# University of Michigan
# Institutional Review Board
# Joint Standard Operating Procedures
# (SOPs)

**Working Draft v.2 November 17, 2025**

**Medical School Institutional Review Board**
**(IRBMED)**

**Health Sciences and Behavioral Sciences Institutional Review Board**
**(IRB-HSBS)**

## REVISION HISTORY

IRBMED and IRB-HSBS Standard Operating Procedures (SOPs) have been harmonized to represent joint operating procedures common to both IRBs. Archived versions of the previous IRBMED SOPs (September, 2022) and IRB-HSBS SOPs (July, 2020) remain available for reference. These newly harmonized SOPs remain as a working draft to facilitate any necessary iterative improvements in the transition for the IRBs. Future revisions will be recorded in Part 14.

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# Part 1 – Introduction, Purpose, and Ethical Principles

This section describes the mission of the University of Michigan Human Research Protection Program (HRPP), Institutional Review Boards (IRBs): Institutional Review Boards Medical School (IRBMED) and Institutional Review Boards IRB Health Sciences and Behavioral Sciences (IRB-HSBS), the purpose of the IRBs, the authority under which they operate, and the scope of research conducted at the University.

## I. Mission Statement and Organizational Summary

*Refer to* HRPP OM Part 1.II

The Vice President for Research (VPR), who serves as the Institutional Official (IO) for human research oversight, has established the Human Research Protection Program (HRPP) as a comprehensive, institution-wide initiative to ensure ethical and high-quality research involving human participants. The HRPP includes research leadership, administrative and compliance oversight, Institutional Review Boards (IRBs), other review bodies, education programs, and quality assurance activities. Together, these components work to protect the rights and welfare of research participants and uphold excellence in human research.

The Office of the Vice President for Research (OVPR) maintains a research website that provides comprehensive information about research conducted at the University by its faculty, staff, and students.

HRPP policies are compiled in the HRPP's Operations Manual (OM) which outlines the system's structure and governing rules. The OM serves as a key reference for investigators, IRBs, administrators, and others involved in human research. The IRB's Standard Operating Procedures (SOPs) detail how the IRBs apply the policies outlined in the OM and additional regulatory requirements.

The mission of the IRBs is to protect the rights and welfare of participants in human research studies by careful review and monitoring of research in accordance with applicable laws, regulations, and University policies. The IRBs support investigators with the design and conduct of research projects to minimize risk to human participants, provide guidance to the University and its researchers on ethical and procedural issues related to the use of human participants in research, and facilitate compliance with governmental and University policies pertaining to human subjects research. The safeguarding of participants' rights and welfare must, at all times, take precedence over the goals and requirements of any research endeavor overseen by the IRBs. IRB members and staff, as well as researchers submitting applications to the IRB, must be informed of and understand this obligation.

Except for research that is specifically exempted in accordance with applicable laws and regulations, as described in OM Part 4.VI, a U-M IRB or an external IRB reviews and monitors all U-M research involving human participants, regardless of funding source. In addition, certain types of research involving human participants must be reviewed and approved by additional departments, divisions, or units of the University. Depending on the nature and scope of a project, a University IRB may withhold its approval pending confirmation of approval by and/or receipt of additional information from any of these units and/or from review units at other performance sites or other external agencies or offices.

To perform its review, approval, and monitoring functions, each IRB complies with applicable regulations concerning membership and conduct. The IRBs are designated by the University to review and monitor human participants research under its Federalwide Assurance (FWA). The IRBs maintain these written SOPs, consistent with and supplemental to the HRPP OM, and may issue additional guidance as necessary.

The IRBMED is comprised of six (6) separately constituted boards and oversees the protection of human participants in research conducted at Michigan Medicine which includes the University of Michigan Medical School and the University of Michigan Health, FDA-regulated research or medical intervention research conducted by faculty and staff from other U-M units including Dentistry and the campuses of U-M Ann Arbor, Flint, and Dearborn.

The IRB-HSBS consists of two (2) separately constituted boards providing primary support for researchers from U-M Ann Arbor, Dearborn and Flint academic campuses.

Each IRB also oversees research conducted off-site by faculty and staff as University employees or in connection with their University appointments, research conducted internationally, and as single IRB ([sIRB] also referred to as Reviewing IRB or IRB of Record) for multi-site research or for individual investigators via use of IRB Authorization Agreements or reliance agreements including the National IRB Reliance Initiative: SMART IRB.

## II. AUTHORITY UNDER WHICH THE U-M HRPP AND IRBS OPERATE

*Refer to* HRPP OM Part 1.III

*Refer to* HRPP OM Part 11

The U-M HRPP, of which the U-M IRBs are a part, operates under the authority of and in accordance with applicable federal regulations and its FWA, including:

### A. Department of Health and Human Services (HHS)

The Public Health Service Act and its amendments, which empower the Department of Health and Human Services (HHS) to issue regulations for the protection of human participants. These are compiled in the "Common Rule", 45 CFR 46 Subpart A. The Common Rule codifies and expands on the ethical principles described in the Belmont Report.

HHS maintains additional regulations for federally funded research involving pregnant women, fetuses, and neonates (45 CFR 46 Subpart B); prisoners (45 CFR 46 Subpart C); and children (45 CFR 46 Subpart D). (Note: Except for regulatory citations necessitating use of the term "pregnant women," these SOPs will utilize the terms "pregnant woman/person" or "pregnant women/persons.")

HHS provides guidance and information concerning its interpretation of the Common Rule and related regulations through determination letters directed to organizations performing research under Federalwide or other assurances following investigations of research noncompliance, and other guidance documents.

The Common Rule has been adopted by numerous federal agencies conducting human participant research. The full list of agencies and their regulatory citations are found at: Federal Policy for the Protection of Human Subjects ('Common Rule') | HHS.gov.

The Common Rule and the subparts of 45 CFR 46 providing special protections for identified vulnerable populations may not be uniformly interpreted or enforced. The special protections applicable to federally supported research under these subparts have not been widely adopted by other agencies but generally are applicable to University research, as further described in Part 7 of the SOPs and OM. When a federal agency other than OHRP is responsible for oversight of a particular project or category of projects, the standards set by that agency's interpretation of the Common Rule and adoption or failure to adopt the additional subparts of 45 CFR 46 generally will inform the manner in which the corresponding University research is reviewed and conducted. For non-federally supported research, administrative requirements involving reports or applications to the relevant federal agencies are addressed through alternative mechanisms. Part 7 of the OM and these SOPs provide additional information on University policy for research involving vulnerable research participants.

IRB review of non-federally sponsored research is guided by the principles of the Belmont Report, University policy, the HRPP Operations Manual and state and federal regulations. If federal regulations are not applied per HHS regulations, research is reviewed and conducted under equivalent protections for the human participants.

**B.** Food and Drug Administration (FDA)

FDA regulations for human subjects protections are found in 21 CFR 50; for institutional review boards, 21 CFR 56; for investigational drugs and biologics, 21 CFR 312; and for investigational devices, 21 CFR 812. Additional information about research regulated by the FDA and special requirements for that research is provided in Part 6.II and Part 8 of this SOP and the HRPP OM and at the FDA website.

**C.** National Institutes of Health (NIH)

Rules for research involving recombinant DNA or synthetic nucleic acid molecules issued by the National Institutes of Health (NIH). The NIH Office of Science Policy (OSP), through its Biosafety and Biosecurity Policy Area, issues the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines). The Institutional Biosafety Committee (IBC) at the University of Michigan provides oversight for this research and human gene transfer clinical trials.

**D.** Department of Education (ED)

Research regulated by the Department of Education (34 CFR 97, 98, 99).

*Refer to* U. S. Department of Education Protection of Human Subjects.

**E.** Health Insurance Portability and Accountability Act (HIPAA)

Privacy regulations issued under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 (45 CFR 160 and 164).

**F.** International Council for Harmonization (ICH)

Principles stated in International Council for Harmonization (ICH) Efficacy Guidelines

*Refer to* U-M IRB SOP Part 6 – Roles and Responsibilities of Investigators and Research Staff

*Refer to* HRPP OM Part 6 – Roles and Responsibilities of Investigators and Research Staff

**G.** Additional Governing Laws, Regulations and Other Standards

*Refer to* HRPP OM Part 11

## III. Limitation on Institutional Authority

*Refer to* HRPP OM Part 1.III.B

All regulated human participant research conducted by the University must be approved by an IRB or granted an exemption through the University IRB system. All exempt human participant research must be granted an exemption according to the procedures outlined in Part 3 III.C.1(d)(3) as applicable and specified in these SOPs and the OM. Research that has been reviewed and approved with the necessary expertise by a U-M IRB may be subject to further review and disapproval by other review bodies or officials (including the Vice President for Research). However, no person or organization may override a U-M IRB disapproval determination.

## IV. Ethical Principles

*Refer to* HRPP OM Part 1.IV

## V. Protection from Undue Influence

*Refer to* HRPP OM Part 1.V.

## Part 2 – Organization of the HRPP and U-M IRBs

This section describes the organization of the University of Michigan IRBs and the roles and responsibilities of the various units that guide and support the program.

### I. Key Organizational Representatives

Organizational charts identify key roles and units in the University, Medical School, and IRBs.

*Refer to* the OVPR, IRBMED, and IRB-HSBS websites.

### II. Organizational Entities that Support U-M IRBs

*Refer to* HRPP OM Part 2

Numerous organizational entities contribute to the operation of the U-M HRPP and the IRBs including but not limited to:

- University of Michigan Office of Research (OVPR)
- Office for Research Compliance Review (ORCR)
- Office of Research and Sponsored Projects (ORSP)
- Michigan Institute for Clinical Health Research (MICHR)
- HRPP Advisory Council
- Office of the Vice President and General Counsel
- Research Administrative Deans
- Conflict of Interest Committees
- Information and Technology Services (ITS)
- Health Information Technology & Services (HITS)

Additional entities supporting IRBMED:

- Medical School Office of Research (OoR)
- Medical School Office of Regulatory Affairs
- Michigan Medicine Corporate Compliance
- Executive Vice President for Medical Affairs (EVPMA)

Additional entities supporting IRB-HSBS:

- U-M Office of the Provost
- Chancellors of U-M Flint and Dearborn Campuses
- U-M Flint Office of Research
- U-M Dearborn Office of Research

**A.** University of Michigan Office of Research

*Refer to* HRPP OM Part 2.II.A

**B.** Academic Units

*Refer to* HRPP OM Part 2.II.B

**C.** Other Research Review and Support Units

*Refer to* HRPP OM, Part 2.II.D

Other HRPP and U-M committees review the science, ethics, and additional regulatory requirements that apply to a given study to protect the rights and welfare of the research participants.

Certain types of research involving human participants must be reviewed and approved by additional departments, divisions, or units of the University. Depending on the nature and scope of a project, a U-M or external IRB may withhold its approval pending confirmation of approval by or receipt of additional information including but not limited to any of the following:

- University of Michigan Medical School (UMMS)
- Michigan Institute for Clinical and Health Research (MICHR; includes MIAP [MICHR IND/IDE Investigator Assistance Program])
- Clinical Trials Support Offices (CTSO)
- Michigan Clinical Research Unit (MCRU)
- Clinical Research Calendar Review Analysis Office (CRAO)
- Central Biorepository (CBR)
- Institutional Biosafety Committee (IBC)
- Human Pluripotent Stem Cell Research Oversight Committee (HPSCRO)
- Research Pharmacy, formerly the Investigational Drug Service (IDS)
- Radioactive Drug Research Committee/Subcommittee on the Human Use of Radioisotopes (RDRC/SHUR)
- Michigan Medicine Clinical Engineering
- Michigan Alzheimer's Disease Center (MADC)
- Tissue Procurement Core (TPC)
- OVPR Conflict of Interest Committee
- Michigan Medicine Medical School Conflict of Interest Review Board (MEDCOI)
- Institutional Conflict of Interest Committee (iCOI)
- Department or organization peer review committees (e.g., Rogel Cancer Center Protocol Review Committee)
- Data stewards of individual data sets

Any other unit issuing a decision that impacts a contingent or final determination by a U-M or external reviewing IRB is responsible for informing the IRB of their decision.

**D.** Independence of Research Review Units and Response to Undue Influence

*Refer to* HRPP OM Part 2 II.E.

**E.** Resources

*Refer to* HRPP OM Part 2.II.F.

The Medical School Office of Research provides oversight, administrative and financial support for the IRBMED office; the Office of the Vice President for Research provides equivalent support for IBB-HSBS. On an annual basis, the fiscal year operating budget for the IRBs is reviewed and approved by the applicable authorities in each unit and reviewed by OVPR.

# Part 3 – HRPP and U-M IRB Policy

This section describes the process by which the University's HRPP and U-M IRB policies are developed, approved, and implemented.

## I. Rulemaking

Rulemaking at the University of Michigan is divided three ways: (i) the Bylaws of the Board of Regents; (ii) rules initiated by University authorities that become effective only upon approval by the Board of Regents (Regents Policies); and (iii) rules adopted by subordinate University authorities, under delegated legislative powers, that become effective as provided by such subordinate authorities.

Human Research Protection Program (HRPP) policies fall within the third class of rulemaking. In Standard Practice Guide (SPG) 303.05, the University has delegated to the VPR general executive responsibility for the research programs of the University and, in that role, the responsibility for implementing the HRPP, including the legislative powers to adopt and enforce HRPP policy and procedures.

## II. HRPP Operations Manual

The HRPP Operations Manual (OM) is the primary location for compiling, organizing, integrating, and pointing to the rules, policies, practices, and guidance encompassing the University's HRPP. Revisions to the OM are approved as outlined in the HRPP OM Part 3. Records of such approvals are maintained by OVPR.

At least once every five years, typically in conjunction with the Association for the Accreditation of Human Research Protection Programs (AAHRPP) re-accreditation cycle, OVPR initiates a comprehensive review of the OM, IRB SOPs, and supporting HRPP/IRB guidance documents. Revisions may be made at any time, however, as required by changes in law, ethical standards, institutional policy, quality assurance activities, or other considerations.

## III. IRB Standard Operating Policies and Procedures

*Refer to* HRPP OM Part 3.III

### A. General Provisions

*Refer to* U-M IRB SOP Part 5.IV-VII

*Refer to* HRPP OM Part 5.IV

The U-M IRB members and staff to which these SOPs refer are accountable to the Institutional Official (IO) (and designees) and operate under the authority of OVPR with regard to the oversight of human participants research. The IO may appoint designees including a Deputy Institutional Official (DIO) and/or HRPP Director (collectively, "designees") to perform indicated duties. These designees, in turn, may delegate specified duties to other qualified individuals. The U-M IRBs cooperate with the IO/designees, OVPR, and applicable institutional offices to establish content, revise, and review these SOPs. These SOPs and any substantive revisions thereto, are subject to final approval by the IRB Directors, HRPP Director, and DIO. Non-substantive revisions such as correction of typographical errors, corrections of website links, modifications to enhance regulatory flexibility and workflows, inclusion of standard forms, guidance documents, and similar information developed by the U-M IRBs

are approvable by the HRPP Director. The IRBs maintain an outline of these vetting and approval procedures.

Outdated sections of these SOPs will be archived in such a way that modifications and dates of approval are indicated.

The U-M IRBs maintain guidance documents on the IRBMED and IRB-HSBS websites, Medical School Research A-Z, and OVPR webpages on topics of relevance for the U-M IRB boards, U-M IRB Staff, and researchers. In many cases the guidance expands on the information contained within these SOPs and is therefore referenced in the SOPs where appropriate.

Generally, U-M IRBs have oversight of human participant research aligning with their respective expertise domains as noted in section Table 1. When review of an IRB submission would be better served by a different U-M IRB, oversight of a research project can be moved between IRBMED and IRB-HSBS. When an application must be transferred between IRBs, U-M IRB administrative staff work in consultation with the respective IRB Chairs, as necessary, to assess the submission and make the necessary transfer.

U-M IRBs conduct business through multiple IRBs, each of which is a separately registered IRB with the Office of Human Research Protections (OHRP) for purposes of University policy and the Federalwide Assurance (FWA).

**Table 1: IRBs**

| Board Name | Registration No. | FWA No. | Content |
|---|---|---|---|
| A1 IRBMED | 00000244 | 00004969 | Biomedical |
| A2 IRBMED | 00001996 | 00004969 | Biomedical |
| B1 IRBMED | 00001999 | 00004969 | Biomedical |
| B2 IRBMED | 00001995 | 00004969 | Biomedical |
| C1 IRBMED | 00005467 | 00004969 | Biomedical |
| C2 IRBMED | 00012211 | 00004969 | Biomedical |
| Maize IRB-HSBS | 00000245 | 00004969 | Health/Behavioral |
| Blue IRB-HSBS | 00000246 | 00004969 | Health/Behavioral |

The IRBMED also provides review of cooperative group-sponsored projects through an agreement with the National Cancer Institute - Central Institutional Review Board (NCI-CIRB).

IRBMED and IRB-HSBS are signatories to SMART IRB relationships which include accepting IRB oversight and ceding oversight to external IRBs. The U-M IRBs also permit ceding to independent IRBs with whom master agreements are executed (e.g., WIRB, Advarra).

## B. Organization and Personnel (Chairs, Members and Staff)

### 1. IRB Composition, Rosters, and Meeting Procedures

U-M IRB membership is selected to be sufficiently qualified through the experience, expertise, and diversity of its members (including consideration of race, gender, cultural background, and sensitivity to such issues as community attitudes), thereby to promote respect for its advice, counsel, and determinations in safeguarding the rights and welfare of human participants.

Each of the eight (8) registered IRBs consists of primary voting members and alternate members with expertise augmented as necessary by consultants. As appointed, an individual member may serve as a primary on more than one Board. Members are automatically appointed as alternates to all other Boards where they do not serve as primary members. They may only fill a role in their appointed capacity as defined by the roster.

Each IRB will have at least five (5) voting members, including the Chairs, with varying backgrounds to promote comprehensive review of research activities affiliated with the specific IRB as commonly conducted at the U-M Medical School, Michigan Medicine, and U-M academic units including Ann Arbor, Flint, and Dearborn.

No IRB may consist entirely of members of one profession.

Every nondiscriminatory effort will be made to ensure the IRB does not consist entirely of individuals identifying as the same gender. No selection will be made, however, solely on the basis of gender.

In addition to possessing the professional competence necessary to review specific research activities, each IRB that regularly reviews research involving one or more vulnerable categories of participants, such as children, prisoners, pregnant persons or physically or mentally disabled individuals will include members on the IRB of one or more individuals knowledgeable about and experienced in working with these participants.

When reviewing FDA-regulated studies, the designated IRB must include at least one physician.

The IRB must include at least one scientist member as defined at HRPP OM Part 3.III.B.1.e.1. Scientist members include physician scientists (e.g., MDs or DOs), non-physician scientists (e.g., DDS, PhDs, nurses, geneticists, pharmacists and biomedical engineers), and social and behavioral scientists (e.g., psychologists, social workers, counselors). Scientist members have significant educational background (e.g., a science degree) and experience in scientific disciplines. Scientist members are recruited from among active and emeritus members of the university faculty and staff or from the community.

Any scientist who is an experienced primary member (i.e., those members designated as having enough experience to serve as expedited reviewers) or alternate scientific member with appropriate IRB experience may serve as a substitute chair of that IRB in the absence of the appointed Co-Chair or Vice-Chair.

The IRB must include at least one non-scientist member as defined at HRPP OM Part 3.III.B.1.e.2. They may be recruited from active or emeritus University faculty or staff or from the community.

The IRB must include at least one member who is not otherwise affiliated with the University (including by relationship with an immediate family member; spouse, domestic partner, or dependent) who represents the general perspective of participants, are sensitive to community attitudes in promoting respect of research participants regardless of race, gender and cultural

background, and safeguard the rights and welfare of human participants. See examples of affiliated and unaffiliated individuals at HRPP OM Part 3.III.B.1.f.

All primary members, including unaffiliated members, are expected to attend, actively participate in the discussion, and vote at the majority of IRB meetings during a calendar year. Members are also expected to complete a review of assigned applications. Poor attendance by members will be addressed by the IRB Chair and directors on a case-by-case basis.

Each IRB maintains current membership rosters containing a list of specified Chair(s), members and alternate members that are identified by name, earned degree, representative capacity (physician scientist, scientist, social-behavioral scientist, non-scientist); indications of experience sufficient to describe each member's contributions to the IRB deliberations; and any employment or other affiliation or non-affiliation between each member and the University.

Membership rosters are revised approximately quarterly (ad hoc updates may be issued as necessary) to indicate:

- Newly appointed primary or alternate members and Chairs
- Current primary members or alternate members extending their membership, resigning, or no longer eligible for membership
- Primary members or alternate members who are otherwise modifying some aspect of their membership appointment

Revised membership rosters are forwarded to IRB and HRPP Leadership. Following each roster change the IRBs forward approved membership rosters to OVPR, who then post changes to OHRP as applicable. The IRBs post the current membership rosters of primary and alternate on their websites.

a) IRB Chairs and Vice-Chairs

- Each Board is overseen by one Chair and may have one or more Vice-Chairs (collectively referred to as the "Chairs" throughout these SOPs; if an IRB has more than one individual serving as Chair of separate boards, they are referred to as co-Chairs and are considered voting members. IRB-HSBS will have Vice-Chairs representing the U-M Flint and Dearborn campuses with the relevant expertise noted below.
- Each Chair and Vice-Chair must be a respected, active member of UM faculty who qualifies as a scientist member with significant educational background, is concerned and knowledgeable about human rights and ethical issues, is well informed concerning the laws, regulations, and University policies and procedures that govern the conduct of human participants research, and has previous IRB experience.
- The DIO is responsible for the appointment and reappointment of Chairs. When a vacancy arises, the DIO/HRPP Director may solicit nominations for a new Chair or a Vice-Chair from the University faculty, IRB members, staff, and consultants.
- The DIO then considers all available information and issues the appointment.
- An individual is appointed to serve a three (3) year term as a Chair or a Vice-Chair. In consideration of reappointment, a chair is evaluated for their contribution to leadership as

well as their concern and knowledge of human rights and ethical issues, laws, regulations, University policies and procedures that govern the conduct of human participants research, and their performance of assigned duties. Appointments are renewable with the agreement of the parties but at the discretion of the DIO.

