BENAROYA RESEARCH INSTITUTE
Virginia Mason

Cooperative IRB Review Agreement

Institution A - Name of Institution Providing and Relying on designated IRB Review:
Benaroya Research Institute at Virginia Mason (BRI)
IRB Registration #: (00000057)
Federalwide Assurance (FWA) #: FWA00001994 and FWA00001995

Institution B - Name of Institution Providing and Relying on designated IRB Review:
Fred Hutchinson Cancer Research Center (FHCRC)
IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619), Com D (00009831)
Federalwide Assurance (FWA) #: FWA00001920

Fred Hutchinson Cancer Research Center and Benaroya Research Institute at Virginia Mason (BRI) share a mutual concern for safeguarding the rights and welfare of human subjects involved in research activities conducted under the direct and indirect sponsorship of their respective institutions. Each institution has on file with the Office for Human Research Protections (OHRP) a Federalwide Assurance (FWA) to which OHRP has assigned compliance certification numbers listed above.

This agreement applies to all research involving both institutions, except in the circumstances described below and except for oncology-related research for which (1) research subject consent will be obtained and (2) the Fred Hutchinson Cancer Research Center's principal investigator is a member of the local Cancer Consortium. Such oncology research must be reviewed by the IRB at the Fred Hutchinson Cancer Research Center.

The IRB of record shall be determined as follows. (1) The IRB of the grantee or contracting institution will review for both participating institutions. (2) If funded through both Fred Hutchinson Cancer Research Center and BRI and/or if subcontracted monies are involved, the IRB Directors (or designees) shall confer (in consultation with the IRB Chairs or others as appropriate) and have the authority to decide which IRB shall review for both. Their decision will be documented and provided to the appropriate committing official of each institution if requested. (3) Research that is not externally funded shall generally be reviewed by the IRB of the institution that will conduct most of the participant contact and research procedures, but the decision will be determined on a case-by-case basis by the IRB Directors (or designees) shall confer (in consultation with the IRB Chairs or others as appropriate) and have the authority to decide which IRB shall review for both. Their decision will be documented and provided to the appropriate committing official of each institution if requested. (4) If one of the institutions chooses to rely on an external IRB of record for research that involves both institutions, the other institution can choose to rely on that external IRB as well if the institution wishes. Each institution must establish its own relationship and agreement with that external IRB.

Each institution reserves the right to insist on review by its own IRB or another IRB regardless of this agreement, so long as that preference is documented and provided to each respective IRB office. IRB review shall occur with voting

membership and/or consultant supplementation appropriate to any given activity. The cooperating institutions agree that the reviewing IRB shall be adequately supported in its function, cooperate with reporting requirements and requests for additional information, and abide by IRB decisions. Either cooperating institution may not administratively overrule disapprovals. Relevant minutes of IRB meetings, pertinent file documents and/or the entire study file shall be made available to both cooperating institutions upon request.

Additional specific operating procedures to implement and support this agreement may be developed, as needed, by the IRB Directors, in cooperation with appropriate institutional officials. As such, it is the responsibility of the Principal Investigator to contact his/her IRB Office to familiarize himself/herself with current cooperative review procedures and requirements.

This overarching Cooperative Agreement becomes effective upon the date of the last signature by the Institutional Officials below and will be continuous, but may be revised by either party upon submission of written notice 30 days in advance of the effective amendment or termination date and subject to the approval of OHRP. Following termination of this Agreement, each institution agrees to provide continued IRB oversight of ongoing research for the reasonable time necessary to appropriately transfer oversight of the protocol(s) to the relying institution's IRB. This document must be kept on file at both institutions and will be provided to OHRP upon request. Additional terms and responsibilities are outlined on the attachment and shall be deemed incorporated herein by reference.

The Officials signing below agree that this agreement applies to all non-exempt human subject research covered by each Institution's FWA for review and continuing oversight of all human subject research at described above and in the attachment.

