



**University of Michigan  
Medical School**

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

**Standard Operating Procedures (SOPs)**

**May 2015**

## REVISIONS

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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 subject 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 subjects, provides guidance to the University and its researchers on ethical and procedural issues related to the use of human subjects 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 five (5) 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 the Medical School and the UM Hospitals and Health Centers (UMHHC), including research conducted off-site by UM Health System (UMHS) 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.

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 subject research. HRPP policies are compiled in the Operation's 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 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, including:

- A. The Public Health Service Act and its amendments, which empower the 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, which seventeen federal departments and independent agencies have adopted (see below), codifies and expands on the ethical principles described in the [Belmont Report](#).

DHHS has issued additional rules for federally funded research involving [pregnant women, fetuses, and neonates \(45 CFR 46 subpart B\)](#); [prisoners \(45 CFR 46 subpart C\)](#); and

[children \(45 CFR 46 subpart D\)](#). 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.

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 more than a dozen federal agencies involved with human subjects research. These are:

- [Agency for International Development/International Development Cooperation Agency \(22 CFR 225\)](#)
- [Central Intelligence Agency](#) (by Executive Order 12333, 46 FR 59941)
- [Consumer Product Safety Commission](#) (16 CFR 1028)
- [Department of Agriculture](#) (7 CFR 1c)
- [Department of Commerce](#) (15 CFR 27)
- [Department of Defense](#) (32 CFR 219)
- [Department of Education](#) (34 CFR 97)
- [Department of Energy](#) (10 CFR 745)
- [Department of Health and Human Services](#) (45 CFR 46)
- [Department of Housing and Urban Development](#) (24 CFR 60)
- [Department of Justice](#) (28 CFR 46)
- [Department of Transportation](#) (49 CFR 11)
- [Department of Veterans Affairs](#) (38 CFR 16)
- [Environmental Protection Agency](#) (40 CFR 26)
- [National Aeronautics and Space Administration](#) (14 CFR 123)
- [National Science Foundation](#) (45 CFR 690)
- [Social Security Administration](#) (See P.L. 296 [103rd Congress])

The Office of Science and Technology Policy signed the federal policy for protection of human research subjects but did not codify the Common Rule, because it does not conduct or sponsor research.

Although they have not issued the Common Rule in regulations, three other departments and agencies comply with all subparts of 45 CFR 46. These include:

- The Central Intelligence Agency, by executive order, (Executive Order 12333, paragraph 2.10)
- The Department of Homeland Security, created after issuance of the Common Rule, applies all subparts of 45 CFR 46 (6 U.S.C. section 112)
- The Social Security Administration separated from HHS in 1994. Absent action by the Administrator, it applies all regulations previously applied to SSA before the separation. (42 U.S.C. section 901)

The Common Rule is not uniformly interpreted or enforced. In addition, the subparts of [45 CFR 46](#) imposing special protections for identified vulnerable populations (other than children) have not been widely adopted. 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.

Absent an interpretation from a federal funding agency to the contrary, the requirements of all of the subparts of [45 CFR 46](#) are applied to all University research, regardless of funding source. 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.

- 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 Parts 6 and 8 of the IRBMED SOPs, [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 \(NIH\) Office of Biotechnology Activities \(OBA\)](#). The OBA develops and implements NIH policies and procedures for the safe conduct of recombinant DNA activities and human gene (see [NIH guidelines for rDNA and Gene Transfer](#)). 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, 350, and 356).  
*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 [Guidelines for Good Clinical Practice \(GCP\) of the International Conference of Harmonization \(ICH\)](#)  
*Refer to IRBMED SOP Part 6 – Roles and Responsibilities of Investigators and Research Staff*  
*Refer to [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.II](#)*

#### IV. LIMITATION ON INSTITUTIONAL AUTHORITY

*Refer to [HRPP OM Part 1.III.B](#)*

All regulated human subject research conducted by the University must be approved by an IRB or granted an exemption by a University IRB (through its members or staff, as specified in the IRBs 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](#)
- [Medical School Office of Regulatory Affairs](#)
- [UMHS Compliance Office](#)
- [Office for Human Research Compliance Review \(OHRCCR\)](#)
- [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 subjects.

Certain types of research involving human subjects 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:

- [Michigan Clinical Research Unit](#) (MCRU), formerly the General Clinical Research Center (GCRC)
- [Research Pharmacy](#) (formerly the Investigational Drug Service)
- [Clinical Research Calendar Review Analysis Office](#) (CRAO), formerly the Clinical Research Billing Unit (CRBU)
- [University of Michigan Medical School](#) (UMMS)
- [Radioactive Drug Research Committee/Subcommittee on the Human Use of Radioisotopes](#) (RDRC/SHUR)
- [Central Biorepository](#) (CBR)
- [Institutional Biosafety Committee](#) (IBC)
- [Human Pluripotent Stem Cell Research Oversight Committee](#) (hPSCRO)
- [Hospital Biomedical Engineering Unit](#) (BEU)
- [Tissue Procurement Core](#) (TPC)
- [Medical School or UMOR Conflict of Interest Committees](#) (COI)
- [Michigan Alzheimer's Disease Research Center](#) (MADRC)
- Department or organization peer review committees (e.g., Comprehensive Cancer Center Protocol Review Committee)
- IRBs at other performance sites or coordinating centers
- Core service groups (e.g., Biomedical Engineering Unit (BEU))

The IRBMED is responsible for review and final approval of the human subject 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 Senior Associate Dean for Research and the Dean of the Medical School.

The IRBMED works closely with the Office of Regulatory Affairs, for example, to obtain assistance with FDA inspections, board member recruitment, and mandatory training requirements.



## 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. Rule making 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 rule making. In Standard Practice Guide 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. See, [SPG 303.05](#).

### 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. The VPR has approved the OM and approves each substantial modification or amendment to it. Records of such approval are maintained in the UM Office of Research (UMOR).

At least once every five years, typically in conjunction with the AAHRPP re-accreditation cycle, UMOR initiates a comprehensive review of the OM. Revisions may be made at any time, however, as required by changes in law, ethical standards, institutional policy, quality assurance activities, or other considerations. Non-substantive revisions (e.g., to correct typographical errors, update links, or incorporate summaries of new or revised laws or regulations governing the HRPP) may be made upon approval of the HRPP Director with notice to the VPR.

### III. IRB STANDARD OPERATING POLICIES AND PROCEDURES

Refer to [HRPP OM.Part 3.II](#)

#### A. General Provisions

The IRBMED members and staff to which these SOPs refer are accountable to the Medical School Associate Deans for Research and Regulatory Affairs and operate under the authority of UMOR with regard to the oversight of human subject research.

The IRBMED cooperates with the Medical School Associate Deans for Research and Regulatory Affairs, UM Health System (UMHS) Compliance Committee, and UMOR to establish, review, and revise these SOPs. These SOPs and any substantive revisions thereto, are subject to review and approval by the Medical School Associate Deans for Research and Regulatory Affairs, UMHS Compliance Committee, 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, in conjunction with Medical School Associate Deans for Research and Regulatory Affairs, UM Health System (UMHS) Compliance Committee, and the OVPR

maintains guidance documents on a number of topics targeted to the IRBMED, IRBMED Staff and researchers on the [IRBMED](#) website. In many cases the guidance expands on the information contained within these SOPs and are therefore referenced where appropriate.

IRBMED primarily has oversight of human subject 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) with approval by the Chair of the Board (referred to in the SOPs as the “Chair”) and guidance from UMOR.

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

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

Refer to [IRBMED SOP Part 5.II.A-D](#)

Refer to [HRPP OM Part 5.II.A-D](#)

## **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 subjects.

Each of the five (5) registered IRBs consists of regular voting members and alternate voting members, with expertise augmented as necessary by consultants. New regular members first serve as alternate members for 6 month’s or other time period based on recommendation of the IRBMED Co-Chairs. An individual member may serve as a regular or alternate board member concurrently on more than one Review Board.

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 UM Health System (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 subjects, 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 subjects.

For projects supported by the U.S. Dept. of HHS's National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR) that "purposefully requires" inclusion of children with disabilities or individuals with mental disabilities, the IRB must include at least one member who is primarily concerned with the welfare of these research subjects (refer to [34 CFR 350 and 34 CFR 356](#)).

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, 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 regular member (i.e., those members designated as having enough experience to serve as Single IRB Member reviewers) or alternate member of an IRB 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 (or an immediate family member; spouse, domestic partner, or dependent) of a person affiliated with the University. The University supports efforts of the IRBs to include additional unaffiliated members.

"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 five (5) 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 provide updates to include:

- new members or alternate members are approved by the Medical School Associate Dean for Regulatory Affairs;
- current members or alternate members extending their membership;
- members or alternate members who are moving from one IRB to another or serving on multiple IRBs;
- members or alternate members renewing membership after a period of time away from an IRB;
- 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 Medical School Associate Dean for Regulatory Affairs 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 full 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).