- Retiring Chair(s) who wish to continue their service at the end of their term may be reappointed as a full or alternate member of the IRB.

b) IRB Members

*Refer to* HRPP OM Part 3.III.B

- The DIO, HRPP Director, IRB Chairs/directors/members/staff, or units conducting research may solicit nominations from members of the University faculty, staff, and the University community. Individuals affiliated with the University may also nominate themselves for service on the IRB. Unaffiliated representatives may be recruited through similar methods, by community advertisements, or nomination by third parties. IRB-HSBS will have members representing U-M Flint and Dearborn campuses.
- Solicitations may, as necessary, include information concerning the background, qualifications, and experience needed to promote diversity of experience and to provide or supplement necessary expertise on the IRBs.
- The DIO or HRPP Director will consult with the IRB Chairs on potential new members with regard to each individual's qualifications, past participation (in the case of a reappointment), and other relevant criteria.
- A potential new member will undergo an interview with the IRB Chairs and DIO or HRPP Director. As delegated by the DIO, the HRPP Director has final authority to make each member appointment or reappointment.
- All members should be sufficiently qualified through experience, expertise, and diversity and be able to determine the acceptability of proposed research in terms of institutional commitments and policies, applicable laws and regulations, and standards of professional conduct and practice.
- Each member is typically appointed to an initial term not to exceed three years, which may be renewed at the discretion of the HRPP Director.
- Members are evaluated for reappointment by the HRPP Director after seeking evaluation from the IRB Chairs and Office staff of the member's level of participation, adequacy of reviews, regulatory/ethical interpretations. Evaluations are conducted at the conclusion of the first year of appointment and thereafter prior to any reappointment to assess fulfillment of IRB duties and their ability to apply regulatory criteria to their reviews. Members having unsatisfactory evaluations in one or more areas will receive feedback and recommendations from the IRB Chairs toward improving their efforts.
- Members are assigned reviews of IRB applications within their appropriate scientific and/or regulatory experience.

To ensure that the IRBs are maintained as sufficiently diverse in experience, expertise, education, ethnicity, gender, cultural background, and sensitivity to such issues as community attitudes, the DIO or HRPP Director and IRB Chairs will periodically review the membership composition by examination of the rosters and discussion with IRB Directors. Additional primary or alternate members will be recruited to ensure sufficient breadth of the registered board composition should members' terms expire, vacancies arise, new expertise is required, or the submission review workload necessitates.

c) IRB Staff

- The IRBs are supported by a professional staff hired and supervised by the Director(s) of each IRB with specific authority delegated to any Assistant Directors. The Directors report to the Assistant Vice President for Research - Human Research Protection Program (AVPR-HRPP).
- The Director and staff are responsible for facilitating IRB operations (e.g., human research application regulatory review; documentation and record retention; review of noncompliance allegations, including fact-finding; serving as an informational resource; conducting educational activities) in such a manner as to maintain compliance with applicable State and Federal regulations and University policies, and for performing related activities as designated by the DIO, AVPR-HRPP, or HRPP Director.
- The Director assigns to each staff member the appropriate permission to perform regulatory and/or primary reviews; and/or coordinate the human participant research submissions in the web-based eResearch Regulatory Management (eRRM) system which centralizes the review and approval process for IRB Applications and IBC Biosafety Registrations.
- The IRB Offices include staff dedicated to review submitted materials for clarity, completeness, and compliance with regulations and other institutional requirements in support of each of the eight (8) IRBs. The IRB offices are further supported by other administrative, educational, compliance, quality assurance and quality improvement roles. Day-to-day operations are overseen by the specific authority assigned to any Assistant Directors or other designated roles. All IRB staff ultimately report to the Director.
- Each IRB Office also tracks and manages membership information, including, but not limited to: membership role (physician scientist, non-physician scientist, non-scientist, and unaffiliated members), areas of expertise, COI, university affiliation, and advocacy for minority populations such as decisionally or physically disabled individuals, prisoners, and children or minors.

d) IRB Meetings

- The Institution provides appropriate resources for board meetings, as applicable:
    - Electronic meetings: technological equipment and support
    - In-person meetings: private meeting facilities with appropriate devices including overhead screens, projectors and individual computers (issued for meeting use) for each member present that does not bring a personal laptop computer to the meeting
    - Informational booklets containing copies of regulations (available at in-person

meetings and electronically).

- The Chair, or in their absence, a Vice-Chair or senior scientist member of the IRB leads each meeting. The IRB staff monitors and documents attendance to ensure that quorum and member composition meet requirements defined by Federal Regulations (45 CFR 46.107 and 21 CFR 56.107). A quorum (defined as more than half the number of primary members of an IRB) must be present for each formal vote.
- Quorum must include at least one nonscientist member.
- At convened meetings at least one unaffiliated member who represents the general perspective of participants should be present at the majority of meetings in a given year but is not required for quorum.
- When reviewing research involving prisoners, the prisoner representative must be a voting member of the IRB.
- If quorum is lost during a meeting, no voting will occur until quorum is restored.

e) IRB Meeting Schedules and Format

Each IRB convenes regularly to fulfill the mandate to oversee research involving human participants subject to IRBMED's jurisdiction. The IRBMED is comprised of six (6) IRBs each convening every two weeks. IRB-HSBS is comprised of two (2) boards, each convening monthly. Additional meetings may be convened as necessary. The IRBs typically convene electronically or may meet in person.

(1) Meeting Cancellation

If circumstances dictate that a meeting should be canceled (e.g., an anticipated lack of quorum), the IRB staff will make a request of the Chairs and the Director(s) to cancel the meeting after efforts to secure a meeting have failed. If the Chairs agree the IRB office staff will notify the board members of the change. Agenda items will be reviewed for timely reassignment to other scheduled boards, if possible.

(2) Ad Hoc Meetings

Occasionally additional board meetings are needed to address a significant increase in submissions, submissions from a previously canceled meeting, or other pressing issue. The Chairs are notified of the recommendation. If there is no disagreement, the members of the designated boards are notified by the IRB staff to verify the availability of a quorum.

(3) Electronic Board Meeting Format

The IRBs typically utilize electronic technology (e.g., videoconference or teleconference) to facilitate the participation of the members. The agenda and all review materials will be available to the remote member via eResearch in advance of and throughout the meeting. The Chair of a meeting utilizing these technologies will facilitate the active and equal participation of the remote members.

f) Agendas & Review Items

Prior to each convened IRB meeting the designated IRB staff will prepare an electronic IRB meeting agenda in eResearch with items for review, discussion, deliberation, and vote, as appropriate. Other scheduled reports including expedited reviews and exempt reviews are also presented. Updated working agendas are available at all times to IRB members, the DIOs, OVPR, and authorized consultants. The IRB staff assigns incoming applications to meeting agendas based on necessary expertise (e.g., clinical or scientific expertise), urgency of the submission, and availability of the designated primary reviewer.

Convened board reviews are assigned to primary and any secondary reviewers via eResearch approximately one week but not less than four calendar days before the assigned meeting date. Before a scheduled meeting, all IRB members are notified electronically of the planned meeting agenda. The agenda contains links to all relevant items and documentation for review. IRB members and alternate members in voting status are expected to review the items attached to the agenda in advance of the IRB meeting. Primary reviewers prepare a brief presentation of any submissions under their purview and recommendations for outcome. U-M IRBs provide a review template to facilitate a standard presentation format at the convened meetings and assure that applicable regulatory requirements are considered. IRB members and alternate members are encouraged to RSVP to the IRB Office regarding their availability for each IRB meeting. As members respond, the IRB staff review IRB meeting agenda items for potential conflicts of interest and provide recommendations for substitute alternate members.

g) Convened Meetings

(1) IRB Staff Responsibilities

On the day of, and in advance of each convened IRB meeting, the IRB staff will oversee set-up of resources for the electronic meeting or in-person meeting.

During the convened IRB meeting the IRB staff will monitor attendance to ensure quorum, member composition, and any required special representatives (e.g., prisoner representative) are represented for each vote. All voting outcomes and determinations are recorded and saved by the IRB office. The IRB staff support each meeting by projecting information for discussion and any additional supporting or backup documents as needed.

The IRB staff record information necessary for meeting minutes including member attendance and assigned reviews, discussion, outcomes, contingencies, and determinations of agenda items, required federal, state, or local determinations, and any additional IRB requirements.

Additional information is provided to all board members by the IRB staff at the time of the convened meeting, including, but not limited to, continuing educational presentations, announcements, and other relevant information to assist them in serving on the board.

(2) Changes to the Agenda

When an IRB meeting commences, all IRB members in attendance are alerted to any changes to the planned agenda. In the rare event that an application is discussed that did not appear on the published agenda (e.g., an emergency use or time-sensitive submission), a narrative summary of the protocol and sample informed consent forms, any recruiting

materials, and other documents in the file are made available to all board members to review at the time of the meeting. Members will be afforded a reasonable period of time to review before a discussion and vote is taken.

(3) Board Member Reviews

IRB meetings are generally scheduled for 2-3 hours to permit adequate time for reviewing assigned applications. However, if a board member feels they have been given inadequate time to review a specific submission, that item will be rescheduled to a future meeting.

(4) IRB Deliberations and Voting

At the convened IRB meeting, the primary reviewer and any additional reviewer or consultant presents their review of the submission according to any IRB-defined methodology (e.g., reviewer checklist or other standard format) and recommends a determination to the IRB, including any suggested changes. The IRB staff and primary reviewer must complete their reviewer checklists prior to presentation to the convened IRB.

Following the primary reviewer's presentation, board members discuss the submission and deliberate prior to voting.

An initial, amendment, or Continuing Review (CR) submission may be approved or disapproved only upon a majority vote by the voting members present. The Principal Investigator (PI) or study team designee may be requested to attend the convened board meeting in person or electronically to address any questions raised by the board. However, neither the PI nor the study team will be permitted to be present for the discussion or vote of the submission.

h) IRB Meeting Minutes

(1) Content Requirements

Following a convened IRB meeting, designated office staff shall prepare minutes consisting of at least the following information:

- Attendance of the members at the convened board meeting, including a notation of absences of board members
- Documentation of any conflicted members or staff
- The time a primary or alternate member leaves the room and rejoins the meeting
- Acknowledgement of submissions reviewed by expedited and exempt review procedures
- The names of PIs, guests and/or consultants in attendance
- A list of submissions reviewed at the convened board meeting, including the type of review that was conducted (e.g., initial, amendment, continuing review, adverse events and other reportable information)
- For each submission reviewed, any votes or other actions taken, and the vote on each action including:
  - the number and names of members voting for or against
  - the number and names of those members abstaining

  - the names of alternate members standing in the capacity of an absent primary member—based on designation: for example, non-physician scientist alternate member *a* is standing-in for non-physician scientist primary member *b*
- The names of conflicted members, consultants, PIs or guests who leave the room for the deliberation and vote
- For initial and SCRs, the approval period
- Protocol-specific information supporting any waiver of informed consent or documentation of consent, e.g., The waiver of HIPAA authorization or the inclusion of vulnerable participants in the research
  - Research involving pregnant women/persons, fetuses and neonates
  - Research involving prisoners
  - Research involving children
  - Research involving adults with cognitive impairment or otherwise impaired decision-making capacity
- The name of any consultant reviewer used for an application
- Actions taken by the IRB, including documenting the criteria for approval are met
- The basis for requiring changes in or disapproving research
- Separate deliberations for each action
- A written summary of controverted issues and their resolution
- A summary of any continuing education provided to IRB members
- Documentation of expedited studies that were reviewed by single-member reviewers prior to the meeting
- Documentation of board deliberations and determinations involving Unanticipated Problems Involving Risks to Subjects or Others (UaPs):
  - An evaluation of unexpectedness, in terms of nature, severity or frequency
  - An evaluation of relatedness
  - An evaluation of harm
    - representative of potential increased risk to participants or others, or
    - representative of risk of actual harm to participants or others
- When following HHS regulations or guidance, documentation of justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in a HHS-approved sample consent document
- When following FDA regulations or guidance, documentation of the rationale for significant risk/non-significant risk device determinations

(2) Review and Ratification Process

Meeting minutes are drafted by IRB staff following convened IRB meetings, sent electronically to Board members for review, and are acknowledged (no vote is required) at a subsequent meeting of the convened IRB.

- If Board members indicate necessary changes and the minutes require amending, strict version control is applied to preserve the original minutes
- The acknowledged minutes are maintained in accordance with applicable legal requirements and institutional policy and are archived in eResearch
- The Chair of the board will notify the board members if there is an anticipated delay in

preparation of minutes for acknowledgement beyond 2 meeting cycles for IRBMED or 1 meeting cycle for IRB-HSBS

Additional guidance is provided to IRB staff regarding preparation, acknowledgement, and amending of IRB meeting minutes.

**2.** Use of IRB Consultants

*Refer to* HRPP OM Part 3.III.B.2

During IRB meetings or otherwise, the IRBs may utilize individuals including consultants, advisors, and ad hoc reviewers whose experience or expertise may serve the IRB if there is not at least one IRB member with appropriate scientific or scholarly expertise or other experience or knowledge to conduct an in-depth review of a protocol.

These individuals may participate in the discussions of, or provide written documentation concerning an application, but shall not be counted for the purposes of establishing quorum, nor shall they vote on the approval, disapproval, or other disposition of any application.

As appropriate, key information from consultants, advisors, and ad-hoc reviewers will be recorded in the minutes. These individuals will be granted access only to the assigned research project. Any individual asked to serve a U-M IRB in this manner will be required to sign the standard U-M IRB confidentiality agreement, follow the standard U-M IRB member conflict of interest procedures, and comply with appropriate application review requirements.

**3.** Alternate IRB Members

*Refer to* HRPP OM Part 3.III.B.3

The IRBs may appoint alternate members to serve in the absence of primary members to establish quorum and participate in deliberations and votes on applications pending before the IRBs. A primary member of IRBMED designated IRBs is automatically considered to be an alternate member of the other IRBMED designated IRBs. The same circumstances apply to IRB-HSBS. These cross-designations are not required on the rosters.

Each alternate IRB member has experience, expertise, background, professional competence, and knowledge comparable to that of the primary IRB member whom the alternate would replace.

Alternate members may attend IRB meetings even when their attendance is not necessary to establish a quorum and may participate in the discussion; however, they may not vote unless designated to serve in the absence of a primary member.

A primary member from one IRB may serve as a reviewer on another IRB in the capacity of ad hoc reviewer and is not counted towards quorum or utilized as an alternate.

The IRB Chairs may reassign a previously appointed primary member of one IRB as a primary member of another IRB, or may reclassify a primary member as an alternate member or vice versa, by notifying the member, the HRPP Director, and updating the membership rosters. The HRPP Office maintains the membership information for all IRBs.

Experienced IRB staff members are also appointed as alternate members, in alignment with their qualifications.

**4.** IRB Educational and Training Activities

*Refer* to HRPP OM Part 13

*Refer to* U-M IRB SOP Part 13

a) Orientation of IRB Members

The IRB orientation program for new members is a multi-component program designed to enhance retention and applicability of information to application reviews. The program includes workshops, directed mentoring, completion of human research educational modules in Program for Education and Evaluation in Responsible Research and Scholarship (PEERRS) (or alternative courses completed under a U-M issued PEERRS waiver) and the HHS Health Insurance Portability and Accountability Act (HIPAA) training as applicable, attendance at convened IRB meetings as a non-voting member, and practice protocol reviews. Topics covered include but are not limited to:

- U-M HRPP Overview including IRB SOPs and the HRPP OM
- Federal Regulations and background including 45 CFR 46, applicable 21 CFR sections, the Belmont Report and OHRP information and guidance
- The IRB Review Process
- Use of eResearch

New members are typically appointed as alternate members and undergo an orientation phase providing an overview of regulatory and institutional requirements, eResearch training, and reviewer checklist training. They also attend convened board meetings as an observer and conduct practice reviews. New members are assigned a mentor from among experienced IRB staff or board members during a practicum period which concludes when the mentor determines that the new member has sufficient understanding of IRB requirements to conduct independent reviews. The practicum period typically lasts about two months.

The IRB Chairs determine when each new member's cumulative experiences qualify them for appointment as a primary member and if they qualify to serve as a Single-Member reviewer (including expediting reviewer). This may occur at any time after the member concludes the practicum period.

b) Orientation of IRB Staff

IRB staff members are required to complete an orientation program and take all required PEERRS human research modules.

Depending upon the role of the new staff member, completion of additional orientation and continuing education workshops, as well as public workshops offered to research personnel, are required at the discretion of the employee's direct supervisor.

Staff members are encouraged to attend local, regional, and national conferences on ethics, State and Federal laws, and regulations for human participants research per opportunities identified

and supported by IRB leadership (and as budget permits). The IRBs also subscribe to numerous webinars for which attendance by staff is encouraged.

c) Orientation of U-M IRB Chairs

IRB Chairs are appointed per IRB SOP Part 3.III.B.1(a). Chairs meet with the DIO to review roles and responsibilities of the Chair role in association with relevant federal and state regulations, laws, guidance materials, University (including Medical School and Michigan Medicine policies, as applicable). The Directors of IRBs, relevant IRB staff, and other supporting offices also meet with the Chairs to provide orientation to the working procedures associated with the IRB.

d) Continuing Education for IRB Members and Office Staff

All IRB Chairs, members, and staff participate in continuing education within the context of the IRB meeting and elsewhere. Continuing education on ethics, regulations, federal guidance, university policies, and eResearch are provided in the form of webinars, workshops, presentations at IRB meetings, and electronically forwarded materials. U-MIC (University of Michigan IRB Collaborative) audio/video tips are presented at IRB meetings.

IRB Chairs, members, and Office staff are offered an opportunity to attend IRB conferences (the number of attendees varies based on budget). The IRB staff also participate in ongoing continuing education within the context of weekly all-staff meetings. The IRB Seminar Series is typically presented semi-annually to the research community at-large and covers regulatory requirements and topics of current relevance.

Reference materials such as U-MICs and the slides from Seminar Series are posted to the IRBMED website and other units link to this site. IRBMED also prepares topic-specific guidance which is posted to Research A-Z and IRB-HSBS posts topic-specific materials on its website or the OVPR website.

e) Researcher Education

*Refer to* HRPP OM Part 13.I and .IV

*Refer to* IRB SOP Part 13

**5.** IRB Compensation and Liability Coverage

a) Compensation of Chairs

IRBMED Chairs are compensated a portion of their salary for the effort required to perform their duties as Chairs.

IRB-HSBS Chairs are compensated at a rate determined by OVPR in consultation with the academic units, if necessary.

b) Compensation of Committee Members

IRBMED members are compensated for their service on the IRB in an amount corresponding to their attendance and completed reviews. Community members are compensated similarly taking

into account the number of meetings attended.

IRB-HSBS regular expediting members are compensated at a rate determined by the DIO in consultation with academic units, if necessary. Community members are compensated at a rate determined by the DIO in consultation with the relevant IRB Director and the IRB Chair(s). Rates of compensation for U-M Flint and U-M Dearborn members are determined by these respective campuses in consultation with the DIO, as necessary.

c) Periodic Review of Compensation

The amount of compensation for Chairs and members is reviewed periodically and may be modified by the DIO.

d) Liability Coverage

Liability coverage to cover the actions of faculty, staff, trainees, and non-affiliated volunteers performing authorized activities on behalf of the University (such as membership on an IRB) is a matter of institutional policy and is described in HRPP OM Part 3.III.B.5.

**6.** Evaluations of IRB Chairs, Members, Staff and Regular Consultants

*Refer t*o HRPP OM Part 3.III.B.6.

a) Chairs and Member Performance Review

Annually, the DIO will evaluate the Chairs (excluding Vice-Chairs) of the boards to ensure that their expertise adequately addresses the types of protocols reviewed and to ensure that each Chair is an active participant and is trained in current interpretations of federal regulations and other relevant ethical principles for the protection of human participants. The Vice-Chairs will be evaluated by the Co-Chairs at the conclusion of their first year of appointment as Vice-Chair. Thereafter, the Vice-Chair will be evaluated prior to renewal as Vice-Chair. A Vice Chair may be evaluated more frequently if there is a concern as to their ability to fulfill the role. Feedback is provided to the Chair or Vice-Chair along with any suggested corrective actions such as additional educational requirements or direction on improving workflows associated with the convened IRB meetings.

IRB Chair(s) evaluate new members of their boards at the conclusion of their first year of service to ensure that the expertise of each primary and alternate member adequately addresses the types of protocols reviewed and to ensure that each member is an active participant trained in current interpretations of federal regulations and other relevant ethical principles for the protection of human participants. Feedback is provided to the member, by the Chair(s) along with any suggestions for improving performance via additional education or mentoring.

Annually, each board member receives information regarding their level of participation in the previous calendar year, including the member's total number of reviews by type, and their attendance record at meetings of their primary board. A summary of this information is provided to the appropriate Chair and Vice-Chair for evaluation and any indicated feedback and/or corrective action. It is also provided to the member's unit, upon request.

Prior to renewal of a member's term, the Chair (excluding Vice Chair) receives information from IRB staff regarding the member's performance and performs their own evaluation prior to recommending renewal of the appointment. Members are provided pertinent feedback. An evaluation of a member's performance may also occur at any time during their term if there is concern about their level of participation, adequacy of reviews, regulatory interpretations, or other ethical concerns. The Chair may also ask for input from the IRB and HRPP Directors.

b) Removal of a Chair or Member from an IRB

If necessary, the DIO may relieve a Chair or Vice-Chair from IRB service due to repeated non-attendance, lack of participation in continuing education, failure to understand and/or apply regulations, or other problematic performance issues. Should this action be required, the DIO will notify the Medical School Dean (in the case of IRBMED) and the Vice President for Research in all cases.

Similarly, the Chairs may recommend to the HRPP Director that a board member be relieved from U-M IRB service due to repeated non-attendance, lack of participation in continuing education, or other problematic performance issues. Should this action be required, the HRPP Director will notify the Medical School Dean (in the case of IRBMED) and the Vice President for Research in all cases.

c) IRB Staff Performance Review

Staff members are evaluated at least annually in a performance appraisal conducted by the IRB Director or their functional supervisor as instructed by the IRB Director. The IRB Directors are evaluated by the HRPP Director in a yearly performance appraisal. If circumstances dictate, the Directors and staff are evaluated more often. Constructive feedback is provided to effectuate additional learning or corrective action as necessary.

In addition, the IRB Directors monitor staff workloads and review metrics received from the eResearch system on a routine basis. Feedback is provided to IRB staff and elevated to the HRPP Director, as indicated.

d) Consultant Performance Review

In the rare event that an IRB routinely uses a particular consultant to conduct primary reviews of applications, they will be reviewed annually.

**7.** Conflicts of Interest involving Chairs, Members, Consultants and Staff

*Refer* to HRPP OM Part 9.III

It is the responsibility of IRB Chairs, members, consultants and staff to disclose both actual and perceived conflicts of interest (COI) throughout their terms of service or employment. The financial disclosure sections of the eResearch application indicate disclosure of a financial interest in a sponsored project or technology transfer agreement. This information is on file in the IRB offices.

