

Title:	Engagement in Research: Determining when Activities are Research Involving Human Research Participants
Responsible Office:	Institutional Review Office (IRO)
Responsible Official:	Karen Hansen, IRO Director
	<i>Signature/date</i>
Effective Date:	January 14, 2008
Policy:	1.14

POLICY STATEMENT

It is the policy of the Fred Hutchinson Cancer Research Center (FHCRC) that the FHCRC Institutional Review Board (IRB) will review and determine if activities are “research” (also referred to as a “clinical investigation”) and if they involve “human participants” (also referred to as “human subjects”). Principal Investigators (PIs) whether their activities involve human participants research or not must submit an application to the IRB for review prior to initiating the research. At FHCRC, the PI may not exclusively make a determination whether an activity involves research and the IRB will make the independent determination regarding human research participant involvement.

DEFINITIONS

Engaged in Research: An institution becomes "engaged" in human subjects research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102]. For purposes of this definition, the term “agents” include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility. Solicitation of consent by performance site staff would be considered engagement in research.

Research:

The regulations of the United States Department of Health and Human Services (“DHHS”) define research as a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research even if they are a component of a larger non-research activity (e.g., instruction, demonstration).

The regulations of the United States Food and Drug Administration (“FDA”) use the term “clinical investigation” rather the term “research.” A “clinical investigation” as defined by the FDA means any experiment that involves a test article and one or more human subjects, and that is either subject to requirements for prior submission to the FDA under section 505(i) or 520(g) of the Federal Food, Drug and Cosmetic Act; or, is not subject to requirements for prior submission to the FDA under these sections of the Act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit. [21 CFR 50.3(c)]. Additional information regarding FDA clinical

investigation definitions for drug or device studies are found at 21 CFR 312.3(b) and 21 CFR 812.3(h) respectively. For study-specific assistance with FDA regulations in the protocol development phase, contact the FHCRC Research Trials Office. The following activities are FDA-regulated research:

- Any use of a drug other than the use of a marketed drug in the course of medical practice. (Clinical investigations subject to requirements for prior submission to the FDA under section 505(i) of the Federal Food Drug and Cosmetic Act.)
- Any use of a device to evaluate its safety or efficacy. (Clinical investigations subject to requirements for prior submission to the FDA under section 520(g) of the Federal Food Drug and Cosmetic Act.)
- Any collection of data to submit to FDA or hold for inspection by FDA in support of a marketing application.

Human Subjects (also known as Human Research Participants):

The DHHS regulations define a human subject as a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. Intervention includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact (e.g., questionnaires, interviews) between the investigator and the subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., medical record information). [45 CFR 46.102]

The FDA regulations define a human subject as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used. [21 CFR 50.3]

Under Washington State law, the term “human subject(s)” is not defined but the authority of institutional review boards to approve the release of “health care information” of “patients” for research purposes without the consent of the patient or a legally authorized representative (in the case of death or incapacity) is recognized and confirmed. The Washington Uniform Healthcare Information Act protects the confidentiality of “health care information” of “patients” who are deceased. [RCW Chapter 70.02]

Research Not Involving Humans Subjects: This is a determination made by the IRB for research projects that exclusively evaluate de-identified or coded data or biologic specimens derived from humans. It is a determination recognized by the Office for Human Research Protections of DHHS, but is not recognized by the FDA. Special application forms have been developed by the Institutional Review Office for assisting the investigators making this determination with the IRB.

Minimal Risk: A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests [45 CFR 46.102(i) and 21 CFR 50.3(k)]. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination.

The definition of minimal risk for research involving prisoners differs somewhat from that given for noninstitutionalized adults. [See 45 CFR 46.303(d) and Guidebook Chapter 6, Section E, "Prisoners."]

Exempt Research: DHHS regulations have defined broad categories of research that are "exempt" from IRB review provided that they meet conditions detailed in 45 CFR 46.101(b). FDA regulations define very limited exemptions from the IRB requirement in 21 CFR 56.104.

Expedited Review: A review process of proposed research by either the IRB chair or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research [45 CFR 46.110 and 21 CFR 56.110].

Full Committee Review: Review of proposed research at a convened IRB meeting at which a majority of the membership of the IRB is present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting [45 CFR 46.108 and 21 CFR 56.108].

Test Article: Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food Drug and Cosmetic Act or under Sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

REFERENCES

OHRP Guidance: Engagement of Institutions in Research
OHRP Guidance: Human Subject Regulations Decision Charts
45 CFR 46.101 (b)
45 CFR 46.102(d), (f), (i)
45 CFR 46.108
45 CFR 46.110
21 CFR 50.3(k), (g)
21 CFR 56.104
21 CFR 56.108
21 CFR 56.110
Revised Code of Washington ("RCW") Chapter 70.02

PRINCIPLES/OVERVIEW

The IRB is charged in reviewing all research governed by the HRPP and authorized to make determinations of research involving humans. This policy also describes the documents required to ensure that the IRB reviews relevant information to evaluate the research study in accordance with the regulations and guidance.