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 subject research.

The Medical School Associate Dean for Regulatory Affairs is responsible for the appointment and reappointment of Chairs. When a vacancy arises, the Medical School Associate Dean for Regulatory Affairs may solicit nominations for a new Co-Chair or a Vice-Chair from the Medical School faculty, IRBMED members, staff, and consultants.

The Medical School Associate Dean for Regulatory Affairs then makes a recommendation to the UMHS Compliance Committee, which may adopt or reject the recommendation and in turn communicates its position to the Medical School Associate Dean for Regulatory Affairs.

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 subject research.

#### **b) IRB Members**

Refer to [HRPP OM Part 3.III.B.1](#)

The Medical School Associate Dean for Regulatory Affairs 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 Medical School Associate Dean for Regulatory Affairs or solicited through advertisements in local news media or by other means.

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 Medical School Associate Dean for Regulatory Affairs 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 Medical School Associate Dean for Regulatory Affairs. The Medical School Associate Dean for Regulatory Affairs has final authority to make each member or chair appointment or reappointment.

All members should be sufficiently qualified through experience, expertise, and diversity and be able to determine the acceptability of proposed research in terms of institutional commitments and policies, applicable laws and regulations, and standards of professional conduct and practice.

Each member is appointed to an initial three-year term, which may be renewed at the discretion of the Medical School Associate Dean for Regulatory Affairs for an unlimited number of consecutive three (3) year terms.

Members are evaluated for reappointment at the discretion of the Medical School Associate Dean for Regulatory Affairs after seeking evaluation from the IRBMED Chairs and Office staff of the member's level of participation, adequacy of reviews, regulatory/ethical interpretations.

Members will be assigned proposals to review that fall 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 Associate Dean for Regulatory Affairs and IRBMED Chairs will periodically review the membership composition. Additional full or alternate members will be recruited to ensure sufficient breadth of the registered board composition should members' terms expire, vacancies arise, or the submission review workload necessitate.

#### c) IRB Staff

The IRBMED is supported by a professional staff hired and supervised by the Director of the IRBMED. The Director reports to the Medical School Senior Associate Dean for Research through the Director of the Office of Research.

The Director and staff are responsible for facilitating IRBMED operations (human subject 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 Medical School Senior Associate Dean for Research.

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 a Regulatory Team for each of the five (5) IRBs. Each Regulatory Team is typically composed of a Senior Associate Regulatory Analyst (SARA), a Junior Associate Regulatory Analyst (JARA) and an Assistant Regulatory Analyst (ARA). 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.

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 regular voting 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 subjects 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 subjects subject to IRBMED’s jurisdiction. The IRBMED is comprised of five IRBs. IRBs A1, A2, B1 and B2 each convene twice monthly; two of the IRBs convene on weeks 1 and 3, and the other two IRBs convene on weeks 2 and 4. One Board (C1) convenes weekly to review studies with an oncology. Additional meetings may

be convened throughout the academic year, as necessary. The IRBs may meet by conference call only when necessary.

(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 IRB meeting agenda listing, and linking electronic items for review, discussion, deliberation; and vote, as appropriate; and other information of relevance to the IRB meeting's purpose such as scheduled reports, i.e., Single IRB Member reviews (expedited, Single IRB Member for AE/ORIOs, or NCI-CIRB research projects). Updated working agendas are available at all times to IRBMED members, the Medical School Associate Dean for Regulatory Affairs, UMOR, and authorized consultants. The IRBMED Regulatory Team assigns incoming applications to upcoming meeting agendas generally based on the board assignment 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, and diversity 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

**(a) 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 twice monthly IRB meetings are scheduled for 3-5 hours which allows adequate time for assigned applications. The weekly (C1) board meets weekly for 2-3 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.

**(b) 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 Review Board meeting, designated office staff shall prepare minutes consisting of at least the following information:

- Attendance of the members at the full convened board meeting, including a notation of absences of board members;
- Documentation of any conflicted members or staff;
- The time a full or alternate member leaves the room and rejoins the meeting;
- Acknowledgement of reviews approved by the Single IRB Member (expedited, Single IRB Member for AE/ORIOs, or NCI-CIRB research projects) review procedure;
- The names of PIs, guests and/or consultants in attendance;
- 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 regular member—based on designation: for example, non-physician scientist alternate member *a* is standing-in for non-physician scientist regular member *b*;
- The names of conflicted members, consultant, 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 subjects 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 subjects or others; or
  - representative of risk of actual harm to subjects 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 one (1) week (for the C1 board) but not more than four (4) weeks from the meeting date, an IRB's DRAFT minutes shall be prepared. The DRAFT minutes are reviewed for quality, completeness and compliance with regulatory requirements by the IRBMED Regulatory staff and then sent electronically to Board members for review.

- Board members may request changes to the DRAFT if needed;
- IRB members will vote to ratify them at a subsequent meeting;
- The ratified 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 should a delay in ratifying the IRB's minutes is necessary.
- Minutes are archived in the eResearch System.
- In the event that minutes require amending due to a discovered error, for example, 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

The IRBMED, the Medical School Dean for Regulatory Affairs, or the VPR may, at their discretion, invite persons whose experience or expertise may aid the IRBMED in performing its responsibilities. Whether during meetings or otherwise, such individuals may include consultants, advisors, and ad hoc reviewers, or others who may serve the IRBMED, for example, by assisting in the review of a complex research project.

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.

Refer to [HRPP OM Part 3.III.B.2.](#)

### 3. Alternate IRB Members

The IRBMED may appoint alternate voting members to serve in the absence of regular voting members to establish quorum and participate in deliberations and votes on applications pending before the IRBMED. A regular voting member of one IRB (A1, A2, B1, B2, or C1) 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 quorum. Alternate members may participate in the discussion; however, they may not vote unless designated to serve in the absence of a regular voting member.

A regular member from one IRB may serve as a primary 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 voting member of one IRB as a voting member of another IRB, or may reclassify a regular voting member as an alternate voting member or vice versa, by notifying the member, the Medical School Associate Dean for Regulatory Affairs, and UMOR. When a reassignment of a voting member is made, i.e., a member moves from one IRB to another, the membership rosters are revised to reflect this change and the Medical School Associate Dean for Regulatory Affairs and UMOR are notified. 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. At the conclusion of the orientation period a new member will be asked to conduct a mock review with the IRBMED Chairs and to present the review in the context of an IRB meeting. If the mock review is deemed to provide information in compliance with the regulations, the member enters a practicum period during which new members attend meetings and review protocols as primary reviewers but are not permitted to vote unless a regular member is for whom they qualify as an alternate is absent.

IRBMED Chairs determine when each new member's cumulative experiences qualify them for appointment as a regular member and if they qualify to serve as a Single IRB Member reviewer (including expediting reviewer). This may occur at any time after presenting a mock review and usually occurs within one (1) year for bi-weekly members and six (6) months for weekly members.

**b) Orientation of IRB Staff**

Depending upon the role of the new staff member, completion of some or all of the IRBMED member orientation and continuing education workshops, as well as [workshops offered to research personnel](#), are required at the discretion of the employee's direct supervisor.

IRBMED staff members are required to complete all PEERRS human subject modules. Staff members are encouraged to attend local, regional, and national conferences on ethics, State and Federal laws, and regulations for human subject research protection.

**c) Orientation of IRBMED Chairs**

IRBMED Chairs are appointed per [IRBMED SOP Part 3.III.B.1.a](#). Chairs meet with the Medical School Dean for Regulatory Affairs 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 web-based tips are presented at each IRB meeting; annually, IRB Chairs, members and Office staff are offered an opportunity (the number of attendees varies based on budget) to attend national IRB meetings, IRB Seminar Series are presented to the research community, IRB Seminar Series are offered on specifically for board members on selected topics. IRBMED staff also participate in ongoing continuing education within the context of weekly 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 the website.

**e) Researcher Education**

Refer to [HRPP OM Part 13](#)

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 Medical School Associate Dean for Regulatory Affairs or department Chair.

b) Compensation of Members of the Community

Unaffiliated members of the community are paid for their service on the IRB in an amount to compensate their time and expenses to attend the meeting, unless waived by the unaffiliated member. This may include, but is not limited to: parking expenses, computer support, and a per-meeting stipend. Members of the community that are deemed affiliated are offered compensation at the same rate.

