



SOP: Directed Review (For Cause) Audits

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1 PURPOSE

- 1.1 This procedure establishes the process to conduct for-cause Directed Reviews.
- 1.2 The process begins when a question relating to non-compliance (perceived or confirmed) is raised. A directed review may be required as a result of:
 - 1.2.1 Reportable new information. (See SOP: Reportable New Information - HRP-024).
 - 1.2.2 Any review of submitted materials via eIRB+.
 - 1.2.3 Any allegation of non-compliance (perceived or confirmed).
 - 1.2.4 A suspension or termination of IRB approval (See SOPs: Suspension or Termination Issued Outside of Convened IRB - HRP-026 and Suspension or Termination of IRB Approval by Convened Panel - HRP-029).
 - 1.2.5 Request by an external entity that the Northwestern University IRB cedes IRB review for research conducted at Northwestern University and/or affiliates.
 - 1.2.6 Request by an IRB Chair, convened panel, Executive IRB Director or IRB Manager.
- 1.3 The process ends when the Directed Review is complete and the Audit Report with the Investigator's response has been provided to the Institutional Review Board (IRB), Vice President for Research, Institutional Official or designee.

2 PREVIOUS VERSION

- 2.1 Revised from previous version dated 02/12/2021.

3 POLICY

- 3.1 The IRB Office has the responsibility to: (1) Implement a Directed Review program to monitor and compliance in identified problem areas, and (2) Investigate and remediate identified systemic problem areas and, where necessary, request that the Vice President for Research remove individuals from involvement in the Human Subject Protection Program. (See: Human Research Protection Program Plan - HRP-101)
- 3.2 The IRB Office and IRB investigate allegations of non-compliance in Human Subject Research and impose corrective actions as needed. In addition to Directed Reviews conducted by the IRB Office in response to reports of alleged non-compliance, the IRB Office also conducts routine post-approval monitoring of non-exempt Human Subject Research to ensure the compliant conduct of Human Subject Research at the University and affiliates. (See: POLICY: Human Research Protection Program Compliance)

4 RESPONSIBILITIES

- 4.1 The IRB, Vice President for Research, Institutional Official or designee:
 - 4.1.1 Requests that the IRB Office Compliance Team (Compliance Team) review the Investigator and study materials as needed to answer the questions raised by the review of non-compliance or other eIRB+ submissions.
 - 4.1.2 Charges the Compliance Team with the question(s) to be answered and the scope of the review.
- 4.2 The Compliance Team creates an investigational plan and carries out these procedures upon notification of directed review request.
 - 4.2.1 When the Northwestern University IRB serves as the IRB of record for an external participating site that must undergo a directed review, the Compliance Team will collaborate with the IRB Office Reliance Team (Reliance Team) and the external site Quality Assurance and Auditing Team to conduct the Directed Review.
 - 4.2.2 When the Northwestern University IRB cedes review to an external IRB, and the external IRB requests a directed review, the Compliance Team will collaborate with the Reliance Team and the external IRB contact to conduct the Directed Review.



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- 4.2.3 When the Northwestern University IRB cedes review to an external IRB and an internal entity requests a directed review, the Compliance Team will conduct the review as an internal review.
- 4.3 The Compliance Team makes their observations and recommendations for the next steps based on the available materials, interviews, or information obtained during the Directed Review.
- 4.4 The Compliance Team will document their observations and recommendations in writing in the form of an audit letter and provide it to the following individuals:
 - 4.4.1 Principal Investigator (PI)
 - 4.4.2 Primary contact
 - 4.4.3 With a copy to:
 - 4.4.3.1 Investigator's Department Chair or designee
 - 4.4.3.2 IRB Compliance Manager
 - 4.4.3.3 IRB Office Executive Director
 - 4.4.3.4 Other Institutional Officials as appropriate