Disclosed COI information associated with IRB members and consultants is obtained from either OVPR and/or the relevant COI Committee. This information is considered during review assignment

in order to ensure a member is not assigned to review research for which they are identified as a conflicted member.

a) Financial Disclosures

At the beginning of their service and annually thereafter, each IRB member and any routinely used consultants complete an M-Inform disclosure for their financial disclosures. The financial disclosure section collects any significant financial interest in a sponsored project or technology transfer agreement. The disclosures are available to IRB staff during review and assignment of submissions to reviewers.

Staff members in leadership or management roles, such as the Director, are required to complete an annual M-Inform disclosure (or more frequently as needed).

b) Conflicts of Interest with Research Involving Chairs and Members

An IRB member (including the Chairs) or a consultant with the IRB will not be assigned to review an application if he/she (and/or their spouse, domestic partner, or dependents):

- Is a PI or study team member on the study
- Has a significant financial interest in the research (as defined by University and Medical School policies on COI)
- Has other conflicts that the member, IRB, DIO, COI Committee, or OVPR believes might hamper the member's ability to perform an impartial review of the research

Any conflicted reviewer (Chair, member, or consultant) shall not be present for, count for quorum, participate in deliberations on, or vote on the disposition of research for which the individual has a conflict as described above. The conflicted reviewer or consultant may, however, be invited by the IRB to provide information relevant to the board's consideration of the research.

The conflicted reviewer or consultant must be absent from the room during both relevant deliberation and voting.

A conflicted Chair or member shall not participate in the investigation of actual or alleged noncompliance on behalf of the U-M IRB (other than to cooperate with the investigation) if conflicted as described above.

All conflicts of interest for studies reviewed at the convened IRB are documented in the IRB meeting minutes.

An IRB member may be affiliated with a unit that involves provision of a service to a study (e.g., a Pharmacist from the Research Pharmacy, a Radiologist from the Department of Radiology, or a technical service provider from Information Technology Services) as long as these individuals do not administer any study intervention being tested or evaluated under the protocol. The IRBs do not consider this to be a conflict of interest with regard to reviewing an eResearch submission.

c) Conflicts of Interest with Research Involving IRB Staff

An IRB staff member would be recognized as having a COI with research in which he/she has a

significant personal or financial interest.

When a conflict is identified by OVPR, the University, any COI committee, or other University unit (i.e., ORSP), and/or by self-disclosure, the U-M IRB staff person must excuse him/herself from administrative handling of the research and from the U-M IRB board meeting where there is deliberation and vote on the research. IRB staff document all conflicts of interest in the IRB meeting minutes. Staff members should consult with their IRB director if they have questions regarding any actual or perceived COI.

IRB staff shall not participate in the investigation of actual or alleged noncompliance or other misconduct if the staff person has a conflict as described above.

d) Conflicts of Interest Involving Consultants

*Refer to* HRPP OM Part 9.III

*Refer to* U-M IRB SOP Part 9.III

Consultants are not voting members of the IRB. No consultant to a U-M IRB may participate in the IRB's review of an initial application, amendment or continuing review application, or participate in the investigation of actual or alleged noncompliance or other misconduct investigation in a research protocol, if a conflict of interest exists (as defined in Part 9 of the HRPP OM). The consultant may be invited by the IRB to provide information relevant to the IRB's consideration of the application taking into account the consultant's special qualified expertise and their ability to provide an objective assessment. Any conflict will be disclosed to the board at the convened meeting prior to any participation of the consultant in the discussion.

The IRB staff will evaluate whether an actual or perceived COI exists prior to contacting a consultant and also ask the consultant to disclose any perceived, potential, or actual conflicts. The relevant COI Committee will be consulted, if needed. Conflicts of interest involving consultants will be evaluated according to the same definition as applied to IRB members.

e) Conflicts of Interest Involving a Convened Board

Prior to each convened IRB meeting, the IRB Staff will determine, to the extent possible, if a COI is documented for submissions undergoing convened IRB review and will note the conflict on the agenda. However, it is ultimately the responsibility of the board member to self-identify any COI at the time it is known.

No IRB member, including the Chairs, shall be present for or participate in, the deliberations or vote on the disposition of an application for which the member has a conflict as described above. The member may, however, be invited by the IRB to provide information relevant to the board's consideration of the application.

IRB Chair and staff will ensure that all identified, conflicted IRB members are:

- Excused from discussion, except to provide information requested by the IRB
- Excused from deliberation
- Excused (absent from the room) during voting
- Not counted towards quorum for a particular vote; and

- Documented appropriately in the meeting minutes

To facilitate the identification of any previously unreported conflicts, the U-M IRB Chair shall, at each meeting, inquire whether any members should excuse themselves from discussion and voting as outlined above.

For guests attending a board meeting during which a conflict is identified either by the IRB staff, board members, and/or by self-disclosure, the guest will leave the room during the discussion and vote on the research protocol. IRB staff will document the name of the guest, conflicted project(s), and the time the guest leaves and returns to the meeting.

f) Conflicts of Interest Involving Expedited Review

Prior to expedited or limited IRB review for qualifying submissions the IRB staff will assess the application to determine, to the extent possible, whether the reviewer has a COI. However, it is ultimately the responsibility of the member to self-identify any COI at the time it is known. IRB staff will not assign an application to a conflicted IRB Member reviewer. If a previously unreported conflict is identified in the course of reviewing an application, a different reviewer will be assigned to the application.

g) Conflicts of Interest Involving the Institution

*Refer* to HRPP OM Part 9.IV.

## C. IRB Review Policies and Procedures

*Refer to* HRPP OM Part 3.III.C

### 1. IRB Jurisdiction and Authority

a) Human Research Studies Reviewed by the IRB

U-M IRBs review studies submitted per the assigned jurisdiction in HRPP OM Part 5.II. Submissions include all materials associated with new project (initial) applications, scheduled continuing review applications, amendments, adverse events (AEs), Other Reportable Information or Occurrences (ORIO) reports (including UaPs), and research that may qualify for exemption. Submissions are routed to the appropriate IRB via eResearch Regulatory Management (eRRM), the web-based system for submission, routing, approval and management of human participant research information.

b) Authority of the IRB to Approve, Disapprove or Require Modification to a Study

*Refer to* HRPP OM Part 3.III.C

All regulated, nonexempt human participant research conducted by the University must be approved by an IRB prior to initiation of the research. All exempt human participants must be granted an exemption according to the procedures outlined in Part 3 III.C.1(d)(3), prior to initiation of the research.

The IRBs have the authority to approve, disapprove or require modifications to human participants research under their jurisdiction.

c) Authority of the IRB to Suspend, Terminate or Place Restrictions on a Study

*Refer to* HRPP OM Part 12.II

*Refer to* HRPP OM Part 3.III.C

The U-M IRBs have the authority to suspend or terminate approval of a study or to place restrictions on the performance of the study. It must document the circumstances under which these actions are taken and make a report to OVPR.

d) Not-Regulated projects, Research without U-M Engagement, and Exempt Research

The IRBs require their staff, consistent with the OHRP Guidance and in consultation with the IRB Director or Chairs as appropriate, to make the following determinations with respect to every submission for initial or continuing review:

- That the activity described in the application is "research" as defined in the Common Rule
- If considered research, whether the activity involves "human research" as defined in the Common Rule or "clinical investigation" as defined by the FDA regulations; and
- Whether U-M is engaged in the research; and
- Whether the research is exempt from IRB oversight.

(1) Not-Regulated Research

*Refer to* HRPP OM Part 4.V

For activities not regulated as human participants research per HHS and FDA definitions of human participants research, the IRBs do not require PIs to seek a determination of 'Not Human Participant Research' from the IRB (e.g., review of records preparatory to research, QA/QI, or case studies).

Some not-regulated activities are subject to HIPAA regulations (e.g., review of records containing Protected Health Information (PHI) preparatory to research, research on decedents' PHI, or research involving a HIPAA-defined "limited data set" with data use agreement); these commonly require an eResearch application for tracking or publication purposes. *Refer to* IRB SOP Part 3.III.C.6(e)(5).

PIs seeking documentation of the not-regulated status may submit an application in eResearch to confirm the status and seek a confirmatory letter.

Determination letters of 'Not Human Participant Research' are provided via eResearch.

For "Not Regulated" projects that will be conducted outside of the University, in addition to meeting University requirements, researchers are strongly encouraged to consult proactively with the external institution to ensure that their work aligns with all relevant requirements at the collaborating institution.

(2) Research without U-M engagement

*Refer to* HRPP OM Part 4.III, HRPP OM Part 4.V.A, *and* HRPP OM Part 5.III

The University does not require investigators to seek a formal determination from the IRB where the University is not engaged in the research per Engagement of Institutions in Human Subjects Research: OHRP Guidance (2008). PIs seeking confirmation and documentation may submit an application in eResearch for IRB review.

(3) Exempt

*Refer to* HRPP OM Part 4.VI

Determination of ***exemption*** from 45 CFR 46 may be requested by an investigator via an eResearch application submitted to a U-M IRB. Exemption may be granted by the IRB Chair(s) or designee, IRB board members, qualified members of IRB Office staff or the VPR. Certain exemption categories permit the PI to obtain a eResearch system-generated exemption determination (as available). Limited IRB review is also required for specific exemption categories and must include:

- A protocol document or a protocol summary that describes the participant population, study procedures, and research locations
- Documents relevant to the research (e.g. recruitment materials, a proposed consent document, survey instruments); and
- Information regarding the sensitivity of data to be collected and when appropriate provisions to protect the privacy of participants and to maintain the confidentiality of data (45 CFR 46.111(a)(7))

Some exempt studies are subject to HIPAA regulations (e.g. use of medical records to identify eligible participants); these may require an IRB-approved waiver of HIPAA authorization. *Refer to* IRB SOP Part 3.III.C.6(e)(5).

Once approved as exempt from the regulations, the research activity is not monitored by the IRB. Assuming the project does not exceed the scope of the assigned exemption, it also is not subject to continuing IRB oversight. Exempt status does not lessen the ethical obligations to human participants as articulated in the Belmont Report and in disciplinary codes of professional conduct.

e) International Research

*Refer to* International Human Subject Research Resources
*Refer to* International Compilation Human Research Standards

The University of Michigan adheres to the requirements of its FWA when U-M personnel are "engaged" in human subject research or U-M is the direct recipient of federal funding for the research. An international site must rely upon the approval of an IRB that is registered with HHS when it receives a direct federal award or a sub-contract of federal funding. U-M IRBs will consider whether to function as the reviewing IRB or to cede IRB oversight on a study-specific basis.

(1) Additional Requirements for IRB Review

U-M investigators must also follow foreign laws and regulations (e.g., data security and privacy requirements) providing protections to human subjects and be familiar with local requirements to ensure that the terms of funding agreements and the content of IRB submissions are consistent with those expectations.

In some instances, review of the study will be separated into discrete components: the U-M IRB will review and provide oversight of study activities conducted by the U-M study team (e.g., data analysis) and the international site IRB/Ethics Committee (EC) will review and provide oversight of research activities (e.g., participant interaction and data collection, review of local context, in-country standards and necessary document translation(s)) performed in-country by non-UM members of the study team.

The U-M IRB will communicate with the local IRB/EC as indicated to assure that all requirements are met. Where the international research site is not engaged in the conduct of the research, the U-M IRB may request a letter of collaboration from an appropriate official agreeing to the conduct of the research.

(2) U-M IRB Review

Research conducted by U-M investigators in international settings or under the oversight of a U-M IRB is subject to U.S. IRB requirements for review and approval of initial applications, continuing review (as necessary), amendments, AEs, UaPs, handling of complaints, and assessment of the informed consent process and documents. Informed consent procedures and materials are evaluated to ensure cultural sensitivity, that the information is in a language understandable to the participants, and that the complexity of the information is appropriate for the research population. Informed consent documents and other study materials must be provided to the U-M IRBs in the languages in which they will be offered, as well as in English. When U-M is the reviewing IRB in single IRB circumstances, research participants are provided with the U-M IRB's email address and international phone number as part of the consent process.

U-M IRBs must also consider the following when acting as the reviewing IRB:

A. Local Context:

The U-M IRBs consider local research context when reviewing research conducted in international settings. Elements of consideration include:

- Laws and regulations
- Local customs and cultural norms
- Political and socio-economic conditions
- Language and literacy issues

When U-M IRB members do not possess the appropriate cultural knowledge to review research in a particular country or region, the U-M IRBs will seek guidance from consultants with cultural expertise to assist with the review. The U-M IRB may require local (in-country) IRB/EC or regional government agency review to contribute to review of local

context/culture, particularly for studies involving more than minimal risk to participants. The eResearch application elicits information from the study team regarding their experience with and knowledge of the community and culture in which the research will take place.

B. Monitoring

Post-approval monitoring, such as interim project reports to the U-M IRB by the PI, may be imposed when necessary. As with domestic projects, PIs are obligated to report participant complaints, UaPs and other reports of potential non-compliance to the U-M IRB.

(3) Exempt Research

U-M generally does not enter into a reliance agreement when a study meets criteria for and is determined to be exempt, unless the international collaborator does not have their own IRB/EC. For international collaborators with their own IRB/EC, it is their responsibility to obtain a determination from the international site. For exempt research, U-M IRBs do not require documentation of IRB review or other approvals from international sites unless requested by the IRB reviewer.

(4) DoD funded Research

*Refer to* *Guidance: Additional Requirements for Department of Defense (DoD) Sponsored Research*

**2.** Institutional Approval/Disapproval of IRB Decisions

*Refer* to IRB SOP Part 1.III

**3.** Submission of IRB Applications and Reports

*Refer to* HRPP OM Part 3.III.C.3

The University utilizes eResearch Regulatory Management (eRRM), a web-based system for submission, routing, approval, and management of human research information. eResearch relies upon a role-based structure that permits only a single PI per application and requires the PI to be the individual that functionally submits the initial, continuing review, amendment, and termination applications within the electronic system. The PI may delegate authority to co-investigators or faculty advisors for the submission of AE/ORIO reports. The PI is responsible for the content of each eResearch submission and assumes responsibility for compliance with all regulations, laws, and policies associated with the conduct of the research.

**4.** General IRB Review and Approval Procedures

a) Determining Whether and Under What Authority the Research is Regulated

*Refer to* HRPP OM Part 3.III.C.4.a

*Refer to* IRB SOP Part 3.III.C.1

Beyond the requirements of Common Rule and FDA regulations, the IRB staff considers additional

regulatory requirements associated with the study design such as HIPAA or required by federal sponsors such as the Department of Defense (DoD) or Department of Education (ED). IRB staff utilize guidance documents and a reviewer checklist in the eResearch application to ascertain any additional requirements.

b) Reviewing IRB Applications (Initial Applications, Amendments, Continuing Reviews (CRs), and Termination Reports per 45 CFR 46.111 and 21 CFR 56.111 and 21 CFR 50.

(1) Information Required for IRB Review

*Refer to* HRPP OM Part 3.III.C.4.b

A submission to the IRB that is an initial application, amendment or CR and regulated by 45 CFR 46 (the Common Rule) or 21 CFR 56 (FDA) must contain the indicated information.

For initial applications and SCRs, the IRBs may request other supporting documentation that, in its discretion, will facilitate a complete and meaningful review of the study, such as sponsor or contract research organization contracts governing the conduct of the research, conflict of interest management plans or FDA documents.

(a) Initial Applications

A PI who intends to initiate a new research study involving human participants must submit an initial application in eResearch for IRB review and approval. No aspect of the project (including testing performed solely to determine eligibility for the project) may begin until the application has been approved in the eResearch system. The application should include the following, as appropriate to study design and sponsorship:

- Description of the professional qualifications of the investigator conducting the research
- Study Protocols that address:
  - Study title
  - Purpose of the study
  - Foreseeable risks and potential benefits to human participants
  - Sponsors of the study and any relevant federal grant applications
  - Results of previous related research
  - Participant inclusion/exclusion criteria
  - Justification for use of any special/vulnerable participant populations (e.g., decisionally impaired or populations protected under 45 CFR 46 subparts B, C, D)
  - Test article accountability procedures
- Description of study design including, as needed, a discussion of the appropriateness of research methods and the scientific or scholarly rationale
- Description of individually identifiable data to be collected or used
- Description of interactions and interventions and procedures to be performed, including as applicable, any questionnaires, surveys, or scripts used by PIs or the study team to communicate with participants or their LARs
- Description of any procedures already to be performed for diagnostic or treatment purposes (if applicable)

- Provisions for managing adverse events
- Copies of the proposed informed consent documents (including all requirements of 45 CFR 46.116 and 21 CFR 50 Subpart B as appropriate to the study and including translated consent documents, as necessary, considering likely participant population(s)); or a request for IRB approval of a waiver of informed consent
- A description of the accommodations that will surround the informed consent process, including setting, participant autonomy concerns, language barrier concerns, vulnerable population needs
- The procedures for documentation of informed consent, including any procedures for obtaining assent from minors; using witnesses, Legally Authorized Representatives (LAR), translators; and the plan for secure storage of informed consent documents
- Any compensation for injured participants
- Extra costs to participants for partaking in the study
- Adequate provisions to protect the privacy of participants (i.e., individually identifiable health information) and to maintain confidentiality (security) of the data;
- Copies of advertisements and any other recruiting materials (including, but not limited to, posters, website contents, videotapes, scripts for telephonic communications), if used
- An adequate monitoring plan to review data, where appropriate, to ensure the safety of study participants
- Documentation of approval from other University departments or divisions from which the IRB requests approval or certification that such approval will be obtained before the study begins
- Documentation of approval, disapproval, or other action from other performance sites (partners) performing the research, if the University (directly or through the PI) has ultimate responsibility for the conduct of the study or performs any coordinating functions including, without limitation, study coordination, recruitment, data management, data storage, monitoring, or otherwise; or certification that such approval will be obtained before the study begins
- For multi-center trials supported by HHS, the approved sample informed consent documents and complete HHS-approved protocol (if any)
- The Investigators Brochure, Investigational New Drug (IND)/Investigational Device Exemption (IDE) application or exemption documentation (e.g., an IDE letter), if any, (for studies involving the use of an investigational drug, biologic, or device)

(b) Continuing Reviews (CRs)

*Refer to* HRPP OM Part 3.III.C.4.c

The PI of an approved research study is responsible for submitting an application for continuing review (CR) approval sufficiently in advance of the expiration date of the current approval period to obtain IRB approval prior to expiration.

The eResearch system generates automatic reminders at 90, 60, and 30 days prior to

study expiration. If approval for continuation is not issued prior to the expiration date, the PI must cease all research activity until the IRB has issued its approval, with the exception of research-related interventions that are necessary to avoid harm to a participant. If the study expires, the eResearch system generates an automatic expiration notice notifying the PI of study expiration and indicating that all study procedures must cease, including subject recruitment, experimental procedures or treatments, and data collection or data analysis, except as necessary to eliminate apparent immediate hazards to research subjects. Additionally, expenditure of federal research funds must stop, including salary support associated with human subject activities.

Note that expiration of an approval does not constitute a "suspension" of IRB approval reportable under HHS or FDA regulations, or these SOPs.

An application for CR must include at least the following information:

- The number of participants accrued since the initial application or the previous continuing review application
- The number of participants expected to be recruited in the future
    - The study team's risk-benefit assessment based on current study status and results and any changes in the risk level determination
- A summary or tabulation of any reports including:
    - UaPs involving risks to participants or others
    - participant withdrawals from the project, including the reasons for withdrawals
    - complaints received along with the resolution
    - protocol deviations/violations
    - accidents/incidents involving data, specimens, or facilities
    - information about risks associated with the research
    - reports from or to an oversight entity
    - documentation of any findings made by external inspectors reviewers or auditors such as sponsors, contract research organizations, or government agencies relevant to the conduct of the research project, as well as the PI's response to the findings or progress reports submitted to study sponsors or the FDA
    - reportable adverse events and adverse outcomes experienced by participants
    - amendments or modifications made to the human participants research
    - any interim findings that may have an impact on the IRB's risk-benefit assessment or on a participant's willingness to participate in the study
    - pertinent publications/public announcements obtained or discovered (e.g., articles whose findings may have an impact on the IRB's risk-benefit assessment or on a participant's willingness to participate in the study)
- A copy of the informed consent documents approved by the IRB and currently in use
- Copies of the FDA-required Annual Reports, which should be uploaded to eResearch for FDA research in which the PI holds an IND or IDE necessary for the study (as

applicable)
- Any relevant multi-center research reports

These materials provide the primary reviewer and IRB members with the relevant information necessary to determine whether the study continues to meet the regulatory criteria for approval.

If continuing review approval is not issued prior to the study's expiration date, PIs are expected to cease all study activity except activities necessary to prevent harm to enrolled participants. PIs are expected to contact the IRB to outline the plan for any continuity of study activities due to safety concerns, including whether it is in the best interest of participants to continue until regulatory approval is reestablished.

(c) Information Required for Study Closure (Termination)

The PI of an approved project is expected to notify the IRB upon completion (and/or termination) of a study. A study termination report should include at least the following information:

- Affirmation that the involvement of human participants and use of identifiable human data or specimens in research has concluded
- Any changes to the plan for secure storage of data including maintaining confidentiality of identifiable data as outlined in the initial study submission.
- Number of participants enrolled in the study
- Number of participants completing the study
- Number of participants that withdrew from the study and the reasons for withdrawal
- Number of participant complaints about the project and description/resolution of those complaints
- Number of AEs reported to IRB during the study period (including any reported concurrently with submission of the termination report
- For FDA regulated research where a U-M PI is the IND/IDE sponsor-investigator, the final report that is submitted to the FDA (if final reports are not available at the time of study termination, they may be submitted via an ORIO submission, once available)

(2) Review Process / Primary Reviewers

*Refer* to HRPP OM Part 3.III.C.4.b

(a) Review Process

IRB staff and primary reviewers must receive sufficient information prior to review of submissions to prepare their recommendations for approval of the research.

IRB staff and primary reviewers assess and review the eResearch submission and all other supporting documentation depending on the submission type, to satisfy requirements for completeness, consistency, and compliance with University policy, 45

CFR 46.111 (the Common Rule), FDA regulatory requirements (21 CFR 56.111), or other regulatory rules or regulations (HIPAA Privacy Rule and HITECH Act, FERPA, or other federal, oversight activities) prior to presentation for board review. (*Refer to* HRPP OM Part 11 for additional information specific laws, regulations and standards).