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 Medical School Associate Dean for Regulatory Affairs.

d) Liability Coverage

Liability coverage is a matter of institutional policy and is further 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 Medical School Associate Dean for Regulatory Affairs 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 Chair is an active participant and is trained in current interpretations of federal regulations and other relevant ethical principles for the protection of human subjects. 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- 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 Co-Chairs and Vice-Chairs will evaluate new members of their boards at the conclusion of their first year of service to ensure that the expertise of each full 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 subjects. Feedback on the performance evaluation will be provided to the member by the Co- or Vice-Chair along with any suggestions for improving performance via additional education or mentoring.

Each board member reaching the end of their term is evaluated and provided feedback by the Co-Chairs or Vice-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.II-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, review board, Medical School Associate Dean for Regulatory Affairs, COI Committee, or UMOR believes might hamper the member's ability to perform an impartial review of the research.

Any conflicted reviewer (Chair or member) 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 the conflict is 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's Guidance on Engagement of Institutions in Human Subject's Research, October 16, 2008, Section III.B.1.](#)

**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](#)*

*Refer to [IRBMED SOP Part 3.III.B.7.b.](#)*

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) except in limited circumstances as requested by the IRB. 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 Medical School [COI Committee](#) or UMOR 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 if, to the extent possible, if a COI statement is documented for any research submissions for 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 Subject Research Studies Reviewed by the IRB**

IRBMED reviews studies submitted per the assigned jurisdiction in [HRPP OM Part 5.I](#). 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, and research that may qualify for exemption. Submissions are routed to the IRBMED office by the PI via [eResearch](#), the web-based system for submission, routing, approval and management of human subject 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 subject 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 subject 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.D-F](#)

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 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

For activities not-regulated as human subject research per HHS and FDA definitions of human subject 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).

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) Exempt

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 or designee, including qualified members of the IRBMED Office staff, or the VPR. 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 subjects 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.

e) International Research

Generally, the IRBMED will review all international human subject 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 subject, 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 subject complaints, UaP/UPIRSOs and other reports of potential non-compliance to IRBMED. Research subjects 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.III-IV.](#)

## 3. Submission of IRB Applications and Reports

Refer to [HRPP OM Part 3.III.C.3](#)

The University utilizes eResearch, 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 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.d](#)

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 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.

Refer to [HRPP OM Part 3.III.C.4.b](#)

###### (1) Information Required for IRB Review

Refer to [HRPP OM Part 3.III.C.4.b1](#)

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 subjects 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.

- Description of the professional qualifications of the investigator conducting the research;
- Study Protocols that address:
  - Study title;
  - Purpose of the study;
  - Risks and expected benefits to human subjects;
  - 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 children (21CFR50subparts B, C, D));
- Test article accountability procedures;
- Description of study design (including as needed, a discussion of the appropriateness of research methods);
- 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;
- Provisions for managing adverse reactions;
- Copies of the proposed informed consent documents (including all requirements of 21 CFR 50.25(a); including requirements of 21 CFR 50.25(b) that are appropriate to the study; meeting all requirements of 21 CFR 50.20; translated consent documents, as necessary, considering likely participant population(s); or a request for IRB approval of a waiver of written 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)

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 subject. Note that expiration of an approval does not constitute a “suspension” of IRBMED approval reportable to OVPR and federal regulations under KHHS, FDA regulation, or these SOPs.

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

- The number of subjects accrued since the initial application or the previous continuing review application;
- The number of subjects expected to be recruited in the future;
- Any changes in the risk level determination;
- A summary or tabulation of any reports including:
  - unanticipated problems involving risks to subjects or others;
  - subject withdrawals from the project;
  - 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, amendments, or modifications made to the research and a summary of 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 subject’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.
- 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.

(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 subjects 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 subjects enrolled in the study
- Number of subjects completing the study
- Number of subjects that withdrew from the study and the reasons for withdrawal
- Number of subject 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.2](#)

(a) Review Process

IRBMED Regulatory Teams and primary reviewers must receive sufficient information (IRBMED SOP Part 3.III.C.4.b) 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, HITECH Security Rule FERPA or other federal, oversight activities) prior to presentation for board review. (*Refer to [IRBMED Part 3.II.C.4.b](#)*).

An 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 (or designee) 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 subject 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. and the elements detailed in [IRBMED SOP Part 3.III.4.b](#)).
- 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 subjects, if any will be in accordance with University policy. The IRBs will review payment arrangements offered to subjects. 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 subject at risk.
- Where appropriate, credit for payment accrues as the study progresses and may not be contingent upon the subject completing the entire study.
- Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects 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 MICHHR 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 56.11 are met and that the study design is adequate to protect the subjects from increased risk and yield expected knowledge. This includes examination of the following:

- Risks to subjects are minimized
  - by using procedures that are consistent with sound research design and do not unnecessarily expose subjects to risk;
  - whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes; and
  - when adequate resources are available to protect and minimize harm to human subjects.
- Sound Research Design / Scientific Review
  - Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result;
  - Selection of subjects 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 subjects and to maintain the confidentiality of data (Refer to [IRBMED SOP Part 3.III.C.6.g](#));
  - When appropriate, additional safeguard have been included in the study to protect the rights and welfare of vulnerable subjects.

- (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 system;
  - For studies conducted in the Comprehensive Cancer Center, all studies are reviewed by the Protocol Review Committee (as a Core Committee of eResearch).
  - Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, 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 Guidance – Risk 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 subjects for participation in the project is equitable. In making this assessment, the IRBMED takes into account the characteristics of the subject 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 subjects 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 subjects.
  - When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
  - When some or all of the subjects 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 subjects (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 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 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; 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

Approval will be contingent on specified changes to the protocol, ICDs or other items that will be made by the PI prior to initiating the research.

- *Approved Pending Office (APO)*

Approval of the submission is contingent on specified administrative changes requested and clearly defined by the IRB. The requested changes, such as correction of typographical errors, specified wording changes, or other items will be made by the PI or study team.

- *Approved Pending Reviewer (APR)*

Approval of the submission is contingent on specified changes requested by the board. If there are contingencies remaining and they are of an administrative nature as clearly defined by the Board (e.g., correction of typographical errors or specified wording changes to an informed consent) the reviewer may request that the IRBMED Regulatory Team verify those changes. Once all contingencies are met and they meet with the reviewer's approval (and that of the designated IRBMED Regulatory Team approval may be granted.

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.C.4.b.1.c](#)

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 subjects; and/or
- cannot minimize risks to subjects 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 subject research project or discontinuing a PI's privilege to conduct human subject 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 subject research or a PI's privilege of conducting human subject research except for the continuation of follow-up activities necessary to protect human subject 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

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.
- 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 unless the IRBMED reviews, approves, and document that it is in the best interest of individual subjects currently participating in the study to continue the research interventions or interactions;
- Enrollment of new subjects or intervention and interaction with subjects during a lapse is prohibited, as is data analysis.
- Sponsored project resources (e.g., government or private) must not be expended for unallowable activities;

(b) Lapses in Approval and Administrative Termination

If an approved research project is not renewed or terminated within three 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 Medical School Associate Dean for Regulatory Affairs, 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 9/30/15 and an expiration date of 9/29/16.

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.

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

#### d) Monitoring and Verification by IRB

Refer to [IRBMED SOP Part 12.II.G](#)

The IRBMED is responsible for overseeing the safety of human research subjects and has the authority to suspend or terminate human subject 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 Human Research Compliance Review (OHRCR) – 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 subjects;
- 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;
- Subject 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 subjects;
- 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 subject incentive) without prior IRBMED review and approval, unless necessary to eliminate apparent immediate hazards to the subjects. Any change made without prior approval to avoid a hazard must be reported promptly to the IRBMED.

The IRBMED will scrutinize any proposed amendments to determine the degree to which risks to human subjects 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 subjects of the changes and if reconsenting of the subjects is necessary.

Reportable changes may include, but are not limited to:

- Proposed changes in risks or benefits to subjects;
- Proposed amendments to the study protocol, including changes to the eligibility criteria, recruitment materials, questionnaires, surveys, scripts and subject 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 subject 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 subject 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](#)

**5. Expedited Review**



Refer to [HRPP OM Part 3.III.C.5.](#)

DHHS regulations at 45 CFR 46.108(b) and FDA regulations at 21 CFR 56.08(c)(i) identify certain types of research that may be reviewed and approved by “expedited review.” The following types of research may be considered for an expedited review process:

- The research involves no more than minimal risk to subjects;
- The identification of the participants on 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 45CFR46.110 and 21CFR56.110).
- Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

Under an expedited review procedure, the IRBMED Chairs, or an experienced IRBMED reviewer designated by the Chair from among the members of the IRBMED 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 full or alternate members of the IRBMED boards.

The research submitted for expedited review requires the same materials that a convened board would receive for standard submission.

The IRBMED Regulatory Team performs a regulatory review of the application followed by assignment to an expediting reviewer. Following reviewer assignment, and at the reviewer's discretion, submissions eligible for expedited review may be referred to the full IRBMED for a discussion and vote.