5 PROCEDURE

- 5.1 The Compliance Analyst(s) will notify the Investigator that a Directed Review is being conducted, the question to be answered and/or reason for the Directed Review, and the timeline for completion using template letter Directed Review Notification (HRP-1814).
- 5.2 Determine what information to gather and what individuals to interview.
 - 5.2.1 The Compliance Analyst(s) prepare and maintain the Directed Review file, which typically consists of the following elements (but may vary depending on the circumstances of a particular Directed Review):
 - 5.2.1.1 IRB Submission(s)
 - 5.2.1.2 Consent Document(s)
 - 5.2.1.3 Protocol(s)
 - 5.2.1.4 Continuing Review (most recent)
 - 5.2.1.5 Applicable Post Approval Monitoring Checklists
 - 5.2.1.6 Report (official Directed Review report)
 - 5.2.1.7 Final findings and IRB determinations (The response from the Investigator and the IRB Panel's determination)
- 5.3 Gather information and interview individuals.
 - 5.3.1 This might involve one or more of the following activities:
 - 5.3.1.1 Interviewing research staff
 - 5.3.1.2 Reviewing regulatory and all applicable documentation made available to the Compliance Analyst(s)
 - 5.3.1.3 Reviewing a sample of the consent forms (e.g., 20% of consent forms depending on study enrollment and audit focus) made available to the Compliance Analyst(s)
 - 5.3.1.4 Reviewing a sample of data or case report forms (e.g., 10% of participant files depending on study enrollment and audit focus) made available to the Compliance Analyst(s)
 - 5.3.2 The Compliance Analyst(s) may complete the following applicable checklists:
 - 5.3.2.1 HRP-427: Drug or Device Clinical Trial Checklist
 - 5.3.2.2 HRP-428: Participant File Checklist
 - 5.3.2.3 HRP-430: Human Research Checklist
 - 5.3.2.4 HRP-1405: Registry, Data Review, and/or Specimen Collection Checklist
 - 5.3.2.5 HRP-1406: Studies Under External IRB Review Checklist



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- 5.3.2.6 HRP-1407: Site File Checklist
- 5.3.2.7 HRP-1409: Humanitarian Use Device Checklist
- 5.4 The Compliance Analyst(s) may conduct information gathering and interviews until sufficient information is obtained.
- 5.5 At the conclusion of the Directed Review, the Compliance Analyst(s) will verbally debrief the investigator and/or designated study team members regarding their observations, applicable recommendations and next steps.
- 5.6 The Compliance Analyst(s) will formally document their observations and recommendations in writing in an Audit Report using template Directed Review Observations (HRP-18-15) and provide it to the Investigator and other individuals listed in 4.4.3 above.
 - 5.6.1 The Audit Report will include the following:
 - 5.6.1.1 Executive Summary
 - 5.6.1.2 Instructions for Investigator about how to submit a formal response
 - 5.6.1.3 A list of observations and corresponding corrective actions and/or best practice recommendations.
- 5.7 The Audit Report cannot be revised or amended following submission to the IRB. The study team is encouraged to contact the compliance analyst(s) prior to the finalization of the audit report if there are additional queries.
- 5.8 The Investigator will submit the Audit Report and his or her response to each observation to the Institutional Review Board (IRB) for review and acknowledgement through an RNI submission in eIRB+.

6 MATERIALS

- 6.1 SOP: Reportable New Information (HRP-024)
- 6.2 SOP: Suspension or Termination Issued Outside of Convened IRB (HRP-026)
- 6.3 SOP: Suspension or Termination of IRB Approval by Convened Panel (HRP-029)
- 6.4 CHECKLIST: Post-Approval Monitoring: Human Research (HRP-430)
- 6.5 CHECKLIST: Post Approval Monitoring: Drug or Device Clinical Trial (HRP-427)
- 6.6 CHECKLIST: Post Approval Monitoring: Participant File (HRP-428)
- 6.7 CHECKLIST: Post Approval Monitoring: Registry, Data Review, and/or Specimen Collection (HRP-1405)
- 6.8 CHECKLIST: Post Approval Monitoring: Studies Under External IRB Review (HRP-1406)
- 6.9 CHECKLIST: Post Approval Monitoring: Site File (HRP-1407)
- 6.10 CHECKLIST: Post Approval Monitoring: Humanitarian Use Device (HRP-1409)
- 6.11 TEMPLATE: Directed Review Notification (HRP-1814)
- 6.12 TEMPLATE: Directed Review Observations (HRP-1815)

7 REFERENCES

- 7.1 POLICY: Human Research Protection Program Compliance
- 7.2 GENERAL DOCUMENT: Human Research Protection Program Plan (HRP-101)
- 7.3 GENERAL DOCUMENT: Investigator Manual (HRP-103)