



Title:	Monitoring of Institutional Review Board, IRB Operations, and Research Studies
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Responsible Office:	Institutional Review Office (IRO)
Responsible Official:	Meghan Scott, IRO Director
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	<i>Signature/date</i>

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POLICY STATEMENT

It is the policy of Fred Hutchinson Cancer Research Center (Fred Hutch) to require appropriate monitoring of research studies involving human subjects to help ensure that the rights and welfare of research participants are adequately protected and that the research is conducted in compliance with applicable laws and regulations. The required monitoring will include assessing the effectiveness of the

Fred Hutch human research protection program (HRPP) and the determinations of the Institutional Review Board (IRB). Improvement plans for the HRPP will be developed based on the results of the monitoring. Principal Investigators, IRBs, and IRB staff subject to the HRPP must comply with the monitoring policies and procedures established by the Institutional Review Office (IRO) and Clinical Research Support (CRS) as described in this policy.

DEFINITIONS

See *IRB Glossary of Terms and Acronyms* (050) for full definitions of the following:

Cancer Consortium

Clinical Research Support (CRS)

Data and Safety Monitoring Board (DSMB)

Data Safety Monitoring Committee (DSMC)

Data and Safety Monitoring Plan (DSMP)

Good Clinical Practice (GCP)

Scientific Review Committee (SRC)

INDIVIDUALS AFFECTED BY THIS POLICY

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

PROCEDURES

1. Initial Monitoring for New Studies

- a. IRB Scientific Review and Evaluation of Data Monitoring Plans.

The IRB has the ultimate responsibility for determining whether the risks to participants have been appropriately minimized through the use of sound research design and whether those risks are reasonable in light of the anticipated benefits to the participants and the importance of the research. The IRB will review studies and determine whether the proposed research presents minimal risk or more than minimal risk to research participants and then determine whether a data safety monitoring plan is required.¹

The IRB Members are reminded on the *IRB Member Checklist* (071) that it is the IRBs responsibility to determine the level of risk for each proposed research proposal submitted for IRB approval. For studies that involve no more than minimal risk, a monitoring plan is usually not required.

- b. Other Scientific Review Requirements.

In addition to the IRB scientific review, research studies conducted at Fred Hutch may also be required to obtain scientific review by one or more of the following methods:

- NIH peer review
- Scientific Review Committee (SRC) review

¹ HHS: 45 CFR 46.111(a)(6); FDA: 21 CFR 56.111(a)(6)

- Scientific division review by the Division Director (or designee), Research Group Review, or other peer review as determined by the scientific divisions.

All Cancer Consortium intervention research studies must comply with the *Fred Hutch / UW Cancer Consortium Data and Safety Monitoring Plan (CCDSMP)*. The CCDSMP requires that all protocols must incorporate in their design a data and safety monitoring plan consistent with the potential risks and size of the study. The plan also outlines when an independent DSMB is required.

For Cancer Consortium intervention research studies, the PI will include the SRC Report, details of the DSMB (when appropriate) and the DSMP in the materials submitted with the *Application for Review Interventional Research (0324)* as outlined in the *IRB Policy 2.1 New Application (028)* for IRB review.

The IRB will also review the SRC report, the DSMP, and the plans for a DSMB to determine if appropriate monitoring of the study is in place to provide adequate protection for research participants. The IRB may require that a research study be returned to the SRC for additional review if it has concerns about the scientific merit of or the proposed monitoring plan for the study.

2. Ongoing Monitoring of IRB Approved Studies

a. Cancer Consortium Study Monitoring

Ongoing monitoring of Cancer Consortium research studies will occur as provided in the CCDSMP. The DSMC will review each approved protocol on an ongoing basis as provided in the CCDSMP.

CRS will conduct monitoring visits of Cancer Consortium research studies as outlined in the CRS CCDSMP. The results of the monitoring will be provided to the PI and study team. The PI is responsible for reviewing the monitoring findings and submitting any reports of potential serious or continuing noncompliance and any unanticipated problems involving risks to subjects or others on an expedited basis per *IRB Policy 1.11 Reporting Obligations for Principal Investigators (032)*. The PI will include the DSMC and the DSMB reports in the *Continuing Review Report (CRR) Form (045)* for the IRB's review.

b. IRB Monitoring at Continuing Review

At the time of IRB continuing review of a study (see *IRB Policy 2.2 Continuing Review [010]*) the IRB will review any DSMC and DSMB minutes for that study to determine if appropriate monitoring of the study has taken place to adequately protect the rights and welfare of research participants. See *IRB Member Checklist (071)*.

Where applicable, the IRB Chair or IRB members may request additional information by contacting the Clinical Research Support Director or Clinical Research Monitoring Coordinator.