A qualified member of the IRB staff will be assigned to each IRB submission in eResearch. In general, research submitted by the PI for review via eResearch is assigned to the IRB staff overseeing the department, academic area, or type of research (e.g., exempt, secondary use, or multi-site) being conducted. Additional guidance is available to address whether a submission should be transferred between staff due to staff absences, to manage time-sensitive submissions, a high volume of submissions, or between IRBs for purposes of reviewer expertise.

To facilitate the review process, the IRB staff member may request clarification or revisions from the study team for any or all of the application materials prior to sending to a primary reviewer. Upon completion of their review, the IRB staff forwards their Staff Reviewer checklist and comments to an IRB member selected to function as the "primary reviewer" for convened board or expedited review based on, but not limited to, the member's expertise, experience, and/or representation of pertinent participant population, as indicated on the member's Curriculum Vitae, documentation of community experience, or other information available to the IRB.

If the submission qualifies for expedited review the primary reviewer must also have the appropriate education and experience as determined by the IRB to be designated as an expedited reviewer. *Refer to* IRB SOP Part 3.III.C.5 for the expedited review procedure.

The primary reviewer:

- Assesses the initial application, amendment or CR, together with, ICDs, and all supplemental materials as applicable (e.g., the grant application, protocol, recruitment materials).
- Documents their review in the eResearch Reviewer Checklist of the application before the convened board meeting where it will be presented.
- May contact the PI in advance of the board meeting for additional information or clarification.
- Leads the discussion of the application under review at the convened meeting.
- May not have a COI regarding the project under review and is expected to notify the IRB staff and Chair of any conflict at the time the review assignment is offered or if previously unanticipated conflict arises during the review.

Compensation to participants, if any, will be in accordance with University policy. The IRBs will review payment arrangements offered to participants. Their review will ensure the following:

- The amount of payment, the proposed information collected, and the method and timing of disbursement neither is coercive nor presents undue influence or places the participant at elevated risk.

- Where appropriate, credit for payment accrues as the study progresses and may not be contingent upon the participant completing the entire study.
- Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn due to likely or serious risks associated with participation.
- All information concerning payment, including the amount and schedule of payments, is set forth in the consent document.

No aspect of a study (including review of medical or other records performed solely to determine eligibility for the study) may begin until the submission has been approved in eResearch by the IRB.

In some instances, the IRB staff, in consultation with the PI and/or study team, may enter changes into the eResearch application for the purposes of assisting the study team and facilitation of the review process. Parameters for this process are defined by the IRB.

The IRB staff may consult with advisory units (i.e., the MICHR IND/IDE Assistance Program [MIAP]) for preliminary review and assistance with research that may require an Investigational New Drug (IND) or Investigational Device Exemption (IDE) application. (*Refer to* IRB SOP Part 2.II)

(b) Timing of Distribution of Materials

The IRB staff assign applications to the eResearch meeting agenda until the agenda is full. Adjustments may be made to the final agenda to accommodate any reviews that are time-sensitive in nature. Distribution of application materials to the Primary Reviewer and board members typically one week but not less than four calendar days before the meeting unless a time-sensitive submission is added after that date.

A secondary reviewer may be assigned if additional expertise is deemed necessary. The secondary reviewer may be another voting member of the Board or a non-voting member/consultant to the Board. All study documents will be made available to the secondary reviewer.

(c) Regulatory Criteria for Board Review

Initial Applications and Amendments

All eResearch applications are first reviewed by qualified IRB staff to assure that the application is complete, all relevant materials are provided, and that the investigator has addressed all necessary regulatory criteria. The application is then assigned for review by experienced IRB board member(s) to determine that the criteria in 45 CFR 46.111 or 21 CFR 56.111 are met and that the study design is adequate to protect the participants from increased risk and yield expected knowledge. Criteria for IRB approval are listed in IRB SOP Part 3.III.C.6.

Continuing Reviews (including Terminations)

The IRB conducts scheduled continuing review of any non-exempt research study subject to its oversight at intervals appropriate to the magnitude of risk of the study and other considerations, but not less than once each year (except for research meeting the federal criteria for no continuing review or any criteria for regulatory flexibility). The IRB will:

- Assess the current risk level of the project and, if necessary, revise the risk level (decrease or elevate) commensurate with the activity being conducted
- Consider if the protocol needs verification from sources other than the researchers that no material changes had occurred since previous IRB review
- Verify that the current consent document is still accurate and complete
- Consider any significant new findings that might relate to participants' willingness to continue participation and whether these finding will be provided to participants
- Review the project to ensure that the criteria in 45 CFR 46.111 or 21 CFR 56.111 continue to be met
- Require any other changes warranted in accordance with the changes in risk level

Termination of a study, whether due to completion or other reason, is submitted via the CR mechanism. For further information about termination reports *refer to* IRB SOP Part 3.III.C.4.b(1)(c).

(d) Board Actions

The IRB may vote to take any of the following actions with respect to an application for initial, amended, or scheduled continuing review:

*(i)* Approve the Submission as Presented to the Review Board

Submissions will be eligible for approval only if the criteria listed IRB SOP Part 3.III.C.6 as well as other applicable regulatory and institutional requirements are met.

*(ii)* Approve the Submission Pending Contingencies

Approval will be contingent on specified changes to the protocol, ICDs or other application materials that must be made by the PI prior to initiating the research. These requested changes will be reviewed for completeness as indicated by a staff member or IRB Chair or IRB member designated by the IRB Chair via the expedited approval process, prior to issuance of approval.

If the PI disagrees with the IRB's request or proposes an alternate change, the approval status of the application will be "deferred," and the application must be re-presented at a subsequent board meeting in order to obtain approval, unless the application under the regulations qualifies for review in an expedited fashion.

The date of the vote as "Approved Pending Contingencies" shall be deemed the date of approval, regardless of when the specified changes are made by the PI and submitted to the IRB. The IRB may, in its discretion, require that the Pl respond to

required changes within a specified period and instruct that if the response is not received, the application will be considered withdrawn or reassigned to a board action deferred status.

*(iii)* Board Action - Deferred

In the event that a submission requires changes that are significant or substantively require more than simple concurrence of the PI, action on the submission shall be deferred.

Board action may be deferred on any submission. In this case, the PI may be instructed to submit additional information or revisions required by the IRB before reconsideration of the submission. The IRB may, in its discretion, require that the PI respond within a specified period and instruct that if the response is not received, the application will be considered withdrawn.

*(iv)* Board Action - Tabled

If a submission on the agenda is not discussed during the meeting (e.g., if the board reviewer is absent), it is considered tabled without a vote and will be assessed for placement onto a future agenda.

*(v)* Disapproval of the Application

*Refer to* IRB SOP Part 3.III.B.1(g)(4)

PIs will be notified of the reasons for disapproval and afforded the opportunity to appeal the decision. After reviewing information provided by the PI, the IRB may decide to issue a final disapproval or it may choose to reverse its disapproval if new facts are presented that were previously unknown or if the investigator modifies the project to address the IRB's concerns.

*(vi)* Suspension or Termination of IRB Approval

*Refer to* HRPP OM Part 12.III

The IRB also may suspend or terminate approval of research that it determines, after appropriate review and deliberation:

- is not being conducted in accordance with IRB requirements; or,
- has been associated with unexpected harm to participants; or,
- cannot minimize risks to participants or maintain a favorable risk-benefit balance.

Any suspension or termination of approval under this provision shall include a statement of the reasons for the action and inform the PI of institutional notification and reporting requirements.

- Suspension of Research Activity
  Suspension is the temporary closing of a human participant research project or discontinuing a PI's privilege to conduct human participant research. The

suspension may be partial, in that certain activities may continue while others may stop; or it may be complete, in that no activity related to the research may proceed.

- Termination of Research Activity
  Termination is the ending of all activities related to human participant research or a PI's privilege of conducting human participant research except for the continuation of follow-up activities necessary to protect human participant safety.

*Refer to* IRB SOP Part 12 for reporting a suspension or termination of IRB approval.

(3) Timeliness of Submissions and Reviews

(a) Notices of Expiration and Lapses of Approval

It is the PI's responsibility to submit an application for continuing review (SCR) before expiration of U-M IRB approval and in ample time for U-M IRB review.

- eResearch-generated reminder notices are sent to PIs and designated study team members at 90, 60 and 30 days prior to the expiration date of the current approval period. A notice of expiration is sent on the final date of the approval period indicating that all study activities must cease.
- If the IRB has not reviewed and approved the CR application by the expiration date of the current approval (regardless of the reason or circumstances), the study will be considered lapsed and the research must stop including: enrollment of new participants, any intervention or interaction with participants, and data analysis.
- The IRB may permit ongoing interaction and intervention with participants if it reviews, approves, and documents that it is in the best interest of individual participants currently participating in the study to continue the research interventions or interactions; the PI shall provide relevant information at the request of the IRB to inform the IRB's decision.
- Sponsored project resources (e.g., government or private) must not be expended for unallowable activities; ORSP is informed of such lapses in approval.
- Studies that are FDA regulated are sent additional notifications prior to expiration to remind PIs to terminate or renew studies as indicated.

(b) Administrative Termination for Lapses in Approval

If an approved research project is not renewed or terminated after the date of previous approval expiration, the IRB may consider the research to have been completed or discontinued, and may administratively terminate the research project (utilizing approved procedures) notwithstanding the lack of a study completion or termination report.

- Notification to the study team will be posted in eResearch prior to termination; the IRB will consider evidence from the PI in the event the PI wishes to submit a

continuing review. The IRB may determine that submission of a new application is necessary, rather than renewing approval of the now-lapsed application.

- An administrative termination under this provision does not constitute a suspension or termination of IRB approval reportable under HHS or FDA regulations, or these SOPs.

For projects reviewed, but not approved, by the IRB due to outstanding contingencies, the IRB staff may administratively withdraw the project after notification to the PI. Withdrawals of applications by IRB staff may occur after abandonment of an application or communication with the PI of their intent to modify their plans not to finalize the contingencies.

(4) Notice and Appeal of IRB Determinations

(a) Notification of Determinations

Following an IRB meeting, the IRB staff shall prepare electronic notification to inform the PI of each submission upon which a vote was taken, and on the outcome of the vote. The notification shall include at least the following information:

- The IRB's decision and date it was reached
- For an approved submission requiring continuing review, the approval expiration date and notification of any interim reporting requirements
- A list of currently approved documents, e.g., the informed consent and protocol with specific reference to version number as applicable
- For a project approved contingent on specified changes to be made to the protocol, ICDs, or otherwise, a description of the specific modifications necessary to secure approval
- The IRB may, in its discretion, require that the PI respond to required changes within a specified period and instruct that if the response is not received, the application will be considered withdrawn or reassigned to deferred status
- For a disapproved, suspended, or terminated project, the reasons for the IRB's decision and notification of the PI's right to respond in person or in writing

Documentation of all IRB determinations shall be available for review by applicable institutional leadership, OVPR including the IO and DIO, IRB members, and authorized consultants.

Written notice of a board suspension or termination of a project shall be delivered to OVPR for further disposition and notification to other interested parties, as necessary, such as government authorities with jurisdiction (i.e., the FDA and OHRP) and, in the case of a sponsored project, ORSP.

The U-M IRB's may, in their discretion, report disapprovals, or other actions to OVPR as it deems necessary or appropriate.

(b) Appeal of Determinations

The PI may appeal any decision by the board through written (e.g., email)

communication to the IRB.

c) Frequency of Review

In general, the approval period for an initial research application begins on the date it receives full or contingent approval by the IRB and expires 364 days later (365 in a leap year), which is the last date of the approval period. For example, an application will have an approval date of 1/1/24 and an expiration date of 12/31/24.

The IRB may approve an initial application or SCR for intervals of less than one year when warranted. Criteria for this consideration include, but are not limited to:

- The overall risk of the study, with the highest risk studies reviewed more frequently
- Data and safety monitoring plan requirements
- Demonstrated the need for additional oversight of the PI and study team
- Questions about sufficiency of the data to lead to generalizable knowledge
- Excessive numbers of serious adverse events (SAEs) or protocol deviations
- The protocol is subject to complex regulatory compliance requirements, such as research involving investigator-held IND or IDE
- The research is being conducted in an off-site location(s) and the IRB is serving as the IRB-of-record
- An investigator conducting the research has a potential COI that warrants more frequent reporting and review

There may be additional circumstances that the IRB would consider as significant to warrant the additional oversight.

The University permits IRBs to undertake flexibility or demonstration projects that may lengthen an approval period beyond one year.

d) Monitoring and Verification by IRB

*Refer to* IRB SOP Part 12.III.E

The IRBs are responsible for overseeing the safety of human research participants and have the authority to suspend or terminate human participant research that:

- Is not being conducted in accordance with federal and IRB requirements (45 CFR 46.103(b)(5)), 45 CFR 46.113, 21 CFR 56.113 and IRB SOP Part 12); and/or
- Has been associated with unexpected serious harm to human participants in research.

The IRBs may, at their discretion:

- Perform monitoring of studies both for-cause (e.g., alleged noncompliance) and not-for-cause (e.g., random review for quality assurance purposes) in addition to evaluating information received through the initial application, any amendments, annual SCRs, and analyses of interim reports, such as AEs (considering the frequency and nature of AEs reported to-date) and audit reports. For example, the IRBs may choose to undertake extra monitoring for research which presents greater than minimal risk, or to gauge the progress of recruitment of vulnerable participants, or to follow the research progress on controversial subject matter

- Request monitoring of a study from the Office of Research Compliance Review (ORCR) by contacting the HRPP Director

Criteria for additional monitoring may include, but is not limited to, the following:

- Complex projects involving unusual levels or types of risk to participants
- Projects conducted by PIs who previously have failed to comply with applicable regulations, institutional or IRB requirements
- Projects where other concerns about possible material changes occurring without IRB approval have been raised (e.g., major changes to the study protocol were made without an amendment)
- Projects involving vulnerable populations
- Complaints received regarding the study
- Multi-site projects where a U-M IRB serves as the sIRB
- One or more of the projects of a single PI in consideration of the experience of the PI or as follow-up to previous reports of complaints, non-compliance, or prior IRB interactions with the individual

Monitoring actions may include, but are not limited to, evaluating study materials (including providing the IRB copies of or access to materials) or any of the additional measures as necessary:

- Signed informed consent documents
- Study files and research records
- Drug dispensing/Research Pharmacy logs
- Participant records
- Lab test procedures, results and raw data
- Observation of study activity (e.g., witnessing the informed consent process)
- Review of study by an outside auditor
- Interviews of study personnel
- Interviews of research participants
- Site visits to research locations
- Monitoring reports/findings
- Independent third party monitoring reports
- Projects involving vulnerable populations
- Reports by the Data and Safety Monitoring Board (DSMB)

e) Reporting Changes in Research to IRB (Amendments)

All amendments to research must continue to meet the requirements of 45 CFR 46.111 or 21 CFR 56.111 in order to be approved.

Once a project has been approved, a PI may not make any changes to the project (e.g., changes to the protocol, ICD, recruitment materials or participant incentive) without prior IRB review and approval, unless necessary to eliminate apparent immediate hazards to the participants. Any change made without prior approval to avoid a hazard must be reported promptly to the IRB (*Refer* to the IRBMED AE/ORIO Reporting Guidance and IRB-HSBS Incident Reporting).

The IRB will scrutinize any proposed amendments to determine the degree to which risks to

human participants may have changed, whether there is any need to revise the ICDs or informed consent process, whether proposed changes in the ICD are appropriate, and/or whether there is any need to notify previously enrolled participants of the changes and if reconsenting of the participants is necessary. At its discretion, the IRB may authorize its staff to acknowledge non-material changes to protocols and informed consent documents, such as corrections of typographical or grammatical errors and changes in contact information, without submission of the application to a chair, review board, or expediting member.

Reportable changes may include, but are not limited to:

- Proposed changes in risks or benefits to participants
- Proposed amendments to the study protocol, including changes to the eligibility criteria, recruitment materials, questionnaires, surveys, scripts and participant payments
- Proposed amendments to the Investigator's Brochure or equivalent documentation
- Proposed amendments to previously approved ICDs
- Proposed changes in Investigators (including PIs, Co-Is, researchers) or performance sites
- Proposed changes to participant population
- Proposed changes in any other aspect of the research

At the request of a PI, the IRB Chairs or IRB will consider or agree to acknowledge a *voluntary hold* on participant enrollment or delay any portion of research activities to facilitate significant changes to a research study and further IRB review and/or fact-finding of the study or its conduct. This is not considered a reportable suspension of the research.

The date of U-M IRB approval of an amendment does not extend the approval period of the study. However, the IRB may shorten the approval period of the study if the amendment introduces new study procedures requiring more frequent review.

f) Preventing Lapses in IRB Approval

*Refer* to IRB SOP Part 3.III.C.4.b.3

5. Expedited Review

*Refer to* HRPP OM Part 3.III.C.5.

HHS regulations at 45 CFR 46.110 and FDA regulations at 21 CFR 56.110 identify certain types of research that may be reviewed and approved by "expedited review." The following types of submissions may be considered for an expedited review process:

- The research falls into one of more of the categories of projects or applications appearing on a list of expeditable studies published by the Secretary of HHS, and only in those categories, subject also to the following limitations:
  - The research involves no more than minimal risk to participants
  - The identification of the participants or their responses will not reasonably place them at risk of criminal or civil liability or be damaging to their financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are not greater than minimal
  - The research is not classified

- Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.
- Research for which limited IRB review is a condition of exemption under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8).

Research submitted for expedited review requires the same materials to be submitted that a convened board would receive for standard submissions.

Under an expedited review procedure, an IRB Chair, or an experienced IRB member designated by a Chair, reviews the research submission (refer to IRB SOP Part 3.III.C.5.b). Consultants may assist the IRB in the review of issues which require expertise beyond, or in addition to, that available with current primary or alternate members of the IRB's boards.

IRB staff performs a regulatory review of the application followed by assignment to an expedited reviewer. Following the reviewer assignment, and at the reviewer's discretion, submissions eligible for expedited review may be referred to a convened board for a discussion and vote.

When applicable, questions or requirements pertaining to an expedited submission will be communicated to the PI by the IRB staff or the expedited reviewer and must be addressed to their satisfaction prior to approval of the submission. IRB staff and the expedited reviewer will document findings, determination, or recommendations on the Reviewer Checklists in eResearch.

Additions to, and extrapolation from, this list by the institution or the IRBs are not appropriate. For example, it is inappropriate to use an expedited review procedure for the initial review of research that involves minimal risk but does not appear in the categories of research published in the Federal Register or for research that involves greater than minimal risk.

**a)** Expedited Review of Minor Changes

The IRB also may use expedited procedures to review minor changes in previously approved research during a period for which approval is authorized. For purposes of this policy, a proposed change in research is deemed "minor" if it does not significantly affect an assessment of the risks and benefits of the study and does not substantially change the aims or design of the study. A modification cannot be deemed minor if it involves the addition of procedures that involve more than minimal risk or that do not fall into federal categories (1) – (7) of research that can be reviewed by expedited procedures.

Examples of minor changes to a research study include, but are not limited to:

- Addition or deletion of study team members
- Addition of procedures that do not significantly increase risk to participants, considering the original purpose and study design of the approved study (i.e., new procedures that fall under any of the expedited categories can usually qualify as minimal risk)
- Removal of research procedures that would thereby reduce the risk to no more than minimal (i.e., procedures now meet expedited research categories)
- Addition of non-sensitive questions to unvalidated survey or interview procedures
- Addition of or revision to recruitment materials or strategies
- Changes to improve the clarity of statements or to correct typographical errors, provided that

such changes do not alter the content or intent of the statement

**b)** Expedited Reviewers

Generally, IRB Chairs appoint experienced IRB members to serve as expediting reviewers. For purposes of this policy, a member is deemed experienced if he or she has completed all mandatory education for IRB members, has served on the IRB for a minimum of six (6) months or has described and documented prior appropriate experience, and has been approved by the IRB chairs as qualified to perform expedited reviews.

**c)** Expedited Review Determinations

In conducting expedited review, the IRB reviewers may exercise all of the authorities of the IRB, except that they may not disapprove the research, in accordance with the non-expedited review procedure set forth in 45 CFR 46.108(b) and 21 CFR 56.108(c)(i). The reviewer may either approve, require modifications (to secure approval), or refer the research to the convened IRB for review (for example, if they determine the study has a change in risk level due to a change in the protocol).

When conducting an expedited initial or continuing review, the expedited reviewer must confirm the following:

- The research involves no more than minimal risk to participants
- The identification of the participants or their responses will not reasonably place them at risk of criminal or civil liability or be damaging to their financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are not greater than minimal
- The research is not classified; and
- The research falls into one or more of the categories of projects or applications appearing on a list of expeditable studies published by the Secretary of HHS, and only in those categories (see 45 CFR 46.110 and 21 CFR 56.110).

If the expedited reviewer cannot confirm that the submission qualifies for expedited review, the reviewer must document the rationale for this determination and the rationale for review by the convened board.

When conducting an expedited continuing review for clinical studies subject to FDA regulations, the expedited reviewer will additionally determine if there needs to be verification from sources other than the clinical investigator that no material changes in the research have occurred since the previous IRB review by considering the following:

- The nature and risks posed by the clinical investigation
- The degree of uncertainty regarding the risks involved
- The vulnerability of the participants
- The experience of the clinical investigator in conducting clinical research
- The board's previous experience with that researcher or sponsor (e.g., compliance history, previous problems with obtaining informed consent, prior complaints from participants about

the researcher)
- The projected rate of enrollment
- Whether the study involves novel therapies

The IRB may, at its discretion, require that the Pl respond to required changes within a specified period and instruct that, if the response is not received, the application will be considered withdrawn or reassigned to deferred status. The PI may appeal any decision by the board per procedures outlined in IRB SOP Part 3.III.C.4.b(4)(b).

IRB staff will provide on a monthly, but not less than quarterly basis, a list of all expedited review approvals inclusive to that period for inclusion on an IRB meeting agenda for acknowledgement at a convened IRB meeting.

The notification shall include at least the following information:

- the reviewer's name
- the submission title and study number
- a description of the qualifying research category; and
- the expediting reviewer's decision and the date it was reached

**d)** Requirements for Continuing Review

Continuing review for projects qualifying for expedited review is not required except in instances where the research is FDA regulated. Expedited reviewers must provide documented rationale for requiring continuing review in eResearch. If a project qualifying for expedited review requires continuing review, the expedited reviewer is provided with the complete protocol, a status report, and any amendments previously approved by the IRB. If continuing review is required, the following should be assessed:

- Assess the current risk level of the project and, if necessary, revise the risk level (decrease or elevate) commensurate with the activity being conducted
- Consider if the protocol needs verification from sources other than the researchers that no material changes had occurred since previous IRB review
- Verify that the current consent document is still accurate and complete
- Consider any significant new findings that might relate to participants' willingness to continue participation and whether these finding will be provided to participants
- Review the project to ensure that the criteria in 45 CFR 46.111 or 21 CFR 56.111 continue to be met; and
- Require any other changes warranted in accordance with the changes in risk level.

