Fred Hutch Cancer Center

Institutional Review Board

Policy/Procedure

Title:	Noncompliance
Version:	1.00
Effective Date:	February 3, 2025
Responsible Office:	Institutional Review Office (IRO)
Responsible Official / Approved By:	Meghan Scott, IRO Director

POLICY STATEMENT

Confirmed or suspected serious or continuing noncompliance with (i) federal laws relating to research involving human subjects, (ii) the Human Research Protection Program (HRPP) of Fred Hutchinson Cancer Research Center (Fred Hutch) or (iii) the requirements or determinations of the Fred Hutch Institutional Review Board (IRB), must be reported promptly to either the Institutional Review Office (IRO) Director, the Institutional Official (IO), the Vice President and Chief Compliance Officer, the Office of General Counsel or through other normal organizational channels as provided in this policy.[1]

Principal Investigators (PI) and study staff are required to report all serious or continuing noncompliance within ten (10) calendar days of discovering it. If there is any question or possibility that noncompliance could constitute serious or continuing noncompliance, it should be reported.

"Noncompliance" does not include protocol deviations that are beyond the immediate control of the principal investigator and his or her study staff (e.g., delays caused by weather or by the acts or omissions of third parties such as outside labs or scheduling changes not caused by the principal investigator or his or her staff). However, this type of protocol deviation may constitute an unanticipated problem involving risks to research subjects or others reportable under *HRP-131 - POLICY - Unanticipated Problems Involving Risks to Subjects or Others*.

The IRB will determine if the reported event constitutes serious or continuing noncompliance.

Allegations of noncompliance reported under this policy will be promptly investigated. Noncompliance which is or is possibly serious or continuing will be reviewed by the IRB in accordance with this policy and appropriate steps will be taken to minimize any risks to research participants. Confirmed instances of serious or continuing noncompliance will be reported to appropriate institutional and government officials as provided under applicable law, *HRP-117 - POLICY - Requirements for Reporting to Institutional and External Officials* and this Policy. The IO or VP & Chief Compliance Officer may impose sanctions on employees responsible for serious or continuing noncompliance.

DEFINITIONS

See *HRP-001 - Glossary of Terms and Acronyms* for full definitions of the following:

Allegation of noncompliance

Confirmed noncompliance

Noncompliance ***(including Continuing, Minor, and Serious Noncompliance)***

INDIVIDUALS AFFECTED BY THIS POLICY

The contents of this policy apply to IRO staff, IRB members, employees of Fred Hutch, Fred Hutch investigators, investigators from other institutions who submit research studies to the Fred Hutch IRB for

[1] HHS: 45 CFR 46.108(a)(4)(i); FDA: 21 CFR 56.108(b)(2)

review and approval, study monitors, auditors or sponsors. Instructions for reporting are posted on the IRO website. When Fred Hutch investigators are relying on an external IRB, the reporting requirements of the external IRB must be followed instead of this policy.

PRINCIPLES/OVERVIEW

Ensuring that noncompliance with the HRPP is promptly and effectively addressed is essential to protecting the rights and welfare of research participants and to the integrity of the HRPP. The HRPP requires that Fred Hutch employees and agents and persons conducting research for which the Fred Hutch IRB is the IRB of record report any serious or continuing noncompliance or suspected serious or continuing noncompliance of which they become aware. In addition, federal law requires that the IRB follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials and certain government agencies of (i) serious or continuing violations of federal regulations governing human subjects research, or (ii) the requirements or determinations of the IRB. This policy establishes procedures for reporting, investigating and addressing noncompliance relating to the HRPP, applicable laws and regulations and the requirements or determinations of the IRB.

PROCEDURES

1. Reporting Requirements

a. Reporting by Principal Investigators and Study Staff. Principal Investigators and their study staff are required to report **each event** of serious or continuing noncompliance relating to human subjects research which they are conducting. Reports must be made **within ten (10) calendar days of learning of the event**.

If there is any question or possibility that noncompliance could constitute serious or continuing noncompliance, it should be reported.

The following types of noncompliance events must also be reported to the IRB within ten (10) calendar days of learning of the event, **even if** the Principal Investigator, or study staff, do not believe the event constitutes serious or continuing noncompliance:

(i) The failure to obtain IRB approval of human subjects research when required under the HRPP or applicable laws and regulations,

(ii) Enrolling a research participant who does not fit the inclusion and exclusion criteria in the protocol,

(iii) Failing to obtain or document informed consent,

(iv) Administering radiation, drugs, biologics, or cell products, or using devices required by the protocol at a dose or schedule that has not been approved by the IRB except when necessary to eliminate apparent immediate hazards to the research participant (see *HRP-119 - POLICY - Modifications to Ongoing Activities*).

The IRB will determine if the reported event constitutes serious or continuing noncompliance.