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

#### a) Expedited Review Categories of Research

The interactions and interventions in the research must present no more than minimal risk to subjects. The regulatory definition of minimal risk is that “the probability and magnitude of harm or discomfort to participants that is 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 examination or tests”.

- (1) The research conducted must meet the list of research categories as defined in [UM's HRPP OM](#) –Categories of Research and cited below: The categories apply regardless of the age of subjects, except where noted.

Clinical studies of drugs and medical devices only when one of the following conditions is met:

- (a) Research on drugs for which an IND (21CFR312) is not required or
  - (b) Research on medical devices for which an IDE application (21CFR812) is not required; or the medical device is cleared /approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
- (2) Collection of blood samples by finger stick, heel stick, ear stick or venipuncture as follows:
- (a) From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
  - (b) From other adults and children (for definition see 45CFR46.402(a)), considering age, weight and health, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50ml or 3ml/kg in an 8 week period and collection may not occur more frequently than 2 times per week.
- (3) Prospective collection of biological specimens for research purposes by noninvasive means (e.g. hair and nail clippings, teeth in need of extraction, saliva, excreta, dental plaque and calculus, mucosal and skin cells, sputum);
- (4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves; where medical devices are used they must be cleared/approved for marketing (but not for new indications).
- (5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). Refer to 45 CFR 46.101(b)(4) for some examples in this category that are exempt).
- (6) Collection of data from voice, video, digital, or image recordings made for research purposes.
- (7) Research on individual or group characteristics or behavior (including, but not limited to research on perception, cognition, motivation, identity, language, cultural beliefs, social behavior) or research employing survey, interview, oral history, focus group, human factors evaluation or quality assurance methodologies. Refer to 45 CFR 46.101(b)(2) and (b)(3) for some examples in this category that are exempt.
- (8) Continuing review of research previously approved by a convened IRB as follows:
- (a) Where the research is permanently closed to the enrollment of new subjects; all subjects have completed all research-related interventions; and the research remains active only for long-term follow up of subjects; or
  - (b) Where no subjects have been enrolled and no additional risks have been identified; or

(c) Where the remaining research activities are limited to data analysis

- (9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (ii) through eight (viii) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and not additional risks have been identified.

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.

#### **b) 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 does 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 subjects, 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.

#### **c) 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.

#### **d) 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).

The IRBMED Regulatory Team 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.](#)

#### e) Limitations of Use of Expedited Review

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

- identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability;
- would be damaging to the subjects' financial standing, employability, insurability, or reputation; and/or
- would be stigmatizing, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.;
- research is classified; 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.](#)

#### f) Demonstration/Flexibility Projects

Research demonstration/flexibility projects allow for the addition of expedited review

categories for research that are not federally sponsored or FDA regulated and meet other qualifying criteria. Refer to [Innovation and Demonstration](#) website.

## 6. Criteria for IRBMED Approval

Regulations at 45 CFR 46.111 (Common Rule) or 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 subjects 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[i])”. *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 subjects, the IRBMED considers the following:

- The PI’s assessment of the subjects’ 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 subjects 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.I.](#)

**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 subject population;

- the purposes of the research;
- the setting in which it will be conducted;
- the recruiting methods and materials used; and
- the subject 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 benefitting 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 subjects or the groups to which they belong. Non-English-speaking subjects should not be systematically excluded because of inconvenience in translating ICDs. The IRBMED should also ensure that subjects 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 subjects 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.III.A](#)

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

##### (1) General Requirements

Refer to [IRBMED SOP Part 11](#)

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

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 subjects, 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 subjects 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 subjects' 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 subject in research unless the PI has obtained the legally effective informed consent of the subject or the subject'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 subject 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 subject (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 subject 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 subject or the subject'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.IV.C](#)

Federal regulations (45 CFR 46.402 and 21 CFR 50.3(n)) require that IRBMED determine that adequate provisions are made for soliciting the assent of children involved as study subjects 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 subject or the subject's LAR in the presence of a witness. For subjects who do not speak English, the witness must be conversant in both English and the language of the subject.

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

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

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

<b>Short Form Consent Requirements</b>				
	<b>Subject</b>	<b>Translator (when needed)</b>	<b>Researcher</b>	<b>Witness</b>
<b>Forms Required to Sign</b>	Short form	Recommended but not required UNLESS also serving as the witness or the researcher	Oral script	Short form and oral script
<b>Forms Required to Receive or Keep</b>	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 subject or subject'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

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 appropriate conditions of 45 CFR 46.116(c) or (d) are satisfied and the research is not under FDA oversight.

Waiver of informed consent may be approved by the IRBMED only if it finds and documents that:

- The research involves no more than minimal risk to subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably (i.e. feasibly) be carried out without the

waiver of alteration; and

- Whenever appropriate the subjects will be provided with additional pertinent information after participation.

Alternatively, the IRB may approve a waiver or alteration of consent if it determines and documents that:

- The project is to be conducted by or subject to the approval of state or local government officials; and
- The project is designed to study, evaluate, or otherwise examine:
  - Public benefit or service programs;
  - Procedures for obtaining benefits or services under those programs;
  - Possible changes or alternatives to those programs or procedures; or
  - Possible changes in methods or levels of payment for benefits or services under those programs; and
- The research could not practicably be carried out without the waiver or alteration.

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 subjects, IRBMED may waive the requirement to obtain parental permission if it determines and documents that:

- The research involves no more than minimal risk to the subjects;
- The waiver or alteration does not adversely affect the rights and welfare of the subject;
- The research cannot practicably be carried out with the waiver or alteration;
- When appropriate, the subjects will be provided with additional pertinent information after participation; and
- The research is not FDA-regulated.

Alternatively, the IRBMED may waive the requirement to obtain parental permission if it determines and documents that:

- The research is designated for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects;
- An appropriate mechanism for protecting the children who will participate as subjects is substituted; and
- 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 subjects’ 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

subjects if the requirements of 45 CFR 46.117(c) and/or 21 CFR 56.109(c)(1) are satisfied:

- The only record linking the subject and the research would be the ICD and the principal risk would be potential harm resulting from a breach of confidentiality (in which case each subject must be offered the opportunity to receive the documentation); or
- The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

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 subject verbally or by electronic or printed text. Even though subjects do not sign a document, the IRBMED may still require that subjects be provided with written information about the study. The text of the written or oral informed consent scripts and any informational documents provided to subjects must be reviewed and approved by the IRBMED before their use.

#### Emergency Research Exception from Informed Consent (EFIC)

Refer to [HRPP OM Part 3.III.C.6.e.iii.](#)

Refer to [IRBMED Guidance – Emergency Research with Exception From Informed Consent](#) on the IRBMED website.

Refer to [IRBMED Position Statement January 11, 2007](#) on the IRBMED website.

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

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 subjects 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 under 21 CFR 50.24 for an EFIC project each of the following:

- (i) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

- (ii) Obtaining informed consent is not feasible because:
- The subjects will not be able to give their informed consent as a result of their medical condition;
  - The intervention under investigation must be administered before consent from the subjects' LAR is feasible; and
  - There is no reasonable way to prospectively identify the individuals likely to become eligible for participation in the clinical investigation.
- (iii) Participation in the research holds out the prospect of direct benefit to the subjects because:
- Subjects are facing a life-threatening situation that necessitates intervention;
  - Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
  - Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
- (iv) The clinical investigation could not practicably be carried out without the exception from informed consent requirements.
- (v) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the Principal Investigator has committed to attempting to contact a LAR for each subject within that window of time and, if feasible, to asking the LAR contacted for consent within that window rather than proceeding without consent. The Principal Investigator summarizes efforts made to contact the LAR and makes this information available to the IRBMED within fourteen (14) business days of each subject enrollment without consent.
- (vi) The IRBMED reviews and approves informed consent procedures and an acceptable informed consent document. These procedures and the informed consent document are to be used with subjects or their LAR in situations where use of such procedures and documents is feasible. The IRBMED reviews and approves procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation.
- (vii) Additional protections of the rights and welfare of the subjects will be provided, including, at least:
- Consultation (including, where appropriate, consultation carried out by the IRBMED) with representatives of the communities in which the

clinical investigation will be conducted and from which the subjects will be drawn;

- Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
- Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study (including the demographic characteristics of the research population) and its results;
- Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
- If obtaining informed consent is not feasible and a LAR is not reasonably available, the Principal Investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a LAR, and asking whether he or she objects to the subject's participation in the clinical investigation. The Principal Investigator will summarize efforts made to contact family members and make this information available to the IRBMED within fourteen (14) days of subject enrollment without consent.