For projects where continuing review has been eliminated, the eResearch system sends an annual touchpoint message to investigators to remind them of their continuing responsibilities to submit amendments and AE/ORIOs while the project is active and to terminate the application at study completion. ORCR conducts random audits of minimal risk projects for which continuing review has been eliminated.

**e)** Limitations of Use of Expedited Review

The expedited review procedure may **not** be used where:

- A breach of confidentiality that identifies participants and/or their responses
  - Would reasonably place them at risk of criminal or civil liability; and/or
  - Would be damaging to the participants' financial standing, employability, insurability, or reputation; and/or
  - Would be stigmatizing unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal
- Research is classified
- Research involves prisoners except as outlined in HRPP OM Part 7.B

Other limitations may be placed on expeditable research by an IRB Chair, the VPR, or, for research that is federally supported or FDA-regulated, the relevant department or agency head per HRPP OM Part 3.III.C.5.

6. Criteria for IRB Approval

Regulations at 45 CFR 46.111 (Common Rule) and 21 CFR 56.111 (FDA-regulated research) delineate specific criteria for the approval of research. The IRB shall determine that all of the following requirements are satisfied before approving proposed research:

**a)** Scientific Merit and Feasibility

*Refer to* HRPP OM Part 3.III.C.6.a.

Unless projects have undergone a prior scientific review process (the researcher should identify the organization that conducted the review), the IRBs review all initial protocols for scientific merit and feasibility and consider supporting background scientific information. Scientific merit is examined in relationship with the risks and benefits of the research to human participants. For student applications, the faculty advisor is expected to have reviewed the study for scientific merit before it is submitted to the IRB. The Protocol Review Committee (PRC) reviews all prospective clinical research with aims focused on cancer-related outcomes prior to IRB review and approval.

When performing the scientific review using the eResearch Reviewer Checklist, the primary reviewer shall ascertain and indicate that each of the listed elements is adequately addressed. The primary reviewer may also add additional comments and provide specific information regarding any scientific shortcomings identified in the proposal.

No protocol may be approved unless its scientific validity has been ascertained and documented using the Reviewer Checklist.

**b)** Minimizing Risk: 45 CFR 46.111(a)(1)

*Refer to* HRPP OM Part 3.III.C.6.b.

To approve research, the IRBs must determine that risks are minimized by using procedures that are consistent with sound research design and do not expose participants to unnecessary risks.

Where appropriate, the research project design should include procedures that are already used with the participants for diagnostic or treatment purposes.

The IRBs verify that the research plan, including research design and methodology, will not place participants at unnecessary risk. This includes the risk that the research is inappropriately designed or is lacking in statistical power, such that meaningful results cannot be obtained. To assist the IRB staff with making these determinations, the eResearch application provides guidance materials, including checklists.

The IRBs shall also consider the professional qualifications of the research team, as well as the resources available to the research team at the specific location(s) where the research will be conducted, including but not limited to facility resources such as the testing and safety equipment. PIs and Co-Is are expected to maintain appropriate professional credentials and licensing privileges, if required.

**c)** Risk-Benefit Analysis

*Refer to* HRPP OM Part 3.III.C.6.c.

*Refer* to IRB guidance: Evaluating Risks to Participants on the IRB website.

All research studies, regardless of the type of review (initial or SCR; convened board or expedited), undergo a risk/benefit assessment.

The IRB will review the eResearch application to evaluate the risks versus benefits of the study, using supporting documents, scientific references, IRB staff and primary reviewer Checklists, and recommendations provided by consultants (as appropriate).

The initial step in evaluating a study for risk is to determine if the study meets the federal regulatory definition of minimal risk, i.e., "the probability and magnitude of harms or discomfort anticipated in the 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[j])". *Note: Prisoner research utilizes a different definition of minimal risk (45 CFR 46.303[d]).*

In determining whether a study presents no more than minimal risk to the participants, the IRBs consider the following:

- The PI's assessment of the participants' risk level as presented in the eResearch submission
- Whether the study procedures are consistent with sound research design
- An evaluation of the probability (likelihood) of harm occurring and the magnitude (potential severity) of possible harm
- An evaluation of whether the participants are vulnerable in some way
- An evaluation of the steps taken, or planned, by the PI to alleviate the potential harms (including the quality of the data safety monitoring plan, as appropriate)
- The PI's history of compliance with research protocols and IRB procedures

Generally, studies with a low probability of harm are considered no more than minimal risk. If the study does not meet the federal definition of minimal risk, then IRBs evaluate the design of a proposed study to ensure that:

- It is consistent with fulfilling its scientific mission
- Risks are minimized:
  (i) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and
  (ii) Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Potential benefits of the research are maximized as much as possible within the confines of the research study

The IRBs do not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) to be among those research risks that fall within the purview of its responsibility.

The IRBs will rely on the expertise of its membership to evaluate the risks and benefits of a research proposal. Alternatively, if risks are difficult to assess or are outside the scope of expertise of IRB, the protocol may be referred to another IRB according to the policies outlined in the HRPP OM Part 5.II.C.

**d)** Equitable Subject Selection: 45 CFR 46.111(a)(3)

*Refer to* HRPP OM Part 3.III.C.6.d

To approve research, the IRBs must determine that the selection of participants is equitable. This reflects U-M's adherence to the Belmont Report's concept of "Justice". In making this determination, the IRB will evaluate:

- The characteristics of the participant population
- The purposes of the research
- The setting in which it will be conducted
- The recruiting methods and materials used
- The participant inclusion/exclusion criteria

The IRB should be especially cognizant of special considerations for research involving vulnerable participant populations such as, but not limited to neonates, children, prisoners, pregnant persons, and fetuses, decisionally impaired persons, or economically or disadvantaged persons. Generally, a population that stands no chance of benefiting from the research should not be selected to assume the risk.

The IRBs should be mindful of the importance of including members of minority groups in research, particularly when the research holds out the prospect of benefit to individual participants or the groups to which they belong. Non-English-speaking participants should not be systematically excluded because of inconvenience in translating ICDs. The IRBs should also ensure that participants are not selected from only one group of people simply because it is convenient.

The IRBs should be mindful of the desirability of having gender diversity among research participants and should not arbitrarily exclude the participation of persons of reproductive age. Exclusion of such persons must be fully justified and based on sound scientific rationale.

**e)** Informed Consent, Parental Permission, and Assent

*Refer to* IRB SOP Part 11.II.A

*Refer* to guidance webpages on Informed Consent (IRBMED and IRB-HSBS).

(1) General Requirements

*Refer to* IRB SOP Part 11

Comprehensive informed consent requirements and application of those requirements are provided in IRB SOP Part 11 and the guidance webpages linked above. *Throughout this section the term "consent" refers to both "consent" and "parental permission".*

Informed consent (IC) will be sought from each prospective subject or the participant's legally authorized representative (LAR), in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20 Subpart B. Except as otherwise approved by the IRB or allowed under FDA regulations (21 CFR 50.23 Subpart B), no PI may involve a human participant in research unless the PI has obtained the legally effective informed consent of the participant or the participant's legally authorized representative (LAR).

The PI will submit ICDs for IRB review (including written ICDs, oral scripts), descriptions of the process to obtain informed consent from participants, and any requests for waiver(s) or alteration of informed consent or waiver(s) of documentation of informed consent, in the eResearch submission to the IRB.

The IRB will review the proposed informed consent process, including ICDs for each submitted application to assure that participants or their LARs provide legally effective, voluntary, informed consent.

In its review of ICDs, the IRB will ensure that all required elements of consent as well as any additional elements, as appropriate, are included per 45 CFR 46.116. It will also ensure that the documents do not contain any exculpatory statements suggesting that any of the participants' legal rights are being waived, or that the Pl, sponsor, or U-M may be released from liability for negligence.

The IRB will assess applications and issue waivers of documentation or waivers of some or all of the elements of informed consent, where appropriate under regulatory guidance.

The IRB will evaluate the plans for obtaining consent by confirming the following:

- The consent process is facilitated by a person knowledgeable about the study, its enrollment criteria, its risks and benefits, and alternatives to participating in research (usually a PI or Co-I, although other study team members, for example, a research study coordinator or research nurse, may also be qualified and designated by the PI).
- The prospective participant or LAR will be provided with information and materials in a location appropriate to the study and offering the privacy necessary to ask questions about the study before deciding to participate.
- In obtaining informed consent, the PI will give the participant (or LAR) sufficient opportunity, commensurate with the risk level of the research, to consider whether or not to participate. Time should be allowed for questions and full discussion.

Information about the study should be presented in a neutral, non-coercive manner and in a language readily understandable to the participant or LAR.

- Except as otherwise approved by the IRB, informed consent shall be documented by the use of a written consent form approved by the relevant IRB and signed by the participant or the participant's LAR. A copy will be given to the person signing the form. Studies following International Council for Harmonisation: Good Clinical Practice (ICH-GCP) require that a copy (paper or electronic) of the signed informed consent and any other informed consent materials be provided to the participants.
- The informed consent document used by the researchers must be the most recent version approved by IRB and is valid only after its approval by the convened board or through expedited review.

Evaluation of Parental Permission

Generally, a parent (the child's biological or adoptive parent) or guardian (an individual who is authorized under applicable state or local law to consent on behalf of the child) must agree to the child's participation in the research.

The IRB assesses the procedures and appropriateness of the parental permission process.

The specific requirements for obtaining parental permission for HHS conducted or supported studies are found at 45 CFR 46.406 and 407. For information about waivers of parental permission see IRB SOP Part 3.III.C.6.e.3.

Assent of Children

*Refer* to IRB SOP Part 7.II.C

Federal regulations (45 CFR 46.408 and 21 CFR 50.55) require that IRBs determine that adequate provisions are made for soliciting the assent of children involved as study participants when, in the judgment of the IRB, the children are capable of providing assent (i.e., a child's affirmative agreement to participate in research). The IRB uses its best judgment, on a study-specific basis, to ensure that the assent process is tailored to the level of comprehension of the prospective participants. Mere failure to object will not, absent affirmative agreement, be construed as assent. The assent process will determine when children are capable of assent based on age and maturity of the children, psychological state of the children, and nature of the proposed research activity.

Research conducted in public schools may be subject to additional regulatory consent requirements such as PPRA (Protection of Pupil Rights Amendment) and FERPA (Family Educational Rights and Privacy Act) (see 34 CFR 98, 20 USC 1232g, 34 CFR 99, and OM Part 11.I.B.5).

(2) Short Form ICD

*Refer to* HRPP OM Part 6.II.B.2.g

*Refer to* additional guidance on the IRBMED website.

A short form written ICD may be used in certain circumstances (45 CFR 46.117(b)(2)). The

short form consent process requires that the elements of informed consent required by HHS and/or FDA regulations are presented orally to the participant or the participant's LAR in the presence of a witness. For participants who do not speak English, the witness must be conversant in both English and the language of the participant and may be the interpreter.

The IRB must approve the short form and a written summary (oral script) of what will be said to the participant or participant's LAR.

The short form must include signature lines for the participant, or participant's LAR and the witness.

The participant or participant's LAR, the researcher consenting the participant, and a witness, if appropriate must sign the short form and/or the oral script according to the following table:

**Table 2: Short Form Consent Requirements**

| **Short Form Consent Requirements** | | | |
|---|---|---|---|
| | **Participant or Legally Authorized Representative (LAR)** | **Researcher** | **Witness** |
| **Forms Required to Sign** | Short form | Oral script | Short form and oral script |
| **Forms Required to Receive or Keep** | A copy of the short form and oral script. Studies adhering to ICH GCP should provide signed copies as applicable. | Original signed short form and signed oral script | Nothing |

The participant or participant's LAR will receive a copy of the short form and oral script. Studies following ICH GCP should provide signed copies as appropriate.

(3) Informed Consent Waivers, Alterations, Exceptions and Substitutions

<u>Waiver or Alteration of Informed Consent</u>

*Refer* to HRPP OM Part 3.III.C.6.e.3

*Refer* to IRBMED guidance webpage Emergency Research (Planned and Approved) with Exception from Informed Consent.

The IRB may approve a consent procedure which does not include or which alters some or all of the basic elements of informed consent or which waives the requirement to obtain informed consent, if the IRB finds that the research complies with either:

- Appropriate conditions of 45 CFR 46.116(e) and/or (f) and, if appropriate, FDA regulations at 21 CFR 50.22 for Exception from informed consent for minimal risk investigations.
- Exception from informed consent (EFIC) for emergency research that satisfies criteria at 21 CFR 50.24 and Office for Human Research Protections (OHRP) Secretary's Waiver.

Projects involving the use of deception or concealment in the consent process must meet the same criteria as required for waiver of informed consent.

Waiver of Requirement for Parental Permission

For research involving children as human research participants, the IRB may waive the requirement to obtain parental permission if it determines and documents requirements per 45 CFR 46.408 and applicable requirements under 45 CFR 46.116 and 21 CFR 50.22.

The IRB may also waive the requirement to obtain parental permission if the protocol is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants (e.g., neglected or abused children) and if it determines and documents requirements per 45 CFR 46.408(c) and applicable requirements under 45 CFR 46.116 and assures the research is not FDA-regulated.

Waivers of Documentation of Informed Consent

"Waiver of documentation" is a regulatory term that means the informed consent process takes place but the requirement to "document" that process does not involve obtaining participants' signatures on a written document. The IRB may waive the requirement for the PI to obtain a signed ICD for some or all of the participants if the requirements of 45 CFR 46.117(c) and/or 21 CFR 56.109(c)(1), and requirements of 21 CFR 50.22 are satisfied.

Situations in which a waiver of documentation of informed consent is allowed include, but are not limited to:

- Telephone or web-based surveys
- Blood draws or urine collection (where HIPAA does not apply or the requirement for an Authorization signature can be altered)
- A minimal risk FDA regulated clinical investigation that does not require procedures that would otherwise require written consent
- Research involving illegal activities or illegal behavior
- Research involving socially sensitive issues, such as HIV status

When the IRB waives the requirement for documentation of informed consent, the required

elements of informed consent, as well as any additional elements of consent disclosure, as appropriate, must be conveyed to the participant verbally or by electronic or printed text. Even though participants do not sign a document, the IRB may still require that participants be provided with written information about the study. The text of the written or oral informed consent scripts and any informational documents provided to participants must be reviewed and approved by the IRB before their use.

Emergency Research Exception from Informed Consent (EFIC)

*Refer* to HRPP OM Part 3.III.C.6.e.4

*Refer* to FDA

- Information Sheet: Informed Consent heading "Exceptions to Informed Consent"
- 21 CFR 50.23 and .24

*Refer* to OHRP Informed Consent Requirements in Emergency Research (OPRR Letter, 1996)

Emergency Research with Exception from Informed Consent (EFIC) is *planned* research conducted where participants are in an emergent need of clinical care. "Emergency Research" is distinct from "Emergency Use", in that the latter is an *unplanned* need to use an investigational agent that arises emergently for a single patient/participant.

In the course of its review, approval, and continuing review of clinical research proposals, the IRB may approve a research proposal without requiring that informed consent of all research participants is obtained prior to the commencement of the research. The IRBMED (with the concurrence of a licensed physician who is a member of, or consultant to, the IRBMED and who is not otherwise participating in the clinical investigation) must find and document all requirements under 21 CFR 50.24 for EFIC research.

(4) Research Subject to Both HHS and FDA Regulations

*Refer* to HRPP OM Part 3.III.C.6.e.5.

(5) Research Subject to HIPAA Regulations

Waiver of HIPAA Authorization

*Refer* to HRPP OM Part 3.III.C.6.e.6

Under HIPAA Privacy Rule, researchers must obtain written authorization from a research participant for release of protected health information that the researcher will collect, use or disclose for the study, unless criteria are met for a waiver of authorization or other exception to the authorization requirement.

A PI may submit as part of an eResearch application a request for review and approval of a waiver or alteration of HIPAA authorization for the use and disclosure of PHI for research purposes, which may be part of an application for IRB approval according to 45 CFR 46.111 or 21 CFR 56.111, or may be a stand-alone application for research projects not otherwise subject to IRB oversight, in which PHI may be used or disclosed without patient authorization, including decedents, PHI and review of PHI preparatory to research (e.g.,

Certification Preparatory to Research).

The IRBs exercise authority in accordance with HIPAA (45 CFR 164) and applicable University policies and procedures to grant waivers or alterations of HIPAA authorization. The IRB expedited reviewer(s) or convened IRB Boards may approve a waiver or alteration only if all of the 45 CFR 164.512(i)(2)(ii) criteria are met. Where the PI anticipates the disclosure of PHI outside the Covered Entity (as that may be determined from time to time), the PI must account for each disclosure and retain records of such disclosures.

Refer to HRPP OM Part 3.III.C.6.g for a detailed description of points the IRBs should consider in determining whether a protocol includes plans sufficient to address privacy and confidentiality concerns.

Other exceptions to the HIPAA authorization requirement

eResearch applications regarding other exceptions to the HIPAA authorization requirement (decedents, review of PHI preparatory to research, and Limited Data Sets) are usually research projects not otherwise subject to IRB oversight. These are processed by IRB office staff (or any qualified individual designated to review such submissions) including verification of the required assurances from the researcher [45 CFR 164.512(i)(1)(ii)-(iii) and/or cognizance of data use agreement requirement(s) [45 CFR 164.514(e)].

The IRB expedited reviewer(s) or convened Board considers all applicable HIPAA provisions for submissions requesting IRB approval according to 45 CFR 46.111 or 21 CFR 56.111.

**f)** Data and Safety Monitoring

*Refer to* HRPP OM Part 7.III.

With respect to any research project or class of research projects, the IRBs may impose additional conditions on the conduct of the research at any time prior to, concurrent with, or following approval, when in the judgment of the IRBs such additional conditions are necessary or appropriate for the protection of human research participants.

(1) Considerations for the Imposition of Special Monitoring Requirements

The IRB may, at its discretion, perform monitoring or request monitoring of a study and its relevant study documentation from ORCR (the request is routed through the HRPP Director). For example, the IRB may choose to undertake extra monitoring for research which presents greater than minimal risk, to gauge the progress of recruitment for vulnerable participants, to follow the research progress on a controversial subject matter, or to evaluate the frequency and nature of AEs reported to date.

The U-M IRBs may also choose to monitor one or more of the projects of a single PI in consideration of the experience of the PI or as follow-up to previous reports of complaints, non-compliance, or prior IRB interactions with the individual.

(2) Examples of Special Monitoring Requirements

*Refer to* IRB SOP Part 3.III.C.4.d

The U-M IRBs shall communicate with the PI as appropriate, regarding the outcomes of these additional monitoring efforts.

**g)** Privacy and Confidentiality Protection

*Refer to* HRPP OM Part 3.III.C.6.g.

*Refer to* Code of Federal Regulations 45 CFR 46 (OHRP), 21 CFR 56 (FDA), 45 CFR 160 and 164 (HIPAA)

*Refer to* University of Michigan Website Guidance for Sensitive Human Subjects Data: safe computing.umich.edu

To approve research, including under the provisions of limited review for exemptions 2 and 3, the IRB must determine that, where appropriate, there are adequate provisions to protect the privacy of participants and the confidentiality of data. Regulatory, institutional, and IRB policies and guidance are used to confirm that the protocol appropriately and adequately protects privacy.

The PI must include a plan to protect participants' privacy and confidentiality in the eResearch application, protocol or other documents submitted to the IRB to include a description of the types of privacy and confidentiality information that the researcher must include in its plan. The IRB reviews the PI's plan to protect participants' privacy and confidentiality to assess the adequacy of the protection.

In reviewing confidentiality protections, the IRB shall consider the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research context. It shall evaluate the effectiveness of proposed techniques to anonymize, code, encrypt, store, or access the information, and any other relevant factor in determining the adequacy of confidentiality protections.

**h)** Vulnerable Participants

*Refer to* HRPP OM Part 7.II.
*Refer to* IRB SOP Part 7.II

Special federal regulations apply to research involving vulnerable populations. These groups include, but are not limited to:

- Children (individuals who have not attained the legal age for consent to the treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted (45 CFR 46 Subpart D; 21 CFR 50 Subpart D)
- Pregnant women/persons, fetuses, and neonates, including those of uncertain viability (45 CFR 46 Subpart B)
- Prisoners:
    - Individuals involuntarily confined or detained in a penal institution, including:

  - Individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, as well as individuals detained pending arraignment, trial, or sentencing (45 CFR 46 Subpart C)
- Individuals who lack decision-making capacity (45 CFR 46.111(b) and 21 CFR 56.111(b))
- Individuals who otherwise may be subject to coercion or undue influence (e.g., economically or educationally disadvantaged persons, employees or students of investigators conducting the study, or patients of physician-investigators (45 CFR 46.111(b) and 21 CFR 56.111(b))

When members of any of these groups participate in research, the IRB requires investigators to specify what additional protections, if any, will be provided to these persons to protect their rights and welfare (e.g., to minimize risks unique to these groups and the possibility of coercion or undue influence). In reviewing these research projects, the U-M IRBs will ascertain that inclusion of a vulnerable population is adequately justified and that safeguards are implemented to minimize risks unique to that population.

Laws governing research involving vulnerable populations, including laws on who may consent on behalf of children or incapacitated adults, vary from state to state.

Michigan Law

*Refer* to IRB SOP Part 11 for a detailed description of State of Michigan requirements and references to guidance for determining the nature of requirements applicable to Michigan and to research proceeding outside of Michigan.

