANCE

According to Policy 802 Non-Compliance in Human Subjects Research, it is the responsibility of any member of the human research protection program (HRPP), or any individual or organization within the University of Rochester who suspects possible non-compliance to report such an occurrence to the RSRB. All institutional members, research subjects and others are encouraged to report any potential, observed, suspected, or apparent non-compliance. Reports of non-compliance may also arise from calls to the University of Rochester Medical Center Integrity Hotline (585-756-8888), the confidential institutional number to call with any concerns about improper, unethical or non-compliant activities; as a result of internal or external audits; as a result of report through the OHSP Feedback website; as a result of RSRB review or discussion with chairs, supervisors, or colleagues; or through other avenues. Regardless of how they arise, all allegations of non-compliance must be referred to the RSRB.

A. Initial Notification of an Allegation of Non-Compliance

Allegations of non-compliance may be initiated by a number of mechanisms, as described below. Note that validated allegations of non-compliance received by the RSRB, when the RSRB is the relying IRB, will be referred to the reviewing IRB for further review and assessment.

1. Continuing Review:

The RSRB may learn of potential non-compliance through its continuing review of ongoing research. Examples of possible non-compliance based upon the items Investigators must address during continuing review:

- Date the first subject was enrolled precedes the RSRB approval date.
- Accrual exceeds the number requested by the Investigator.
- Copy of the last signed consent was obtained by individuals not RSRB approved to obtain consent.
- Copy of the last signed consent is the incorrect version (e.g., an expired consent was used, an amended consent was not used).
- Copy of the last signed consent does not include all applicable dates of signature (e.g., the subject and/or person obtaining consent), or the year of the dated signature is incorrect.
- Copy of the last signed consent containing optional procedures to be confirmed (e.g., by checking a box) were not completed.

2. Quality Improvement (QI) Review by Office for Human Subject Protection (OHSP):

As part of its activities, the OHSP conducts routine and for cause QI reviews of research studies conducted or supported by employees or agents of the University of Rochester. When the RSRB is the reviewing IRB, OHSP provides all final reports to the convened board for further review and assessment. When the RSRB is the relying IRB, reports will be forwarded to the reviewing IRB, as

applicable. These reports may reveal area(s) of non-compliance (e.g., protocol deviations, unqualified personnel conducting study procedures, repeated cases of not following RSRB policies or guidelines). The convened board will make an assessment regarding any reported non-compliance as applicable.

3. QI Review or Audit by Department or Organization:

An internal University department (e.g., University Audit) or external organization may conduct QI reviews or audits as per individual department or organizational policies and procedures. The RSRB may receive documentation of final reports for further review and assessment regarding any allegations of non-compliance as applicable.

4. Direct Report to the RSRB:

An allegation of non-compliance may be reported directly to the RSRB office by any of the following individuals or organizations:

- Any individual, including a subject, subject's family member or representative, or a UR employee (who may or may not be associated with the research team);
- OHSP 'Feedback' Website
 - A mechanism via the OHSP website for someone to provide feedback, either anonymously or not, that will be emailed directly to the OHSP Director who will forward the communication as needed.
- The University of Rochester (UR) Office of Compliance
 - Concerns regarding non-compliance that arise during a compliance office investigation involving an employee who may also be involved in a UR research study will be forwarded to the RSRB Director or OHSP Director.
 - The UR Office of Compliance maintains a confidential hot line, through which any individual may report a concern. Concerns regarding research are forwarded to the RSRB Director or OHSP Director, who will verify that the concern involves a UR research study. If so, the concerns are addressed as described in B1 below.
- Organizations including funding agencies (e.g., NIH) and oversight agencies (e.g., OHRP and FDA);

5. Other Mechanism of Notice:

If an allegation of non-compliance is reported by a mechanism other than the categories indicated above, the RSRB Chair, RSRB Director and OHSP Director, in consultation with Office of Counsel as necessary, will determine the appropriate process to follow for evaluation and review of the report.

B. Managing Allegations of Non-Compliance

There is a two-step process for handling allegations of non-compliance. The first is to determine whether reports of non-compliance contain enough information to determine whether the report is sufficiently credible and specific so that potential evidence of non-compliance may be identified and acted upon. The second is to evaluate whether the allegation is valid (i.e., non-compliance occurred).