INDIVIDUALS AFFECTED BY THIS POLICY

The contents of this policy apply to Institutional Review Office (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. Determination Authority

As outlined in the *Policy on Human Research Protection Program*, the FHCRC IRB is charged with reviewing all research governed by the HRPP to determine if it meets

applicable ethical standards and other requirements of this policy and the HRPP. The IRB will also approve, disapprove or require modifications to research based on its review. In carrying out these duties the IRB is authorized to make the following determinations for research involving humans.

- The IRB will determine whether or not the proposed research satisfies the definition of human subjects research as defined under the federal regulations; and,
- For research that satisfies the definitions of human subjects research, the IRB will determine if:
 - a) the proposed research is exempt from federal human research subjects protection regulations as outlined in 45 CFR part 46, or
 - b) the proposed research is minimal risk and qualifies for expedited review
 - c) the proposed research is more than minimal risk and requires review by the convened IRB.

The IRB, IRB Chair (or designee) will make the determination as to whether an activity is human subjects research or not. All determinations will be made in accordance with the applicable federal regulation and guidance, and each determination and its basis will be documented and communicated to the investigator.

2. Investigator Submission Methods

When an Investigator submits proposed research to the IRB for review, the Institutional Review Office (IRO) will forward the research to the IRB, or IRB Chair (or designee) for a confirmatory determination regarding human subjects research involvement. The IRB Chair (or designee) may make the one of following determinations when reviewing proposed research. The four mechanisms for submitting research to the IRB include:

Research Not Involving Human Subjects: If the proposed research involves only de-identified data and/or human biological specimens it may be considered research that does not involve human subjects. The Investigator will complete and submit the *Human Subjects Research Determination Form*, and summary of the proposed research for the IRB to review.

The IRB Chair (or designee) will independently evaluate the *Human Subjects Research Determination Form* any appended materials to ensure the research:

- fits the definition of “research”,
- does not involve “human subjects”,
- the specimens or information/data used is not able to be identified either by the investigator or collaborators, directly or indirectly, via coding systems,
- does not involve human biological specimens or information/data that will be used to support the marketing of a FDA regulated drug, biologic, or device product

Exempt from IRB review: If the proposed research fits the criteria of exempt research; the Investigator will complete and submit the *Exempt Checklist*, and summary of the proposed research for the IRB to review.

The IRB Chair (or designee) will use the *IRB Member Checklist* to evaluate the application and additional documents, as outlined in IRB Policy 2.1 *New Application* to ensure that:

- the activity fits the definition of “research”,
- the research activity involves “human subjects”,

- the information provided by the PI falls under one of the 6 exempt category(ies) for research,
- that the research activity does not involve specimens or information/data that will be used to support the marketing of a FDA regulated drug, biologic, or device product; and,
- the research activity does not involve participants who are known to be prisoners,
- the research activity meets the ethical principles of conducting research
- the participants are protected

The IRB Chair (or designee) reserves the right to forward any proposed research for full Committee Review if they determine the proposed research does not meet the criteria established or is determined to be more than minimal risk.

Minimal Risk Qualifying for Expedited Review: If the proposed research fits the criteria of minimal risk research and falls within “Categories of Research that may be Reviewed by the IRB through an Expedited Review Procedure”; the Investigator will complete and submit a *Application for Review*, as outlined in IRB Policy 2.1 *New Application* of the proposed research for the IRB to review.

The IRB shall determine using the *IRB Member Checklist* and the *IRB Member Consent Process and Documentation Checklist* if the proposed research is minimal risk and governed under human subject protections with such decisions being made in accordance with:

- the definition of “research”,
- involvement of “human subjects”,
- types of activities which are considered minimal risk and fall within the “Categories of Research that may be Reviewed by the IRB through an Expedited Review Procedure” as defined by federal regulations
- any proposed inclusion of participants who are known to be prisoners, or other vulnerable populations (e.g. pregnant women, children, decisionally impaired). See IRB Policy 2.15 *Research Involving Vulnerable Populations* for further guidance on these participants.

The IRB Chair (or designee) reserves the right to forward any proposed research for full Committee Review if they determine the proposed research does not meet the criteria established or is determined to be more than minimal risk.

More than Minimal Risk requiring full committee review: The IRB shall determine using the *IRB Member Checklist* and the *IRB Member Consent Process and Documentation Checklist* if the proposed research is more than minimal risk and governed under human subject protections with such decisions being made in accordance with:

- the definition of “research”,
- involvement of “human subjects”,
- types of activities which are considered more than minimal risk
- any proposed inclusion of participants who are known to be prisoners, or other vulnerable populations (e.g. pregnant women, children, decisionally impaired). See IRB Policy 2.15 *Research Involving Vulnerable Populations* for further guidance on these participants.

3. Communicating IRB determinations to the Investigator

All IRB determinations shall be communicated in writing to the Investigator as defined in IRB Policy 1.8 *Approval Date Guidelines and Turnaround Times*.

SUPPORTING DOCUMENTS

Policy on Human Research Protection Program
IRB Policy 1.8 Approval Date Guidelines and Turnaround Times
IRB Policy 2.1 New Application
IRB Policy 2.2 Continuing Review
IRB Policy 2.5 Modification to Ongoing Activities
IRB Policy 2.15 Research Involving Vulnerable Populations
IRB Member Consent Process and Documentation Checklist
Human Subjects Research Determination Form
Exempt Checklist
Application for Review
Expedited Review Checklist for Minimal Risk Activities
IRB Member Checklist