



**University of Michigan
Medical School**

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

**Standard Operating Procedures
(SOPs)**

September 2022



REVISIONS

Working draft of major revision (2010)

- Approved by the UMHS Compliance Committee – 1/28/2010
- Approved by the Office of the Vice President for Research – 2/1/2010

Final version (2010)

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Part 1 – Introduction, Purpose, and Ethical Principles

This section describes the mission of the Medical School Institutional Review Board (IRBMED), the purpose of the IRBMED, the authority under which it operates, and the scope of research conducted at the University.

I. MISSION STATEMENT AND ORGANIZATIONAL SUMMARY

The mission of the IRBMED is to protect the rights and welfare of participants in clinical trials and other human subjects research studies by careful review and monitoring of research in accordance with applicable laws, regulations, and University policies. The IRBMED assists investigators with the design and conduct of research projects to minimize risk to human participants, provides guidance to the University and its researchers on ethical and procedural issues related to the use of human participants in research, and facilitates compliance with governmental and University policies pertaining to human subjects research. To perform its review, approval, and monitoring functions, the IRBMED is composed of six (6) review boards, each of which complies with applicable regulations concerning membership and conduct.

The IRBMED oversees the protection of human participants in research conducted at Michigan Medicine which includes the University of Michigan Medical School and the UM Health System (UMHS) as well as research conducted off-site by faculty and staff as University employees or in connection with their University appointments. The IRBMED also reviews 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. IRBMED serves as IRB of Record for multi-site research or for individual investigators via use of IRB Authorization Agreements, including the nationally recognized SMART IRB agreement.

The [Human Research Protection Program \(HRPP\)](#) is an integrated institution-wide program for promoting excellence in all aspects of research with humans. Components include the IRBs, other review units, oversight functions, and educational and quality assurance activities, which together seek to assure the rights and welfare of human subjects participating in biomedical and behavioral research and promote excellence in all aspects of human subjects research. HRPP policies are compiled in the HRPP's [Operations Manual \(OM\)](#).

The IRBMED, designated by the University to review and monitor human subjects research under its Federal-Wide Assurance, maintains written SOPs, and may issue additional guidance as necessary. These SOPs are consistent with and supplemental to the HRPP OM.

II. SCOPE OF HUMAN RESEARCH AT THE UNIVERSITY

Refer to HRPP OM Part 1.II

III. AUTHORITY UNDER WHICH THE HRPP AND IRBMED OPERATES

Refer to HRPP OM Part 1.III

Refer to HRPP OM Part 11

The HRPP, of which the IRBMED is a part, operates under the authority of and in accordance with applicable federal regulations and its Federalwide Assurance (FWA), including:

- A. The Public Health Service Act and its amendments, which empower the [Department of Health and Human Services \(DHHS\)](#) to issue regulations for the protection of human subjects. 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](#).

DHHS 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).

DHHS provides guidance and information concerning its interpretation of the Common Rule and related regulations through [determination letters](#) directed to organizations performing research under federal-wide or other assurances following investigations of research noncompliance, and other [guidance documents](#).

The Common Rule has been adopted by numerous federal agencies conducting human subjects research. The full list of agencies and their regulatory citations are found at:

<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html>

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 subjects.

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. FDA regulations for human subjects protections 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 the [IRBMED SOP](#) and the [HRPP OM](#) and at <http://www.fda.gov>.
- C. Rules for research involving recombinant DNA or research otherwise regulated by the [National Institutes of Health](#) (NIH). The [Office of Biosafety, Biosecurity, and Emerging Biotechnology](#) develops and implements NIH policies and procedures for the safe conduct of recombinant DNA activities and human gene (see [Biosafety and Recombinant DNA Policy](#)). Its duties include review and evaluation of the research that is subject to oversight by the University's [Institutional Biosafety Committee](#).
- D. Research regulated by the Department of Education (34 CFR 97, 98, 99).
Refer to <http://www.ed.gov/about/offices/list/ocfo/humansub.html>.
- E. Privacy regulations issued under the [Health Insurance Portability and Accountability Act \(HIPAA\) of 1996](#) (45 CFR 160 and 164).
- F. Principles stated in [International Conference of Harmonization \(ICH\) Efficacy Guidelines](#)
Refer to [IRBMED 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

IV. LIMITATION ON INSTITUTIONAL AUTHORITY

Refer to HRPP OM Part 1.III.B

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All regulated human subjects research conducted by the University must be approved by an IRB or granted an exemption through the University IRB system (including "system-generated determination," IRB staff review, and/or "limited IRB review," as applicable and specified in these SOPs and the OM) or the Vice President for Research. Research that has been reviewed and approved with the necessary expertise by the IRBMED 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 an IRBMED disapproval determination.

V. ETHICAL PRINCIPLES

Refer to HRPP OM Part 1.IV

VI. PROTECTION FROM UNDUE INFLUENCE

Refer to HRPP OM Part 1.V.

Part 2 – Organization of the HRPP and IRBMED

This section describes the organization of the University of Michigan Medical School Institutional Review Board (IRBMED) and the roles and responsibilities of the various units that guide and support the program.

I. KEY ORGANIZATIONAL REPRESENTATIVES

An organizational chart identifies key organizational officials and units in the University, Medical School, and IRBMED.

Refer to [UMOR website](#) and the [IRBMED website](#)

II. ORGANIZATIONAL ENTITIES THAT SUPPORT IRBMED

Refer to HRPP OM Part 2

Numerous organizational entities contribute to the operation of the University's HRPP and the IRBMED. Entities closely associated with IRBMED providing oversight and assistance include but are not limited to:

- [University of Michigan Office of Research \(UMOR\)](#)
- [Medical School Office of Research \(OoR\)](#)
- [Medical School Office of Regulatory Affairs](#)
- [UMHS Compliance Office](#)
- [Office for Research Compliance Review \(ORCR\)](#)
- [Office of Research and Sponsored Projects \(ORSP\)](#)
- [Michigan Institute for Clinical Health Research \(MICHHR\)](#)
- IRB Council (advisory)
- [Executive Vice President for Medical Affairs \(EVPMA\)](#)
- [Office of the Vice President and General Counsel](#)

A. University of Michigan Office of Research

Refer to HRPP OM Part 2.II.A

B. The Academic Units

Refer to HRPP OM Part 2.II.B

C. Other University of Michigan Institutional Review Boards

Refer to HRPP OM Part 2.II.C

D. Other Research Review and Support Units

Refer to HRPP OM, Part 2.II.D

Other HRPP and UMHS 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, the IRBMED may withhold its approval pending confirmation of approval by or receipt of additional information from any of the following:

- [University of Michigan Medical School \(UMMS\)](#)

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- [Michigan Institute for Clinical and Health Research](#) (MICHR; includes MIAP (MICHR IND/IDE Investigator Assistance Program))
- [Clinical Trials Support Office](#) (CTSO)
- [Michigan Clinical Research Unit](#) (MCRU), formerly the General Clinical Research Center (GCRC)
- [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, formerly Biomedical Engineering Unit (BEU)
- [Michigan Alzheimer's Disease Center](#) (MADC)
- [Tissue Procurement Core](#) (TPC)
- [UMOR Conflict of Interest Committee](#)
- [Michigan Medicine Medical School Conflict of Interest Review Board \(MEDCOI\)](#)
- [Institutional Conflict of Interest Committee](#)
- Department or organization peer review committees (e.g., Rogel [Cancer Center](#) Protocol Review Committee)

The IRBMED is responsible for review and final approval of the human subjects research application in those cases where other committees are also involved in the review process.

E. Independence of Research Review Units and Response to Undue Influence

Refer to HRPP OM Part 2 II.E.

F. Resources

Refer to HRPP OM Part 2.II.F.

The [Medical School Office of Research](#) provides oversight and administrative support for the IRBMED office. On an annual basis, the fiscal year operating budget for the IRBMED is reviewed and approved by the applicable Medical School Deans.

The IRBMED works closely with the [Office of Regulatory Affairs](#) regarding FDA inspections and other regulatory matters.

Part 3 – HRPP Policy

This section describes the process by which the University's Human Research Protection Program (HRPP) policies, including the IRBMED policies, are developed, approved, and implemented, and articulates minimum requirements for IRBMED SOPs and Policies.

- I. 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 Vice President for Research (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 in the [UM Office of Research \(UMOR\)](#).

III. IRB STANDARD OPERATING POLICIES AND PROCEDURES

Refer to HRPP OM Part 3.III

A. General Provisions

The IRBMED members and staff to which these SOPs refer are accountable to the applicable Medical School Deans (or designees) and operate under the authority of UMOR with regard to the oversight of human subjects research. Further references in this document to applicable Medical School Deans also incorporate "designees" by reference.

The IRBMED cooperates with the applicable Medical School Deans, UM Health System (UMHS) Offices, and UMOR to establish content, review, and revise these SOPs. These SOPs and any substantive revisions thereto, are subject to review and approval by the applicable Medical School Deans, and the VPR or designee. Non-substantive revisions such 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 IRBMED in consultation with the applicable Medical School Deans, relevant U-M offices, and UMOR do not require further review or approval. Outdated sections of these SOPs will be archived in such a way that changes and dates of approval may be followed.

The IRBMED, in conjunction with applicable Medical School Deans, UMHS Offices, and UMOR maintains guidance documents on the [IRBMED](#) website and [Medical School Research A-Z](#) on topics of relevance for the IRBMED boards, IRBMED Staff, and researchers. In many cases the guidance expands on the information contained within these SOPs and are therefore referenced where appropriate.

IRBMED has oversight of human subjects research conducted by the Medical School faculty and staff or in the Health System facilities. Under certain conditions, oversight of a research project can be moved between IRBMED and the Health Science-Behavioral Science IRB (IRB-HSBS). In cases where an application must be transferred between IRBs, the administrative staff of each IRB work together and in consultation with the respective Chairs, as necessary, to assess the submission and make the necessary transfer.