Michigan Law requires special consent for procedures or treatments for the following conditions:

- Breast cancer
- Electroconvulsive therapy
- HIV/AIDS testing
- Pregnancy termination
- Surgery for mental health patients
- Terminal illness

**i)** Test Article Accountability Procedures (FDA)

*Refer to* HRPP OM Part 8.VIII.D

*Refer* to HRPP OM Part 3.III.C.6.i

(1) The IRB may not approve an application for research involving drugs, biologics or devices unless it determines that the test articles will be used only in approved research protocols, under the direction of approved investigators, or in emergency circumstances, consistent with FDA requirements and University policies on emergency use
(2) Research protocols must describe local drug/biologic or device accountability procedures, as applicable, including procedures required by:
    (a) Michigan Medicine Research Pharmacy; and
    (b) Clinical Engineering

(3) Investigational drug management and accountability is performed according to Department of Pharmacy Services Policies
(4) Investigational device accountability, under most circumstances, is performed by the PI and study teams, who are responsible for documenting the processes for handling and dispensing of investigational devices according to the plan approved by the IRB. Note that investigational devices may need to undergo additional quality control measures to ensure they are safe and may need to be registered with the University

**j)** Resources

*Refer* to HRPP OM Part 3.III.C.6.j

IRBs will determine that research studies have the resources necessary to protect participants by evaluating all of the following as outlined in the application materials submitted for review:

- There is adequate time for the investigators to conduct and complete the research
- There are an adequate number of qualified staff
- Financial resources and budget are adequate to support the research to its completion
- The facilities where the research will be conducted are adequate
- PIs have access to a population that will allow recruitment of the necessary number of participants
- Medical or psychosocial resources that participants may need as a consequence of the research are available

**7.** IRBMED Review and Monitoring of FDA-Regulated Research

*Refer to* HRPP OM Part 8

*Refer to* IRB SOP Part 8

## D. IRB Administrative Functions

### 1. IRB Meetings

a) An IRB must review submissions requiring IRB determinations at convened meetings at which a majority of the members of the IRB are present.
b) At convened meetings at least one non-scientist member must be present in order to meet quorum; at least one unaffiliated member, who represents the general perspective of participants, should be present at the majority of meetings in a given year. Attendance of all present members is recorded in the meeting minutes.
c) In order for the research to be approved, it must receive approval by majority vote of the quorum (as described above). If, during the course of the meeting, quorum is lost, votes may not be taken until it has been restored.
d) When convened board review is not required, expedited review procedures (as described in Part 3.III.C.5 above) or other approval procedures (to address administrative approvals, not-regulated determinations and exempt review) may be used to supplement the IRB's review responsibilities.

e) IRB members may agree, during an appropriately convened meeting, to issue conditional approval for a project only if any requested clarifications or modifications are not relevant to the determinations required by the IRB under the Common Rule or its Subparts (45 CFR 46) or, as applicable, FDA regulations (21 CFR 56/50). If substantive clarifications or modifications regarding the protocol or informed consent documents are required as a condition of approval, approval must be deferred pending subsequent review of responsive material by the convened IRB.

f) IRB meetings may occur as remote (electronic), in-person with members physically present, or hybrid with a combination of members joining electronically and some attending live.

**2.** Notification of Decisions

a) The IRB will notify investigators in writing of its decision to approve or disapprove a proposed research activity or of modifications to the proposal that are required to secure IRB approval.

b) If the IRB decides to disapprove a research activity, it must include a statement of the reasons for its decision in its written notification and the investigator must be afforded the opportunity to appeal the decision.

c) The IRB will notify the IO or DIO and other institutional officials, when appropriate, of its decisions regarding proposed research activities by formal or informal means, such as through access to relevant electronic databases.

**3.** IRB Response to Noncompliance, ORIOs and Other Required Reporting

*Refer* to IRB SOP Part 12

**4.** IRB Records and Reports

a) Documentation Uploaded into eResearch

The following documentation associated with eResearch submissions, determinations and tracking will be uploaded (and permanently archived) to the appropriate submission itself, or submitted via AE/ORIO Reports:

- Protocols or research plans
- Any investigator brochures
- Any scientific evaluations, when provided by an entity other than a U-M IRB
- Recruitment materials
- Approved consent documents
- Reports of injuries to participants
- Unanticipated problems involving risks to participants or others
- Documentation of non-compliance including if non-compliance is serious and/or continuing
- Amendments or modifications to previously approved research
- Any data and safety monitoring reports
- Documentation of exemption determinations, include the category by which research was

determined to be exempt
- Documentation of approvals using the expedited procedure, including the applicable criteria by which the research was approved using the expedited procedure
- If applicable, the rationale for conducting continuing review of research that otherwise would not require continuing review
- If applicable, the rationale for determining that research appearing on the list of eligible expedited review categories is greater than minimal risk
- Description of action taken by a reviewer
- Records of continuing review activities
- Significant new findings and those that have been provided to participants
- Progress reports submitted by PIs
- Submission approval letters
- Correspondence with study team members
- Documentation of Institutional Authorization Agreements, Individual Investigator Agreements, or Collaborating Institutional Agreements

Approved meeting minutes are uploaded to the agenda work-space of the convened meeting for which they were recorded.

b) Reports and Communications Archived by each IRB

- Current and previous IRB membership rosters for primary and alternate members describing their qualifications (degrees earned, area of expertise, membership role) sufficient to describe each member's anticipated contribution to the IRB's deliberations and any employment relationship between members and UM.
- Resumes or curricula vitae for each board member.
- Written SOPs
- Documentation of member and staff training
- Noncompliance reports

c) Retention

*Refer to* HRPP OM Part 11.II.F

*Refer* to IRB SOP Part 11.II.F

*Refer to* IRB Guidance – Record Retention for information for the HRPP on the length of time study records are to be kept on file.

Any retained hard copy materials (from prior IRB application systems) are logged and stored off-site in a secure manner in a commercial storage facility. Retrieval of documents stored off-site is arranged by contacting the IRB office, who will notify the facility for the appropriate records to be delivered on an assigned date.

- IRBs must maintain records for at least three (3) years after the completion of a research study

- If a research application is terminated without participant enrollment, IRB records must be maintained for at least three (3) years following termination
- If an IRB performs functions on behalf of a "covered entity (such as the University of Michigan Hospitals and Health Centers) related to HIPAA and research, those records must be retained for at least six (6) years, either by the IRB, or by the covered entity; and
- Administrative units responsible for IRB operations may impose longer retention and specific destruction standards.

d) Inspection of Records

Paper and electronic documents will be made accessible for inspection and copying by authorized representatives of U-M, relevant sponsors, and government authorities with jurisdiction (such as OHRP, FDA, and NIH) at reasonable times and in a reasonable manner.

**E.** Quality Assurance and Quality Improvement

*Refer to* HRPP OM Part 12.I.A-B

**1.** SOPs

The IRB SOPs are evaluated, amended, reviewed, and approved as indicated in Part 3 III.A. Outdated sections of these SOPs will be archived in such a way that changes and dates of approval may be followed.

Revisions to SOPs may be made at any time as required by changes in law, ethical standards, institutional policy, quality assurance activities, IRB Chair, member or stakeholder input, advisory councils, the IO or designee(s), or other considerations at the discretion of the IRB.

**2.** Internal Quality Assurance

The IRB routinely conducts internal review of its staff and board member operations, as well as review of the eResearch application and its workflows, as part of its continuous quality improvement efforts to measure the effectiveness of its human research protection program and to determine if its review processes are performed and recorded in compliance with established standards.

Review will be conducted periodically by the following means:

- Solicitations in writing or by survey of the IRB Chairs, members, staff, and affiliated Pls and study team personnel as well as from standing and ad hoc research advisory councils within the jurisdiction of the IRB
- Peer assessments
- Periodic internal checks for quality improvement
- Review by other institutional units, such as the ORCR review of convened board meeting minutes

## IV. OTHER REVIEW UNIT STANDARD OPERATING POLICIES AND PROCEDURES

*Refer to* HRPP OM Part 3.IV

## Part 4 – Activities Subject to the HRPP

The conduct of human participants research triggers a broad array of regulatory and institutional requirements, including advance approval from IRBs and other review units. To determine whether a particular activity is subject to U-M's HRPP or when the requirements of the HRPP are triggered, four questions must be answered:

- Is it human participants research under the Common Rule?
- Is it human participants research under FDA regulations?
- Is U-M engaged in the research?
- When does the research begin and end?

Analysis of these questions is described below and in the decision aids attached to the Appendix.

### I. Determining What is and what is not human subjects Research

*Refer to* HRPP OM Part 4.I

### II. Determining Whether Research Involves Human Subjects

*Refer to* HRPP OM Part 4.II

### III. Determining Whether the University is Engaged in Human Subjects Research

*Refer to* HRPP OM Part 4.III

### IV. Determining When Human Subjects Research Begins and Ends

*Refer to* HRPP OM Part 4.IV

### V. Authority to Make Regulated/Not-Regulated Determinations (Per the Common Rule and FDA) and Notification of Decisions

*Refer to* HRPP OM Part 4.V

#### A. Authority to Make Regulated/Not-Regulated Determinations

*Refer to* HRPP OM Part 4.V.A

As part of the administrative and regulatory review process of submitted eResearch applications, qualified IRB staff members assess whether the project meets the definition of human participant research using the charts and guidance found in HRPP OM Part 4. The IRB Chairs or Directors may be consulted, as necessary.

PIs may consult informally with an IRB staff member to determine if their research project involves human participants. To obtain a formal, documented regulated/not-regulated determination, an eResearch "Projects Not Regulated as Human Subjects Research" application must be prepared for review and determination. The outcome determination letter may be used for funding or publication purposes.

Applications submitted in eResearch as "Projects Not Regulated as Human Subjects Research" are reviewed administratively by designated IRB staff who have completed appropriate training and demonstrated a working knowledge to assess whether the project meets the definition of human

participant research. Applications may also be reviewed by expedited review or convened board review for confirmation of the appropriateness of the determination, as indicated. PIs may contact the IRB Office to initiate a consultation.

**B.** Illustrations

*Refer to* HRPP OM Part 4.V.B

**C.** Student Practicum and Internships

*Refer to* HRPP OM Part 4.V.C

**D.** Notification of Decisions

*Refer to* HRPP OM Part 4.V.D

**E.** Review of Emergency Use of Investigational Agents

*Refer to* HRPP OM Part 8 and IRB SOP Part 8

**F.** Review of Humanitarian Use Devices (HUD) Under a Humanitarian Device Exemption (HDE)

*Refer to* IRB SOP Part 8

**G.** Non-Research Use of Investigational Products Regulated by the FDA

*Refer to* HRPP OM Part 8 and IRB SOP Part 8

## VI. POLICY ON EXEMPT RESEARCH

*Refer to* HRPP OM Part 4.VI

**A.** Introduction

*Refer to* HRPP OM Part 4.VI.A

IRB SOPs require an IRB application be submitted for exempt projects. The application includes specific questions to evaluate the protection of human subjects and to determine eligibility under each exemption category.

Once an exemption has been granted, the project is not subject to continuing IRB oversight, unless the scope of the project changes such that it no longer meets the criteria required for exemption.

**B.** Categories of Eligibility for Exempt Determination

*Refer to* Federal Exemption Categories

*Refer to* HRPP OM Part 4.VI.B.

Research involving prisoners may not be granted exempt status, even if it falls into one or more of the federal exemption categories.

Special limitations on exemptions apply to research with children.

In addition to the federal exemption categories, U-M permits IRBs to issue exemptions to qualifying research under additional categories. These are described at the HRPP Flexibility Initiatives and currently include:

- Expansion of Exemption 5 (to accommodate research sponsored by the State of Michigan)

Exempt applications requiring limited IRB review must include the following information:

- Adequate information in the application or protocol to determine that the research fulfills the criteria for approval under limited IRB review
- Any proposed consent documents and
- Any recruitment materials

**C.** Authority to Grant Exempt Status

*Refer to* HRPP OM Part 4.VI.C

Designated IRB staff that have completed appropriate training and demonstrate a working knowledge of the regulations, Chairs, or board members may determine as exempt any project that meets the exemption criteria set out at 45 CFR 46.104 or in institutional policy. However, final determination of Exemption 5 may not be issued by the IRB but instead according to the parameters of OM Part 4.VI.C. Exempt determinations may not be conducted by PIs or others who may have a conflict of interest regarding the studies. Any practice involving regulatory flexibility permitting PIs or individuals (other than those listed above) to issue exempt determinations must be approved by the IO or their designee. Investigators are permitted to generate an exemption determination letter for some projects qualifying for exemption categories 1, 2, and 3, based upon their responses to key qualifying questions in the eResearch system, subject to at least the following limitations/requirements of the research:

- Does not involve data subject to HIPAA or FERPA
- Does not include studies requiring "limited IRB review" (Exemptions 2 and 3)
- Cannot involve undisclosed deception or concealment (Exemption 3)
- Does not involve research conducted in comprehensively embargoed countries
- Student investigators must include a faculty advisor as a member of the study team
- No financial conflicts of interest are disclosed by study team members
- Key study team members have completed PEERRS human subjects training

System-generated exemption determinations are subject to audit by the IRB to validate the outcome. If determination errors are identified, the IRB requires amendments to correct those errors.

**D.** Notification and Documentation of Exempt Status

*Refer to* HRPP OM Part 4.VI.D

The exempt determination is issued to the PI via eResearch. The eResearch application and determination letter remind researchers of the ethical obligation to ensure that participants are fully informed about the nature of a research project so that they can make an informed decision to participate. The notification letter includes the exemption category assigned to the study, as well as instructions to amend the eResearch application for IRB review should the scope of the project change beyond the criteria for exemption.

# Part 5 – IRB Jurisdiction, Cooperative Research, and Reliance Agreements

This section describes the scope of jurisdiction of the various University IRBs as well as policies on cooperative research and reliance agreements for accepting and ceding of IRB oversight.

## I. UNIVERSITY OF MICHIGAN IRB JURISDICTION

*Refer to* HRPP OM Part 5

### A. University of Michigan Medical School IRB (IRBMED)

#### 1. Primary Jurisdiction

All research proposed by faculty, staff, students, or other trainees with a primary appointment in the Medical School or in affiliation with Michigan Medicine.

All research using the patients, medical records, or facilities of the University of Michigan Hospitals and Health Centers.

All research where the results will be submitted to FDA as part of an application for a research or marketing permit. This includes research involving investigational drugs, biologics or significant risk devices.

All clinical investigations conducted by the School of Dentistry.

Any research involving invasive techniques, such as deep muscle biopsies by the School of Kinesiology.

Research using the Functional MRI (fMRI) Laboratory (also see below under IRB-HSBS exceptions B.2.).

#### 2. Exceptions

By agreement of the IRBs, some categories of exempt research are reviewed by IRB-HSBS.

### B. IRB–Health Sciences and Behavioral Science (IRB-HSBS)

#### 1. Primary Jurisdiction

*Refer to* the list maintained at HRPP OM Part 5

All research conducted by the faculty, staff, students or other trainees with a primary appointment in UM-Ann Arbor, UM-Flint, and UM-Dearborn schools, colleges, units or programs not subject to IRBMED jurisdiction.

#### 2. Exceptions

*Refer to* the list of exceptions maintained at HRPP OM Part 5

By agreement with IRBMED, qualifying PIs with a primary appointment to IRB-HSBS may submit fMRI protocols to IRB-HSBS for review under the terms of the IRBMED-approved Master Protocol.

### C. General Exceptions

1. If the IRB with primary jurisdiction does not have the appropriate expertise or is not appropriately constituted to review a research proposal, the project may be transferred to the IRB with

appropriate expertise for review and approval.

2. When conflicts of interest preclude a quorum for review, the project may be transferred to an alternate IRB with appropriate expertise for review and approval. The selection of an alternative IRB will be made by the chair of the referring IRB in consultation with the receiving IRB, if the chair does not have a disqualifying conflict. If the chair has a disqualifying conflict of interest, the selection will be made by the Vice President for Research or designee.
3. When an IRB or a faculty member, staff member, student, or other trainee requests review by an alternate U-M IRB, the Director or designee of the initially assigned IRB will review the reasons for such a request. If the request has merit, they will consult with the Director or designee of the other IRB to finalize the transfer. If additional input is necessary or the requester is dissatisfied with the decision, the IRB Chairs of both IRBs will be consulted and they will decide which IRB shall review the proposal. In extraordinary circumstances, the Vice President for Research may overrule a Chair's refusal to refer an application to another U-M IRB.
4. In rare instances, in which the rules below do not clearly define which IRB to use and the Chairs cannot agree on jurisdiction, the matter may be referred to the Vice President for Research or designee for a determination.

The IRB is also authorized, in its discretion, to invite individuals (consultants) with special expertise to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals will identify any conflicts of interest to the IRB and they may not vote with the IRB.

## II. COOPERATIVE RESEARCH

*Refer to* HRPP OM Part 5.III

Researchers at U-M frequently interact with entities or individuals outside the University. Relationships may include:

- Establishing research collaborations by subcontract from or to the University
- Serving as the coordinating site for a multi-center clinical trial being conducted elsewhere or serving as a performance site in a multi-center clinical trial
- Conducting research at clinics, schools, etc., where the outside site provides only access to the facility or participants, or where the outside site has or will have identified data
- Conducting research in another country, but not in partnership with an established entity in that country, and establishing relationships with individuals, such as volunteer research assistants, who will provide services
- Conducting research with the UM Health Statewide Network of Care Sites

The OM Part 5.III describes overall roles and responsibilities of the institution, IRBs, and PIs when interacting with performance sites determined to be engaged or not engaged in the conduct of the research.

## III. RELIANCE AGREEMENTS

*Refer to* HRPP OM Part 5.IV
*Refer to* IRBMED Guidance - Single IRB and Multi-site Research
*Refer to* IRB-HSBS Guidance - Collaborative Research IRB-HSBS sIRB Process

NIH policy, the Common Rule, and certain sponsors require that multi-site and collaborative research use a sIRB model. When one IRB acts as the Reviewing IRB on behalf of other institutions, referred to as Relying IRBs, a written reliance agreement (also called an IRB Authorization Agreement) among the involved institutions is required. Whether using a single IRB or conducting duplicate review when appropriate, the U-M IRB must approve the arrangement either for individual studies or categorically (e.g., Master Agreements with commercial IRBs). The University does not enter into Reliance Agreements with external entities for projects that have been determined to be exempt unless mandated by federal agencies sponsoring the research or by exception approved by the HRPP Director.

U-M is a signatory to multiple Master Agreements as well at the SMART IRB agreement. The IRBs have developed numerous procedures as well as guidance documents that address IRB, U-M study team, and external site responsibilities when U-M is either ceding IRB oversight or accepting oversight as the sIRB. Records of executed Reliance Agreements are stored in eResearch submissions and by each IRB.

In a centralized process, U-M IRB and HRPP leadership representatives meet routinely to conduct an Authorization Agreement Meeting to discuss the appropriateness of specific requests to either cede IRB oversight or accept IRB oversight in association with specific Reliance Agreements or Master Agreements. Information is collected from study teams and presented to facilitate the discussion and decision-making and additional information can be requested. Assessments include but are not limited to the reason for requesting the Reliance action, information about the external entities (e.g., FWA and AAHRPP status), the nature of study activities, any special IRB expertise necessary to assess whether the IRB has appropriate composition/expertise IRB to conduct the review, and appropriateness of study budget. The HRPP Director, in consultation with the IRB Directors, determines the appropriateness of arrangements to accept or cede IRB oversight.

Each multi-site agreement apportions roles and responsibilities between the Reviewing IRB and the Relying Site and are described below. Any concerns are addressed at the Authorization Agreement Meeting. These agreements cover adverse event and protocol deviation reporting, conflict of interest management, non-compliance reviews, external reporting requirements and other elements necessary for the conduct of the research.

eResearch includes application-types that support ceding or accepting IRB oversight responsibilities in association with Reliance Agreements. The ceding application provides notice to the IRBs of the intent to cede the research and collects information relevant to the local conduct of the research and permits routing of the application to the relevant U-M ancillary committees. The multi-site research application utilizes participating site modules to collect information from sites intending to rely upon a U-M IRB for IRB oversight.

## IV. IRB RESOURCES

The IRBs have dedicated staff to facilitate the intake of multi-site information and prepare the information for consideration of efforts to cede or accept oversight.

New information about regulatory guidance or procedures is published in newsletters or distributed by email and is posted to each IRB's website.

The IRBs also conduct a Quality Assurance process to evaluate procedures associated with ceding and accepting oversight. Studies are selected and sites (U-M and external) are asked to provide evidence that study procedures are maintained in a compliant manner. Information is evaluated for correctness and accuracy and any corrective action or identified noncompliance is addressed through normal channels.

## V. REVIEWING IRB RESPONSIBILITIES

*Refer* to HRPP OM Part 5.IV.A.2

U-M IRBs may be asked to serve as sIRB in association with the requirements of a multi-site study. As described earlier, Reliance Agreements will govern the relationships and reporting obligations between the parties.

The IRBs utilize eResearch to collect information from/about individual relying sites including, but not limited to: FWA and AAHRPP status, study team members and qualifications, relevant state laws or institutional procedures, conflict of interest management plans for study team members, required ancillary committee reviews, site-specific information for the informed consent document (e.g., HIPAA and subject injury language), how the consent process will be conducted, how vulnerable populations will be protected during the conduct of the study, and local educational requirements. The information is stored securely and distributed to IRB reviewers for inclusion during the review process and in association with determining whether to extend U-M IRB oversight to the site.

After a U-M IRB has agreed to be the sIRB through the appropriate convened or expedited review pathway as determined by study risk level, individual sites may be approved via the expedited review process.

U-M IRBs provide templates for relying sites to facilitate development of informed consent documents and reporting of adverse events and protocol deviations associated with the study.

The U-M IRBs transmit approved materials and regulatory determinations to the participating sites via the eResearch application. Participating sites report required information (e.g., reportable events including UaPs, protocol deviations, and potential noncompliance as well as site-specific requests for amendments) directly to the U-M IRBs via the participating site section of the eResearch application.

Any relying site may communicate directly with the U-M IRBs to discuss questions, concerns, or obtain interpretation of determinations by contacting the IRB Chairs, Director, or IRB staff members.

## VI. RELYING IRB RESPONSIBILITIES

*Refer* to HRPP OM Part 5.IV.A.4

U-M IRBs may be required to rely upon external IRBs as required by regulation, grant or contract issued by a funding source, or other non-financial study sponsor, as a condition of participating in the research (e.g., NCI cIRB, independent IRBs as delineated by a sponsor, or federally sponsored research in compliance with the Common Rule). U-M IRBs may also voluntarily choose to cede IRB oversight at the request of the

institution, sponsor, PI, or other external party associated with the research. As described earlier, Reliance Agreements will govern the relationships and reporting obligations between the parties.

U-M IRBs utilize the eResearch ceding application to collect and maintain U-M required information for the compliant local conduct of the research throughout the lifespan of the study.

## VII. UNAFFILIATED INVESTIGATORS

*Refer to* HRPP OM Part 5.V

## VIII. COMMUNITY-BASED PARTICIPATORY RESEARCH (CBPR)

*Refer to* HRPP OM Part 5.VI

# Part 6 – Roles and Responsibilities of Investigators and Research Staff

Every person involved in human research plays a critical role in protecting the rights and welfare of research participants. This section describes the roles and responsibilities of investigators and research staff engaged in University research.