To report noncompliance, the PI will submit a Reportable New Information (RNI) submission in Hutch IRB, attaching *HRP-255 - FORM - Reportable New Information (RNI) Supplement* and any other relevant information. Unless circumstances clearly indicate otherwise, reports by Principal Investigators or study staff under this Section 1a will be considered confirmed noncompliance.

b. Reporting by Others. Persons other than Principal Investigators and study staff should report any actual or suspected noncompliance to the IRO Director, the IO, the VP & Chief Compliance Officer, the Office of General Counsel or through other normal organizational channels such as the Fred Hutch Scientific Ombuds. If possible, the person reporting the event should submit a Reportable New Information (RNI) submission in Hutch IRB. To keep the report confidential from the PI and study team, do not associate the event with a study record in Hutch IRB. Generally, reports of noncompliance involving the IRO Director or members of the IRB (in their capacity as such) should be made to the IO, VP & Chief Compliance Officer, or the Office of the General Counsel.

For Anonymous reporting, employees may use the EthicsPoint website to file a report. This is an independent third party selected to help Fred Hutch fulfill its commitment to compliance, ethical

conduct and workplace respect in all its programs and activities. The report will be forwarded to the Chief Compliance Officer with no identifying information about the individual reporting the event, unless they provide such information. Employees may also contact an EthicsPoint representative by calling the hotline at 866.353.6098.

c. Minor Noncompliance. Minor noncompliance does not need to be reported unless required by the IRB-approved protocol. It is recommended that principal investigators initially prepare and, as necessary, amend protocols to minimize instances of minor noncompliance.

2. Preliminary Assessment of Reported Noncompliance

Any Fred Hutch official receiving a report that such person determines is a report of actual or suspected noncompliance will promptly notify and forward the report to the IRO Director (or designee) unless the noncompliance involves the IRO Director or a member of the IRB in his or her capacity as such, in which case the person will notify and forward the report to the IO or the VP & Chief Compliance Officer.

The IRO Director (or designee), the IO or the VP & Chief Compliance Officer will preliminarily assess whether or not there is (i) confirmed noncompliance or (ii) an allegation of noncompliance. In making this determination, the IRO Director (or designee), the IO or the VP & Chief Compliance Officer may collect additional information necessary to making this determination, although it is not intended that a full investigation of alleged noncompliance be conducted at this stage of review.

If the allegation of noncompliance involves a Participating Site outside of Fred Hutch, where the Fred Hutch IRB is the IRB of record, the IRO Director, the IO or the VP & Chief Compliance Officer may contact the outside institution to assess whether or not there is (i) confirmed noncompliance or (ii) an allegation of noncompliance.

If the IRO Director (or designee) determines that the report is an allegation of noncompliance, Section 3 will be followed.

If the IRO Director (or designee) determines that the report is confirmed noncompliance, Section 4 will be followed.

For reports of noncompliance made under Section 1a. by Principal Investigators and study staff, IRO staff will complete their pre-review of the RNI submission using *HRP-364 - WORKSHEET - Reportable New Information (RNI)*.

3. Review of Allegations of Noncompliance

IRO staff will generally assign RNI submissions to the Chair of the committee that initially approved the study to which the allegation of noncompliance relates; however, any Designated Reviewer may review the RNI. The Designated Reviewer will review the RNI submission and any supporting documentation including *HRP-378 - WORKSHEET - IRB Chair or Designee Report Checklist for Unanticipated Problems or Noncompliance*. This review should normally occur within 2 business days of the time the RNI is submitted to the IRO. Based on this review, the Designated Reviewer will determine whether the allegation of noncompliance is confirmed noncompliance or has no basis in fact. In making this determination the Designated Reviewer will collect or instruct others to collect additional information necessary to making this determination and may, in his or her discretion conduct or ask others to conduct a full investigation of the alleged noncompliance.

- If the Designated Reviewer determines that the allegation of noncompliance has no basis in fact, then no further action will be taken under this policy.
- If the Designated Reviewer determines that the allegation of noncompliance is confirmed noncompliance, then Section 4 will be followed.

The Designated Reviewer, in his or her discretion, may refer the determination of whether an allegation of noncompliance is confirmed noncompliance or has no basis in fact to the full IRB. In that case, the RNI submission and all appropriate supporting documentation will be scheduled for Committee Review. The IRB will collect or instruct others to collect additional information necessary to making its determination and may, in its discretion conduct or ask others to conduct a full investigation of the alleged noncompliance.

If the allegations of noncompliance involve the IRO Director or members of the IRB (in their capacity as such), the IO or the VP & Chief Compliance Officer (or designee) rather than the IRB Chair will conduct the review and make the determinations required under this Section 3.

4. Review of Confirmed Noncompliance

a. Review by the Chair. IRO staff will generally route RNI submissions to the Chair of the committee that initially approved the study to which the noncompliance relates; however, any Designated Reviewer may review an RNI. The Designated Reviewer will review the RNI SmartForm, *HRP-255 - FORM - Reportable New Information (RNI) Supplement,* and any supporting documentation including *HRP-378 - WORKSHEET - IRB Chair or Designee Report Checklist for Unanticipated Problems or Noncompliance*. This review should normally occur within two business days of receipt of the RNI by the IRO. Based on the review, the Designated Reviewer will determine whether (i) the confirmed noncompliance is definitely neither serious nor continuing or (ii) or is possibly serious or continuing.