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The IRBMED conducts its 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 Federal-Wide Assurance (FWA).

Board No.	Registration No.	FWA No.	Content
A1	00000244	00004969	Biomedical
A2	00001996	00004969	Biomedical
B1	00001999	00004969	Biomedical
B2	00001995	00004969	Biomedical
C1	00005467	00004969	Biomedical
C2	00012211	00004969	Biomedical

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 is a signatory to numerous SMART IRB relationships which include accepting IRB oversight and ceding oversight to external IRBs. IRBMED also permits ceding to independent IRBs with whom master agreements are in-place (e.g., WIRB, Advarra).

Refer to [IRBMED SOP](#) Part 5.IV-VII

Refer to HRPP OM Part 5.IV

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

1. IRB Composition, Rosters, and Meeting Procedures

The IRBMED 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 six (6) 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.

Each IRB will have at least five (5) voting members, including the Chairs, with varying backgrounds to promote comprehensive review of research activities commonly conducted at the Medical School and UMHS.

No IRB may consist entirely of members of one profession.

Every nondiscriminatory effort will be made to insure the IRB does not consist entirely of men or entirely of women. 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 women 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 IRB must include at least one physician.

The IRB must include at least one scientist member. A scientist is a member whose training, background, and occupation would incline him or her to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline. Scientist members include physician scientists (MDs or DOs), non-physician scientists (e.g., DDS, PhDs,

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nurses, geneticists, pharmacists and biomedical engineers), and social and behavioral scientists (e.g., psychologists, social workers, counselors). Scientist members have significant educational background (a science degree) and experience in scientific disciplines.

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

The IRB must include at least one non-scientist member. Non-scientist members are individuals without significant scientific educational background or experience and whose training, background and occupation would incline him or her to view scientific activities from a standpoint outside of any biomedical or behavioral scientific discipline. 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 subjects. They must be present at the majority of meetings in a given year.

“Unaffiliated” individuals include:

- University patients or research subjects or former students of the University who have no other affiliation with the University
- Alumni, former faculty or staff of the University
- Individuals contributing to fund-raising drives
- Unaffiliated IRB members who have been paid at reasonable market rates for their services to an IRB.

“Affiliated” individuals include:

- Part-time employees;
- Current students;
- Members of any governing panel or board of the University;
- Paid and unpaid consultants of the University;
- Healthcare providers with medical staff membership or other credentials to practice at University clinical sites; and
- Volunteers working at the University on business unrelated to the University
- Active emeritus faculty

The IRBMED Staff maintains current membership rosters for each of the six (6) IRBs. Each membership roster contains 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 to indicate:

- new primary or alternate members and chairs as approved by the applicable Medical School Dean;
- current primary members or alternate members extending their membership;
- primary members or alternate members who are moving from one IRB to another or serving as a primary member on additional Boards;

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- primary members or alternate members renewing membership after a period of time away from an IRB;
- primary members or alternate members that are resigning or are no longer eligible for membership.

The IRBMED will forward drafts of the revised membership rosters to the applicable Medical School Dean for review and approval. Following each roster change the Medical School approved membership rosters will be submitted to UMOR, which is then responsible for forwarding the approved membership rosters to OHRP. The IRBMED posts the current membership rosters of primary and alternate on the IRBMED website.

a) IRB Chairs and Co-Chairs

- Each Board has one Co-Chair and may have one or more Vice-Chairs (collectively referred to as the “Chairs” throughout these SOPs) who are considered voting members.
- Each 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, and is well informed concerning the laws, regulations, and University policies and procedures that govern the conduct of human subjects research.
- The applicable Medical School Dean is responsible for the appointment and reappointment of Chairs. When a vacancy arises, the applicable Medical School Dean may solicit nominations for a new Co-Chair or a Vice-Chair from the Medical School faculty, IRBMED members, staff, and consultants.
- The applicable Medical School Dean then considers all available information and issues the appointment.
- An individual may serve an unlimited number of three (3) year terms as a Vice-Chair or a Co-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, and University policies and procedures that govern the conduct of human subjects research.

b) IRB Members

Refer to HRPP OM Part 3.III.B

- The applicable Medical School Dean may solicit nominations (including self-nominations) from members of the Medical School faculty, staff, and the University community. Unaffiliated representatives may be recruited by the applicable Medical School Dean, community advertisements, or word of mouth via existing IRBMED members or office staff.
- 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 IRBMED.
- The applicable Medical School Dean will consult with the IRBMED 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 IRBMED Chairs and applicable Medical School Dean or designee. The applicable Medical School Dean or designee has final authority to make each member appointment or reappointment.

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- 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 appointed to an initial three-year term, which may be renewed at the discretion of the applicable Medical School Dean for an unlimited number of consecutive three (3) year terms.
- Members are evaluated for reappointment by the applicable Medical School Dean after seeking evaluation from the IRBMED 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 at the time of their three-year reappointment.
- Members are assigned reviews of IRB applications within their appropriate scientific and/or regulatory experience.

To ensure that the IRBMED is maintained as sufficiently diverse in experience, expertise, education, ethnicity, gender, cultural background, and sensitivity to such issues as community attitudes, the applicable Medical School Dean and IRBMED 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 IRBMED is supported by a professional staff hired and supervised by the Director of the IRBMED with specific authority delegated to designated Assistant Directors. The Director reports to the applicable Medical Dean through the Director of the Office of Research.
- The Director and staff are responsible for facilitating IRBMED operations (human participants research application regulatory review; documentation and record retention; review of noncompliance allegations, including fact-finding; serving as an informational resource; conducting educational activities, etc.) 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 applicable Medical School Dean .
- 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 "eResearch", i.e., the web-based [eResearch](#) Regulatory Management (eRRM) system which centralizes the review and approval process for Human Subjects Research Applications and IBC Biosafety Registrations.
- The IRBMED Office includes Regulatory Teams dedicated full board and expedited review to support each of the six (6) IRBs. The IRBMED office is further supported by other administrative, educational, compliance, quality assurance and quality improvement roles. All IRBMED staff ultimately report to the Director. Day-to-day operations are overseen by the specific authority assigned to the Assistant Directors.
- The IRBMED 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 cognitively or physically disabled individuals, prisoners, and children or minors.

d) IRB Meetings

- The Institution provides appropriate resources for board meetings including private meeting facilities equipped with appropriate electronic devices including overhead screens, projectors and individual notepad computers (issued for meeting use) for each member present that does not bring a personal laptop computer to the meeting. In addition, informational booklets containing copies of regulations are available at board meetings.
- The Co-Chair, or in his or her absence, a Vice-Chair or senior scientist member of the IRB leads each meeting. The IRBMED regulatory team monitors and documents attendance to ensure that the quorum, member composition, and diversity are present for each meeting as defined by Federal Regulations (21CFR56). 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) IRBMED 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 IRB convenes every two weeks. Additional meetings may be convened as necessary. The IRBs may meet by conference call as circumstances dictate.

(1) Meeting Cancellation

If circumstances dictate that a meeting should be cancelled (e.g., an anticipated lack of quorum), the IRBMED Regulatory Team will make a request of the Co-Chairs and the Director(s) to cancel the meeting after efforts to secure a meeting have failed. If the Co-Chairs agree the IRBMED 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 or submissions from a previously cancelled meeting or other pressing issue. The Chairs are notified of the recommendation and asked for comment. If there is no disagreement, the members of the specific boards for which the additional meeting is necessary are notified by the IRBMED Regulatory Team to verify the availability of a quorum.

(3) Alternate Board Meeting Format

In the event that a quorum of IRBMED members cannot be convened face-to-face, the IRBMED may utilize electronic technology (e.g., teleconference or videoconference) 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 alternative technologies will facilitate the active and equal participation of the remote members. Minutes of meetings utilizing assistive technology must document that these two additional conditions have been satisfied.

f) Agendas & Review Items

Prior to each convened IRB meeting the designated IRBMED Regulatory Team will prepare an electronic IRB meeting agenda in eResearch listing and linking items for review, discussion, deliberation; and vote, as appropriate. Other scheduled reports as appropriate, including Single IRB Member expedited reviews and exempt reviews are also presented. Updated working agendas are available at all times to IRBMED members, the applicable Medical School Deans, UMOR, and authorized consultants. The IRBMED Regulatory Team assigns incoming applications to meeting agendas based on necessary clinical and scientific expertise, urgency of the submission and availability of the designated primary reviewer.

Before a scheduled meeting, all IRBMED members are notified electronically of the planned meeting agenda generated by the IRBMED Regulatory Team. The agenda will contain links to all relevant items and documentation for review. IRB Members and Alternate Members will review the items attached to the agenda in advance of the IRB meeting. Primary reviewers will prepare a brief presentation of any submissions under their purview and recommendations for outcome.

IRB members and alternate members are encouraged to provide an RSVP to the IRBMED Office regarding their availability for each IRB meeting. Based on Member response the IRBMED Regulatory Team will review IRB meeting agenda items for potential conflicts of interest with Members and provide recommendations for substitute Alternate Members.

g) Convened Meetings

(1) IRBMED Regulatory Team Responsibilities

On the day of, and in advance of each convened IRB meeting, the IRBMED Regulatory Team will oversee IRB meeting room facilities and supplies; the set-up of audio/visual projection equipment, laptop or notebook computers, and vote cards (as appropriate) for members, alternate members and others.

During the convened IRB meeting the IRBMED Regulatory Team will monitor attendance to ensure that quorum, member composition, diversity, and any required special representatives (e.g., prisoner representative) are represented for each vote and record all voting outcomes and determinations on Voting Record sheets that are later archived in the IRBMED Office. The IRBMED Regulatory Team will provide support to the IRB by electronic projection of each agenda item for discussion, and any additional supporting or backup documents as needed.