Signatures:

Authorized Official of BRI (Institution A):

Lynn M. Rose 11/8/16
(signature) (date)

Name: Lynn M. Rose, PhD
Title: Director, Scientific Administration

Mailing Address: 1201 Ninth Avenue
Mailstop: IN-RC
Seattle, WA 98101

Phone: (206) 287-1085 Fax: (206) 342-6580
Email: LRose@benaroyaresearch.org

Authorized Official of the Fred Hutchinson Cancer Research Center (Institution B):

Karen Hansen 11/21/16
(signature) (date)

Name: Karen Hansen
Title: Director, Institutional Review Office

Mailing Address: 1100 Fairview Avenue N
Mailstop: J2-100
Seattle, WA 98109

Phone: (206) 667-4867 Fax: (206) 667-6831
Email: khansen@fhcrc.org

Attachment to IRB Authorization Agreement:

Division of Responsibilities between BRI IRB and Fred Hutchinson Cancer Research Center IRB

The following Division of Responsibilities is based on the premise that the IRB of record will be providing IRB oversight for non-exempt human subjects research activity occurring at another institution (the "Cooperative Institution"), and that institution's primary function is (a) to contribute local context to the IRB of record's review (as needed) and (b) conduct oversight of local performance of these studies.

Applicable regulations. The IRB of record will conduct all reviews in accordance with 45 CFR 46; 21 CFR 50,56, 812; 45 CFR 164; and RCW 70.02 as applicable, in addition to any other applicable regulations as required by the researcher sponsor or location where the research will be conducted. Studies that are not regulated by 45 CFR 46 or 21 CFR 50,56,812 will generally nonetheless be reviewed according to 45 CFR 46 except that the IRB of record may apply its institution's Flexibility Policy concerning such situations. Each institution is required to meet all applicable NIH requirements regarding genetic data (e.g., the Genomic Data Sharing policy) when the institution is the primary awardee of the grant funding the research and is serving as the IRB of record for the other party.

The responsibilities of the IRB of record:

- Perform initial review of new studies, discuss any issues with the Principal Investigator, require necessary modifications to the study, and make a final decision of approval or disapproval of the study;
- Conduct continuing review of the research and review study amendments;
- Conduct review of serious, unexpected, and related adverse events; serious or continuing noncompliance; and other unanticipated problems;
- Inform the Principal Investigator (PI) at the institution of the IRB of record that it is his/her responsibility to inform the PI at the other institution (non-IRB of record site) in writing of all IRB determinations, including approvals and disapproval, required modifications, determinations related to unanticipated problems and noncompliance, and any changes in the study approval status as needed;
- Inform the PI at the institution of the IRB of record that it is his/her responsibility to notify the Pi at the other institution (non-IRB of record site) of new materials that have been reviewed for an active study and any changes in the study approval status;
- Promptly notify the Principal Investigator from the IRB-of-record site the IRB office of the non-IRB of record site, and appropriate officials any determinations that require reporting to institutional officials and/or regulatory agencies under 45 CFR 46.103(b)(5) and 21 CFR 56.108(b) and 56.113 . The IRB of record will submit required reports to the applicable federal department (e.g. OHRP, FDA) and/or funding agency head(s). The IRB of record will make best efforts to provide other institution (non-IRB of record site) an opportunity to review and provide input on any reports prior to transmission to regulatory agencies, especially when the issue is in regard to non-compliance involving subjects from the non-IRB of record's institution.
- Maintain an IRB membership that satisfies the requirements of 45 CFR 46 and 21 CFR 56 and provides special expertise as needed to adequately assess all aspects of each study;
- Make available the roster of IRB membership and the IRB Standard Operating Policies and Procedures as needed (SOPs) to the non-IRB of record site;

- Ensure all IRB members receive orientation and continuing education on topics relevant to human subjects protection;
- Ensure the IRB has adequate meeting space and sufficient staff to support the IRB's review and recordkeeping duties;
- Notify the non-IRB of record site immediately if there is ever a suspension or restriction of IRB authorization to review a study; and
- Notify the non-IRB of record of any changes in the IRB of record's SOPs that might affect the institution's reliance on the IRB of record's review or performance of the research at the local institution.

