

Cornell University
Office of Research Integrity and Assurance
Human Research Participant Protection Program

SOP 7: REPORTING UNANTICIPATED PROBLEMS, NONCOMPLIANCE, SUSPENSIONS, AND TERMINATIONS,
TO REGULATORY AGENCIES AND SPONSORS

1. Subject of Policy & Procedure

Federal regulations and Cornell's Federalwide Assurance Registration (FWA) require the Institutional Review Board (IRB) to report the following promptly to appropriate institutional officials; federal departmental or agency heads at the Office of Human Research Protections (OHRP) or the Food and Drug Administration (FDA); and sponsors: (1) unanticipated problems involving risk to human research participants or others (*see* SOP 4); (2) instances of serious or continuing noncompliance (*see* SOP 5); and (3) suspensions or terminations of IRB approval of research protocols (*see* SOP 6).

The Institutional Official has delegated this reporting authority to the Assistant Vice President for Research Compliance (AVPRC). This policy sets forth the procedures for complying with federally mandated reporting requirements concerning unanticipated problems, noncompliance, and suspensions and terminations involving human research protocols previously approved by the IRB.

2. Scope of Policy & Procedure

This Policy & Procedure applies to all on-going and future human participant research projects conducted by Cornell faculty, staff, or students or by anyone conducting a research activity supported by Cornell or on property maintained by Cornell. This Policy & Procedure refers only to reporting to outside agencies and entities. Internal communication procedures are referenced in this policy, but please consult SOPs 4, 5, and 6 for details.

3. Terms and Definitions

All parties to whom this policy applies (*e.g.*, faculty, students, staff, IRB members) should consult the IRB Glossary at <http://www.irb.cornell.edu/glossary/>.

4. Attachments

All parties to whom this policy applies should also consult the Cornell University Federal Wide Assurance Registration: <http://www.irb.cornell.edu/regulations/fwa.htm>

5. Regulations Applicable to Reporting Requirements

5.1. 45 CFR 46.109; 21 CFR 56.109: IRB Review of Research, mandating IRB review and approval of human participant research.

5.2. 45 CFR 46.103(5), mandating compliance with "written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to human subjects or others or any serious or

continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.”

- 5.3. 45 CFR 46.113: “Any suspension or termination of [IRB] approval shall include a statement of the reasons for the IRB’s action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.”
- 5.4. 21 CFR 56.108, mandating compliance with “written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of: (1) any unanticipated problems involving risks to human subjects or others; (2) any instance of serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB; or (3) any suspension or termination of IRB approval.”
- 5.5. 21 CFR 56.113: “Any suspension or termination of [IRB] approval shall include a statement of the reasons for the IRB’s action and shall be reported promptly to the investigator, appropriate institutional officials, and the Food and Drug Administration.”

6. Reporting Responsibilities & Requirements

- 6.1. Content of Reports: *Final Reports*: A final report should include the following information: (1) the name of the Protocol PI; (2) the IRB’s OHRP registration number, Cornell’s FWA number; (3) protocol title; (4) sponsor of the study; (5) any applicable grant numbers; (6) the date(s) and nature of the event(s); (7) details concerning how the event was discovered; (8) the IRB’s and the AVPRC’s response to the event; (9) the Protocol PI’s response to the event; (10) ORIA’s investigatory/audit findings; (11) IRB’s actions and rationale and any response by the Protocol PI; (12) details of the corrective plan; (13) any pertinent details concerning the Protocol PI’s implementation of the corrective plan; (14) participants’ response to corrective measures; (15) IRB plan for monitoring the outcome of the event; (16) certification of destruction of data resulting from un-approved research activities, if applicable; (17) outcomes of withdrawal and follow-up of participants, if applicable; and (18) any general educational activities inspired by the incident. *Initial Reports*: While this information is being compiled for the final report and the corrective plan is being implemented, the IRB and the AVPRC may elect to have ORIA submit an initial report to OHRP and/or FDA in order to ensure prompt reporting. An initial report should include as much of this information as is available.
- 6.2. Drafting, Approval, and Distribution of Reports: ORIA will draft initial and final reports, and the AVPRC will be responsible for signing and finalizing them. After initial and final reports are signed and finalized, ORIA will distribute them to all required recipients.
- 6.3. Required Recipients of Reports: *Final Reports*: Copies of final reports concerning serious adverse events, other unanticipated problems, noncompliance, suspension or termination, will be sent to OHRP and/or FDA, as well as to the Protocol PI, appropriate institutional officials, department chair/center director/college dean of the PI, Office of Sponsored Programs, and if appropriate, the sponsor. The sponsor should always receive a final report relating to serious adverse events; serious or continuing noncompliance; and/or terminations of IRB approval of a research protocol. A final report concerning non-serious and non-continuing noncompliance will not be sent to OHRP or FDA or other federal sponsoring agency. *Initial Reports*: Copies of initial reports will be sent to OHRP and/or FDA and to the other aforementioned parties, including, if appropriate, the sponsor.
- 6.4. Serious Adverse Events (*see* SOP 4): The timing of the notification of a serious adverse event to OHRP and/or FDA depends on the nature of the risk, the availability of relevant information