The IRBMED Regulatory Team will also take meeting minutes to document IRB meeting attendance, reviews, discussion, outcomes, contingencies and determinations with regard to IRB meeting agenda items, federal and other state or local regulations, and IRBMED requirements.

Additional information will also be provided to all board members by the IRBMED Regulatory Team at the time of the convened meeting, including, but not limited to, continuing educational presentations and other relevant information to assist them in serving on the board.

(2) Changes to the Agenda

When an IRBMED meeting commences, all voting IRBMED members are alerted to any changes that may have been made to the planned agenda. In the event that an application is discussed that does not appear on the 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 before a discussion and vote is taken.

(3) Board Member Reviews

The IRBMED Regulatory Team will assure that Board members have adequate time to review all aspects of the submissions for review. The IRB meetings are scheduled for 2.5-3 hours which allows adequate time for assigned applications. However, if a board member feels they have been given inadequate time to review a specific submission then that item will be rescheduled to the next available meeting.

(4) IRBMED Deliberations and Voting

At the convened IRBMED meeting, the primary reviewer and any additional reviewer or consultant presents their review of the submission, including comments documented on their Review Checklist in advance of the meeting, and their recommendation to the IRB, including any suggested changes. The IRBMED Regulatory Team 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 SCR submission may be approved or disapproved only upon a majority vote by the voting members present. The PI or study team designee may be requested to attend the convened board meeting in person or by telephone 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) IRBMED 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 reviews (expedited and exempt) approved by the Single IRB Member review procedure;
- 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, fetuses and neonates;
 - Research involving prisoners; and
 - Research involving children
- The name of any consultant reviewer used for an application;
- 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 expeditable studies that were reviewed by single-member reviewers prior to the meeting.
- Documentation of board deliberations and determinations involving UaPs/UPIRSOs that must be made separately:
 - 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 DHHS regulations or guidance, documentation of justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in a DHHS-approved sample consent document; and
- When following FDA regulations or guidance, documentation of the rationale for significant risk/non risk device determinations.

(2) Review and Ratification Process

Typically, within four (4) weeks from the IRB meeting date, meeting minutes are drafted by IRBMED staff and are reviewed for quality, completeness and compliance with regulatory requirements before being sent electronically to Board members for review and approval at a convened IRB meeting.

- Board members indicate changes as needed;
- The approved minutes will be maintained in accordance with applicable legal requirements and institutional policy.
- In circumstances where the minutes require further scrutiny or review, i.e., after an outcome of serious and/or continuing noncompliance, the minutes may be presented to the board later than four (4) weeks after the meeting date. The Co-Chair of the board will notify the board members at the next available full convened board meeting if a delay in approving the IRB's minutes is necessary.
- Minutes are archived in the eResearch System.
- In the event that minutes require amending, strict version control is applied to preserve the original minutes.

Additional guidance is available to IRB Regulatory Teams and staff regarding preparation, approval and amending IRBMED meeting minutes.

2. Use of IRB Consultants

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

During IRB meetings or otherwise, IRBMED may utilize individuals such as consultants, advisors, and ad hoc reviewers whose experience or expertise may serve the IRBMED 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 the IRBMED in this manner will be required to sign the standard IRBMED confidentiality agreement, follow the standard IRBMED 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 IRBMED 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 IRBMED. A primary member of one IRB (A1, A2, B1, B2, C1, or C2) is automatically considered to be an alternate member to each of the other IRBs. Specific designation on each of the rosters is not required.

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. Alternate members 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 IRBMED 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 applicable Medical School Dean, UMOR and updating the membership rosters. The IRBMED Office maintains the membership information.

4. IRB Educational and Training Activities

Refer to HRPP OM Part 13

Refer to [IRBMED SOP](#) Part 13

a) Orientation of IRB Members

The IRBMED orientation program for new members is a multi-component program designed to permit new members to assimilate information in a manner that enhances retention and appropriate application of the material to 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),

the UMHS Health Insurance Portability and Accountability Act (HIPAA) training for researchers, and mock protocol reviews. Topics covered include but are not limited to:

- Human Subject Protections Overview
- Federal Regulations and the IRBMED Review Process
- Federal Regulations—Special Populations
- Review of eResearch Applications

New members are initially considered alternate members. New members undergo an orientation phase where they receive an overview of regulatory and institutional requirements, eResearch training, reviewer checklist training, observe at least four board meetings, and conduct at least two practice reviews. At the conclusion of the orientation period, a new member is assigned as a secondary reviewer for an application with the IRBMED Chair or an experienced member acting as primary reviewer. If the review is deemed to provide information in compliance with the regulations, the member enters a practicum period. During the practicum period, new members review protocols as primary reviewers, attend IRB meetings, and present reviews, but are not permitted to vote unless a primary member for whom they qualify as an alternate is absent. During the practicum period, the new board member receives mentoring from IRBMED staff or an experienced board member. The practicum period 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.

IRBMED 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 IRB Member reviewer (including expediting reviewer). This may occur at any time after the member concludes the practicum period.

b) Orientation of IRB Staff

IRBMED staff members are required to complete a standardized IRBMED orientation program and all required [PEERRS](#) human subjects modules.

Depending upon the role of the new staff member, completion of additional orientation and continuing education workshops, as well as [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 IRBMED leadership (and as budget permits).

c) Orientation of IRBMED Chairs

IRBMED Chairs are appointed per [IRBMED SOP](#) Part 3.III.B.1.a Chairs meet with the applicable Medical School Dean(s) to review roles and responsibilities of the role in association with relevant federal and state regulations, laws, guidance materials, and University and Medical School policies. The Directors of IRBMED and Regulatory Affairs as well as relevant IRBMED Office staff also meet with the Chairs to provide orientation to the working procedures associated with the IRB. Feedback associated with the orientation sessions are provided to the Dean for Regulatory Affairs.

d) Continuing Education for IRB Members and Office Staff

All IRBMED 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 and presentations at meetings. Printed and electronic materials are provided

on an on-going basis.

[U-MIC \(University of Michigan IRB Collaborative\)](#) audio/video tips are presented at IRB meetings. IRBMED Chairs, members, and Office staff are offered an opportunity (the number of attendees varies based on budget) to attend IRB conferences, and the IRBMED Seminar Series is presented at least semi-annually to the research community on topics of relevance (these typically include a mock IRB review). IRBMED staff also participate in ongoing continuing education within the context of weekly all-staff meetings.

Reference materials such as U-MICs and the slides from Seminar Series are posted to the [IRBMED website](#). IRBMED also prepares topic-specific guidance which is posted to [Research A-Z](#).

e) Researcher Education

Refer to HRPP OM Part 13.I and .IV

Refer to [IRBMED SOP](#) Part 13

5. IRB Compensation and Liability Coverage

a) Compensation of Chairs

The IRBMED Chairs are compensated for the portion of their effort required to perform their duties as Chair. The IRBMED Chairs are paid a portion of their salary for the time and effort involved in performing the duties of a Co-Chair or Vice-Chair. The stipend is commensurate with the required time to perform the IRBMED duties in negotiation with the applicable Medical School Dean and department Chair.

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, also taking into account the number of meetings attended and expenses associated with attendance, such as parking.

c) Periodic Review of Compensation

The amount of compensation for Chairs and members of the community is reviewed periodically and may be changed by the applicable Medical School Dean.

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 to HRPP OM Part 3.III.B.6.

a) Chairs and Member Performance Review

Annually, the applicable Medical School Dean will evaluate the Co-Chairs of the board to ensure that their expertise adequately addresses the types of protocols reviewed and to ensure that each Co-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 on the performance evaluation will be provided to the Co-Chair or Vice-Chair along with any suggested corrective actions such as additional educational requirements or direction on how to improve workflows associated with the convened IRB meetings.

The IRBMED Chairs will 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 who is trained in current interpretations of federal regulations and other relevant ethical principles for the protection of human participants. Feedback on the performance evaluation will be provided to the member by the Chairs along with any suggestions for improving performance via additional education or mentoring.

Each board member is annually provided with details 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 Co-Chairs and Vice-Chairs for evaluation.

Feedback about necessary performance improvement provided by the Chairs prior to renewal. At any time during a member's term an evaluation may be conducted if there is concern about the level of a member's participation, adequacy of reviews, regulatory interpretations or other ethical concerns.

b) Removal of a Chair or Member from an IRB

If necessary, the Medical School Associate Dean for Regulatory Affairs may relieve a Chair or Vice-Chair from IRBMED service due to repeated non-attendance, lack of participation in continuing education, or other problematic performance issues. Should this action be required, the Medical School Associate Dean for Regulatory Affairs will notify the Medical School Dean and UMOR.

Similarly, the Chairs may recommend to the Medical School Associate Dean for Regulatory Affairs that a board member be relieved from IRBMED service due to repeated non-attendance, lack of participation in continuing education, or other problematic performance issues. In this situation, as described above for the Chair or Vice-Chair, the Medical School Associate Dean for Regulatory Affairs will notify the Medical School Dean and UMOR.

c) IRB Staff Performance Review

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

d) Regular Consultant Performance Review

In the rare event that an IRB regularly uses a consultant to conduct reviews, 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 IRBMED 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 IRBMED office.

Disclosed COI information associated with IRBMED members and consultants is obtained from UMOR and the Medical School's 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 IRBMED member or consultant completes an [M-Inform](#) disclosure for their financial disclosures. The financial disclosure section divulges any significant financial interest in a sponsored project or technology transfer agreement. This information is periodically reviewed by the IRBMED office and relevant information is entered into eResearch. IRBMED members and consultants are also queried periodically as to any other relationships (e.g., familial) that might create a conflict of interest. This information is entered into eResearch.

