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Responsible Official:	Meghan Scott, IRO Director
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	<i>Signature/date</i>

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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 Associate Vice President and Chief

Ethics and Compliance Officer (CECO), 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 *IRB Policy 2.6 Unanticipated Problems Involving Risks to Subjects or Others (0224)*.

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, *IRB Policy 2.8 IRB Requirements for Reporting to Institutional Official and External Officials (021)* and this Policy. The IO or CECO may impose sanctions on employees responsible for serious or continuing noncompliance.

DEFINITIONS

See *IRB Glossary of Terms and Acronyms (050)* 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 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

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

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 *IRB Policy 2.5 Modifications to Ongoing Activities* [025]).

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

The *Expedited Reporting Form for Unanticipated Problems or Noncompliance* (0203) should be used for reporting noncompliance. 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 Associate Vice President and Chief Ethics and Compliance Officer (CECO), the Office of General Counsel or through other normal organizational channels such as the Fred Hutch Scientific Ombuds. Generally, reports of noncompliance involving the IRO Director or members of the IRB (in their capacity as such) should be made to the IO, CECO or the Office of the General Counsel. If possible, use the *Allegation of Human Subjects Research Noncompliance Reporting Form* (0200) for such reporting.
- 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 CECO.

The IRO Director (or designee), the IO or the CECO 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 CECO 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 CECO 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 the *Screener: Expedited Reporting Form for Unanticipated Problems or Noncompliance (0296)* or *Screener: Allegation of Human Subjects Research Noncompliance Reporting Form (0297)* to screen these reports.

3. Review of Allegations of Noncompliance

The Chair of the IRB that approved the research to which the allegation of noncompliance relates (or designee) will review the report and any supporting documentation including the *IRB Chair or Designee Report Checklist for Unanticipated Problems or Noncompliance (074)* and relevant *Allegation of Human Subjects Research Noncompliance Reporting Form (0200)*. This review should normally occur within 2 business days of the time the report is received by the IRO. Based on this review, the IRB Chair (or designee) will determine whether the allegation of noncompliance is confirmed noncompliance or has no basis in fact. In making this determination the IRB Chair (or designee) 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 IRB Chair (or designee) determines that the allegation of noncompliance has no basis in fact, then no further action will be taken under this policy.
- If the IRB Chair (or designee) determines that the allegation of noncompliance is confirmed noncompliance, then Section 4 will be followed.

The IRB Chair, 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 IRB Chair (or designee) will provide the report and all appropriate supporting documentation to the IRB. 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 CECO (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 IRB Chair. The Chair of the IRB that approved the research to which the noncompliance relates (or designee) will review any supporting documentation including the *IRB Chair or Designee Report Checklist for Unanticipated Problems or Noncompliance (074)* and relevant *Expedited Reporting Form for Unanticipated Problems or Noncompliance (0203)*. This review should normally occur within 2 business days of the time the report is received by the IRO. Based on the review, the IRB Chair (or designee) will determine whether (i) the confirmed noncompliance is definitely neither serious nor continuing or (ii) or is possibly serious or continuing.
- If the IRB Chair (or designee) determines that the confirmed noncompliance is definitely neither serious nor continuing, the IRB Chair (or designee) may work with the investigator, if appropriate, to develop a corrective action plan.
 - If the IRB Chair (or designee) 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 CECO (or designee) rather than the IRB Chair 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.

IRO staff will provide the following documentation to all IRB members in connection with any report of noncompliance that is or is possibly serious or continuing:

- The protocol.
- The current consent document(s).
- Copy of the reported information along with any supporting documents.
- The *Expedited Reporting Form for Unanticipated Problems or Noncompliance (0203)* and *IRB Chair or Designee Report Checklist for Unanticipated Problems or Noncompliance (074)*.

The IRB first 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, then the report will be referred to the IRB Chair (or designee) for development of a corrective action plan 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
- 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
- Requiring the re-consenting of and/or providing additional information to past research participants
- Requiring more frequent 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.

In appropriate cases, the IRB may also recommend to the IO or the CECO 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, IRO staff will notify the Principal Investigator of the IRB's conclusions and any actions. IRO staff will then follow *IRB Policy 2.8 IRB Requirements for Reporting to Institutional and External Officials* (021).

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 CECO (or designee) will appointment 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 Chief Ethics and Compliance Officer. The IO and CECO (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 CECO or their designee.

SUPPORTING DOCUMENTS

IRB Policy 2.5 Modifications to Ongoing Activities (025)

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

IRB Policy 2.6 Unanticipated Problems Involving Risks to Subjects or Others (0224)
IRB Policy 2.8 IRB Requirements for Reporting to Institutional and External Officials (021)
Allegation of Human Subjects Research Noncompliance Reporting Form (0200)
Expedited Reporting Form for Unanticipated Problems or Noncompliance (0203)
IRB Chair or Designee Report Checklist for Unanticipated Problems or Noncompliance (074)
IRB Glossary of Terms and Acronyms (050)
 Screener: Allegation of Human Subjects Research Noncompliance Reporting Form (0297)
 Screener: Expedited Reporting Form for Unanticipated Problems or Noncompliance (0296)

REFERENCES

21 CFR 50.25
21 CFR 56.108
45 CFR 46.108
45 CFR 46.116
OHRP Guidance on Reporting Incidents to OHRP