and evidence, and the estimated timeframe for full implementation of a corrective plan. Where a serious adverse event has occurred, the IRB Chair and the AVPRC may require ORIA to notify OHRP and/or FDA with an initial report following suspension of the protocol by the IRB Chair, *see* SOP 4, Section 6.3.2, but at some point before ORIA's for-cause audit, the IRB's issuance of a corrective plan, or the Protocol PI's implementation of the corrective plan. Where the IRB Chair and the AVPRC estimate that full implementation of the corrective plan will require more than 75 days, an initial report is recommended. Upon full implementation of the corrective plan, ORIA will draft a final report for comment by the IRB at the next available meeting. The final report should be distributed by ORIA to all required recipients within 75 days of any official action taken by the IRB, including its issuance of a corrective plan.

6.5. Other Unanticipated Problems (*see* SOP 4): In the case of unanticipated problems that are not serious adverse events, formal notification to OHRP and/or FDA generally will be made after completion of an investigation or formal audit by ORIA, if appropriate, and implementation of the IRB's corrective plan. Upon full implementation of the corrective plan, ORIA will draft a final report for comment by the IRB at the next available meeting. The final report should be distributed by ORIA to all required recipients, within 75 days of any official action taken by the IRB, including its issuance of a corrective plan.

6.6. Serious or Continuing Noncompliance (*see* SOP 5):

The timing of the notification to OHRP and/or FDA of a finding of serious or continuing noncompliance as per SOP 5, depends on the nature of the risk, the availability of relevant information and evidence, and the estimated timeframe for full implementation of a corrective plan. Where serious or continuing noncompliance has occurred, the IRB Chair and the AVPRC may instruct ORIA to notify OHRP or FDA with an initial report at some point before ORIA's for-cause audit, the IRB's issuance of a corrective plan, or the Protocol PI's implementation of the corrective plan. Where the IRB Chair and the AVPRC estimate that full implementation of the corrective plan will require more than 75 days, an initial report is recommended. Upon full implementation of the corrective plan, ORIA will draft a final report for comment by the IRB at the next available meeting. The final report should be distributed by ORIA to all required recipients within 75 days of any official action taken by the IRB, including the issuance of a corrective plan.

6.7. Suspensions and Terminations (*see* SOP 6): Upon the Protocol PI's implementation of the corrective plan following a suspension notice or upon the IRB's termination of a research protocol, ORIA will submit a final suspension or termination report to OHRP and/or FDA and other required recipients. The final report should be distributed by ORIA to all required recipients within 75 days of a suspension or termination. However, where the IRB votes for termination, ORIA may be instructed by the IRB Chair and the AVPRC to notify OHRP and/or FDA with an initial report at some point before ORIA's for-cause audit, the IRB's issuance of a corrective plan, or the Protocol PI's implementation of the corrective plan. Where the IRB Chair and the AVPRC estimate that full implementation of a corrective plan (including any required withdrawal or follow-up of participants) in response to a suspension or termination will require more than 75 days, an initial report is recommended. The IRB Chair or the AVPRC may also instruct ORIA to draft an initial report in the case of a suspension, if the circumstances so warrant.

- 6.8. Follow-up Communications with OHRP/FDA:** ORIA is responsible for drafting and sending responses to any comments by federal officials or sponsors on the final reports after coordination with the Principal Investigator, IRB, Institutional Official, and other as appropriate.

7. Documentation Relating to Reporting

All documents relating to reporting unanticipated problems, noncompliance, suspensions, and terminations will be maintained by ORIA for a period of not less than 5 years, in accordance with SOP ___: Document Retention.

These documents include but are not limited to: Unanticipated Problem Report Forms; Noncompliance Report Forms; correspondence with the Protocol PI; documentation of implementation of corrective plans; audit reports; preliminary notification reports; and final notification reports.