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 IRBMED member (including the Chair) is not assigned to review research if the member:

- Is a PI on the study or the PI's immediate relative (spouse, domestic partner or dependent);
- 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, applicable Medical School Dean, COI Committee, or UMOR 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 IRBMED (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 by IRBMED staff in the IRB meeting minutes.

In some instances, an IRBMED member may have involvement in a research study that solely involves the provision of a service to a study (e.g., a Pharmacist from the Research Pharmacy who prepares and dispenses study medication, or a Radiologist who performs a diagnostic imaging study that is part of the research). The IRBMED does not consider this to be a conflict of interest with regard to reviewing an IRBMED submission, provided the member's role in the study is limited to providing a service to the PI and they are not

otherwise engaged in the research study. For example, a board member is not permitted to be listed on the FDA Form-1572. If additional clarification is needed, contact IRBMED. This is consistent with the examples of non-engagement in research provided in OHRP Guidance [Engagement of Institutions in Human Subjects Research \(2008\)](#)

c) Conflicts of Interest with Research Involving IRB Staff

An IRBMED 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 UMOR, the University, the Medical School COI Board or other University unit (i.e., ORSP), and/or by self-disclosure, the IRBMED staff person must excuse him/herself from administrative handling of the research and from the IRBMED board meeting where there is deliberation and vote on the research. IRBMED staff document all conflicts of interest in the IRB meeting minutes.

IRBMED 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 [IRBMED SOP](#) Part 9.III

Consultants are not voting members of the IRB. No consultant to IRBMED 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 IRBMED Regulatory Team 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 IRBMED members.

e) Conflicts of Interest Involving Guests

For guests attending a board meeting during the course of which a conflict is identified either by the IRBMED staff, board members, and/or by self-disclosure, the guest will leave the room during the discussion and vote on the research protocol. IRBMED 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 a Convened Board

Prior to each convened IRBMED meeting, the IRBMED Regulatory 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 IRBMED 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 IRBMED to provide information relevant to the board's consideration of the application.

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

- excused from discussion, except to provide information requested by the IRBMED; 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 IRBMED Chair shall, at each meeting, inquire whether any members should excuse themselves from discussion and voting as outlined above.

g) Conflicts of Interest Involving Single Member Review and Expedited Review

Prior to a Single Member review (SMR) of an AE or ORIO, or expedited review, the IRBMED Regulatory Team 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. IRBMED 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.

h) 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 Subjects Research Studies Reviewed by the IRB

IRBMED reviews 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 unanticipated problems (UAPs)), and research that may qualify for exemption. Submissions are routed to the IRBMED office by the PI via [eResearch](#) Regulatory Management (eRRM), the web-based system for submission, routing, approval and management of human subjects 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 human participants research conducted by the University must be approved by an IRB or granted exemption by a University IRB;

The IRBMED has the authority to approve, disapprove or require modifications to human participants research under its 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 IRBMED has 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 UMOR.

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

The IRBMED requires its staff, consistent with the [OHRP Guidance](#) and in consultation with the IRBMED 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 IRBMED oversight.

(1) Not-Regulated

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 IRBMED does not require PI to seek a determination of ‘Not Human Subject Research’ from the IRBMED (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 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 [IRBMED SOP](#) Part 3.III.C.6.e.5

PIs seeking documentation of the not-regulated status may submit an application in eResearch and obtain a system-generated determination letter for qualifying circumstances. The PI may also request that the application may be submitted for IRB review to confirm the circumstances of the not-regulated determination.

Determination letters of ‘Not Human Subject Research’ are provided via eResearch.

(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 documentation may submit an application in eResearch for IRB review to confirm the circumstances of research without U-M engagement via a not-regulated determination.

(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 to IRBMED. Exemption may be granted by the IRB

Chair(s) or designee, qualified members of the IRBMED Office staff, or the VPR. Certain exemption categories permit the PI to obtain a system-generated exemption determination. Limited 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 subjects and to maintain the confidentiality of data ([45 CFR 46.111\(a\)\(7\)](#))

Once approved, 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.

By agreement, IRBMED also permits certain qualifying applications for exemption to be reviewed by IRB-HSBS.

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

e) International Research

Generally, the IRBMED will review all international human subjects research projects conducted by U-M investigators under its jurisdiction, rather than deferring review to a collaborating international institution.

(1) Federally Supported

When an international site is engaged in the conduct of a U-M research project and the research is supported by a Common Rule agency, the regulatory requirements of 45 CFR 46 are applied and local IRB or ethics committee review is required. Supporting agencies may require a FWA.

(2) Non-Federally Supported

For international research that is not federally supported, the IRB may apply the same or equivalent protections as those described in the Common Rule and U-M institutional policy. IRBMED may require local IRB review, particularly for studies involving more than minimal risk to participants.

Where the international research site is not engaged in the conduct of the research, IRBMED may request a letter of collaboration from an appropriate official agreeing to the conduct of the research.

(3) IRBMED Requirements

Projects conducted in international settings are subject to the same IRB requirements for review and approval of initial applications, scheduled continuing review and review of amendments as projects conducted domestically. A key element of the review process is the assessment of the informed consent process and documents. IRBMED evaluates the informed consent process to ensure that it is culturally sensitive and in a local language that is 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 IRBMED in the languages in which they will be offered, as well as in English.

(4) IRBMED Review

IRBMED will 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

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. When IRBMED members do not possess the appropriate cultural knowledge to review research in a particular country or region, IRBMED will seek guidance from consultants with cultural expertise to assist with the review. IRBMED may also request that the investigator seek cultural review by an IRB or ethics committee review or from a government agency in the region. For exempt research, IRBMED does not require documentation of IRB review or other approvals from international sites.

(5) Monitoring

Post approval monitoring, such as project reports to IRBMED 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 IRBMED. Research participants are provided with the IRBMED email address and international phone number as part of the consent process.

2. Institutional Approval/Disapproval of IRB Decisions

Refer to [IRBMED SOP](#) Part 1.IV

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-Is or faculty advisors for the submission of Adverse Event and/or Other Reported Incident or Occurrence (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 [IRBMED SOP](#) Part 3.III.C.1

Beyond the requirements of Common Rule and FDA regulations, the IRBMED staff considers additional regulatory requirements associated with the study design such as HIPAA or required by federal sponsors such as DoD or DoEd. 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, Scheduled Continuing Reviews (SCRs), 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 SCR and regulated by 45 CFR 46 (the Common Rule) or 21 CFR 56 must contain the indicated information.

For initial applications and SCRs, the IRB 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 that is subject to IRBMED jurisdiction must submit an initial application in eResearch for IRBMED 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;
 - 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., cognitively 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 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;
- Provisions for managing adverse reactions;
- 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, LARs, 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 DHHS, the approved sample informed consent documents and complete DHHS-approved protocol (if any)
- The Investigators Brochure, IND/IDE application or exemption documentation (e.g., an IDE letter), if any, (for studies involving the use of an investigational drug, biologic, or device);
- The clinical case report form (if any);

(b) Scheduled Continuing Reviews (SCRs)

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

The PI of an approved research study is responsible for submitting an application for scheduled continuing review (SCR) an approval sufficiently in advance of the expiration date of the current approval period to permit IRBMED approval within that period.

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 IRBMED has issued its approval, with the exception of research-related interventions that are necessary to avoid harm to a participant. If the study expires, eResearch system generates automatic expiration notice notifying the PI of study expiration. Note that expiration of an approval does not constitute a “suspension” of IRBMED approval reportable to UMOR under DHHS or FDA regulations, or these SOPs.

An application for SCR 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:
 - unanticipated problems 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 IRBMED 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 IRBMED risk-benefit assessment or on a participant's willingness to participate in the study);
- A copy of the informed consent documents approved by the IRBMED and currently in use;
- Copies of the FDA-required Annual Reports, which should be uploaded to eResearch for FDA research in which the Principal Investigator holds an IND or IDE necessary for the study.
- Any relevant multi-center trial reports.

These materials provide the primary reviewer and IRBMED 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 IRBMED 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 IRBMED 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
- Description of the plan for secure storage of data and indication whether data will be de-identified
- 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 IRBMED during the study (including any reported concurrently with submission of the termination report
- For research governed by the FDA, the final report that is submitted to the FDA by the IND/IDE sponsor

(2) Review Process / Primary Reviewers

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

(a) Review Process

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

IRBMED Regulatory teams and primary reviewers will 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 member of the IRBMED Regulatory Team will be assigned to each IRB submission in eResearch. In general, research submitted by the PI for review via eResearch is assigned to the IRBMED Regulatory Team overseeing the department (e.g., therapeutic area) or type of research being conducted; for example, a clinical trial submitted by an PI in the Department of Orthopedics is generally assigned to the IRBMED Regulatory Team overseeing that department's research as part of their review portfolio. Additional guidance is available to address sharing submissions among Regulatory Teams for purposes of backup.

To facilitate the review process, the IRBMED Regulatory Team member may request clarification or revisions to any or all of the application documents prior to sending to a primary reviewer. Upon completion of their review, the Regulatory Team forwards their Staff Reviewer checklist and comments for primary review to:

- A single member qualified and designated for expedited review (*Refer to HRPP OM Part 3.III.C.5*); or
- A primary reviewer, with relevant scientific expertise, who will present their review to a convened board

Following IRBMED Regulatory Team review and at the time most identified

issues have been resolved with the study team, the IRBMED Regulatory Team will select an IRB member to function as the “primary reviewer” 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 responses to the periodic IRBMED survey of expertise.

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

The primary reviewer:

- Assesses the initial application, amendment or SCR, together with, ICDs, and all supplemental materials (including, if applicable, the grant application, protocol, recruitment materials, etc).
- Documents his/her 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 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.

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 records performed solely to determine eligibility for the study) may begin until the submission has been approved in eResearch by the IRBMED.

