

Title:	Monitoring of Institutional Review Board. IRB Operations, and Research Studies
Responsible Office:	Institutional Review Office (IRO)
Responsible Official:	Karen Hansen, IRO Director
	<i>Signature/date</i>
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POLICY STATEMENT

It is the policy of Fred Hutchinson Cancer Research Center (FHCRC) 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 FHCRC human subjects protection program (“HRPP”) and the determinations of the 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 the Research Trials Office (RTO) as described in this policy.

DEFINITIONS

Cancer Consortium: A research consortium among FHCRC, the University of Washington and Children’s Hospital and Regional Medical Center.

Data and Safety Monitoring Board (DSMB): A committee of scientists, physicians, statisticians, and others that collects and analyzes data during the course of a clinical trial to monitor for adverse effects and other trends that would warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial.

Data and Safety Monitoring Plan (DSMP): A plan for appropriate oversight and monitoring of the conduct of a research study involving human subjects to help ensure the safety of the research participants and the validity and integrity of the research data.

Good Clinical Practice (GCP): A standard for design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate.

Research Trials Office (RTO): The FHCRC Office that promotes supports and facilitates research trials within the Cancer Consortium the following Committees are supported by the RTO:

- **Protocol Data Monitoring Committee (PDMC):** A FHCRC committee of scientists, physicians, statisticians, and others that performs ongoing review and monitoring throughout the accrual life of Cancer Consortium intervention studies.

- **Scientific Review Committee (SRC):** A FHCRC Committee that provides the formal internal peer-review and monitoring for Cancer Consortium intervention studies as required under the terms of the Cancer Consortium's CCSG (Core) Grant.

REFERENCES

21 CFR 56.111(a)(6)

21 CFR 56.109(f)

45 CFR 46.111(a)(6)

45 CFR 46.109(e)

INDIVIDUALS AFFECTED BY THIS POLICY

The contents of this policy apply to IRO staff, IRB members, employees of FHCRC and investigators from other institutions who submit research studies to the FHCRC 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. The IRB Members are reminded on the IRB Member Checklist 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, all research studies conducted at FHCRC must obtain scientific review by one or more of the following methods:

- NIH peer review
- Scientific Review Committee (SRC) review
- Review in accordance with procedures approved by the Division Director (or designee)

All Cancer Consortium intervention research studies must comply with the *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 new IRB application as outlined in the *IRB Policy 2.1 New Applications* 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 Studies' Monitoring.

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

The RTO will conduct monitoring visits of Cancer Consortium research studies as outlined in the RTO CCDSMP Appendix D. The results of the monitoring will be provided to the IRB if there are delinquencies noted that have a reasonable possibility of impacting the safety of research participants.

The PI will include the PDMC and the DSMB reports in the *Continuation Review Report (CRR)* Form for the IRBs review.

b. IRB Monitoring at Continuation Review.

At the time of IRB continuation review of a study (see *IRB Policy 2.2 on Continuing Review*) the IRB will review any PDMC 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*.

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

As part of continuing review, the IRB may observe the consent process of an ongoing study. 45 CFR 46.109(e); 21 CFR 56.109(f). Observation of the consent process may be delegated to appropriate FHCR staff. The FHCR 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 FHCR staff will work with the investigator so that the investigator may inform the research participant that the consent process will be observed.

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

The PDMC 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 IRB after the meeting. Each IRB Chair will then review the monthly minutes of PDMC 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 referred to the convened IRB. A section in the PDMC minutes called "IRB Notification" includes any discussion involving reports of serious noncompliance. The IRO or the IRB may request the full copy of the monitoring report from the RTO Monitoring group. A copy of the signed minutes of the PDMC meeting will be kept on file in the IRO. The Chair may refer the minutes to the full IRB if there is any noted change in the risk.

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*.

- d. The IRO Special Projects Manager (SPM) will monitor the research files of Principal Investigators and their research staff, as outlined in the *IRO Staff Monitoring Procedures*, for the following reasons:
 - i. For-Cause
 - ii. Request of the IRB or IRO Director
 - iii. PI Request
 - iv. Routine monitoring

3. Ongoing Monitoring of IRB Records

The IRO Special Projects Manager (SPM) will periodically conduct monitoring of 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. Generally, the SPM will monitor two IRB files each month but the number of files monitored may vary depending on circumstances. Monitoring procedures will be followed as noted in the *IRB Staff and Research Study Monitoring Procedures* document. Files may be monitored for any of the following reasons:

- a. As part of “for cause” monitoring relating to a particular research study;
- b. At the request of the IRB or IRO Director;
- c. As part of a routine random monitoring of IRB files meeting the criteria described in the *IRB Staff and Research Study Monitoring Procedures*; or
- d. As a result of a report (e.g., suspension of a previously approved study) being forwarded to a regulatory agency.

4. Ongoing Quality Improvement (QI) Review of the HRPP

To improve existing HRPP processes the SPM will conduct annual reviews of:

- a. The OD Policy
- b. the IRO operations
- c. the IRB minute’s binders

The 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 IRB Member information file and the IRB Member roster will be reviewed as needed.

The monitoring process will be followed as outlined in the *IRB Staff and Research Study Monitoring Procedures* document. All action plans will be reviewed and approved by the IRO Director. The findings from all HRPP, IRB Operations or IRB file monitoring will be provided to the IRO Assistant Director with a copy to the IRO Director. The Director or designee will respond to the findings within 30 days of receiving the monitoring report.

5. Quality Assurance Review of the IRO database

The SPM will run periodic reports to check the accuracy and completeness of the data being entered into the database to verify that the data in the paper files are consistent with the data in the database. Any data entry errors noted in these reports will be provided to the Assistant Director who will facilitate the corrections with IRO staff.

6. Action Plans and Evaluation

The SPM will prepare a written report of any findings resulting from monitoring conducted by the SPM and will provide the report to the IRO Assistant Director with a copy to the IRO Director. The IRO Director or designee, with input from the IRB Chairs, may determine if the report is to:

- 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 sources such as FDA, OHRP, or Sponsors in compliance with the *IRB Policy 2.8 Reporting Requirements* and regulatory reporting requirements.

7. 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.

8. Education

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

SUPPORTING DOCUMENTS

IRB Policy 2.1 New Application
IRB Policy 2.6 Unanticipated Problems Involving Risks to Subjects or Others
IRB Policy 2.8 Reporting Requirements
Application For Review
Continuation Review Report
IRB Member Checklist
IRB Staff and Research Study Monitoring Procedure
RTO Protocol Office Scientific Review Committee
RTO Protocol Data Monitoring Committee
RTO Web Page
RTO Cancer Consortium Data and Safety Monitoring Plan