- If the Designated Reviewer determines that the confirmed noncompliance is definitely neither serious nor continuing, the Designated Reviewer may work with the investigator, if appropriate, to develop a corrective action plan.
- If the Designated Reviewer determines that the noncompliance is or is possibly serious or continuing, then Section 4b will be followed.

If the noncompliance involves the IRO Director or members of the IRB (in their capacity as such), the IO or VP & Chief Compliance Officer (or designee) rather than the IRB Designated Reviewer will conduct the review and make the determinations required under this Section 4a.

b. Review and Action by the IRB. The IRB is responsible for reviewing confirmed noncompliance that is or is possibly serious or continuing.

IRB members will have access to the following information in connection with any report of noncompliance that is or is possibly serious or continuing:

- The protocol.
- The current consent document(s).
- RNI SmartForm and any supporting documents.
- *HRP-255 - FORM - Reportable New Information (RNI) Supplement* and *HRP-378 - WORKSHEET - IRB Chair or Designee Report Checklist for Unanticipated Problems or Noncompliance*.

The IRB will determine whether the noncompliance is serious or continuing. The IRB may request that additional facts be collected or that a further investigation be conducted if necessary for it to make this determination.

If the IRB determines that the noncompliance is neither serious nor continuing, the IRB may still provide recommendations related to the corrective action plan, which can be referred back to the Designated Reviewer for final confirmation of the CAPA as described in 4a.

If the IRB determines that the noncompliance is serious or continuing, then the IRB will consider at a minimum the following actions to remedy the noncompliance and protect research participants and others:

- Requiring additional information from the Principal Investigator with a plan for corrective action
- Monitoring or Auditing of the active protocol
- Requiring modification of the protocol
- Requiring modification of the consent
- Requiring the re-consenting of and/or providing additional information to current research participants (must occur when such information may affect the willingness of current participants to continue to take part in the research.)[2]

[2] HHS: 45 CFR 46.116(c)(5); FDA: 21 CFR 50.25(b)(5)

- Requiring the re-consenting of and/or providing additional information to past research participants
- Monitoring of the consent process as described in *HRP-090 – POLICY – Informed Consent*
- Requiring more frequent continuing review of the study
- Requiring additional training of study staff
- Prohibiting use of the data collected for publication
- Suspending or terminating the protocol
- Requesting that the IO (or designee) withhold funding for the study conditioned on appropriate corrective measures or informing other Fred Hutch entities about the noncompliance determination as appropriate.

In appropriate cases, the IRB may also recommend to the IO or the VP & Chief Compliance Officer that disciplinary or other action be taken against any Fred Hutch employee or other person subject to the HRPP including, without limitation, the following:

- Suspending the right to conduct or participate in human subject research at Fred Hutch pending completion of additional training or other requirement
- Terminating or limiting the right to conduct or participate in human subject research at Fred Hutch
- Requiring additional supervision of the Principal Investigator
- Terminating employment
- Conducting an investigation into scientific or other misconduct.
- Terminating an appointment to serve on the IRB
- Discontinuing an investigator's reliance on the Fred Hutch IRB as the IRB of record due to an investigator's repeated serious or continuing noncompliance that subsequently results in an IRB suspension of research activity(ies)

Upon completion of the IRB's review, the individual that submitted the RNI as well as the PI, Primary Contact, and PI Proxies of the related study are notified of the IRB's conclusions and any actions. These individuals will receive an automated email notification from Hutch IRB that provides a link to the RNI submission, where the formal result letter is available for download. IRO staff will then follow *HRP-117 - POLICY - Requirements for Reporting to Institutional and External Officials.*

If the noncompliance involves the IRO Director or members of the IRB (in their capacity as such), the persons involved may not participate in the review under this Section 4b. If necessary, the IO or the VP & Chief Compliance Officer (or designee) will appoint someone else to assume the responsibilities of the person or persons involved in the noncompliance for purposes of the review.

c. Review and Action by the Institutional Official or VP & Chief Compliance Officer. The IO and VP & Chief Compliance Officer (or their designees) will promptly review the conclusions of the IRB including any recommended actions to address the noncompliance. The decision to take disciplinary or other action against a person engaged in noncompliance is within the discretion of the IO, the VP & Chief Compliance Officer or their designee.

SUPPORTING DOCUMENTS

HRP-001 - Glossary of Terms and Acronyms

HRP-117 - POLICY - Requirements for Reporting to Institutional and External Officials

HRP-119 - POLICY - Modifications to Ongoing Activities

HRP-131 - POLICY - Unanticipated Problems Involving Risk to Subjects or Others

HRP-255 - FORM - Reportable New Information (RNI) Supplement

HRP-364 - WORKSHEET - Reportable New Information (RNI)

HRP-378 - WORKSHEET - IRB Chair or Designee Report Checklist for Unanticipated Problems or Noncompliance

REFERENCES

21 CFR 50.25

21 CFR 56.108

45 CFR 46.108

45 CFR 46.116

OHRP Guidance on Reporting Incidents to OHRP

VERSION HISTORY

Version	Effective Date
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