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**POLICY STATEMENT**

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The Institutional Review Board (IRB) and the Institutional Review Office (IRO) staff shall follow special procedures with respect to inclusion of special populations in research studies. A systematic evaluation of initial applications, continuing reviews, and modifications to research studies will be conducted to determine if part or all of the targeted population is or may be considered to be a special population. In all cases where a special population is identified, additional safeguards will be followed. The IRB review will include the review by IRB members and if necessary, consultants to the IRB that have the specific scientific or scholarly knowledge and expertise of the identified special population to protect the rights and welfare of the special population and assure that there is no undue influence or coercion.

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## DEFINITIONS

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

**Assent**

**Children**

**Fetus**

**Individuals with Impaired Decision-making Capacity**

**Legally Authorized Representative**

**Minimal Risk (Prisoners only)**

**Neonate**

**Pregnancy**

**Prisoners**

**Special Populations**

**Vulnerable Populations**

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## PRINCIPLES/OVERVIEW

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### 1. Inclusion of Children in Research

It is the policy of the Fred Hutchinson Cancer Research Center (Fred Hutch) to require adherence to federal regulations regarding the additional responsibilities assigned to the IRB under Subpart D of the DHHS regulations and FDA regulations, as applicable. Investigators, IRB Members, and the IRO staff shall consider the involvement of children in research only after all additional safeguards are considered and in place related to children as research participants as outlined in *Research Involving Special Populations: Children* (0108).<sup>1</sup>

Minimal risk research involving children may be reviewed under the expedited procedure as per 45 CFR 46.110/21 CFR 56.110 and approved under Subpart D 46.404/50.51 or forwarded to the convened IRB as deemed appropriate by the expedited reviewer. When research involving children is reviewed by the convened IRB, the IRB will have at least one member, such as a pediatrician, with the expertise necessary to aid the IRB in determining the risk level of the study and whether there is the prospect of direct benefit to the individual child.

If the research is greater than minimal risk, the IRB will consider whether it holds out the prospect of direct benefit to the individual child, whether their inclusion in the research as well as the risks are justified, and whether the benefit is at least as favorable to children as that presented by available alternatives. If all of these criteria are met, the research may be approvable under 46.405/50.52. All arms of the research will be considered separately for benefit, risks and alternatives to the research, including control/placebo arms or donors.

If the IRB determines the research is greater than minimal risk and there is no prospect for individual benefit of children in one or more arms of the research, the risk level in that affected research population must be limited to a **minor** increase over minimal risk to be approvable under 46.406/50.53. The member with appropriate expertise, such as a pediatrician, will aid in the

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<sup>1</sup> HHS: 45 CFR 46.107(a), Subpart D, 45 CFR 46.403; FDA: 21 CFR 56.107(a), Subpart D, 21 CFR 50.50, 21 CFR 56.111(c)

assessment of what constitutes a minor increase over minimal risk, as well as whether the risks and inclusion of children in the research are justified and the research contributes to knowledge about children who have this disease or condition.

In the case that the IRB determines that research is not otherwise approvable but presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children, the IRB will follow the regulations under HHS 45 CFR 46.407 and FDA 21 CFR 50.54.

In all cases of research involving children, assent and parental/guardian consent shall be sought or appropriately waived according to the Subpart D of DHHS and FDA regulations and IRB Policy 2.11 Informed Consent (017). Who can serve as a guardian to a minor is determined by state or local law.

## **2. Inclusion of Pregnant Women, Human Fetuses and Neonates in Research**

Research involving Pregnant Women, Human Fetuses, or Neonates is very rare at Fred Hutch. If any of these populations have been identified as potential research participants, the Fred Hutch IRB, IRO staff, and investigators will consider all safeguards needed in research activities involving pregnant women, human fetuses, and neonates set forth in Subpart B of DHHS and FDA guidance on pregnant women when developing, reviewing and approving the research. The Fred Hutch IRB will carry out their review as outlined in 45 CFR 46 Subpart B, ensuring that all 10 conditions are met and will request expert consultation as necessary for adequate review. The IRB Members will use the *IRB Member Checklist* (071) to carry out this review.<sup>2</sup>

## **3. Inclusion of Individuals with Impaired Decision-Making Capacity in Research**

When reviewing research involving individuals with impaired decision-making capacity, the IRB will consider whether the protocol includes special safeguards to protect the rights and welfare of such individuals. If the research may include participants with impaired decision-making capacity, the IRB will determine whether the research plan includes an acceptable method for assessing the level of understanding of the potential participant (e.g., post-consent interview, standardized cognitive tests, court guardianship documentation, etc.). If the potential participant is determined to lack the capacity to consent or is expected to lose the capacity to consent during the research study, the IRB will consider whether the research includes an adequate plan to obtain initial and ongoing assent, as appropriate to protect the rights of the participant, and a plan to include a legally authorized representative (LAR) to provide initial and ongoing consent.