The responsibilities of the institution (Cooperative Institution; non-IRB of record) relying on another IRB of record:

- Provide any local context information that is not study-specific to the IRB of record and update it as necessary
- When needed, provide a local context reviewer who has knowledge of the local research context and is able to review the informed consent form and related documents (e.g. authorizations for testing and release of medical records or donation of human specimens) to verify these documents comply with applicable federal, state or local laws, institutional requirements, or IRB policies of the Cooperative Institution;
- Ensure the safe and appropriate performance of the research at the Cooperative Institution. This includes, but is not limited to, conducting the research as approved by the IRB of record, monitoring protocol compliance (after becoming aware of protocol deviations, unanticipated problems or noncompliance), managing any major protocol violations, managing any serious adverse events occurring at the institution, ensuring qualifications and training of research staff are commensurate with the research activity and providing a mechanism by which complaints about the research can be made by local study participants or others and consequently investigated;
- Provide the names and addresses to the IRB of record of local contact persons who have the authority to correspond on behalf of the non-IRB of record (e.g. the local IRB Director);
- Maintain records from the IRB of record approved research at the Cooperative Institution;
- Maintain an OHRP-approved Assurance for human subjects research;
- Promptly notify the IRB of record if the Cooperative Institution becomes aware of events that may change the ability of the site to conduct the research (e.g., suspension of the institution's FWA);
- Maintain a human subjects protection program compliant with 45 CFR 46 and 21 CFR 50 and 56;
- Maintain compliance with state, local, or institutional requirements related to the protection of human subjects; and
- Review and monitor individual and institutional conflicts of interest per the Cooperative Institution's own policies and procedures.

Additional considerations:

Confidentiality Laws and Regulations:

Compliance with confidentiality laws and regulations, including HIPAA and state law requirements, is considered a local institutional issue. The IRB of record expects the designated local context reviewer to have knowledge of these requirements for the Cooperative Institution and to be able to provide comments before or during the IRB review process. The Cooperative Institution remains responsible for how compliance with these confidentiality requirements is implemented at the institution.

Prisoners:

The IRB of record must adhere to 45 CFR 46 Subpart C and would need to re-review a protocol when it becomes aware of an investigator wanting to conduct research on a prisoner. The Cooperative Institution must notify the IRB of record before enrolling prisoners in research overseen by another IRB.

Serious Adverse Events and Other Unanticipated Problems

It is the responsibility of the Cooperative Institution's Principal Investigator to identify and report Serious Adverse Events and/or Other Unanticipated Problems in accordance with the IRB of record policy on reporting to the IRB of Adverse Events and/or Unanticipated Problems. The IRB of record accepts the responsibility to ensure reporting to the appropriate regulatory agencies (i.e. OHRP and/or FDA) and any federal funding agency if they determine the event constitutes an Unanticipated Problem Involving Risk to Subjects or Others. Any reporting to federal agencies regarding a subject at the Cooperative site should only be done after consultation between both institutions' IRBs to assure accurate and consistent reporting.

Noncompliance:

It is the responsibility of Cooperative Institution's Principal Investigator to identify and report Noncompliance in accordance with the IRB of record policy on Non-compliance. For events that must be reported to the IRB ofr record, the Principal Investigator at the Cooperative Institution will be responsible for providing the appropriate documentation directly to the IRB of record's investigator, which will report the event to the IRB of record. The IRB of record accepts the responsibility to ensure reporting to the appropriate regulatory agencies (i.e. OHRP and/or FDA) if the IRB of record determines the event constitutes Serious and/or Continuing Non-compliance per their own policies and procedures. Any reporting to federal agencies regarding noncompliance involving the Cooperative site should only be done after consultation between both institutions' IRBs to assure accurate and consistent reporting.