If an allegation of non-compliance cannot be investigated adequately by the RSRB, or if additional information is needed to ascertain the nature/extent of the allegation, the Chair or convened board may direct additional investigation (e.g., through an OHSP QI review, assistance by the department Chair, or intervention by Office of Counsel) to determine the validity of the allegation.

1. Handling Initial Allegations of Non-Compliance

- a) With the exception of reports of non-compliance arising from OHSP QI reviews (see description in ‘b’ below) and reports arising from a UR Coordinating Center (see description in ‘c’ below), all initial allegations of non-compliance received by the RSRB office are reviewed by the RSRB Chair and RSRB Specialist (in consultation with the RSRB Director or designee, as necessary) to determine whether the allegation has a basis in fact. Additional information or clarification may be requested during this review process.
 - If the RSRB Chair determines that the allegation does not have a basis in fact, the determination is documented within the mechanism the event was originally reported (e.g., modification, continuing review, report of new information) and no further action is taken. The matter may be referred to other institutional entities for evaluation and management as applicable.
 - If the RSRB Chair determines that the allegation has a basis in fact, the process under *Handling Determinations of Non-Compliance* will be followed.
- b) When the RSRB is the Reviewing IRB, OHSP provides all final QI reports to the convened board for further review and assessment. The convened board will make a determination about whether or not the report contains non-compliance.
 - If non-compliance is identified within the QI report and it requires no further action (i.e., corrective action plan is appropriate), the Investigator is notified that the report was acknowledged.
 - If there is insufficient information to determine whether identified non-compliance within the QI report may be serious or continuing, additional information will be requested as needed.
 - If it is determined that the non-compliance is neither serious nor continuing, the process under *Handling Non-Compliance Determined as Neither Serious or Continuing* is followed.
 - If it is determined that the non-compliance is potentially serious and/or continuing, the process under *Handling Non-Compliance Determined as Potentially Serious or Continuing* is followed.

Note: If during a QI review, the QI reviewer has concerns about subject safety, the information will be forwarded directly to the RSRB Chair, OHSP Director and RSRB Director and steps will be taken to suspend the research, if necessary, before the report is finalized and an investigation is initiated.

- c) Reports of non-compliance when the UR is the Coordinating Center will reviewed by the RSRB. When the non-compliance relates to the activities of the Coordinating Center, this guideline will be followed. When the non-compliance relates to activities of the enrolling site, the RSRB will review for acknowledgment. It is the responsibility of the enrolling sites' reviewing IRB to make review determinations for the event occurring at the respective site.
- d) When the RSRB is the relying IRB, reports will be forwarded to the reviewing IRB, as applicable, to make review determinations.

2. Handling Determinations of Non-Compliance

- a) The RSRB Chair will review all non-compliance with a basis in fact (in consultation with the RSRB Specialist and RSRB Director, or designee, as necessary) and evaluate the report to determine whether the non-compliance potentially represents serious and/or continuing non-compliance. Note that nothing shall prohibit an Investigator from voluntarily suspending study enrollment or any research activity (e.g., lab analysis or experimental treatment) during any part of the review process if the Investigator deems appropriate (see *Policy 801 and the Guideline for Reportable Events*).
 - If it is determined that the non-compliance is neither serious nor continuing, the process under *Handling Non-Compliance Determined as Neither Serious or Continuing* is followed.
 - If it is determined that the non-compliance is potentially serious and/or continuing, the process under *Handling Non-Compliance Determined as Potentially Serious or Continuing* is followed.

Examples of Non-Compliance:

- Over-enrollment of subjects
- Minor protocol deviations of protocol procedures, such as out of window visits
- Use of a translated consent without RSRB approval
- Engagement of sites or personnel not approved by the RSRB
- Consent issues (no consent, no signature, wrong version)
- Enrolling subjects who were not eligible
- Drug dosing issue or mis-randomization
- More radiation dosed than expected
- Not performing safety assessments
- Not following URMC clinical procedures
- Not following approved recruitment procedures

3. Handling Non-Compliance Determined as Neither Serious or Continuing

- a) If the non-compliance is considered to be neither serious nor continuing, this determination will be documented where the event was originally reported (i.e., continuing review, modification, report of new information). The RSRB Chair and RSRB Specialist (in consultation with the RSRB Director, or designee, as necessary) will determine whether any

further corrective actions are needed. If a QI report or other allegation of non-compliance was referred to a convened meeting, the board will make the determination regarding corrective actions. Any action item will be communicated to the Investigator or person(s) involved in the allegation, and may include a statement with a cautionary reminder that any additional reports of non-compliance may result in opening an investigation of serious and/or continuing non-compliance. Action items may include, but are not limited to, any of the following:

- Notification to current subjects (when such information may relate to their willingness to continue to take part in the research);
- Modification of the protocol (i.e., amending the previously approved protocol);
- Modification of the information disclosed during the consent process;
- Providing additional information to former subjects;
- Requiring current subjects to re-consent to participation;
- Modification of the continuing review schedule;
- Monitoring of the research;
- Monitoring of the consent;
- Obtaining more information from the Investigator pending a final decision;
- Remedial education of the Investigator (and study team as applicable);

NOTE: The Chair may choose to refer the report of non-compliance to the convened board to determine whether the non-compliance is serious or continuing, in which case the procedures in *Handling Non-Compliance Determined as Potentially Serious or Continuing* will be followed.

- b) The RSRB (inclusive of the Chair, Specialist, RSRB Director, convened board, or designee, as necessary) will work with the Investigator to implement any requested corrective and preventative action (CAPA) plan and will monitor the completion of all required corrective actions. If the RSRB is unable to work with the Investigator to implement the requested corrective actions, the matter may be considered as potentially continuing non-compliance and the procedures in *Handling Non-Compliance Determined as Potentially Serious or Continuing* will be followed.

4. Handling Non-Compliance Determined as Potentially Serious or Continuing

Definition and Examples of Possible Serious Non-Compliance:

- Definition:
 - Non-compliance that, in the judgment of the convened board, results in any of the following:
 - a) an increased risk to subjects or others,
 - b) adversely affects the rights, welfare and safety of the research subjects,
 - c) adversely affects the scientific integrity of the study. Non-compliance may also be deemed serious when it involves fraud and/or scientific misconduct, even in research posing minimal risk to subjects.

- Examples:
 - An act or omission taken by the Investigator that any other reasonable Investigator would have foreseen as compromising the rights and welfare of the subjects (e.g., PI allowing unqualified personnel to perform procedures/consent not approved by the RSRB);
 - Conducting research without IRB approval;
 - Enrollment of subjects who do not meet eligibility criteria.

Definition and Example of Possible Continuing Non-Compliance:

- Definition:
 - Non-compliance that, in the judgment of the convened board, persists when there is:
 - a) evaluation by the convened board,
 - b) notice to the Investigator,
 - c) prior submission of a corrective action plan(s), and
 - d) lack of evidence of effective efforts towards resolution by the Investigator.

These events may or may not result in increased risk to subjects and may be due to a variety of factors. The non-compliance might imply that an Investigator is either unwilling or unable to develop and apply successful corrective measures.

- Examples:
 - The continuation of actions or omissions by an Investigator after identification by RSRB and implementation of non-compliance corrections, thus indicating a deficiency in the ability or willingness of an Investigator to comply with Federal regulations, local policy, or RSRB requirements.
 - Persistent lapse in continuing approval of research for active studies, which may result in an increased risk to subjects.

a) Referral to Board: Some reports of non-compliance are referred to the convened board after the RSRB Chair, Specialist and RSRB Director have determined that the event may represent serious or continuing non-compliance, or to request that the board evaluate whether an event may represent serious or continuing non-compliance. If the board agrees that the non-compliance may potentially represent serious or continuing non-compliance, the board will open an investigation to determine the validity and seriousness of the non-compliance. The investigation will consist of a team of RSRB office staff, board members, OHSP staff (QI) and other University personnel (e.g., legal counsel), as necessary, to further investigate the potential non-compliance. The Investigation of Serious or Continuing Non-Compliance Summary Report will be used to ensure all steps of the investigation and convened board review process are completed.

- NOTE: If a particular issue poses an immediate threat to the safety of subjects, the RSRB Chair may suspend the study prior to notice to and review by the convened board (Policy 402 RSRB Meetings).

b) Notice to Investigator, Opportunity to Respond: Prior to reviewing and acting upon the allegation, the board should confirm that the individual(s) under review were: a) informed in writing of the materials which the board would be reviewing; b) informed of the scheduled convened board meeting date, and c) provided an opportunity to attend the convened board

meeting to make an oral statement, address any questions from board members, or to submit a written response for the board's consideration. Individual(s) under review for potential serious or continuing non-compliance should be provided sufficient information from the RSRB regarding the items which may represent serious or continuing non-compliance in order to understand the issue(s) and have the opportunity to directly address the concern(s). In the case of potential continuing non-compliance, the individual(s) under review should also be provided details regarding the items which may elevate the reported events to continuing non-compliance.