In some instances, the IRBMED Regulatory Team, after 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. This process, designated as Staff Edit Rights (SER) is described in detail, including the types of changes that are authorized in an additional guidance document.

The IRBMED Regulatory Team 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 [IRBMED SOP](#) Part 2.II.)

(b) Timing of Distribution of Materials

The IRBMED Regulatory Teams assign the applications to the eResearch meeting agenda on a rolling basis 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 generally occur not later than 4 business 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 IRBMED Regulatory 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 IRBMED 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. This includes examination of the following:

- Risks to participants are minimized
 - by using procedures that are consistent with sound research design and do not unnecessarily expose participants to risk;
 - whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes; and
 - when adequate resources are available to protect and minimize harm to human participants.
- Sound Research Design / Scientific Review
 - Risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result;
 - Selection of participants is equitable;
 - When appropriate, the research plan has an adequate data and safety monitoring plan; (Refer to [IRBMED SOP](#) Part 3.III.C.6.f)
 - There are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data (Refer to [IRBMED SOP](#) Part 3.III.C.6.g);
 - When appropriate, additional safeguards have been included in the study to protect the rights and welfare of vulnerable participants. (Refer to [IRBMED SOP](#) Part 3.III.C.6.h);
 - Studies that have received peer or scientific review indicate in the eResearch application the name of the unit or person(s) who performed the review;
 - For student applications it is expected that the faculty advisor has

- reviewed the study for scientific merit before it is submitted to IRBMED;
- For studies that receive federal support (and thus a scientific review) the grant application must be uploaded into the eResearch Proposal Management (eRPM) system;
- For studies conducted in the Rogel Comprehensive Cancer Center, all studies are reviewed by the Protocol Review Committee (as a Core Committee of eResearch).
- Necessary resources to protect participants
 - Adequate time to conduct and complete the proposed research;
 - Adequate number of qualified staff;
 - Adequate facilities;
 - Access to the population being studied in order to adequately recruit the necessary number of participants;
 - If necessary, availability of medical or psychosocial resources that participants may need as a consequence of the research
- Risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result.
- Assessment of risks and benefits of the research will include consideration of immediate medical as well as societal benefit. Refer to IRBMED [Guidelines For Using Magnitude Of Harm In Categorizing Risk Level](#).
- In evaluating risks and benefits, the IRBMED will consider risks and benefits that may result from the research. The IRBMED does not consider possible long-range effects of applying knowledge gained in the research (i.e., the possible effects of the research on public policy) to be among those research risks that fall within the purview of its responsibility.
- Selection of participants for participation in the project is equitable. In making this assessment, the IRBMED takes into account the characteristics of the participant population, the purposes of the research, the setting in which it will be conducted, recruiting methods and materials, and other relevant information.
- Informed consent (unless waived) will be sought from prospective participants or their legally authorized representatives before enrollment in the protocol, in a manner that minimizes the likelihood of coercion or undue influence and will be documented on a form approved by the IRBMED (per 46.111[a][5]).
Refer to [IRBMED Informed Consent and Assent Templates](#).
Refer to [IRBMED SOP Part 11.III](#).
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants.
- When appropriate, there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data.
- When some or all of the participants are likely to be vulnerable to coercion or undue influence (such as children, prisoners, pregnant women and fetuses, handicapped, mentally disabled persons or economically or educationally disadvantaged persons), additional safeguards have been included in the study to protect the rights and welfare of these participants (e.g., to minimize risks peculiar to these groups and the possibility of coercion or undue influence).

Scheduled Continuing Reviews (including Terminations)

The IRBMED 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 IRBMED 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 findings 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.

Termination of a study, whether due to completion or other reason, is submitted via the SCR mechanism. For further information about termination reports refer to [IRBMED SOP Part 3.III.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 [IRBMED SOP Part 3.III.C.6](#) are met.

(ii) Approve the Submission with Contingencies (APC)

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 by a staff member (Approved Pending Office: APO) or IRB Chair or IRB member designated by the IRB Chair (Approved Pending Reviewer: APR) prior to issuance of approval.

If the PI disagrees with the IRBMED 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 for approval as APO or APR shall be deemed the date of approval, regardless of when the specified changes are made by the PI and submitted to the IRBMED. The IRBMED 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 a board action deferred status.

(iii) Board Action Deferred (BAD)

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 without a vote. If neither a motion to approve nor a motion to disapprove is carried, the action is automatically deferred. In this case, the PI may be instructed to submit additional information or revisions required by the IRBMED before reconsideration of the submission. The IRBMED 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) Disapproval of the Application

Refer to [IRBMED 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.

(v) Suspension or Termination of IRBMED Approval

Refer to [HRPP OM Part 12.III](#).

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

- is not being conducted in accordance with IRBMED requirements;
- has been associated with unexpected harm to participants; and/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 [IRBMED SOP](#) Part 12 for reporting a suspension or termination of IRBMED 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 IRBMED approval and in ample time for IRBMED 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 IRBMED has not reviewed and approved the SCR 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.
- IRBMED 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.

(b) Administrative Termination of Lapses in Approval

If an approved research project is not renewed or terminated within six months after the date of previous approval expiration, the IRBMED may consider the research to have been completed or discontinued, and may administratively terminate that protocol notwithstanding the lack of a study completion or termination report.

- Notification will be sent to the PI 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 IRBMED approval reportable to UMOR and regulatory agencies under 45 CFR 46.113 or these SOPs.

For projects reviewed, but not approved, by the IRBMED due to outstanding contingencies, the IRBMED staff may administratively withdraw the project after notification to the PI. Withdrawals of applications by IRBMED 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.

Additional guidance is available regarding Administrative Terminations and Withdrawals.

(4) Notice and Appeal of IRB Determinations

(a) Notification of Determinations

Following an IRB meeting, the IRBMED Regulatory Team 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, 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 IRBMED 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 IRBMED determinations shall be available for review by the appropriate Medical School Dean, UMOR, IRBMED members, and authorized consultants.

A copy of any notification of a board suspension or termination of a project shall be delivered under cover letter to UMOR 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 IRBMED may, in its discretion, report disapprovals, or other actions to UMOR as it deems necessary or appropriate.

(b) Appeal of Determinations

The PI may appeal any decision by the board through a telephonic or written (e.g., email) request to the Co-Chairs or Vice-Chairs of the reviewing board.

c) Frequency of Review

In general, the approval period for an initial research application begins on the date it is approved by the IRBMED and expires 364 days later, which is the last date of the approval period. For example, an application will have an approval date of 1/1/20 and an expiration date of 12/31/20.

The IRBMED 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 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 IRBMED 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 [IRBMED SOP](#) Part 12.III.E

**University of Michigan
Medical School Institutional Review Board (IRBMED), Standard Operating Procedures**

The IRBMED is responsible for overseeing the safety of human research participants and has the authority to suspend or terminate human participant research that:

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

The IRBMED may, at its discretion,

- Perform monitoring of studies both for-cause (e.g., alleged noncompliance) and not-for-cause (e.g., random review for quality assurance purposes);
- Request monitoring from the Office of Research Compliance Review (ORCR) – via UMOR– of a study; in addition to information received through the initial application, any amendments, annual SCRs, and analyses of interim reports, such as AEs and audit reports. For example, the IRBMED 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;
- Consider the frequency and nature of AEs reported to date.

Criteria for 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 IRBMED requirements;
- Projects where other concerns about possible material changes occurring without IRBMED 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.

The IRBMED 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 IRBMED interactions with the individual.

Monitoring may include, but is not limited to, providing the IRBMED copies of or access to any or all of the following:

- Signed informed consent documents;
- Study files and research records;
- Drug dispensing/IDS 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 IRBMED (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 IRBMED 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 IRBMED (*Refer to the [IRBMED AE/ORIO Reporting Guidance](#)*).

The IRBMED 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 IRBMED 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 review board or chair.

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 Investigators 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 IRBMED 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 IRBMED review of the study or its conduct.

The date of IRBMED approval of an amendment does not extend the approval period of the study.

f) Preventing Lapses in IRB Approval

Refer to [IRBMED SOP](#) Part 3.III.C.4.b.3

5. Expedited Review

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

DHHS 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 the Department of Health and Human Services, 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 IRBMED Chair, or an experienced IRBMED member designated by a Chair, reviews the research submission (refer to [IRBMED SOP Part 3.III.B.7.g](#)). Consultants may assist the IRBMED in the review of issues which require expertise beyond, or in addition to, that available with current primary or alternate members of the IRBMED boards.

IRBMED 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 IRBMED staff or the expedited reviewer and must be addressed to their satisfaction prior to approval of the submission. IRBMED staff and 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 IRBMED 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 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 IRBMED reviewers may exercise all of the authorities of the IRBMED, 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 IRBMED 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 of more of the categories of projects or applications appearing on a list of expeditable studies published by the Secretary of the Department of Health and Human Services, and only in those categories (see see [45 CFR 46.110](#) and [21 CFR 56.110](#)).

If the expedited reviewer finds that research appearing on the expedited review list is greater than minimal risk, 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 the obtaining informed consent, prior complaints from participants about the researcher);
- The projected rate of enrollment; and
- Whether the study involves novel therapies.

IRBMED staff will prepare notification of any expedited determinations that will be provided electronically to the appropriate IRB. On a monthly, but not less than quarterly basis, a list of all expedited review approvals inclusive to that period will be provided 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.

For an approved project, the notification will also include:

- the approved expiration date; and
- notification of any interim reporting requirements.

For a project approved contingent on specified changes being made to the protocol, ICDs, or otherwise, the notification will include a description of the specific modifications necessary to secure approval.

The IRBMED may, at 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. The PI may appeal any decision by the board per procedures outlined in [IRBMED SOP](#) Part 3.III.C.4.b.4.b.

d) Requirements for Continuing Review

Continuing review for minimal risk research projects qualifying for expedited review is not required. 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 IRBMED. 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 findings 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 for which 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 also 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:

- identification of the 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 minima;
- research is classified; and

- research involves prisoners.