## I. Eligibility to Perform Research at the University of Michigan

*Refer to* HRPP OM Part 6.I

## II. Roles and Responsibilities of Investigators and Research Staff for the Protection of Human Participants

*Refer to* HRPP OM Part 6.II

### A. Generally

*Refer to* HRPP OM Part 6.II.A

*Refer to* IRBMED Guidance – Investigator Responsibilities

*Refer to* IRB-HSBS Guidance - Researcher Roles & Responsibilities

### B. Key Responsibilities

#### 1. Minimizing Risks to Subjects and Protecting Subject Rights and Welfare

*Refer to* HRPP OM Part 6.II.B.1

#### 2. Obtaining and Documenting Informed Consent

*Refer to* HRPP OM Part 6.II.B.2

*Refer to* IRBMED Guidance - Re-consenting Study Subjects and Informed Consent and Assent Templates.

*Refer to* IRB-HSBS Guidance Informed Consent Guidance & Templates

#### 3. Compliance with IRB and Other Requirements

*Refer to* HRPP OM Part 6 II.B.3

*See also* IRB SOP Part 12.II

#### 4. Conflict of Interest Disclosures

*Refer to* HRPP OM Part 6.II.B.4

*See also* IRB SOP Part 9

The U-M IRBs coordinate with the appropriate University Conflict of Interest Committee to ensure that conflict of interest management plans and any relevant imposed terms of conflict management are considered in the review of applications submitted by the personnel in question.

#### 5. ClinicalTrials.gov Registration

*Refer to* HRPP OM Part 6.II.B.5

*Refer to* HRPP OM Part 11.I.A

**C.** Studies Regulated by The Food and Drug Administration

**1.** Generally

*Refer to* HRPP OM Part 8

**2.** Exception from Informed Consent Research

*Refer to* IRBMED Guidance Emergency Research (Planned and Approved) with Exception from Informed Consent.

*Refer to* IRB SOP Part 3.III.C.6.e.4

*Refer* to HRPP OM Part 8.V

**3.** Principal Investigator Responsibilities

*Refer to* HRPP OM Part 8.VIII.

*Refer to* IRBMED Guidance – Investigator Responsibilities

**4.** Sponsor-Investigator

*Refer to* HRPP OM Part 8.VII

*Refer to* University of Michigan Medical School Policy on Requirement to Use MICHR MIAP Services

*Refer to* Michigan Institute for Clinical and Health Research (MICHR) Investigational New Drug / Investigational Device Exemption (IND/IDE) Investigator Assistance Program (MIAP)

**5.** Manufacturers

*Refer to* HRPP OM Part 8.VII.E

**6.** Guidelines for Good Clinical Practice (GCP) of the International Conference of Harmonization (ICH)

*Refer to* IRBMED Guidance - International Council for Harmonisation: Good Clinical Practice (ICH-GCP)

From time to time, especially in multi-site clinical research where U-M is a proposed performance site, a Sponsor may indicate that the FDA-approved protocol and any PI SOPs associated with that protocol, if followed, assure ICH-GCP compliance. In those instances, IRBMED will make the determinations required by institutional policy and will also review the research plan submitted to identify aspects that may be inconsistent with ICH-GCP. Such review will include evaluation of the adequacy of the available nonclinical and clinical information on an investigational product to support the proposed clinical research project, and a review that proposed clinical research is scientifically sound and described in a clear, detailed protocol. IRBMED will bring any area of concern to the attention of the PI, who may in turn ask for clarification from the Sponsor.

PIs who agree to perform research represented to be ICH-GCP compliant are required to follow the protocol as written and will be advised by IRBMED to review all PI obligations in the ICH-GCP as well as any aspects of ICH-GCP incompletely captured or not captured in the research protocol and investigator SOPs.

If a PI In the research contract agrees to conduct an investigation in full compliance with the PI obligations under ICH-GCP, any compliance review conducted by OHRCR will be done against the complete set of ICH-GCP requirements.

## III. EDUCATION

*Refer to* IRB SOP Part 13

The U-M IRB web pages provide educational opportunities for researchers and their research teams. Workshops, conferences, and consults are provided on regulations, institutional policies, and the eResearch application. Further information is available on the IRBMED website, IRB-HSBS website, HRPP website and in Part 13 of these SOPs.

# Part 7 – Participant Protection

All non-exempt human research subject to the HRPP is reviewed and must be approved by the applicable IRB or other duly constituted committee approved by the OVPR, using criteria similar to those applied to federally-funded research and consistent with the principles outlined in the Belmont Report. This section describes some of the ways research participants are protected under the HRPP.

## I. HRPP Protection Extends to All Participants

*Refer to* HRPP OM Part 7.I

## II. Vulnerable Populations

*Refer to* HRPP OM Part 7.II
*Refer to* HRPP OM Part 11.II.D
*Refer to* OHRP Guidance Documents on Vulnerable Populations and FAQs

Special rules apply to research involving vulnerable populations. For federally-supported research, the IRBs comply with the requirements of 45 CFR 46 to the extent the sponsoring agency has adopted its subparts B-D.

For FDA-regulated research involving children, IRBMED complies with the requirements of 21 CFR 50, subpart D.

For research not subject to the above regulations, the IRBs may choose to apply the regulations as stated or apply equivalent protections adopted by the University as stated in HRPP OM Part 7.II.

### A. Research Involving Pregnant Women/Persons, Fetuses, and Neonates

*Refer to* HRPP OM Part 7.II.A

### B. Research Involving Prisoners

*Refer to* U-M IRB Guidance: Research Involving Prisoners
*Refer to* HRPP OM Part 7.II.B
Refer to OHRP Prisoner Research FAQs

**IRB Composition**

The IRBs are permanently constituted with at least one prisoner representative with appropriate background and experience to serve in that capacity.

Prior to enrolling any prisoners on a study, the IRBs must certify to the Institutional Official or Deputy Institutional Official that all requirements have been fulfilled (except as allowed in urgent situations where the best interests of the participant requires participation in the research prior to fulfillment of all requirements) as described in the prisoner research documents at OHRP Guidance Documents on Vulnerable Subjects and FAQs

### C. Research Involving Children

*Refer to* IRB SOP Part 11.II.A.2.a

*Refer to* IRBMED Guidance: Children in Research; Assent of Children in Research; Wards
*Refer to* IRB Guidance on Assent Age Ranges
*Refer to* HRPP OM Part 11.II.A.2
*Refer to* HRPP OM Part 7.II.C
*Refer to* OHRP Research with Children FAQs

**D.** Research Involving Adults with Impaired Decision-making Capacity

*Refer to* HRPP OM Part 7.II.D

## III. Data and Safety Monitoring Plans and Boards

*Refer to* HRPP OM Part 7.III
*Refer to* U-M IRB Guidance Data and Safety Monitoring Plans (DSMP)
*Refer to* IRBMED Education

eResearch instructs PIs to include information about data and safety monitoring plans and boards as applicable to the risk level of the study. The IRB will review the DSMP and information pertaining to any DSMB before approving an initial or amended application, or may require one in response to an adverse event or other report.

## IV. Advertising Materials

*Refer to* HRPP OM Part 7.IV
*Refer to* U-M IRB Guidance Recruitment Communications
*Refer to* OHRP Guidance IRB Review of Clinical Trial Websites (2005)
*Refer to* FDA Guidance Recruiting Study Subjects

## V. Payment to Research Subjects

*Refer to* HRPP OM Part 7.V
*Refer to* U-M IRB Guidance Payments to Research Participants.
*Refer to* U-M Standard Practice Guide 501.07: Research Subject Incentives.

## VI. Compensation for Injuries

*Refer to* HRPP OM Part 7.VI
*Refer to* OHRP 2011 Draft Guidance "Exculpatory Language" in Informed Consent and 1996 Exculpatory Language in Informed Consent
*Refer to* Michigan Medicine Clinical Research Position Statement on subject injury language available through CRAO Billing Calendar & Study Applications

# Part 8 – Studies Regulated by FDA and Use of Investigational Articles

The US FDA enforces the Food, Drug and Cosmetic Act and other laws and regulations governing the use of drugs, biologics, and devices for treatment and in research studies. This section describes when or under what circumstances an Investigational New Drug (IND) application or Investigational Device Exemption (IDE) is needed and describes IRB responsibilities with respect to protocols involving investigational test articles.

IRBMED is designated as the only U-M IRB permitted to conduct reviews of FDA-regulated research.

## I. INTRODUCTION

*Refer to* HRPP OM Part 8.I

## II. RESEARCH INVOLVING INDS OR IDES

*Refer to* HRPP OM Part 8.II

### A. Investigational Drugs and Biologics

*Refer to* HRPP OM Part 8.II.A
*Refer* to MICHR/MIAP Guidance

### B. Investigational Devices

*Refer to* HRPP OM Part 8.II.B
*Refer* to MICHR/MIAP Guidance

1. Generally
2. Significant Risk (SR) / Non-Significant Risk (NSR) Determinations

   *Refer to* HRPP OM Part 8.II.B.1-3

   *Refer to* FDA SR / NSR Device Determinations
3. Device Studies Exempt from IDE Requirements

   *Refer to* HRPP OM Part 8.II.B.5

### C. Humanitarian Use Devices (HUD)

If the proposed use is to collect safety and effectiveness data for a new indication, the IRBMED will require the investigator to submit an IDE application to the FDA, as well as the eResearch Standard Application (not the HUD application). If the use falls under the labeling of the Humanitarian Device Exemption (HDE) or is used off-label under the HDE, an IDE is not required and falls under Section VI, below.

## III. EXPANDED ACCESS

*Refer to* HRPP OM Part 8.III

*Refer to* MICHR/MIAP Guidance

*Refer to* IRBMED Guidance - FDA Expanded Access Program at the University of Michigan

**A.** Expanded Access to Investigational Drugs and Biologics for Treatment Use

*Refer to* HRPP OM Part 8.III.D

**B.** Expanded Access to Investigational Devices

*Refer* to HRPP OM Part 8.III.F

1. Compassionate Use (Devices)

   *Refer to* HRPP OM Part 8.III.F.1

2. Treatment IDE

   *Refer to* HRPP OM Part 8.III.F.2

   Also see: IRBMED Guidance – Emergency Use of Test Articles.

3. Emergency Use (Devices)

   *Refer to* HRPP OM Part 8.IV

## IV. EMERGENCY USE OF INVESTIGATIONAL ARTICLES

*Refer to* HRPP OM Part 8.IV

## V. PLANNED EMERGENCY RESEARCH USING INVESTIGATIONAL ARTICLES

*Refer to* HRPP OM PART 8.V

## VI. HUMANITARIAN USE DEVICES

*Refer to* HRPP OM Part 8.VI

*Refer* to IRBMED Guidance – HUD Requirements for U-M Physicians & Investigators.

*Refer* to U-MIC presentation on HUDs

a. Physicians are required to submit a HUD application in the eResearch System for on-going use of a HUD for clinical purposes without collection of patient safety and effectiveness data to support a Premarket Approval (PMA). The Principal Investigator is required to ascertain whether the manufacturer will require this data and provide documentation to the IRB. The IRB will assure that the documentation is appropriate.

b. Physicians are required to submit a standard application in the eResearch System for on-going use of a HUD for clinical purposes with collection of patient safety and effectiveness data to support a Premarket Approval (PMA). The Principal Investigator is required to ascertain whether the manufacturer will require this data and provide documentation to the IRB. The IRB will assure that the documentation is appropriate.

## VII. FDA SPONSORS AND SPONSOR-INVESTIGATORS

*Refer to* HRPP OM Part 8.VII

## VIII. INVESTIGATOR AND IRB RESPONSIBILITIES FOR FDA-REGULATED RESEARCH

*Refer to* HRPP OM Part 8.VIII

*Refer to* IRB SOP Part 6.II.C

**A.** Ensuring Review by Appropriate IRB

*Refer to* HRPP OM Part 8.VIII.A

**B.** Verification of IND or IDE Acquisition Prior To Release of Final IRB Approval

*Refer to* HRPP OM Part 8.VIII.B

As part of the eResearch or application, the study team is required to upload all documentation submitted to and received from the FDA regarding IND/IDE information. This information is available to the IRB staff as well as IRBMED Chairs and Board Members via eResearch for review. The Regulatory teams verify that this documentation is included in the eResearch application and check the validity of the IND or IDE number.

**C.** Oversight of FDA-Regulated Research

*Refer to* HRPP OM Part 8.VIII.C

**D.** Investigational Article Accountability

*Refer to* HRPP OM Part 8.VIII.D

**E.** Charging for Investigational Articles

*Refer to* HRPP OM Part 8.VIII.E

**F.** Records and Documentation

*Refer to* HRPP OM Part 8.VIII.F

*Refer to* Medical School Data Integrity and Sharing (level 2 login required)

**G.** Required Reporting

*Refer to* HRPP OM Part 8.VIII.G

**H.** ICH-E6 and GCP

*Refer to* HRPP OM Part 8.VIII.H

*Refer* to IRBMED Guidance - International Council for Harmonisation: Good Clinical Practice (ICH-GCP)

**I.** FDA Inspection of FDA-Regulated Research and Related Articles

*Refer to* HRPP OM Part 8.VIII.I

The IRBMED works closely with the Office of Regulatory Affairs regarding FDA inspections and other regulatory matters.

**J.** Additional Exceptions

**1.** Emergency Use Authorizations

*Refer to* FDA Guidance Document Emergency Use Authorization of Medical Products.

In the event of an emergency, or a significant potential for an emergency, involving a heightened risk of attack with a specified biological, chemical, radiological, or nuclear agent or agents, the FDA may issue an Emergency Use Authorization (EUA) for use of an investigational agent. In such an emergency:

- IRB review and approval is not required prior to or after administration of the investigational agent.
- Identifiable private information regarding the use may be collected and submitted to the required federal authorities (e.g., FDA, CDC, or Homeland Security).

Contact the IRBMED for additional information, if needed. If a PI later intends to do research on the collected data, IRB approval must be secured at that time.

**2.** Other Exceptions

The FDA or other federal government entity may issue other types of exceptions. Contact IRBMED for guidance regarding the need for IRB approval in such an event.

# Part 9 – Conflicts of Interest and Commitment

Conflicts of interest and commitment in research can adversely impact the integrity of research results and the confidence of prospective volunteers in the research enterprise. The University seeks to identify, disclose, and avoid or manage conflicts to avoid these negative repercussions.

## I. Applicable Policies

*Refer to* HRPP OM Part 9

Real or perceived conflicts of interest on the part of any individual associated with the use and the protection of human participants in research can seriously undermine the credibility of the process and must be avoided.

## II. Conflicts of Interest of Investigators and Research Staff

### A. Identification and Disclosure of Outside Interests Related to Human Research

*Refer to* HRPP OM Part 9.II.A

#### 1. Sponsored Project Proposals

*Refer to* HRPP OM Part 9.II.A.1

#### 2. IRB Application

*Refer to* HRPP OM Part 9.II.A.2

#### 3. Disclosures First Received by Schools and Colleges Pursuant to COI/COC Policies

*Refer to* HRPP OM Part 9.II.A.3

#### 4. Sponsored Project and Technology Transfer Negotiations

*Refer to* HRPP OM Part 9.II.A.4

### B. Conflict of Interest Review and Management

*Refer to* HRPP OM Part 9.II.B

*Refer to* OVPR Conflict of Interest webpage

### C. IRB Risk/Benefit Analysis

*Refer to* HRPP OM Part 9.II.C

## III. Conflict of Interest of IRB Members, Consultants, And Staff

*Refer to* HRPP OM Part 9.III.

*Refer to* IRB SOP Part 3.III.B.7

*Refer to* OVPR Conflict of Interest webpage

The IRBs and other University staff are subject to University-wide policy (Standard Practice Guide (SPG) 201.65-1), which requires that University employees not use their official University position of influence to further personal gain or the gain of their families or business associates.

The IRBs strive to avoid both actual and perceived conflicts of interest in the performance of required activities. The IRBs communicate regularly with the University COI committees and other University units (e.g., ORSP) to coordinate awareness of actual and perceived conflicts of interest of IRB members, staff (if applicable), and researchers. Legal Counsel is available to the IRBs to discuss a conflict of interest situation.

## IV. Institutional Conflicts of Interest

*Refer to* HRPP OM Part 9.IV.

*Refer to* OVPR webpage Institutional Conflict of Interest

# Part 10 – Sponsored Projects

This section describes policies and procedures for the administration of sponsored project agreements for human participants research.

## I. Role of the Office of Research and Sponsored Projects

*Refer to* HRPP OM Part 10

## II. Agreements with Sponsors

*Refer to* HRPP OM Part 10.II

### A. Assurance of Compliance with Human Research Protection Requirements

*Refer to* HRPP OM Part 10.II.A

### B. Medical Care for Research-Related Injury

*Refer to* HRPP OM Part 10.II.B

*Refer to* HRPP OM Part 7.VI

*Refer to* IRB SOP Part 7.VI

*Refer to* IRBMED Standard Informed Consent Template

*Refer to* IRB-HSBS Informed Consent Templates & Guidance

### C. Communication of Findings that May Affect the Safety of Human Research Participants or their Willingness to Participate or Influence the Conduct of the Research

*Refer to* HRPP OM Part 10.II.C

### D. Dissemination of Findings from the Research

*Refer to* HRPP OM Part 10.II.D

## III. Finders Fees and Bonus Payments

*Refer to* HRPP OM Part 10.III

## IV. Additional Information

*Refer to* HRPP OM Part 10.IV

# Part 11 – Laws, Regulations, and Standards

The University of Michigan and its faculty, staff, and trainees are committed to complying with the laws and regulations that govern the conduct of human research and to upholding the highest ethical standards. This section describes selected laws and regulations impacting human research conducted at U-M and the University's implementation and educational activities to promote compliance with these regulations.

## I. Federal Laws, Regulations, and Requirements Commonly Applicable to Research

*Refer to* HRPP OM Part 11.I

### A. Federal Laws and Regulations Applicable to Research

*Refer to* HRPP OM Part 11.I.A

### B. Federal Agencies and Additional Federal Requirements Applicable to Research

*Refer to* HRPP OM Part 11.I.B

## II. State Laws, Regulations and Requirements Commonly Applicable to Research

*Refer to* HRPP OM Part 11.II

### A. Informed Consent and Legally Authorized Representatives

#### 1. Who May Give Consent

*Refer to* HRPP OM Part 11.II.A

*Refer to* IRBMED Who May Consent or Provide Permission for Participation in Research

*Refer to* IRBMED Wards of the State guidance.

*Refer to* IRBMED Assent of Children in Research

*Refer to* IRB-HSBS Informed Consent Templates & Guidance

### B. Confidentiality of and Access to Research Records and Other Information

*Refer to* HRPP OM Part 11.II.B

*Refer to* IRBMED Guidance - Record Keeping Guidelines.

### C. Mandatory Disclosure Requirements

*Refer to* HRPP OM Part 11.II.C

### D. Additional Protections for Vulnerable Populations

#### 1. Research Involving Prisoners and Other Detained Persons

*Refer to* HRPP OM Part 7

*See also* the U-M IRB guidance on prisoners.

#### 2. Research Involving Pregnant Women/Persons, Fetuses, and Neonates

*Refer to* HRPP OM Part 7

Principal Investigators are encouraged to consult with the IRBs about research involving these populations prior to submitting an IRB application.

**E.** Stem Cell Research

*Refer to* HRPP OM Part 11.II.E

**F.** Document Control and Record Retention and Destruction

*Refer to* HRPP OM Part 11.II.F

*Refer to* IRBMED Guidance – Retention of Research Data/Biospecimens

**G.** State Professional Licensing Laws and Institutional Credentialing Policies

*Refer to* HRPP OM Part 11.II.G

## III. INTERNATIONAL RESEARCH

*Refer to* HRPP OM Part 11.III

**A.** World Medical Association (WMA)

*Refer to* HRPP OM Part 11.III.A

**B.** International Conference on Harmonisation Good Clinical Practice (ICH-GCP)

*Refer to* HRPP OM Part 11.III.B
*Refer to* HRPP Guidance International Conference on Harmonization Good Clinical Practice (ICH-GCP)
*Refer to* IRBMED Guidance International Council for Harmonisation: Good Clinical Practice (ICH-GCP)

**C.** The General Data Protection Regulation (GDPR)

*Refer to* HRPP OM Part 11.III.C
*Refer to* U-M Safe Computing Guidance General Data Protection Regulation (GDPR) Compliance
*Refer to* HSBS GDPR guidance International Human Subject Research Resources

**D.** Export Controls

*Refer to* OVPR Guidance Export Controls

## IV. ACCESS TO LEGAL COUNSEL

*Refer to* HRPP OM Part 11.IV

All University faculty, staff, and trainees conducting human research, as well as members and staff of the IRBs and other review units, have access to legal advice concerning application of the laws and regulations that affect human research through the Office of the Vice President and General Counsel, and through Health System attorneys who specialize in human participant research and healthcare law.

# Part 12 – Quality Assurance and Research Compliance

This section describes the University's and the U-M IRB's quality assurance, quality improvement, and enforcement activities.

## I. Quality Assessment and Improvement

*Refer to* HRPP OM Part 12.I

## II. Reportable Events: Adverse Events, Unanticipated Problems, Non-Compliance, Suspensions and Terminations of IRB Approval

### A. Background

*Refer to* HRPP OM Part 12.II.A

### B. Definitions

*Refer to* HRPP OM Part 12.II.B
*Refer to* IRBMED Guidance - AE Reporting and ORIO Reporting
*Refer to* IRB-HSBS Guidance - Incident Reporting AE/ORIO

### C. Roles and Responsibilities for Required Reporting of Reportable Events

#### 1. Researchers

*Refer to* HRPP OM Part 12.II.C.1

As noted in the OM, guidelines and reporting procedures for reporting AE/ORIOs, including those AE/ORIOs that are also unanticipated problems involving risks to participants or others (UaPs), are posted on each IRB's website. This guidance is also referenced within the "Help" feature in eResearch. It provides the timelines and process for submitting reports.

Researchers are responsible for understanding and following these guidelines and reporting procedures. The IRBs offer educational sessions that review the guidelines and offer individual consultations with PIs and study teams, as indicated, to assist in understanding the reporting requirements.