- c) **Compiling Documentation:** As the investigation is being conducted, information will be compiled by the RSRB into a summary packet, including a summary of any prior events of non-compliance for the Investigator (or other study personnel) leading up to the event under investigation. The Investigation of Serious or Continuing Non-Compliance Summary Report will contain information about the non-compliance being evaluated (e.g., a brief description of the investigation, the basis for recommending that non-compliance is or is not serious and/or continuing and any recommended corrective actions, communications related to the investigation, supporting documentation).
- d) **Consultation with Office of Counsel:** The Summary Report and supporting documentation will be circulated for internal purposes to individual(s) investigating the non-compliance, including consultation with the designated legal liaison. In all cases, this consultation with the legal liaison will take place prior to the presentation of the case investigation to the board. The purpose will be to review the records for legal/procedural purposes. The allegation is then referred back to a convened board for review and action.
- e) **Board Meeting:** A primary reviewer will be assigned to present the non-compliance that is referred to the convened board for review and action. All relevant materials regarding the allegation will be provided to the board members in advance of the convened meeting. These materials (e.g., written reports, complaints or concerns, copies of email, copies of notes to the file made by the Chair/office staff, response provided by the Investigator) will include information resulting from the following, as applicable:
 - any prior events of non-compliance for the Investigator or other study personnel
 - events leading up to the report under investigation
 - initial review of the reported non-compliance by the convened board
 - convened board opening the investigation .

In addition, all study materials (e.g., protocol, consent forms) in the online review system are accessible to all board members. The board may request to hear from or ask questions of individuals involved in the non-compliance or the investigation of the non-compliance. Other individuals familiar with the case of non-compliance may be asked to attend the convened meeting as consultants (e.g., the OHSP QI reviewer or University legal counsel). If attending the board meeting, the individual(s) under investigation will present their response to the convened board. Once the response has been presented and questions from the board answered, the individual(s) involved in the non-compliance will be excused from the meeting.

5. Actions of the Convened Board Regarding Review of Potential Serious or Continuing Non-Compliance

The convened board will confirm by vote whether the non-compliance is serious and/or continuing.

- a) When an investigation is complete and the convened board does not find that the non-compliance is serious or continuing, the process for *Handling Non-Compliance Determined as Neither Serious or Continuing* is followed.
- b) When an investigation is complete and the convened board finds that the non-compliance is serious or continuing, the board will specify and communicate to the Investigator or person(s) under investigation, (i) the finding(s) of the Board, and (ii) any required corrective actions which may include the following in addition to those actions listed under section 3a :
 - Suspension of the research (see *Policy 402 and Guideline for Institutional and Regulatory Reporting of Suspension, Termination, Non-Compliance and UPIRTSO*)
 - Termination of the research (see *Policy 402 and Guideline for Institutional and Regulatory Reporting of Suspension, Termination, Non-Compliance and UPIRTSO*)
 - Restriction of data used for analysis and/or publication;
 - Restriction of the Investigator's current research approvals;
 - Referral to the proper University entities for non-compliance that raises academic discipline issues (e.g., scientific misconduct).
 - Referral to other organizational entities (e.g., OHSP, University Audit, UR Office of Counsel, the privacy office)

The RSRB (inclusive of the Chair, Specialist, RSRB Director, convened board, or designee, as necessary) will work with the Investigator or person(s) involved in the investigation to implement any requested corrective and preventative action plan and will monitor the completion of all required corrective actions.

C. Process for Reporting Board Determinations of Serious or Continuing Non-Compliance

In cases where the convened Board determines that serious or continuing non-compliance has occurred, the IO or designee, with assistance of the RSRB Director or designee and an RSRB Chair, will report the institution's determination and findings to all appropriate entities according to *Policy 403 Notification of RSRB Determinations and the Guideline for Institutional and Regulatory Reporting of Suspension, Termination, Non-Compliance and UPIRTSO*.