In assessing whether it is appropriate for the research to include individuals with impaired decision-making capacity, the IRB will first consider the nature of the research study, its risk level, and whether there is a prospect of individual benefit for the potential participant. The vast majority of research conducted at Fred Hutch that involves individuals with impaired decision-making is therapeutic research that offers the prospect of direct benefit to individual participants.

For IRB review of non-therapeutic research, in which it is unlikely the individual with impaired decision-making capacity will benefit, the IRB will consider whether the research could, instead, be conducted in participants who have the capacity to consent and personally provide appropriate documentation of consent as per ICH-GCP (E6) guidelines.

In cases in which there is no individual benefit for participants with impaired decision-making capacity: If the objectives of the research can only be met by enrolling individuals with impaired

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<sup>2</sup> HHS: Subpart B, 45 CFR 46.203

decision-making capacity, the IRB will consider whether the negative impact of study participation on such individuals is minimized and low and whether inclusion of such individuals in the study contributes to the field of knowledge about the condition or disease in this population. The research-related activities must also be minimal risk or low risk. For all studies, plans for initial and ongoing assent will be reviewed as well plans for consent by an LAR and withdrawal of participants who no longer agree to study activities.

In seeking to enroll an individual with impaired decision-making capacity in a research study, informed consent must be obtained from a legally authorized representative acting on behalf of the research participant. The determination as to who is the legally authorized representative for an individual with impaired decision-making capacity must be made in accordance with the applicable law of the jurisdiction in which the research will be conducted. See *IRB Policy 2.25 Identification and Use of Legally Authorized Representatives (0177)*.

#### 4. Inclusion of Prisoners in Research

In order to conduct research with prisoners, investigators must adhere to additional regulations beyond the basic requirements for research with human participants. The ability of prisoners to exercise free choice may be limited because their autonomy is restricted. In addition, confidentiality of participation and of data are difficult to maintain in a prison setting because privacy of inmates is severely limited. Therefore, additional safeguards are necessary.

Fred Hutch does not routinely review research with a targeted prison population; therefore, investigators must consult with IRO prior to submission of such a study. Fred Hutch generally only reviews research involving prisoners when the incarceration of an individual is incidental to the research. Therefore, most research involving prisoners at Fred Hutch falls under 46.306(a)(2)(iv), "Research on practices that have the intent and reasonable probability of improving the health or well-being of the subject" (for example, clinical trials of cancer therapies that do not involve assignment to placebo).

The involvement of healthy donors in a transplant-related research study generally will not meet the requirements for involvement of prisoners, so prisoners may only be enrolled in the treatment arm of such a study.

It is the policy of Fred Hutch that an IRB member who qualifies as a prisoner representative must be present during the presentation, discussion, and vote of any study in which the research population includes individuals who meet the regulatory definition of "[prisoner](#)" under 45 CFR 46.303(c). For the purposes of human subject research, this definition includes any person who enrolls in a research study, and then becomes a prisoner at any time while in the study **unless** the design of the study is such that it is impossible to determine whether prisoners are involved in the research. It is also the policy of Fred Hutch that the majority of the IRB members (exclusive of the prisoner representative) have no association with the prison involved.

It is the policy of Fred Hutch that the additional responsibilities for IRB review of prisoner research under 45 CFR 46 Subpart C must be fulfilled regardless of funding source.