(4) Research Subject to FDA Regulations – Waiver or Alteration of Informed Consent

Refer to [HRPP OM Part 3.III.C.6.e.iv.](#)

(5) Research Subject to Both HHS and FDA Regulations

Refer to [HRPP OM Part 3.III.C.6.e.v.](#)

(6) Research Subject to HIPAA Regulations

Waiver of HIPAA Authorization

Under HIPAA, researchers must obtain written authorization from a research subject for release of protected health information that the researcher will collect, use or disclose for the study.

A PI may submit for review and approval a waiver of HIPAA authorization for the use and disclosure of PHI for research purposes, which may include a database or registry, or other human subject 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)

Depending on the type of submission (e.g., independent of or as part of an initial application in eResearch), the Privacy Board or full convened IRBMED Board may approve a waiver only if both of the following criteria are met:

- The project has been submitted to the IRBMED for review and has been deemed to be exempt from ongoing IRBMED oversight; and
- The use or disclosure of PHI for the project involves no more than minimal

risk of harm to the privacy of individuals. This criterion may be met where all of the following elements are present:

- An adequate plan is in place to protect patient identifiers and PHI from improper use and disclosure; and
- An adequate plan is in place to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a Privacy Board-approved health or research justification for retaining the identifiers or such retention is otherwise required by law; and
- Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure would be permitted by HIPAA; and
- The Waiver of Authorization will not adversely affect the rights and welfare of the subjects; and
- The research could not practicably be conducted without the Waiver of Authorization; and
- The research could not practicably be conducted without access to and use of the PHI; and
- Whenever appropriate, the subjects (including their physicians, as applicable) are provided with additional pertinent information after participation; and
- 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.

### Privacy Board

The Privacy Board operates under the authority of and in accordance with HIPAA (45CFR164) and applicable University policies and procedures.

The Privacy Board is authorized to review and approve, if found to be in compliance with the requirements of these SOPs and HIPAA, the following:

- Waivers of authorization for research not subject to the Common Rule, or exempt from IRBMED oversight under the Common Rule, including waivers in connection with development and maintenance of research databases and registries;
- Investigator's application for Certification Preparatory to Research for reviews of protected health information;
- Information (PHI) preparatory to research submitted in the eResearch application (also known as "pre-review of clinical data sets" in the initial application in eResearch);
- Investigator's application for Certification Preparatory to Research for research involving decedents' PHI submitted in the eResearch application;
- In consultation with other units (e.g., the UMHS Privacy Office and DRDA), any use or disclosure of limited data sets under data use agreements; and
- Waivers of Authorization for research may also be granted by the IRBMED Board as part of a review for a project under IRBMED jurisdiction.

### Privacy Board Membership

Privacy Review Board Membership includes, but is not limited to, the following members:

- *Chair* – The Privacy Board Chair is an experienced and active member of the IRBMED and is well-informed concerning the laws, regulations, and University policies and procedures that govern the use or disclosure of protected health information in connection with human subjects' research.
- *Voting member(s)* – The Privacy Board shall include at least one member who is a "Community Representative", who is not affiliated with UM or any entity conducting or sponsoring the research, and who is not a family member (e.g., spouse, domestic partner or dependent) to any person affiliated with the University or an entity conducting the research.

#### Procedures for Waiver of Patient Authorization

All applications for Waiver of Authorization require review by the Privacy Board or by the convened IRBMED board where the request is part of an initial application, unless eligible for expedited review. All other applications will be reviewed and approved by the IRBMED Director or designated Privacy Board Administrator, unless consultation with other units (i.e., the UMHS Privacy Office or ORSP) is necessary.

Upon receipt of an application from a PI requiring Privacy Board review the regulatory staff will forward a complete set of documents (in electronic and/or printed form) directly relevant to the application to the Privacy Board members. All of the project documents shall be made available to Privacy Board members and authorized consultants for advance review.

Prior to the Privacy Board meeting, the regulatory staff may request from the PI additional information or documents, or explore proposed revisions that may be required as a condition of Privacy Board approval of the project.

The designated regulatory staff member will present the project to the Privacy Board membership at a convened meeting, unless approval is expeditable as provided below.

An application for Waiver of Authorization for Use or Disclosure of PHI in connection with a research project may be approved by expedited review if the research involves no more than minimal risk of violation of the privacy of the individuals who are the subject of the research for which use or disclosure is being sought. Expedited review may be carried out by the Chair or any member of the Privacy Board as designated by the Chair.

A reviewer has the authority to approve an expeditable project without a vote of the convened Privacy Board. If the reviewer believes that the application is not suitable for expedited review, the reviewer shall defer any decision and instead submit the application to a full review by the Privacy Board.

All applications approved by expedited review are available to the Privacy Board Members, the UMHS Privacy Office, and authorized consultants on an ongoing basis via eResearch.

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.

#### f) Data Monitoring

Refer to [HRPP OM Part 7.II.](#)

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 subjects.

(1) Considerations for the Imposition of Special Monitoring Requirements

The IRBMED may, at its discretion, perform monitoring or request monitoring from the Office of Human Research Compliance Review (OHRCR) – via UMOR– of a project; in addition to information received through the initial application, any amendments, annual continuing reviews, and analyses of interim reports, such as adverse events and audit reports. 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 subjects, or to follow the research progress on controversial subject matter. The IRBMED may also consider 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 access to any or all of the following from the PI:

- Signed informed consent documents;
- Site visits to research locations;
- Shortened approval periods and/or interim scheduled reports from the Principal Investigator during the approval period;
- Interviews with subjects;
- 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/Protection of Human Subjects (45 CFR 46):  
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>

Refer to Food and Drug Administration (FDA)/Protection of Human Subjects (21 CFR 56): <http://www.fda.gov/oc/ohrt/irbs/appendixc.html>

Refer to Health Insurance Portability and Accountability Act (45 CFR Parts 160 and 164): <http://www.hhs.gov/ocr/privacy/hipaa/administrative/index.html>

Refer to University of Michigan Website Guidance for Sensitive Human Subjects Data: <http://safecomputing.umich.edu>



To approve research, the IRBMED must determine that, where appropriate, there are adequate provisions to protect the privacy of subjects 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.IV.](#)

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

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 (21 CFR 50.20);
- 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 (21 CFR 50.20).

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 references to guidance for determining the nature of requirements applicable to Michigan and to research proceeding outside of Michigan.

Refer to HRPP OM Part 11.II for a detailed description on Michigan requirements and guidance for determining the nature of requirements applicable to research proceeding outside of Michigan.

#### i) Test Article Accountability Procedures

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.i](#)

IRBs will determine that research studies have the resources necessary to protect subjects by evaluating all of the following:

- There is adequate time for the investigators to conduct and complete the research;
- There are an adequate number of qualified staff;
- 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 subjects; and
- Medical or psychosocial resources that subjects 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 [HRPP OM Part 3.III.C.7.](#)

Refer to [IRBMED SOP Part 8](#)

Refer to [IRBMED SOP Part 12.II.G](#)

## D. IRB Administrative Functions

### 1. IRBMED Meetings

- 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 subjects, 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, the SOPs must include details of any process, such as expedited review procedures (as described above) or subcommittee procedures, which 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). 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) Although it is preferred that IRB meetings take place with all participating members physically present, an IRB may establish protocols to convene meetings via video conference, teleconference or similar means. Such protocols must provide a means for all participants to receive the meeting materials prior to the meeting and facilitate active and equal participation in the discussion of all protocols. The protocols must further provide that minutes from meetings convened in this manner will reflect that these two conditions have been met, in addition to other mandated information (e.g., presence of a quorum including at least one non-scientist, discussion and resolution of problematic issues, final vote).

### 2. Notification of Decisions

- a) An 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) An 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

Reports Uploaded into eResearch

The following documentation associated with eResearch submissions, determinations and tracking will be either uploaded (and permanently archived) to the appropriate submission itself, or via AE (Adverse Event Report) or ORIO (Other Reportable Information or Occurrences) Reports:

- AEs are reported according to the AE Reporting guidance available on the IRBMED Website;
- Statements of significant new findings provided to subjects;
- 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;
- Description of action taken by a reviewer;
- Records of continuing review activities
- Progress reports submitted by PIs;
- Submission approval letters;
- 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 and protocol-specific findings justifying those determinations for:
    - a. Waiver or alternation 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.

#### Reports and Communications Archived on Network

- A membership roster of the current IRBMED members (and alternates) and 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.
- Written SOPs
- Documentation of member and staff training.

#### Retention

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 subject 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.

#### 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](#)

#### SOPs

The IRBMED cooperates with the Medical School Associate Deans for Research and Regulatory Affairs, UM Health System (UMHS) Compliance Committee, and the OVPR to establish, review, and revise these SOPs. These SOPs and any substantive revisions thereto, are subject to review and approval by the Medical School Associate Deans for Research and Regulatory Affairs, UMHS Compliance Committee, 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 OVPR 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 reviewed at least once every five (5) years in conjunction with the AAHRP accreditation cycle. UMOR initiates a comprehensive review of the HRPP Operations Manual at the same time. IRB SOPs must make provisions for such a review of SOPs on the same cycle, or more frequently, at the IRB's discretion.