The IRB may observe the consent process of an ongoing study during continuing review or at any time throughout the study. Observation of the consent process may be delegated to appropriate Fred Hutch staff. The Fred Hutch staff will contact the investigator, informing them that the next informed consent consultation will be observed. At the time of observing the consent process, the Fred Hutch staff will work with the investigator so that the investigator may inform the research participant that the consent process will be observed.²

² HHS: 45 CFR 46.109(g); FDA: 21 CFR 56.109(f)

c. Ongoing Monitoring of Unanticipated Problems Involving Risks to Research Participants and Others

The DSMC will review unanticipated problems and adverse events involving risks to research participants and others relating to Cancer Consortium intervention studies each month, and the minutes of each meeting will be provided to the Principal Investigator. The Principal Investigator is responsible for evaluating the DSMC minutes to determine if there has been any change in the risk associated with any study and whether there is any unanticipated problem involving risks to research participants or others that needs to be reported to the IRB per *IRB Policy 2.6 Unanticipated Problems Involving Risks to Subjects or Others (0224)*.

The IRB will receive ongoing reports of unanticipated problems involving risks to research participants or others relating to each study as provided in the *IRB Policy 2.6 Unanticipated Problems Involving Risks to Subjects or Others (0224)*.

d. Ongoing Monitoring of IRB Files

The IRO Quality Assurance (QA) Manager will monitor IRB files relating to research studies subject to the HRPP to ensure that the study activities are conducted, recorded, and reported in accordance with the protocol, federal regulations, and the HRPP.

Selection of studies for file monitoring may be random, at the direction of the IRB, or through institutional request. Generally, a minimum of two IRB files each quarter will be monitored but the number of files may vary. Monitoring procedures will be followed as noted in *IRB Staff and Research Study Monitoring Procedures (0244)*.

e. Post-Approval Monitoring

To ensure that research is being conducted per the study protocol as approved by the IRB, the QA manager will conduct post-approval monitoring. Monitoring may be conducted on-site or remotely. This monitoring provides assurance to the IRB that studies are in compliance with local, federal, and state regulations, the HRPP, and institutional policies.

Selection of studies for post-approval monitoring may be random, at the direction of the Fred Hutch IRB or other external IRB, or through institutional request. Random selection will be limited to research not already monitored by another group (e.g., CRS, Sponsor, etc.), open for at least one CRR, and actively accruing participants. Studies that are designated as more than minimal risk will be prioritized over minimal risk studies. Post-Approval monitoring will be conducted as described in *IRB Staff and Research Study Monitoring Procedures (0244)*.

3. Ongoing HRPP Internal Quality Improvement (QI) Activities

In order to improve existing HRPP processes within the IRO, the following QI activities will be conducted:

a. IRB Meeting Minutes and Binder Audit

The IRB meeting minutes will be reviewed annually by the QA manager.

b. IRB Member Review

Annually, the QA manager will conduct a review of IRB member information files and IRB membership roster.

c. IRO Operations Audits

As directed, the QA manager may perform audits to evaluate existing IRO processes.

QI review will be conducted to evaluate existing processes, identify problem areas, develop and implement any necessary action plans, and evaluate the effectiveness of any action plan. The

internal QI activities will be conducted per the *IRB Staff and Research Study Monitoring Procedures* (0244).

4. Monitoring Activity Reporting, Action Plans, and Evaluation

The QA Manager will prepare a written report of any findings resulting from monitoring activities and will provide the report to the IRO Assistant Director. The IRO Assistant Director may determine if the report should:

- a. Be immediately provided to the IRB for consideration due to potential immediate risk to research participants or others;
- b. Include a draft action plan that was developed with the input of the research staff and/or IRO staff and then provided to the IRB for consideration prior to implementation;
- c. Include an action plan that was developed with the input of the research staff and/or IRO staff and then implemented, and re-evaluated within a reasonable time to determine effectiveness; or,
- d. Be reported to additional institutional officials and/or external organizations such as FDA, OHRP, or Sponsors in compliance with the *IRB Policy 2.8 IRB Requirements for Reporting to Institutional and External Officials* (021) and regulatory reporting requirements.

Any corrective action and/or preventative action plans, as well as findings resulting from monitoring activities, will be reviewed and approved by the IRO Assistant Director.

5. External Consultant

The IRO may engage an external consultant with a specific area of expertise to perform or assist with any of the monitoring and reviewing activities described in this policy.

6. Education

The monitoring procedures described in this policy will be made available to the IRB Staff, IRB Members, and investigators and their staff. Monitoring results will be used as appropriate for educating IRB Staff, IRB members, and investigators and their staff and for enhancing institutional understanding of the HRPP.

SUPPORTING DOCUMENTS

IRB Policy 1.11 Reporting Obligations for Principal Investigators (032)
IRB Policy 2.1 New Application (028)
IRB Policy 2.2 Continuing Review (010)
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)
Application for Review Interventional Research (0324)
Continuing Review Report (045)
IRB Glossary of Terms and Acronyms (050)
IRB Member Checklist (071)
IRB Staff and Research Study Monitoring Procedures (0244)
Fred Hutch / UW Cancer Consortium Data and Safety Monitoring Plan

REFERENCES

21 CFR 56.111
21 CFR 56.109

45 CFR 46.111
45 CFR 46.109