The Fred Hutch IRB must make the required determinations when reviewing an application involving prisoner research and will use a *Prisoner Certification Checklist for Investigator (060)* to document the determinations required by the regulations noted in the *Research Involving Special Populations: Prisoners (0109)*. Review of new research applications, major modifications, and continuing review of research involving prisoners will be conducted at a convened IRB meeting with the prisoner representative present. The prisoner representative will receive all materials pertaining to the

research, the same as other IRB members. If the prisoner representative is not present at the convened meeting, research involving prisoners may not be reviewed or approved. The prisoner representative may attend via teleconference as long as they are able to participate in the meeting as if they were present in person. The prisoner representative must present their review regarding the applicability of the Subpart C protections either orally or in writing at the convened meeting.<sup>3</sup>

Minor modifications to research involving prisoners may be reviewed via the expedited procedure. The prisoner representative will provide written concurrence about whether the modification impacts the acceptability of the research under Subpart C. Administrative changes to the research (e.g., addition of funding sources, change in contact information, etc.) do not require input from the prisoner representative unless specifically requested by the Expedited Reviewer.

Fred Hutch does not review new applications or continuing review reports for research involving prisoners through the expedited procedure even if those research studies may otherwise qualify for review through the expedited procedure under 45 CFR 46.110. However, if the research study does not require continuing review under the 2018 Requirements of the Common rule, a study involving prisoners may still be eligible for the Status Report process as described in *Policy 2.28, Status Reports for IRB Files*, unless the IRB determines continuing review is still required and documents its decision with sufficient rationale.

Exempt studies: Fred Hutch does not review research involving prisoners through the exempt procedure, except for research aimed at involving a broader subject population that only incidentally includes prisoners.<sup>4</sup> Exempt applications do not require input from the prisoner representative unless specifically requested by the IRB Chair or designee reviewing the submission.

For federally funded studies, the IRO Director will send the required Prisoner Certification Letter to OHRP certifying the IRB has completed its duties under Subpart C and to seek concurrence and approval from the agency to include prisoners in the study. The PI may not enroll incarcerated participants on a federally funded study until OHRP has issued approval and the approval letter is on file in the IRB file and PI research records.

## **5. Following participants who become incarcerated during a study when the study is not previously approved by the IRB to include prisoners**

If an enrolled participant becomes incarcerated during the course of the research, they must be removed from the research project (and no additional identifiable private information may be obtained from the participant) until such time as the IRB (and OHRP for federally funded projects) approves the study to include prisoners, unless there is an immediate risk to the participant from ending treatments under the protocol. If there is an immediate risk from ending treatments, the Principal Investigator must immediately notify the IRO. The IRO will take appropriate action, including convening an emergency IRB meeting or contacting OHRP to inform them of the situation as appropriate.

If the Principal Investigator would like to keep the incarcerated participant on the research study, they must submit a *Research Modification Form (O62)* requesting the involvement of prisoners in the research. Unless there is an immediate risk as outlined above, no research activity may be conducted on the incarcerated participant until the IRB has approved the research to include prisoners consistent with 45 CFR 46 Subpart C. The Principal Investigator may also consider

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<sup>3</sup> HHS: 45 CFR 46.107(a), 46.304(b); FDA: 21 CFR 56.107(a)

<sup>4</sup> HHS: 45 CFR 46.104(b)(2)

removing the participant from the research and treating them as a patient outside the research context.

If the Principal Investigator does not seek or obtain IRB approval to include prisoners in the study, the now-incarcerated participant can no longer be involved in the study until such time as the participant is released from their status as a prisoner. When the participant is no longer considered a prisoner, 45 CFR 46.303(c) is no longer invoked and the participant may be reintegrated into the research project and resume participation consistent with the IRB-approved research. If, during the participant's period of incarceration, the IRB approved modifications to the research which required re-consent of currently enrolled participants, the participant who is no longer incarcerated must be re-consented using the most current consent form(s) before resuming participation.

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## INDIVIDUALS AFFECTED BY THIS POLICY

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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.

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## PROCEDURES

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### 1. Principal Investigator (PI)

- a. Must complete the appropriate *Application for Review* (0324, 0325, or 0326), *Research Modification Form* (062), or the *Continuing Review Report* (045) and note if a special population will be involved in the research.
- b. Include the *Prisoner Certification Checklist for Investigator* (060) when prisoners are involved in the research.
- c. For research funded by federal grants, the PI must wait for an additional OHRP approval subsequent to IRB approval to include prisoners in the study.