Revisions to SOPs may be made at any time, as required by changes in law, ethical standards, institutional policy, quality assurance activities or other considerations.

Substantive revisions require advance approval by the HRPP Director.

IRBMED SOPs are conducted by the Medical School Associate Deans for Research and Regulatory Affairs, UMHS Compliance Committee, and UMOR.

#### Internal Quality Assurance

The IRBMED routinely conducts internal review of its staff and board member operations, as well as reviewing the human subject research application (eResearch) operations, as part of its continuous quality improvement efforts, in order 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;
- Consultation services by the Chairs, members, or staff, followed by requests for feedback regarding these consultative meetings;
- Peer assessment;
- Periodic checks for quality improvement;
- Review by other institutional units, such as OHRCR.

#### **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 review process of submitted eResearch applications, the IRBMED Regulatory Teams (Senior Associate Regulatory Analysts (SARAs), Junior Associate Regulatory Analysts (JARAs) and Associate Regulatory Analysts (ARAs)) or other qualified IRBMED staff members assess whether the project meets the definition of human subjects 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 or the PI may request IRBMED review to confirm the not-regulated status.

Applications submitted in eResearch as “Projects Not Regulated as Human Subjects Research” may also be reviewed by the HIPAA Privacy Board Coordinator for appropriate determinations. PIs may contact the IRBMED Privacy Board Members, IRBMED Chairs or Directors for 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, only IRBs are permitted to issue an exempt determination.

The IRBMED reviews exempt applications to assure that human subjects 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 six federal exemption categories, U-M permits IRBs to issue exemptions to qualifying research under additional categories. These are described at the [HRPP Innovation and Demonstration website](#) and defined as:

- Exemption 2a (minimal risk interventions are permitted in association with data collection)
- Expansion of Exemption 5 (to accommodate research sponsored by the State of Michigan)
- Exemption 7 (for analysis of identifiable data).

**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 46.101(b) 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. Exempt 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 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 and Cooperative Research

*University research generally must be approved or declared exempt by a University IRB. This section describes the scope of jurisdiction of the various University IRBs and policies on cooperative research and ceded review.*

### I. UNIVERSITY OF MICHIGAN IRB JURISDICTION

Refer to [HRPP OM Part 5.I.](#)

#### 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

##### 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 schools, colleges, units or programs not subject to IRBMED jurisdiction. These include but are not limited to:

- U-M Institutional Research
- College of Architecture and Urban Planning
- College of Engineering
- College of Literature, Science, and the Arts
- College of Pharmacy
- Institute for Social Research (ISR)
- Ford School of Public Policy
- Law School
- Mary A. Rackham Institute
- Rackham Graduate School

- Ross School of Business
- School of Dentistry
- School of Education
- School of Information
- School of Music, Theatre, and Dance
- School of Natural Resources and Environment
- School of Kinesiology
- School of Nursing
- School of Public Health
- School of Social Work
- Stamps School of Art and Design
- University Health Services
- University of Michigan Transportation Institute (UMTRI)

**2. Exceptions**

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. IRB-Dearborn**

**1. Primary Jurisdiction**

- a)** All research conducted by faculty, staff, students or other trainees with a primary appointment at U-M-Dearborn

**D. IRB-Flint**

**1. Primary Jurisdiction**

- a)** All research conducted by faculty, staff, students or other trainees with a primary appointment at UM-Flint

**E. General Exceptions**

- 1.** In any case where the IRB with primary jurisdiction does not have the appropriate expertise or is not appropriately constituted (e.g. prisoner representative) to review a research proposal, the project may be transferred to the IRB with appropriate expertise for review and approval.
- 2.** In those instances in which 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.** In those instances in which another 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 IRB Council for a determination.

The IRB is also authorized, in its discretion, to invite individuals 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.II.A-D](#)

- A. Engagement in Human Research
- B. Default Position on Outside Entities Engaged in University Research: Avoiding Duplicate Review
- C. Researcher and IRB Responsibilities with Regard to Performance Sites not Engaged in Research
- D. Special University IRB Responsibilities for Multi-Site Research in Which the University Is Involved

## III. COORDINATED OR JOINT REVIEW

- A. IRB-of-Record

Refer to [HRPP OM Part 5.IV.A](#)

- B. Responsibilities of the HRPP and Local IRB in Multi-Site Research

Refer to [HRPP OM Part 5.IV.B](#)

## IV. UNAFFILIATED INVESTIGATORS

Refer to [HRPP OM Part 5.V](#)

## V. RESEARCH INVOLVING COMMUNITY MEMBERS IN THE RESEARCH PROCESS

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](#).

##### 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.III](#)

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](#)

### 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 – Position Statement for Emergency Research with Exception from Informed Consent](#).

Refer to [IRBMED SOP Part 3](#)

3. Principal Investigator Responsibilities

Refer to [HRPP OM Part 6.II.A](#)

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

4. Sponsor-Investigator

Refer to [HRPP OM Part 6.II.B.2](#)

Refer to [IRBMED Guidance – Investigational Device Exemption \(IDE\) Application and Investigational New Drug \(IND\) Application](#).

5. Manufacturers

Refer to [HRPP OM Part 8](#)

6. [Guidelines for Good Clinical Practice \(GCP\) of the International Conference of Harmonization \(ICH\)](#)

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 OHRCR 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](#).

## 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](#)

### II. DATA AND SAFETY MONITORING PLANS AND BOARDS

Refer to [HRPP OM Part 7.II](#)

The IRBMED offers a workshop 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 subjects, NIH multi-site clinical trials and higher risk, Principal Investigator (PI)-initiated studies.

The IRB may require PIs to submit a DSMP before approving an initial or amended application, or may require one in response to an adverse event or other report.

Also, see IRBMED educational information [here](#).

### III. PAYMENT TO RESEARCH SUBJECTS

Refer to [HRPP OM Part 7.III](#)

Refer to <http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/payment-research-subjects>.

Refer to [Human Subject Incentive Program Standard Practice Guide \(HSIP SPG 501.7\)](#).

### IV. VULNERABLE SUBJECTS

Refer to [HRPP OM Part 7.IV. A-D](#)

Refer to [IRBMED SOP Part 11.III. 2. A](#)

Refer to [IRBMED Guidance](#).

Refer to [IRBMED Education](#).

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 <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartb>

Refer to [HRPP OM Part 7.IV.A](#)

#### B. Research Involving Prisoners

Refer to [IRBMED Guidance: Incarcerated Subjects](#)

Refer to [IRBMED Guidance: Prisoners](#)

Refer to <http://www.hhs.gov/ohrp/policy/index.html#prisoners>

Refer to [HRPP OM Part 7.IV.B](#)

#### 1. IRB Composition

IRBMED is permanently constituted with a 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 subject requires participation in the research prior to fulfillment of all requirements as described in federal guidance at <http://www.hhs.gov/ohrp/policy/prisoner.html> and <http://answers.hhs.gov/ohrp/categories/1568>.

#### C. Research Involving Children

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

Refer to [IRBMED Assent Guidelines](#)

Refer to [IRBMED Guidance: Wards](#)

Refer to [HRPP OM Part 11.II. A.2](#)

Refer to [HRPP OM Part 7.IV.C](#)

#### D. Research Involving Adults with Cognitive Impairment or Otherwise Impaired Decision-making Capacity

Refer to [HRPP OM Part 7.IV.D](#)

#### V. COMPENSATION FOR INJURIES

Refer to [HRPP OM Part 7.V](#)

Refer to [OHRP "Exculpatory Language" in Informed Consent](#)

Refer to [UM Clinical Research Calendar Review & Analysis Office \(CRAO\)](#)

#### VI. ADVERTISING MATERIALS

Refer to [HRPP OM Part 7.VI](#)

Refer to [IRBMED Guidance: Advertising Materials](#)

Refer to <http://www.hhs.gov/ohrp/policy/clinicaltrials.html>

Refer to <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm>



## 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 [IRBMED Guidance – Investigational New Drug Application](#)

#### B. Investigational Devices

Refer to [HRPP OM Part 8.II.B](#)

Refer to [IRBMED Guidance – IDE Application](#)

##### 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](#)

#### 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](#)

**B. Expanded Access to Investigational Devices**

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

1. Treatment IDE

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

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

2. Compassionate Use (Devices)

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

3. Humanitarian Use (Devices)

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

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.

c) Also refer to [IRBMED Guidance – HUD Requirements for Physicians and Investigators.](#)

4. Continued 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. FDA SPONSORS AND SPONSOR-INVESTIGATORS**

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

**VII. INVESTIGATOR AND IRB RESPONSIBILITIES FOR FDA-REGULATED RESEARCH**

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

**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](#)

Refer to [IRBMED Website – Electronic Signature-Part 11 Compliance Certification](#),

**F. Records and Documentation**

Refer to [HRPP OM Part 8.VIII.F](#)

When a subject withdraws from a clinical trial, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed. The informed consent document cannot give the subject the option of having data removed. In the case of a subject's withdrawal, the subject may either consent to follow up (non-interventional, non-invasive) or not. If the patient wishes to provide continual follow-up, the researcher must obtain the subject's consent for this limited participation if it was not described in the original informed consent document.