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 IRBMED Approval [1] [2]

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 IRBMED 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.

The IRBMED reviews all initial protocols for scientific merit and feasibility and considers supporting background scientific information. Scientific merit is examined in relationship with the risks and benefits of the research to human participants. The Protocol Review Committee (PRC) reviews all UM Comprehensive Cancer Center protocols prior to IRBMED 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 IRBMED 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 IRBMED verifies 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 IRBMED staff with making these determinations, the eResearch application provides guidance materials, including checklists.

The IRBMED 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.

c) Risk-Benefit Analysis

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

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

The IRBMED will review the eResearch application to evaluate the risks versus benefits of

the study, using supporting documents, scientific references, IRBMED Regulatory Team 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 IRBMED considers 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 IRBMED 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 IRBMED evaluates the design of a proposed study to ensure that:

- It is consistent with fulfilling its scientific mission;
- risks are minimized; and
- potential benefits of the research are maximized as much as possible within the confines of the research study.

Refer to IRBMED guidance: [Guidelines for Using Magnitude of Harm in Categorizing Risk Level](#) on the IRB website.

The IRBMED does 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 IRBMED will rely on the expertise of its membership to evaluate the risks and benefits of a research proposal. Alternatively, if physical risks are difficult to assess or are outside the scope of expertise of IRBMED, 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 IRBMED must determine that the selection of participants is equitable. This reflects UM’s adherence to the Belmont Report’s concept of “Justice”. In making this determination, the IRBMED 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; and

- the participant inclusion/exclusion criteria.

The IRBMED should be especially cognizant of special considerations for research involving vulnerable participant populations such as, but not limited to neonates, children, prisoners, pregnant women and fetuses, cognitively 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 IRBMED 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 IRBMED should also ensure that participants are not selected from only one group of people simply because it is convenient.

The IRBMED should be mindful of the desirability of including both women and men as 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 and Parental Permission

Refer to [IRBMED SOP Part 11.II.A](#)

Refer to [IRBMED Guidance on Informed Consent](#) on IRBMED website.

(1) General Requirements

Refer to [IRBMED SOP Part 11](#)

Comprehensive informed consent requirements and application of those requirements are provided in IRBMED SOP Part 11 and on the IRBMED website. Additional guidance on the website includes links to regulations, templates and suggested wording on the IRBMED website. *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 subject’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 subject in research unless the PI has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative (LAR).

The PI will submit ICDs for IRBMED 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.

IRBMED 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, IRBMED 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 PI, sponsor, or U-M may be released from liability for negligence.

The IRBMED 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.

Except as otherwise approved by the IRBMED or allowed under FDA regulations, 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 LAR.

The IRBMED 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 IRBMED, informed consent shall be documented by the use of a written consent form approved by the IRBMED and signed by the participant or the participant's LAR. A copy shall be given to the person signing the form;
- The informed consent document used by the researchers must be the most recent version approved by IRBMED and is valid only after its approval by the convened board or through expedited review.

Assent of Children

Refer to [IRBMED SOP](#) Part 7.II.C

Federal regulations (45 CFR 46.408 and 21 CFR 50.55) require that IRBMED 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). 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.

(2) Short Form ICD

Refer to HRPP OM Part 3.III.C.6.e.2

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.

The IRBMED 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 translator, if appropriate must sign the short form and/or the oral script according to the following table:

Short Form Consent Requirements				
	Participant	Translator (when needed)	Researcher	Witness
Forms Required to Sign	Short form	Recommended but not required UNLESS also serving as the witness or the researcher	Oral script	Short form and oral script
Forms Required to Receive or Keep	A copy of the signed short form and oral script	Nothing UNLESS also serving as the researcher	Original signed short form and signed oral script	Nothing

The participant or participant’s LAR will receive a copy of the signed short form and oral script.

Refer to additional guidance on the IRBMED website.

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

Waiver or Alteration of Informed Consent

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

Refer to FDA Guidance IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects

The IRBMED 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 IRBMED finds that the research complies with appropriate conditions of [45 CFR 46.116\(e\)](#) and/or (f) and, if appropriate, FDA regulations at 21 CFR 50.24 for emergency research with exception from informed consent (EFIC) are satisfied, or the research is no more than minimal risk and meets FDA requirements for waiver or alteration consistent with section 3024 of the Cures Act.

Projects involving the use of deception 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, IRBMED 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 50.25 in accordance with [FDA guidance](#) for waiver or alteration of informed consent for clinical investigations involving no more than minimal risk to human subjects.

IRBMED may also waive the requirement to obtain parental permission if the protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (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 IRBMED 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) 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 can be waived);
- Research involving deviant or illegal behavior;
- Research involving socially sensitive issues, such as HIV status.

When the IRBMED waives the requirement for documentation of informed consent, the required elements of informed consent must be conveyed to the participant verbally or by electronic or printed text. Even though participants do not sign a document, the IRBMED 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 IRBMED before their use.

Research Subject to FDA Regulations – Waiver or Alteration of Informed Consent 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 IRBMED 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.

Minimal Risk Clinical Investigation

Per 2017 guidance, FDA does not intend to object to a sponsor initiating, or an investigator conducting, a minimal risk clinical investigation for which an IRB waives or alters the informed consent requirements as described. FDA intends to withdraw this guidance after promulgating regulations to permit a waiver or alteration of informed consent under appropriate human subject protection safeguards.

Consistent with section 3024 of the Cures Act FDA does not intend to object to an IRB approving a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in 21 CFR 50.25, or waiving the requirements to obtain informed consent when the IRB finds and documents that:

1. The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The clinical investigation could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(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 a waiver 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 maybe a stand-alone application for research projects not otherwise subject to IRBMED 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)

IRBMED serves as the Privacy Board under the authority of and in accordance with HIPAA (45 CFR 164) and applicable University policies and procedures. All requests associated with waiver and/or alteration of HIPAA Authorizations are reviewed by the IRBMED using the expedited review process or the convened IRBMED Board when appropriate. IRBMED expedited reviewer(s) or convened IRBMED Board may approve a waiver and/or alteration only if all of the [45 CFR 164.512\(i\)\(2\)\(ii\)](#) criteria are met. Whenever appropriate, the subjects (including their physicians, as

applicable) are provided with additional pertinent information after participation. Where the Principal Investigator anticipates the disclosure of PHI outside the Covered Entity (as that may be determined from time to time), the Principal Investigator 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 IRBMED 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 IRBMED oversight. These are processed by IRBMED office staff (or any designated Single Member Reviewer) 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 IRBMED 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.

Refer to IRBMED website - [Data Safety Monitoring Boards: Agency for Healthcare Research and Quality \(AHRQ\), Mandatory Use Guidance](#)

With respect to any research project or class of research projects, the IRBMED 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 IRBMED such additional conditions are necessary or appropriate for the protection of human research participants.

(1) Considerations for the Imposition of Special Monitoring Requirements

The IRBMED may, at its discretion, perform monitoring or request monitoring of a study and its relevant study documentation from ORCR (the request is routed through UMOR). For example, the IRBMED 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 IRBMED may also choose to monitor one or more of the projects of a single Principal Investigator in consideration of the experience of the Principal Investigator or as follow-up to previous reports of complaints, non-compliance, or prior IRBMED interactions with the individual.

(2) Examples of Special Monitoring Requirements

Monitoring may include, but is not limited to requesting copies of or access to any or all of the following from the PI:

- Signed informed consent documents;
- Site visits to research locations;
- Interim reports from the PI during the approval period;
- Interviews with participants;

- Interviews with study personnel;
- Drug dispensing/IDS logs;
- Third party witness to the informed consent process;
- Study files and research records;
- Independent Data and Safety Monitoring Board (DSMB) reports; and
- Other independent third-party monitoring reports

The IRBMED 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: <http://safecomputing.umich.edu>

To approve research, including under the provisions of limited review for exemptions 2 and 3, the IRBMED 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 IRBMED 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 Subjects

Refer to HRPP OM Part 7.II.

Refer to [IRBMED 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, 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 are cognitively impaired or 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 IRBMED 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 IRBMED 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 cognitively impaired or incapacitated adults, vary from state to state.

Michigan Law

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

Refer to [IRBMED 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.

i) Test Article Accountability Procedures

- (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) UMHS Clinical Engineering.
- (3) Investigational drug management and accountability is performed according to Department of Pharmacy Services Policies 400.00-400.10 [1];
- (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.

Refer to HRPP OM Part 8.VIII.D

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

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; and
- 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 [IRBMED SOP](#) Part 8

D. IRB Administrative Functions

1. IRBMED Meetings [1]

- a)** An IRB must review proposed research and conduct continuing reviews 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 subcommittee procedures 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 of responsive material.
- f)** IRB meetings typically occur with all participating members physically present, but IRBMED will conduct virtual meetings as indicated (refer to the section on Alternate Board Meeting Format).