### 2. IRB Members

- a. Must consider the following at the time of initial review, when modifications to the study are requested, and at the time of continuing review when making determinations as to the possible inclusion of a special population in research studies:<sup>5</sup>
  - Inclusion and exclusion criteria for selecting and recruiting;
  - Informed consent process;
  - Criteria for selection and recruiting research participants;
  - Willingness of the research participant to volunteer;
  - Possible vulnerability to:
    - coercion and undue influence;
    - being specifically targeted to take on the burdens of research, potentially without the promise of proportionate benefits;
    - being exploited or disrespected during the research process due to inequalities of power or other resources;

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<sup>5</sup> HHS: 45 CFR 46.111(a)(3), 46.111(b); FDA: 21 CFR 56.111(a)(3), 56.111(b)

- taking on excessive risks, for instance because of co-morbidities, or environmental or social factors that make research participation particularly risky for some populations;
  - to being excluded from the opportunity to participate in research for reasons of convenience;
  - Confidentiality of data;
  - Economic, social, physical and environmental conditions.
- b. Use the *IRB Member Checklist (071)* when reviewing New Applications, Continuing Review Reports, and Modifications.
  - c. The IRB Member or consultants to the IRB (e.g., General Counsel) must be knowledgeable about applicable state or local laws (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe) that address potentially special populations.
  - d. Determine if additional safeguards must be taken to protect the potential special populations.
  - e. Follow *Research Involving Special Populations: Children (0108)*; and *Research Involving Special Populations: Prisoners (0109)*.

### 3. IRO Staff

- a. Screen the completed Application, Revision, or the Continuing Review Report and note for the IRB Members if a special population will be involved in the research by using the following:
  - i. *Screener: Modification (0139)*;
  - ii. *Screener: New Application (0335, 0336, or 0337)*;
  - iii. *Screener: Continuing Review Report (0124)*;
  - iv. *Screener: Research Involving Prisoners (0140)* – to be used when prisoners are involved
- b. Provide additional regulatory requirements and considerations to the PI and the IRB Members if on a rare occasion the study might include, pregnant women, human fetus, neonates, or individuals with impaired decision-making capacity.
- c. The IRO staff will document the findings of the IRB and communicate those findings to the PI and study staff as outlined in *IRB Policy 1.6 Meeting and Meeting Records (024)* and screeners noted above.
- d. Follow the *Research Involving Special Populations - Children (0108)*; *Research Involving Special Populations – Pregnant Women, Human Fetuses, and Neonates (0350)*; and the *Research Involving Special Populations - Prisoners (0109)* including the IRO Director sending the prisoner certification letter to OHRP for NIH-funded research to obtain approval by OHRP that the study may involve prisoners.

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## SUPPORTING DOCUMENTS

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IRB Policy 1.6 Meeting and Meeting Records (024)  
 IRB Policy 2.11 Informed Consent (017)  
 IRB Policy 2.25 Identification and Use of Legally Authorized Representatives (0177)  
 IRB Policy 2.28, Status Reports for IRB Files (0403)  
 Application for Review Interventional Research (0324)  
 Application for Review Observational Research (0325)  
 Application for Review Human Specimens or Data Research (0326)  
 Continuing Review Report (045)

IRB Glossary of Terms and Acronyms (050)  
IRB Member Checklist (071)  
Prisoner Certification Checklist for Investigator (060)  
Research Involving Special Populations: Children (0108)  
Research Involving Special Populations: Pregnant Women, Human Fetuses, and Neonates (0350)  
Research Involving Special Populations: Prisoners (0109)  
Research Modification Form (062)  
Screener: Continuing Review Report (0124)  
Screener: Modification (0139)  
Screener: New Application Human Specimen or Data Research (0337)  
Screener: New Application Intervention (0335)  
Screener: New Application Observation (0336)  
Screener: Research Involving Prisoners (0140)

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## REFERENCES

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45 CFR 46 Subpart B  
45 CFR 46 Subpart C  
45 CFR 46 Subpart D  
45 CFR 46.104  
45 CFR 46.107  
45 CFR 46.110  
45 CFR 46.111  
45 CFR 46.203  
45 CFR 46.303  
45 CFR 46.304  
45 CFR 46.403  
21 CFR 50.50  
21 CFR 50 Subpart D  
21 CFR 56.107  
21 CFR 56.111  
OHRP Common Findings 3 & 47 & 48 & 74  
OHRP Guidance Prisoners in Research  
Revised Code of Washington (RCW), Section 7.70.065  
Revised Code of Washington (RCW), Section 11.88.010  
Revised Code of Washington (RCW), Section 26.28.010