For further information, refer to [FDA Guidance](#).

**G. Required Reporting**

Refer to [HRPP OM Part 8.VIII.G](#)

**H. ICH-E6 and GCP**

Refer to [HRPP OM Part 8.VIII.H](#)

**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**

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

- IRB review and approval is not required prior to or after administration of the investigational agent.

- Identifiable private information regarding the use may be collected and submitted to the required federal authorities (e.g., FDA, CDC, or Homeland Security).

Contact the IRBMED for additional information, if needed. Also see the FDA Guidance Document [Emergency Use Authorization of Medical Products](#).

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 subjects 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 <http://www.med.umich.edu/u/coi/index.htm>

#### 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 <http://www.med.umich.edu/u/coi/index.htm>.

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 OVPR, Medical School Conflict of Interest Boards, 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.](#)*

## 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 [IRBMED ICD 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. LEGAL AND REGULATORY BODIES

Refer to [HRPP OM Part 11.I](#)

### II. LAWS, REGULATIONS, AND STANDARDS COMMONLY APPLICABLE TO RESEARCH

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 subject research and healthcare law.

Refer to [HRPP OM Part 11.II](#)

#### A. Informed Consent and Legally Authorized Representatives

##### 1. General Requirements for Informed Consent

Refer to [HRPP OM Part 3.III.C.6](#) for information on the detailed explanation of the elements of informed consent.

Refer to IRBMED Guidance – [Non-English-Speaking Subjects](#)

Refer to IRBMED Guidance – [Informed Consent](#)

Refer to IRBMED [Informed consent templates](#).

##### 2. Who May Give Consent

###### a) Children as Subjects

For research involving children, the IRBMED will, as it deems necessary, seek the additional expertise of consultants to assist in fully evaluating the research proposal.

In order to approve DHHS-funded research or research involving test articles that involves children as subjects, the IRBMED must apply the regulatory components of 45 CFR 46 Subpart D or 21 CFR 50 Subpart D. For research not funded by DHHS, the IRBMED complies with Subpart D in its deliberations, but may also utilize other comparable ethical guidelines, policies, or procedures.

The IRBMED shall determine whether the Principal Investigator (PI) has outlined adequate provisions for obtaining any necessary assent for the children and permission from parents/guardians according to 45 CFR 46.408 or 21 CFR 50.55. When research is funded by the Department of Education and conducted in public schools, additional regulatory requirements such as the Protection of Pupil Rights Amendment and the Family Educational Rights and Privacy Act may need to be considered.

The IRBMED will assess the PI's recruitment strategies, the environment for assenting, the additional resources to assist in the process (e.g., videos, books, and



pictures), and the age of the subjects in assessing the capacity of the child to understand the nature of the research.

The IRBMED will assess the adequacy of plans to obtain the permission of the parents/guardians according to 45 CFR 46.408(b) and (c) or 21 CFR 50.55 (e), including the instances in which both parents must provide permission and instances in which the requirement to obtain permission should be waived in order to protect the subject.

#### (1) Evaluation of Assent

Assent is defined in 45 CFR 46.402 (b) as "...a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent," and in 21 CFR 50.3 (n) as "...a child's affirmative agreement to participate in a clinical investigation. Mere failure to object may not, absent affirmative agreement, be construed as assent."

The IRBMED uses its best judgment, on a study-specific basis, to ensure that the assent is tailored to the level of comprehension of the prospective participants:

- Under age 6, assent is not generally sought.
- Ages 7-9, verbal or simple written assent.
- Ages 10-12, simple written assent.
- Full written assent, mirroring the parental permission document may be appropriate for children older than 14.

Federal regulations do not cite any specific elements of assent or an age above which assent should be possible.

When appropriate, assent will be sought from prospective subjects before enrollment in the protocol in a manner that minimizes the likelihood of coercion or undue influence and will be documented in the manner determined by the IRBMED.

The IRBMED compares the assent materials with the study protocol or application to determine the correctness of the information.

The IRBMED evaluates the procedures for obtaining assent, including the individual who will conduct the assent process. The IRBMED is granted wide discretion in determining whether children are capable of assenting and when discretion for assessing the capability of particular children to assent will be granted to investigators or others (e.g., social workers, teachers, or parents). When assent has been required for a study overall, the IRBMED can waive the requirement for assent of a particular child if the investigator provides evidence to the IRBMED that the child is not capable of assent. Investigators should contact the IRBMED Co-Chair on-call for this permission and report the exception to the IRBMED using the ORIO deviation form.

The IRBMED can grant waivers of child assent or documentation of assent if the research meets the regulatory criteria set forth in 45 CFR 46.408(a) or 21 CFR 50.55(d).

#### (2) Evaluation of Parental Permission

Generally, a parent (the child's biological or adoptive parent) or guardian (an individual who is authorized under applicable state or local law to consent on

behalf of the child) must agree to the child's participation in the research. If a child is a ward of the state (e.g., foster child) the [guidance on the IRBMED website](#) must be followed.

IRBMED assesses the procedures and appropriateness of the parental permission process. The IRBMED can grant waivers of parental permission if the research both meets the regulatory criteria set forth in 45 CFR 46.116 and does not fall under the FDA's definition of "clinical investigation", as defined under 21 CFR 56.102(c). Research subject to FDA oversight can be granted a partial waiver of parental permission to review medical records or otherwise obtain information necessary to recruit subjects.

21 CFR 50.24 allows the IRBMED to approve a waiver of parental permission for FDA research that has fulfilled all the requirements set forth in that regulation. See the IRBMED's [Position Statement of IRBMED on Allowing Exception From Informed Consent for Emergency Care Research January 11, 2007](#).

45 CFR 408(c) also includes provisions for waiving parental permission in research that is designed for conditions or a subject population where parental or guardian permission is not a reasonable requirement to protect subjects (e.g., research on neglected or abused children). The IRBMED will not allow a waiver of documentation of parental permission if the research is subject to FDA oversight.

The IRBMED may allow a waiver of documentation of parental permission if the research meets the regulatory criteria set forth in 45 CFR 46.117 or 21 CFR 56.10r(c)(1).

The specific requirements for obtaining parental permission for HHS conducted or funded studies are found at 45 CFR 46.406 and 46.407. *See also:*

- IRBMED Assent guidance (under "[Children in Research](#)").
- IRBMED [Wards of the State](#) guidance.

**b) Research Involving Adults with Cognitive Impairment or Otherwise Impaired Decision-Making Capacity**

When reviewing the informed consent process for research involving decisionally-impaired adults, the IRBMED considers additional assessments in order to ascertain whether the subjects are vulnerable to coercion or undue influence and whether these risks have been minimized. Adults may have decisional impairment due to conditions such as stroke, brain injury, or mental illness such as schizophrenia or depression. Decisional impairment is reflected in a diminished ability to reason and make sound choices. This impacts the subjects' capacity to provide full, effective informed consent. Some decisional impairment may be transient, whereas other forms are permanent. Individuals with transient impairments may be able to provide consent during lucid intervals, but those intervals may not coincide with the conduct of the research. Lesser degrees of impairment may also allow some prospective subjects to consent to participation, while individuals with more severe degrees of impairment are not competent to consent.

In addition to the usual requirements, the IRBMED assesses the informed consent document and process as outlined by the PI to assure that:

- Adequate assurances are in place to assess the prospective subject's understanding of the research.

- The consent document is written at a language/readability level appropriate to the subject.
- If the subject is likely to be unable to read, that there are provisions, compliant with informed consent requirements, to provide for an oral presentation of the informed consent materials.

The IRBMED may consider the following to provide additional assurances to the integrity of the informed consent process:

- Monitoring of the informed consent process by a third party.
- Obtaining an independent assessment of the prospective subject's cognitive capacity.
- If the subject is unable to provide legally effective informed consent, the PI should outline a plan to obtain assent from the subject and informed consent from a legally authorized representative (LAR).
- The PI should use open-ended questions to assess the individual's understanding of the goals of the study and its risks and benefits.