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 must give the investigator an opportunity to respond in person or in writing.
- 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 [IRBMED SOP](#) Part 12

4. IRB Records and Reports

a) Reports 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 (Adverse Event Report) or ORIO (Other Reportable Information or Occurrences) Reports according to guidance on the IRBMED website:

- Protocols or research plans;
- Any investigator brochures;
- Any scientific evaluations, when provided by an entity other than IRBMED;
- Recruitment materials;
- Approved consent documents;
- Reports of injuries to participants;
- Unanticipated problems involving risks to participants or others;
- Documentation of non-compliance;
- 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
- Minutes of IRBMED meetings sufficiently detailed to show:
 1. Attendance at meetings;

2. Actions taken by the IRB;
3. The vote on these actions including the number of members voting for, against, and abstaining;
4. The basis for requiring changes in or disapproving research;
5. A written summary of the discussion of problematic issues and their resolution;
6. Separate deliberations for each action;
7. When an alternate member replaces a primary member;
8. For initial and continuing review, the approval period;
9. The names of IRB members who leave the meeting because of a conflict of interest along with the fact that a conflict of interest is the reason for the absence;
10. Unless documented in the IRB records, determinations required by the regulations including protocol-specific findings justifying determinations for:
 - a. Waiver or alteration of the consent process,
 - b. Research involving pregnant women, fetuses, and neonates,
 - c. Research involving prisoners, and
 - d. Research involving children;
11. When following DHHS regulations or guidance, documentation of justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in a DHHS-approved sample consent document; and
12. When following FDA regulations or guidance, documentation of the rationale for significant risk/non-risk device determinations.

b) Reports and Communications Archived on the Internal Network

- Current and previous IRBMED 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 IRBMED 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 [IRBMED SOP](#) Part 11.II.F

Refer to [IRBMED Guidance – Record Retention](#) on the IRBMED website for information on the length of time study records are to be kept on file.

Hard copy materials 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 IRBMED 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 UM, 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 IRBMED cooperates with the applicable Medical School Dean for Research and Regulatory Affairs and UMOR to establish, review, and revise these SOPs. These SOPs and any substantive revisions thereto, are subject to review and approval by the applicable Medical School Associate Dean, the HRPP Director and the VPR. Non-substantive revisions such as modifications to enhance regulatory flexibility and workflows, inclusion of standard forms, guidance documents, and similar information developed by the IRBMED in consultation with the Medical School Associate Deans for Research and Regulatory Affairs and UMOR do not require further review or approval. Outdated sections of these SOPs will be archived in such a way that changes and dates of approval may be followed.

The IRBMED SOPs will be comprehensively reviewed in conjunction with the AAHRPP accreditation cycle (typically every 3-5 years). UMOR initiates a comprehensive review of the HRPP Operations Manual at the same time

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 including IRB Council, the IO or designee, or other considerations at the discretion of the IRB.

2. Internal Quality Assurance

The IRBMED routinely conducts internal review of its staff and board member operations, as well as reviewing 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 IRBMED Chairs, members, staff, and affiliated PIs and study team personnel as well as from standing and ad hoc research advisory councils within the jurisdiction of the IRBMED;
- Peer assessment;
- Periodic checks for quality improvement;
- Review by other institutional units, such as ORCR.

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 subjects 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. First, is it human subjects research under the Common Rule? Second, is it human subjects research under FDA regulations? Third, is U-M engaged in the research? And finally, 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, the IRBMED Regulatory Teams (Senior Associate Regulatory Analysts (SARAs), (Intermediate Associate Regulatory Analysts (MARA)), Junior Associate Regulatory Analysts (JARAs) or other qualified IRBMED 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 IRBMED Chairs or Directors may be consulted, as necessary.

Principal Investigators (PIs) may consult informally with an IRBMED Regulatory Team member to determine if their research project involves human subjects. To obtain a formal, documented regulated/not-regulated determination, an eResearch “Projects Not Regulated as Human Subjects Research” application must be prepared. This application permits PIs to respond to questions to determine whether such a determination is applicable. A self-generated determination letter that may be generated for qualifying responses and used for funding or publication purposes; the PI may also request IRBMED review to confirm the not-regulated status.

Applications submitted in eResearch as “Projects Not Regulated as Human Subjects Research” are reviewed administratively by designated IRBMED regulatory 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 IRBMED 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 [IRBMED SOP](#) Part 8

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

Refer to [IRBMED SOP](#) Part 8

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

Refer to HRPP OM Part 8 and [IRBMED 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

The eResearch application provides an exempt application pathway to assist the PI and the IRBMED in identifying exempt research. Under U-M policy, PIs proposing research in alignment with exemption categories 1, 2, 3 are permitted to obtain a 'system generated' approval letter for qualifying studies. Only IRBs are otherwise permitted to issue an exempt determination.

The IRBMED reviews exempt applications to assure that human participants are protected under the relevant regulatory framework. Once an exemption has been granted, the project is not subject to continuing IRBMED 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 IRBMED staff that have completed appropriate training and demonstrate a working knowledge of the regulations (e.g., the Exempt/Not Regulated Coordinator) or Chairs 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 must be issued by the University of Michigan Office Research (UMOR) Institutional Official (IO) or their designee. Except as indicated for exemptions 1, 2, or 3, determinations may not be conducted by PIs or others who may have a conflict of interest regarding the studies.

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 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 IRBMED 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. IRBMED

1. Primary Jurisdiction

All research proposed by faculty, staff, students, or other trainees with a primary appointment with the Medical School or the University of Michigan Health System

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

All research conducted by the faculty, staff, students or other trainees with a primary appointment in U-M Ann Arbor, Flint, and Dearborn schools, colleges, units or programs not subject to IRBMED jurisdiction. Refer to the list maintained at HRPP OM Part 5

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 (e.g., not having a prisoner representative) 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 chair will review the reasons for such a request; and if appropriate, consult with the other IRBs; and 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 the U-M and the IRBMED 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 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.

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](#)

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.

U-M is a signatory to multiple Master Agreements as well as the SMART IRB agreement. IRBMED has developed numerous procedures as well as [guidance documents](#) that address IRBMED, U-M study

team, and external site responsibilities when U-M is either ceding or accepting oversight as the IRB of Record. Records of executed Reliance Agreements are stored at the UMOR level.

In a centralized process, the HRPP Director, UMOR and U-M IRB representatives routinely conduct an Authorization Agreement Meeting (typically weekly) 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 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 IRBMED of the intend to cede the research, collects information relevant to the local conduct of the research and permits routing of the application to the relevant U-M ancillary committees. The 'coordinating center application' utilizes 'participating site' modules to collect information from sites intending to rely upon IRBMED for IRB oversight.

IV. IRBMED RESOURCES

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

IRBMED maintains an area of its website dedicated to information, guidance, and procedures associated with multi-site research and single IRB arrangements. New information is also published in newsletters or distributed by email.

IRBMED also employs 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 compliance 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

IRBMED may be asked to serve as IRB of Record 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.

IRBMED utilizes an electronic software tool 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 IRBMED reviewers for inclusion during the review process and in association with determining whether to extend IRBMED oversight to the site.

After IRBMED has agreed to be IRB of Record through the appropriated convened or expedited review pathway as determined by study risk level, individual sites may be approved via the expedited review process.

IRBMED provides templates for relying sites to facilitate development of informed consent documents and reporting of adverse events and protocol deviations associated with the study.

IRBMED transmits 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 IRBMED via the 'participating site' section of the eResearch application.

Any relying site may communicate directly with the IRBMED to discuss questions, concerns, or obtain interpretation of determinations by contacting the IRBMED Chairs, Director, or dedicated single IRB staff members.

VI. RELYING IRB RESPONSIBILITIES

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

IRBMED 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). IRBMED 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.

IRBMED utilizes 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 SUBJECTS

Refer to HRPP OM Part 6.II

A. Generally

Refer to HRPP OM Part 6.II.A

Refer to [IRBMED Guidance – Investigator 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](#).

3. Compliance with IRB and Other Requirements

Refer to HRPP OM Part 6 II.B.3

See also [IRBMED SOP](#) Part 12.II

4. Conflict of Interest Disclosures

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

See also [IRBMED SOP](#) Part 9

The IRBMED coordinates 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 [IRBMED SOP](#) Part 3

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 MICHHR MIAP Services](#)

Refer to [Michigan Institute for Clinical and Health Research \(MICHHR\) 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 UM is a proposed performance site, a Sponsor may represent that the FDA-approved protocol and any Principal Investigator 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 Principal Investigator, who may in turn ask for clarification from the Sponsor.

Principal Investigators 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 Principal Investigator 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 Principal Investigator in the research contract agrees to conduct an investigation in full compliance with the Principal Investigator Obligations under ICH-GCP, any compliance review conducted by OHRCCR will be done against the complete set of ICH-GCP requirements.

III. EDUCATION

Refer to [IRBMED SOP](#) Part 13

IRBMED provides 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](#) 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 Institutional Review Board (IRB) or other duly constituted committee approved by the University of Michigan Office of Research (UMOR), 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 SUBJECTS

Refer to HRPP OM Part 7.I

Refer to IRBMED educational [information](#)

II. VULNERABLE SUBJECTS

Refer to HRPP OM Part 7.II

Refer to HRPP OM Part 11.II.D

Refer to OHRP [Guidance Documents on Vulnerable Subjects](#) and [FAQs](#)

Special rules apply to research involving vulnerable populations. For federally-supported research, IRBMED complies 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, IRBMED may choose to apply the regulations as stated or apply equivalent protections adopted by the University as stated in HRPP OM Part 7.IV.

A. Research Involving Pregnant Women, Fetuses, and Neonates

Refer to HRPP OM Part 7.IV.A

B. Research Involving Prisoners

Refer to IRBMED Guidance: [Prisoners in Research](#)

Refer to HRPP OM Part 7.IV.B

6. IRB Composition

IRBMED is 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, IRBMED 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 [IRBMED SOP](#) Part 11.II.A.2.a

Refer to [IRBMED Guidance](#): Children in Research; Assent of Children in Research; Wards

Refer to HRPP OM Part 11.II.A.2

Refer to HRPP OM Part 7.II.C

D. Research Involving Adults with Cognitive Impairment or Otherwise 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

[IRBMED Education](#) includes a course to review requirements for developing Data and Safety Monitoring Plans (DSMP) for qualifying studies; and Data and Safety Monitoring Boards (DSMB) to address studies with risks to participants, NIH multi-site clinical trials and higher risk, Principal Investigator (PI)-initiated studies.

eResearch instructs PIs to include information about data and safety monitoring as applicable to the risk level of the study. The IRB will review the DSMP 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 [IRBMED Guidance: Advertising Materials](#)

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 IRBMED Guidance [Payment to Research Subjects](#).