Events that may require reporting in accordance with each IRB's AE and ORIO guidance include:

- Internal AEs that are unexpected, involve new or increased risks, and are related to the research
- External AEs that are UaPs
- Changes made to the research without prior IRB approval in order to eliminate apparent immediate hazards to the participant
- Other unanticipated information that is related to the research and indicates that participants or others might be at increased risk of harm, including information that indicates a change to the risks or potential benefits of the research such as:
  - An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB
  - A paper is published from another study that shows that the risks or potential benefits of the

research may be different than initially presented to the IRB
- A breach of confidentiality
- Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol
- Incarceration of a participant in a protocol not approved to enroll prisoners
- Event that requires prompt reporting to the sponsor
- Sponsor imposed suspension for risk
- Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team
- Protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed participants or others or that indicates participants or others may be at increased risk of harm

Failure to follow these guidelines may require the IRB to halt the study and/or the institution to report the noncompliance to entities that include, but are not limited to, government agencies or study sponsors.

As noted in the guidelines and the OM, PIs should be aware of their option to submit a "Study-Specific AE Reporting Plan" to the IRB, either with their initial IRB application or via an amendment on an approved study. If approved, a study-specific plan would be used to determine the required AE reporting and timing of reports, instead of the requirements in the Standard AE Timetable. Researchers who initiate an approved study using a standard AE reporting plan and then modify the project to a study-specific AE reporting plan must follow the standard reporting guidelines until the IRB approves the modification.

**2.** The IRBs

*Refer to* HRPP OM Part 12.II.C.2

It is essential to human participant protection to identify, analyze the causes of, and respond appropriately to AEs and ORIOs (including UaPs), and provide notification to appropriate institutional entities and external agencies/sponsors.

IRB staff will consider the following when reviewing an AE or ORIO report:
- Whether there is a participant safety concern or a change in participant status (such as incarceration) that may impact study participation such that urgent notification of the IRB's Director, Legal Counsel, IRB Chairs, the DIO, the HRPP Director, or other authority is required
- Completeness of the submission
- Whether necessary supporting documents are included
- Whether the submission occurred within the required timeframe
- Whether the event or information is described in the currently approved informed consent document (when applicable)

Reports of events that are unexpected, related, or linked in a significant way to the research and indicate risks that were previously unknown or unrecognized, will be flagged to enable the reviewer to assess whether the event represents a potential UaP.

The timelines for completion of IRB review are dependent upon:
- Completeness of the report, such that additional information is necessary before IRB review
- Whether the report is a potential UaP and other reporting deadlines may be triggered

- Whether the report indicates a participant safety concern or other serious matter

Requests for additions to incomplete reports should be sent back to the study team in a timely manner after the date of the initial assessment. However, if an incomplete report raises serious concerns related to participant protections or other protocol or regulatory violations, it may be sent to a designated reviewer while the missing information is being collected.

The IRB Chair(s) are authorized to take immediate action to protect the health and safety of research participants, as described in the HRPP OM Part 12.II.C.2.

The IRB may use review by an expedited reviewer for reports of AE/ORIO, as long as those reports do not constitute a potential or identified Unanticipated Problem Involving risks to subjects or others.

Reports identified as potential UaPs, regardless of the risk level of the research study, will receive convened board review as soon as possible. Required changes to the submission or research, if any, will be communicated to the researchers. If an expedited reviewer of an AE/ORIO report requires changes to the research that impact the study risk level based upon that report, or if the report is judged to include potential UaPs, the submission must be sent for convened board review.

If a submission requires convened board review, it will be assigned to a primary reviewer. All supporting documentation included in the AE/ORIO report is available to all IRB members attending the meeting.

If the convened board determines an event to be an UaP, the IRB staff will prepare the UaP report. See below in II.C.2.3 for reporting requirements.

If a study is suspended or terminated by the Chair or convened board, the following must be considered:

- Any actions required to protect the rights and welfare of currently enrolled participants
- Any procedures for withdrawal of enrolled participants and whether these procedures take into account the rights and welfare of participants
- Whether current participants should be informed of the suspension or termination; and
- Any adverse events or outcomes reported to the IRB.

IRB board members consider the following when reviewing an AE report:

- PI's assessment of the AE and concurrence or disagreement with that assessment. The reviewer and board will consider:
  - Causality and relatedness of the event to the research, not just to an investigational agent that is part of the research
  - Seriousness
  - Expectedness
  - Whether the event constitutes an UaP
  - Whether urgent communication with the PI, IRB Director, UM Office of General Counsel, OVPR, or other authority or unit is required (e.g., Office of Patient Relations and Clinical Risk)
  - Safety of participants (including whether the study should be halted or modified)
  - Risk/benefit assessment of the study

- Impact of the AE on participants' willingness to participate in the study
- Whether the continuing review schedule should be modified
- Whether the research and/or the informed consent process should be monitored
- Referral to other organizational entities

For AEs not described in the currently approved informed consent document (ICD), the review will consider:

- Whether the ICD needs modification
- Whether previously enrolled participants should be notified and/or re-consented

IRB board members consider the following when reviewing an ORIO report:

- PI's assessment of the ORIO and concurrence or disagreement with that assessment. The reviewer and board will consider:
  - Causality and relatedness of the event to the research, not just to an investigational agent that is part of the research
  - Whether the event constitutes an UaP
  - Whether remediation is required (e.g., education of the study team or referral to risk management)
  - Whether urgent communication with the PI, IRB director, Office of General Counsel, IRB Chair(s), OVPR or other authority is required
  - Whether the report indicates that serious and/or continuing noncompliance may have occurred
  - Whether the report indicates that an UaP has been identified
  - Safety of participants (including whether the study should be halted or modified)
  - Risk/benefit assessment of the study
  - Impact of the ORIO on participants' willingness to participate in the study
  - Whether the continuing review schedule should be modified
  - Whether the research and/or the informed consent process should be monitored
  - Referral to other organizational entities

For ORIOs involving circumstances not described in the currently approved ICD the review will consider:

- Whether the ICD needs modification
- Whether previously enrolled participants should be notified and/or re-consented

When reviewing an UaP, IRB Board Members consider whether the event is:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research)
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized

**3.** Institution

*Refer to* HRPP OM Part 12.II.C.3

*Refer to* HRPP OM Part 12.III.H

If the convened board determines an event to be an UaP, the IRB staff will prepare the UaP report. After appropriate institutional review, the IRB will send the required reports directly to external entities as required by regulation or sponsor agreement, with notification of the IO, DIO, Associate Vice President for Research, HRPP Director, IRB co-chairs, the principal investigator, and institutional committees or entities as indicated.

Generally, reports to federal agencies for unanticipated problems will be made promptly (not to exceed one month absent special circumstances, such as the need for extensive data gathering or analysis).

If the IRB chair imposes a partial or complete suspension, the IRB chair will promptly (i.e., no later than three business days) report the suspension to the HRPP Director who will follow additional requirements outlined in the OM. The IRB chair shall report any such action taken to the convened IRB at its next regularly scheduled meeting. External reports of serious and/or continuing noncompliance, suspensions, and terminations of IRB approval will be made by the HRPP Director.

## III. COMPLIANCE OVERSIGHT

*Refer to* HRPP OM Part 12.III

### A. Response to Complaints or Allegations of Noncompliance

If information brought to the attention of the IRBs, through any source, indicates the possibility that research participants or others are exposed to unnecessary or excessive risks, or that the requirements of the IRB are not being met (including that IRB approval or exemption was not sought before conducting research activities), the IRB shall collect any additional information necessary to evaluate the credibility or accuracy of the information and determine whether further corrective action (e.g., education of the PI or the PI's research staff, modification of the project, or suspension or termination of the project) appears necessary. In some circumstances, in consultation with the IRB, the PI may place a voluntary "hold" on new participant accrual or research-related interventions during the fact-finding period, unless doing so would place participants in immediate harm or otherwise jeopardize their well-being.

If the IRB is undertaking further inquiry, any voluntary "hold" during this fact-finding period does not constitute a suspension of approval for purposes of the HRPP reporting to external agencies or sponsors.

Under institutional authority and federal regulations (45 CFR 46.113, 21 CFR 56.113), the IRB is responsible for overseeing the safety of human participant research participants and has the authority to suspend or terminate human participant research that is (1) not being conducted in accordance with the federal and the IRB's requirements or (2) has been associated with unexpected serious harm to participants.

The IRB will also consider if notification of current participants is appropriate if such information may relate to willingness to continue in the research.

**B.** Noncompliance Review Procedures

*Refer to* HRPP OM Part 12.III.B

In the event of a credible allegation of noncompliance with applicable law or University policy, including these standard operating procedures, the matter will be handled consistent with University policies.

Should the allegation of noncompliance pose immediate risk to participants, the IRB will assure notification of the IRB Chairs, DIO, Associate Vice President for Research - Clinical and Human Subjects, the appropriate Legal Office(s), and the HRPP Director, as soon as possible.

Allegations or other indications of fabrication or falsification of research results will be reported to the Research Integrity Office, Medical School Associate Dean for Regulatory Affairs, the appropriate Legal Office, and OVPR.

An IRB staff member or IRB Director initiates a review of any complaint or allegation of noncompliance made to the IRB. If assistance with the review is desired, the IRB Chairs will make a written request to the HRPP Director to request assistance from ORCR. The purpose of the review is fact-finding, and may involve examination of study records, including, but not limited to, source documentation, informed consents, and the study protocol. Where appropriate, the IRB staff member may engage in discussion with the research team, research participants, the complainant (if known), and others.

Initial fact-finding by either the IRB or ORCR may include, but is not limited to, any or all of the following:

- Review of:
  - Signed informed consent documents
  - Study files
  - Drug dispensement logs/Research Pharmacy logs
  - Patient records
  - Lab tests
  - Delegation logs
- Observation of study activity (e.g., witnessing the informed consent process)
- Review of study by an outside auditor
- Interviews of study personnel
- Interviews of research participants

If the IRB or other University or Medical School entity believes additional collection of information or further investigation is still necessary in order to facilitate a determination of serious and/or continuing non-compliance, such a request may be made to the HRPP Director.

Upon completion of the review, the relevant documents and findings are provided to the IRB Chair(s) in the context of a Chairs and Director Meeting (CDM). The Chair(s) review the information and determine whether the complaint or allegation of noncompliance constitutes potentially serious and/or continuing noncompliance. If so determined, the matter is referred to the convened board with oversight for the study in order to make a final determination as to the nature of the noncompliance. The convened board will be provided with all relevant findings and documents related to noncompliance.

The IRB shall notify the HRPP Director of any complaints or allegations of noncompliance, as required in HRPP OM Part 12. As necessary, the HRPP Director will notify any applicable federal agencies and provide notification to institutional entities as indicated in the OM Part 12.

The IRB staff maintains records of all complaints and allegations of noncompliance that come to the attention of the IRB.

Reports prepared for the HRPP Director are copied to the IRB Chair(s), Associate Vice President for Research - Clinical and Human Subjects, and other applicable Medical School or other Unit Leadership as indicated by the nature of the report.

The IRB shall promptly notify the HRPP Director of (1) any potentially serious and/or continuing noncompliance; and (2) any suspension or termination of IRB approval for a project, including those instances determined by an external IRB. In certain instances of alleged or apparent noncompliance, the IRB may choose to provide an early notification or preliminary report to the HRPP Director (i.e., where the noncompliance may pose immediate risk to participants) prior to a determination of serious and/or continuing noncompliance. As described in the HRPP OM Part 12, the HRPP Director may choose to further investigate the reports of serious and/or continuing noncompliance or to ask for additional review by the Office for Research Compliance Review (ORCR). On a semi-annual basis, the IRBs will prepare a list of all externally reportable events for review with the IRB Chair(s), Directors and Compliance Specialists, Director and Associate Director HRPP, Associate Vice President for Research - Clinical and Human Subjects, and the Medical School Office of Regulatory Affairs for verification of appropriate reporting and follow-up.

**C.** How Compliance Concerns Are Brought Forward

*Refer to* HRPP OM Part 12.III.C

Reports or allegations of noncompliance may be reported by, but are not limited to, the following means:

- Telephone calls or written communications (e.g., letter or email)
- UM Compliance Telephone Hotline
- Through in-person discussion with staff or faculty of the University

**D.** Receipt and Initial Handling of Allegations of Noncompliance

*Refer to* HRPP OM Part 12.III.D

The IRB, through appropriate members and/or staff (consistent with procedures and guidance, if any), will initiate a fact-finding review. The IRB Director determines whether the complaint or allegation of noncompliance is reportable immediately to the IRB Chair(s) for a determination of potential serious and/or continuing noncompliance. If the IRB Director concludes that the concern clearly is without merit or that the conduct in question:

- Clearly does not constitute potentially serious and/or continuing noncompliance
- Can be addressed through minor corrective action agreed to by the principal investigator (PI) or other involved parties, the matter will be referred as appropriate to the convened board, expedited reviewer, education coordinator, or IRB compliance staff to be addressed and concluded. Some corrective actions as noted in Part 12, Section E (below) may be appropriate to address minor corrective actions.

**E.** Chair and Board Considerations and Determinations

*Refer to* HRPP OM Part 12.III.E

If, according to the results of the IRB's fact-finding, the alleged noncompliance is evaluated by the Chair(s) or Director as credible to be potentially serious and/or continuing non-compliance, the available information will be presented to the IRB Chair(s) at the next available CDM Meeting or ad hoc meeting of the Chairs, but not later than thirty (30) days from the initial evaluation by the Chair(s) or Director. In reviewing the alleged noncompliance, the Chair(s) may request a meeting with the PI and others to discuss the concerns and provide an opportunity for the study team to correct or clarify the fact-finding information.

The Chair(s) determine by vote whether according to definitions in the HRPP OM or federal regulations, the activity:

- Constitutes potentially serious noncompliance
- Separately constitutes potentially continuing noncompliance.

Documentation of the outcome of a decision by the Chair(s) to refer the matter to the convened IRB will be sent to the applicable Medical School Associate Dean for Research, the Associate Vice-President for Research - Clinical and Human Subjects, the applicable Legal Office(s), the DIO, the HRPP director, and the PI.

If the convened IRB determines that the noncompliance was not serious and/or continuing, the Medical School Associate Dean for Research, the Associate Vice-President for Research - Clinical and Human Subjects, the applicable Legal Office(s), the DIO, the HRPP director, and the PI will be notified. A finding of serious and/or continuing noncompliance as determined by the convened IRB will be sent to the PI, the Department Chair and Associate Chair for Research (if applicable), the Medical School Associate Dean for Research, the Associate Vice-President for Research - Clinical and Human Subjects the applicable Legal Office(s), the DIO, and the HRPP Director.

The IRB may also determine that additional monitoring activities are appropriate, and/or additional requirements or restrictions on either a PI or a particular study because of risk level, safety issues, conflict of interest issues, or because of findings of noncompliance.

Monitoring may include, but is not limited to, accessing and reviewing any or all of the following:

- Both clinical and research records
- Review of study by an outside auditor
- Interviews of research participants

Additional requirements or restrictions may include, but are not limited to, any or all of the following:

- Education or certification in the conduct of research:
  - The Association of Clinical Research Professionals (ACRP)
  - The Society of Clinical Research Associates (SoCRA)
  - The Professionalism and Integrity in Research (Washington University School of Medicine in St. Louis)
  - Re-certification of PEERRS
- Less than a one-year approval of the research project
- Submission of reports to the IRB at specific time intervals (in addition to the study's scheduled continuing review submission for renewal of IRB approval)

- Submission of reports to the IRB at specific increments of participant participation (e.g., after every third participant completes the trial or after the first three doses of an investigational agent)
- Restriction on location of study activities
- Requirement for additional supervision of overall study or aspects/activities of the study
- Prohibition, permanently or for a period of time, for specific members of the study team from obtaining informed consent from participants
- Prohibition, permanently or for a period of time, for specific members of the study team from conducting certain types of research
- Prohibition, permanently or for a period of time, for specific members of the study team from serving as a PI or in other study team roles
- Requiring current participants to reconsent to participation in the research project.
- Notification of past participants
- Monitoring of the informed consent process
- Modification of the informed consent process
- Modification of the protocol
- Referral to other organizational entities

**F.** Actions of the HRPP Director as Delegated by the Institutional Official

*Refer to* HRPP OM Part 12.III.F

**G.** Response to Determinations of Serious and/or Continuing Noncompliance

*Refer to* HRPP OM Part 12.III.G

The board's determination will be conveyed to the PI at the conclusion of the board meeting as to whether the noncompliance constitutes serious and/or continuing noncompliance. The PI will be notified in writing if the IRB requires any remediation related to noncompliance. The PI will also be notified in writing if the board makes a determination of serious or continuing noncompliance.

**H.** Institutional Notification and External Reporting Requirements

*Refer to* HRPP OM Part 12.III.H

## IV. QUESTIONS AND CONTACT INFORMATION

Questions from research participants and study team members received by the IRB office through general intake procedures are triaged by the IRB Receptionist or staff designee. The receptionist or designee notes the pertinent information and routes the message to the person most appropriate to respond.

PIs and study team members may request representatives from the IRB office meet with them to discuss a research project or regulatory question by contacting the Office Reception number listed below.

**A.** IRBMED Director and Office

- Director and Office Reception: (734) 763-4768
- E-mail: irbmed@umich.edu
- US Mail: IRBMED, 2800 Plymouth Rd., Building 520, Room 3214, Ann Arbor, MI 48109-2800

**B.** IRB-HSBS Director and Office

- Director and Office Reception: (734) 936-0933

- E-mail: irbhsbs@umich.edu
- US Mail: IRB-HSBS, 2800 Plymouth Rd. Building 520, Room 2144, Ann Arbor, MI 48109-2800

**C.** Questions Concerning University Policies and Procedures

- The Office of the Vice President for Research: (734) 763-1289
- The Medical School Office of Research: (734) 615-1332
- The Medical School Office of Regulatory Affairs: (734) 647-1576
- The Health System Legal Office: (734) 764-2178
- Office of the Vice President and General Counsel (734) 764-0304

# Part 13 – Education and Training

This section describes educational and training opportunities offered to IRB members, office staff, and researchers and study team members comprising the University research community.

## I. Education in General

*Refer to* HRPP OM Part 13.I

### A. Required Training

*Refer to* HRPP OM Part 13.I.A

## II. Tracking and Communicating New FDA and Clinical Developments

*Refer to* HRPP OM Part 13.II

IRBMED monitors FDA and other regulatory communications, including MEDWATCH reports. Based on these reports, as well as new information available through other sources, such as medical and ethical journals, FDA warning letters, or OHRP determination letters, the IRBMED may require changes to ongoing and proposed research. These changes may be communicated to researchers in various ways depending on the nature of the information. Examples include, but are not limited to:

- Postings on the IRBMED website
- IRBMED newsletters
- Global e-mail to all researchers
- Directed e-mail or phone calls to particular researchers, units, or departments
- Announcements in U-M communication venues such as, but not limited to, the Michigan Medicine Headlines, the University Record, the Medical School Office of Research newsletters

When the IRBMED changes or adds posted guidance or informed consent or assent templates, an announcement will appear on the IRBMED homepage, along with any deadlines for compliance. Announcements regarding the changes may also be communicated via the means listed above.

## III. Educational Initiatives for the Research Community

*Refer to* HRPP OM Part 13.III-IV

The IRBs provides researchers, board members, and IRB office staff with opportunities for continuing education comprised of:

- Routine workshops on regulations, institutional policy and procedures, and the application process throughout the year as announced on each IRB's website and upon the request of a department or unit.
  - New workshops as needs are identified
- Special educational events and recorded presentations, including, but not limited to:
  - The Joint IRB Seminar Series or other live conferences featuring multiple speakers on regulatory, ethical, and practical information of concern to researchers
  - Presentations by researchers, regulators, and regulatory experts from within and outside of the university, available on the U-M Human Research Protection Program YouTube channel for convenient access and further learning

  - A web-based archive of materials from prior presentations
- Hosted webinars offered by professional organizations
- Web-based instructional modules developed at U-M by content experts
  - U-MIC (University of Michigan IRB Collaborative) modules on regulatory and procedural topics. Each newly developed module is presented to the convened boards and the IRB office staff before posting to the IRB and HRPP websites. Internal, procedural U-MICs may not be posted publicly.
- Routine publication of electronic newsletters, including the HRPP Pulse, for the research community
- Consultations with study teams either upon the request of the study team or upon the IRB's (staff or boards) identification of the need for a consultation on one or more issues
  - Specified educational sessions as part of a corrective and preventative action plan following a noncompliance assessment
- Guidance posted on the IRB websites (IRBMED and IRB-HSBS)
  - Developing new guidance as needs are identified
- Information and Technology Services (ITS) provides help guides and other resources on using eResearch.

## IV. IRB STAFF MEMBER EDUCATION

IRB staff members are required to complete a standardized IRB orientation program and all required PEERRS human participants modules. Completion of additional orientation and continuing education workshops are required at the discretion of the employee's direct supervisor. Staff members are encouraged to attend local, regional, and national conferences on ethics, State and Federal laws, and regulations for human participants research per opportunities identified and supported by IRB leadership (and as budget permits).

Staff members are evaluated yearly in a performance appraisal conducted by the IRB Director and any functional supervisor as instructed by the IRB Director. If circumstances dictate, staff are evaluated more often. Constructive feedback is provided to effectuate additional learning or corrective action as necessary.

## Part 14 – Revisions

| Effective Date | Part(s) Changed | Description of Changes |
|---|---|---|
| 6/10/25 | First IRB Joint Standard Operating Procedures (SOPs) Working Draft | |
| 11/17/25 | Part 3.III.B.1.h -- IRB Meeting Minutes, Content Requirements (p. 23) | Added: “Research involving adults with cognitive impairment or otherwise impaired decision-making capacity” |
| 11/17/25 | Part 3.III.B.1.h -- IRB Meeting Minutes, Content Requirements (p. 23) | Added: “Actions taken by the IRB, including documenting the criteria for approval are met” |
| 11/17/25 | Part 3.III.C.1.d(1) -- Not-Regulated Research (p. 32) | Added new paragraph:<br>“For ‘Not Regulated’ projects that will be conducted outside of the University, in addition to meeting University requirements, researchers are strongly encouraged to consult proactively with the external institution to ensure that their work aligns with all relevant requirements at the collaborating institution.” |
| 11/17/25 | Part 3.III.C.6.e(3) -- Waivers of Documentation of Informed Consent (pp. 58-59) | Added phrase to statement: "as well as any additional elements of consent disclosure, as appropriate"<br><br>Revised statement: “When the IRB waives the requirement for documentation of informed consent, the required elements of informed consent, as well as any additional elements of consent must still be provided to the subject.” |
| 11/17/25 | Part 3.III.D.4.a -- IRB Records and Reports: Documentation Uploaded into eResearch (p. 64) | Added phrase to statement: "including if non-compliance is serious and/or continuing"<br><br>Revised 8th bullet: “Documentation of non-compliance including if non-compliance is serious and/or continuing.” |