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.

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 [MICHHR/MIAP Guidance](#)

B. Investigational Devices

Refer to HRPP OM Part 8.II.B

Refer to [MICHHR/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 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 IV, below.

III. EXPANDED ACCESS

Refer to HRPP OM Part 8.III

Refer to [MICHHR/MIAP Guidance](#)

Refer to IRBMED Guidance - [FDA Expanded Access Program at the University of Michigan](#)

A. Investigational Drugs and Biologics

Refer to HRPP OM Part 8.III.D

1. Treatment INDs

Refer to [HRPP OM Part 8.III.D](#)

2. Group C Treatment IND

Refer to [HRPP OM Part 8.III.D.2](#)

3. Open Label Protocols or Open Protocol INDs

Refer to [HRPP OM Part 8.III.D.1](#)

4. Parallel Track Studies

Refer to [HRPP OM Part 8.III.D.3 \[1\]](#)

B. Expanded Access to Investigational Devices

Refer to HRPP OM Part 8.III.E.

1. Compassionate Use (Devices)

Refer to HRPP OM Part 8.III.E.1

2. Treatment IDE

Refer to HRPP OM Part 8.III.E.2

Also see: [IRBMED Guidance – Emergency Use of Test Articles.](#)

3. Access (Devices)

Refer to HRPP OM Part 8.III.E.3

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 IRBMED 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 IRBMED Regulatory team 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 [IRBMED Guidance – Electronic Signature-Part 11 Compliance Certification](#)

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

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:

**University of Michigan
Medical School Institutional Review Board (IRBMED), Standard Operating Procedures**

- 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 [UMOR 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 [IRBMED SOP Part 3.III.B.7](#)

Refer to [UMOR Conflict of Interest webpage](#)

IRBMED 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 IRBMED strives to avoid both actual and perceived conflicts of interest in the performance of required activities. The IRBMED communicates regularly with the Medical School Conflict of Interest Committee, UMOR COI committee, and other University units (e.g., ORSP) to coordinate

awareness of actual and perceived conflicts of interest of IRBMED members, staff (if applicable), and researchers. Legal Counsel is available to IRBMED to discuss a conflict of interest situation.

IV. INSTITUTIONAL CONFLICTS OF INTEREST

Refer to HRPP OM Part 9.IV.

Refer to [UMOR webpage Institutional Conflict of Interest](#)

Part 10 – Sponsored Projects

This section describes policies and procedures for the administration of sponsored project agreements for human subjects 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 IRBMED SOP Part 7.VI

Refer to [IRBMED Standard Informed Consent Template](#)

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 UM 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 can Consent or Provide Permission for Participation in Research](#)

Refer to IRBMED [Wards of the State](#) guidance.

Refer to IRBMED [Assent Guidelines](#)

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 [guidance on prisoners](#).

2. Research Involving Pregnant Women, Fetuses, and Neonates

Refer to HRPP OM Part 7

Principal Investigators are encouraged to consult with the IRBMED about research involving these populations prior to submitting an IRBMED 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 – Recording Retention](#)

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](#)

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 IRBMED 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 in particular 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 IRBMED'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](#)

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 Adverse Events (AEs) and Other Reportable Information or Occurrences (ORIOs), including those AEs and ORIOs that are also unanticipated problems involving risks to participants or others (UaPs), are posted on the [IRBMED 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 IRBMED offers educational sessions that review the guidelines and offers individual consultations with PIs and study teams, as indicated, to assist in understanding the reporting requirements.

Examples of events that may require reporting in accordance with IRBMED 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. For example:
 - Information that indicates a change to the risks or potential benefits of the research.
For example:
- An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRBMED
- 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 IRBMED
- 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 IRBMED 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 IRBMED, either with their initial IRBMED 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 IRBMED 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.

IRBMED 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 IRBMED Director, Health System Legal Counsel, IRBMED Chairs, the applicable Medical School Deans, 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.

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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 IRBMED may use review by a Single IRB Member for reports of Adverse Events or Other Reportable Events or Occurrences, as long as those reports do not constitute a Potential or Identified Unanticipated Problem Involving 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 a Single IRB Member reviewer of an AE or 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 or ORIO report is available to all IRB members attending the meeting.

If the convened board determines an event to be an UaP, the IRBMED 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.

IRBMED 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, IRBMED Director, UM Office of General Counsel, UMOR, 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

IRBMED 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, IRBMED director, Office of General Counsel, IRBMED Chair(s), UMOR 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, IRBMED 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 IRBMED will prepare the UaP report. After appropriate institutional review, the IRBMED will send the required reports directly to external entities as required by regulation or sponsor agreement, with notification of the IO, the Associate Vice President for Research, the HRPP Director, the IRBMED 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. 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 IRBMED, through any source, indicates the possibility that research participants or others are exposed to unnecessary or excessive risks, or that the requirements of the IRBMED are not being met, the IRBMED shall collect any additional information necessary to evaluate the credibility or accuracy of the information and determine whether further action [such as education of the PI or the PI's research staff, or suspension or termination of the project] appears necessary. In some circumstances, in consultation with the IRBMED, the PI may place a voluntary "hold" on new participant accrual or research-related interventions during the fact-finding period, unless to do 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 IRBMED 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 IRBMED'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 IRBMED will assure notification of the IRBMED Chairs, the applicable Medical School Associate Dean, the Health System Legal Office, and the HRPP Director, as soon as possible.

Allegations or other indications of fabrication or falsification of research results will be reported to the Medical School Associate Dean for Regulatory Affairs, the Health System Legal Office, and the UMOR.

An IRBMED staff member initiates a review of any complaint or allegation of noncompliance made to the IRBMED. If assistance with the review is desired, the IRBMED Chairs will make a written request to UMOR (usually via the IRBMED 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 IRBMED staff member may engage in discussion with the research team, research participants, the complainant (if known), and others.

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

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- Providing the IRBMED with copies of or access to:
 - 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 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 IRBMED 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 IRBMED shall notify the applicable Medical School Deans and 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 IRBMED staff maintains records of all complaints and allegations of noncompliance that come to the attention of the IRBMED.

The IRBMED Chair(s) and applicable Medical School Associate Deans are provided with copies of reports that are prepared for submission to the HRPP Director.

The IRBMED shall promptly notify the HRPP Director of (1) any potentially serious and/or continuing noncompliance; and (2) any suspension or termination of IRBMED approval for a project, including those instances determined by an external IRB. In certain instances of alleged or apparent noncompliance, the IRBMED 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 quarterly basis, the IRBMED will prepare a list of all externally reportable events for review with the IRBMED Chair(s), 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 (and consistent with locally adopted SOPs, 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 (i) clearly does not constitute potentially serious and/or continuing noncompliance; and/or (ii) 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, education coordinator, Single Member Reviewer, or IRBMED compliance staff to be addressed and concluded. Some corrective actions as noted in IRBMED 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 IRBMED 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 IRBMED Chair(s) at the next available CDM Meeting, 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 the activity (1) constitutes potentially serious noncompliance with IRBMED determinations or federal regulations; and/or, (2) separately constitutes potentially continuing noncompliance with IRBMED determination or federal regulations. 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 Deans, the Health System Legal Office, the HRPP director, and the PI.

If the convened IRB determines that the noncompliance was not serious and/or continuing, the applicable Medical School Associate Deans, the Health System Legal Office, 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 applicable Medical School Associate Deans, the Health System Legal Office, and the HRPP Director.

The IRBMED 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 clinical 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 IRBMED at specific time intervals (in addition to the study's scheduled continuing review submission for renewal of IRBMED approval)
- Submission of reports to the IRBMED 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 re-consent 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 Noncompliance

Refer to HRPP OM Part 12.III.G

One of the IRBMED Chair(s) will convey the board's determination by telephone or e-mail to the PI at the conclusion of the board meeting as to whether the noncompliance constitutes serious and/or continuing noncompliance. A formal letter will be sent to the PI outlining the reasons for the board's decision and any required remediation.

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 IRBMED office through general intake procedures are triaged by the IRBMED 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 IRBMED 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

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- US Mail: IRBMED, 2800 Plymouth Rd., Building 520, Room 3214, Ann Arbor, MI 48109-2800

B. Questions Concerning University Policies and Procedures

- The Medical School Office of Research: (734) 615-1332
- The Medical School Office of Regulatory Affairs: (734) 647-1576
- The Office of the Vice President for Research: (734) 763-1289
- The Health System Legal Office: (734) 764-2178

Part 13 – Education and Training

This section describes educational and training opportunities offered to IRBMED 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 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 UMHS Daily Bulletin, Biomedical News, the University Record, the 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 IRBMED provides researchers, board members, and IRBMED office staff with opportunities for continuing education comprised of:

- Routine workshops on regulations, institutional policy and procedures, and the application process throughout the year and upon the request of a department or unit (see the [IRBMED Education](#) page)
 - New workshops as needs are identified
- Special educational events, including, but not limited to:
 - IRBMED 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
- 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 IRBMED office staff before posting to the IRBMED website. Internal, procedural U-MICs may not be posted publicly.
- Routine publication of electronic newsletters for the research community

- Consultations with study teams either upon the request of the study team or upon IRBMED (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 IRBMED website
 - Developing new guidance as needs are identified
- [Information and Technology Services \(ITS\)](#) provides [help guides and other resources on using eResearch](#).
- A [web-based archive](#) of materials from prior presentations

IV. IRBMED STAFF MEMBER EDUCATION

IRBMED staff members are required to complete a standardized IRBMED orientation program and all required PEERRS human subjects modules. Completion of additional orientation and continuing education workshops, as well as [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 IRBMED leadership (and as budget permits).

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