### c) Wards

Additional state and federal requirements exist for all research involving children who are wards of the state or another entity. Investigators must follow the IRBMED guidance on [Research on Wards of the State](#). If the research falls under 45 CFR 46.406 or 46.407, or 21 CFR 50.53 or 50.54, and research does not present a potential of direct benefit to the subjects, the wards may participate only if the research meets the provisions of 45 CFR 46.409 or 21 CFR 50.56. In such cases, the IRBMED will require an advocate to be appointed for each child and will ask the PI for verification of the appointment. Specific instructions are in the guidance noted above.

### d) Legally Authorized Representatives

If subjects are initially capable of providing informed consent, but it is likely that they will lose this capacity during the conduct of the research study, they should be encouraged to appoint a LAR or durable power of attorney while they are capable. Once their appointment becomes legally effective, the representative can consent to continued participation, amendments to the study, or decide to end the subject's participation in the research.

The IRBMED will review the study procedures to assure that the PI has a plan to inform the LAR about the study, its implications for the subject, and their role in providing initial and ongoing consent.

Michigan law describes who is authorized to consent for particular medical interventions.

For a detailed discussion of who may consent for whom under various circumstances, consult [HRPP OM Part 11.II.](#)

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

Refer to [HRPP OM Part 11.II.B](#)

Refer to <http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/record-keeping-guidelines>.

Refer to [IRBMED SOP Part 8.VII.F.](#)

1. Protection of Subject Privacy and Data Confidentiality

The IRBMED will ensure that the research plan contains adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. See [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.

2. Research Involving Use or Disclosure of Patient Health Information

Refer to [HRPP OM Part 11.II.B.2](#)

3. Research Involving Student Records

Refer to [HRPP OM Part 11.II.B.3](#)

4. Research Involving Department Education-funded Surveys, Analysis, or Evaluation

Refer to [HRPP OM Part 11.I.A.6](#)

5. Mandatory Disclosure Requirements

Refer to [HRPP OM Part 11.II.B.4](#)

6. Protecting Against Disclosure: Certificates of Confidentiality

Refer to [HRPP OM Part 11.II.B.5](#)

C. Research Involving Prisoners and Other Detained Persons

Refer to [HRPP OM Part 7](#)

Refer to [HRPP OM Part 11.II.C.](#)

See also the [guidance on prisoners.](#)

D. Research Involving Pregnant Women, Fetuses, and Neonates

Refer to [HRPP OM Part 7](#)

Refer to [HRPP OM Part 11.II.D.](#)

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

1. Generally (including Investigator Responsibilities)

Refer to [HRPP OM Part 11.II.F.1](#)

Refer to [IRBMED SOP Part 3.III.F](#)

Refer to [IRBMED Guidance – Recording Retention](#)

2. IRB Responsibilities

Refer to [HRPP OM Part 11.II.F.2](#)

Refer to [IRBMED SOP Part 3.III.F.](#)

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

*Refer to [HRPP OM Part 11.II.G](#)*

**H. Clinical Trials Disclosure Requirements**

*Refer to [HRPP OM Part 11.II.H](#)*

**III. ACCESS TO LEGAL COUNSEL**

*Refer to [HRPP OM Part 11.III](#)*

## Part 12 - Quality Assurance and Research Compliance

*This section describes the University's quality assurance, quality improvement, and enforcement activities.*

### I. QUALITY ASSURANCE: ASSESSMENT AND IMPROVEMENT

#### A. Performance Measurement and Quality Assessment

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

#### B. Quality Improvement

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

### II. COMPLIANCE OVERSIGHT

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

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

If information brought to the attention of the IRBMED, through any source, indicates the possibility that research subjects 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 Principal Investigator (PI) or Principal Investigator's research staff, or suspension or termination of the project] appears necessary. In some circumstances, in consultation with the IRBMED, the Principal Investigator may place a voluntarily "hold" on new subject accrual or research-related interventions during the fact-finding period, unless to do so would place subjects in immediate harm or otherwise jeopardize their well being.

Under institutional authority and federal regulations (45 CFR 46.103[b][5], 45 CFR 46.113, 21 CFR 56.113), the IRBMED is responsible for overseeing the safety of human subject research participants and has the authority to suspend or terminate human subject research that is (1) not being conducted in accordance with the federal and IRBMED's requirements or (2) has been associated with unexpected serious harm to subjects.

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

1. Should the allegation of noncompliance pose immediate risk to subjects, the IRBMED Director will notify the IRBMED Chairs, the Medical School Associate Dean for Regulatory Affairs, the Health System Legal Office, and the Office of the Vice President for Research (UMOR) immediately.
2. 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 OHRCR. 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:

- Providing IRBMED with copies of or access to:
  - Signed informed consent documents
  - Study files
  - Drug dispensement logs/IDS 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 subjects

Upon completion of the review, the report is provided to the Chairs in the context of a Chairs and Director Meeting (CDM). The Chairs 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 IRBMED shall notify the Medical School Associate Deans for Research and Regulatory Affairs and the UMOR of any complaints or allegations of noncompliance, as required in [HRPP OM Part 12](#). If necessary, the UMOR will notify any applicable Federal Agency.

During the course of investigating an allegation of noncompliance, the IRBMED may request assistance from the OHRCR through the UMOR or the Health System Legal Office.

#### 1. Local Reports

The IRBMED staff maintains records of all complaints and allegations of noncompliance that come to the attention of the IRBMED. These records include communications with the complainant and other parties providing information to the IRBMED, copies of source documents and other information gathered during the fact-finding activity, analysis of the fact-finding results for presentation to IRBMED Chairs and board members, notes and minutes of Chair and board member deliberations and determinations, and communications with the PI and relevant study personnel.

The IRBMED Chairs and Medical School Associate Deans for Research and Regulatory Affairs are provided with any copies of case reports that are prepared for submission to the UMOR.

The IRBMED shall promptly notify the UMOR of (1) any unanticipated problems involving risks to subjects or others or any potentially serious or continuing noncompliance with institutional policy; and (2) any suspension or termination of IRBMED approval for a project. In certain instances of alleged or apparent noncompliance, the IRBMED may choose to provide an early preliminary report to the UMOR (i.e., where the noncompliance may pose immediate risk to subjects) prior to a determination of serious or continuing noncompliance. As described in the [HRPP OM Part 12](#), the UMOR may choose to further investigate the reports of serious or continuing noncompliance or to ask for additional review by the Office for Human Research Compliance Review (OHRCR). For situations reported to the UMOR for additional review and/or reporting, the Vice President for Research makes and reports the institutional conclusions and imposes any institutional sanctions or remediation requirements. Summaries of non-serious or non-continuing noncompliance concerns are reported by IRBs to the UMOR on a quarterly basis, as a way of monitoring the need for attention to policy or to education.

#### 2. Institutional Reports

Refer to [HRPP OM Part 12.II.H](#) which describes the obligations of the University to make additional reports outside the institution to sponsors and government authorities with jurisdiction.

## B. Noncompliance Review Procedures

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

### 1. Definitions

Refer to [HRPP OM Part 12.II.B.1](#)

### 2. Process Summary

Refer to [HRPP OM Part 12.II.B.2](#)

### 3. Rights of Faculty, Staff, or Others Accused of Noncompliance

Refer to [HRPP OM Part 12.II.B.3](#)

### 4. Assurances of Confidentiality

Refer to [HRPP OM Part 12.II.B.4](#)

### 5. Policy Against Retaliation for Reporting

Refer to [HRPP OM Part 12.II.B.5](#)

## C. How Compliance Concerns Are Brought Forward

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

Reports or allegations of noncompliance are brought forward by, but are not limited to, the following means:

- Telephone
- Via electronic mail (e-mail) communications
- Anonymous communications (telephone, mail, e-mail)
- UM Compliance Hotline (1-866-990-0111)
- Through staff or faculty of the UM

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

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

## E. Chair and Board Considerations and Determinations

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

If, according to the results of the IRBMED fact-finding, the alleged noncompliance is determined by the IRBMED Chairs or Director to be credible and potentially serious or continuing, the case is presented to the IRBMED Co- and Vice-Chairs collectively at the next available Chairs and Directors Meeting, not later than thirty (30) days from the fact-finding determination. In reviewing the alleged noncompliance, the Chairs 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 Chairs determine by vote whether or not the activity has (1) possibly caused injury or an unanticipated risk to subjects or others; or (2) possibly constitutes serious or continuing noncompliance with IRBMED determinations or federal regulations. Documentation of the outcome of a decision by the Chairs to refer the matter to the convened IRB will be sent to the Medical School Associate Deans for Research and Regulatory Affairs, the Health System Legal Office, and the PI.



If the convened IRB determines that the noncompliance was not serious and/or continuing, the Medical School Associate Deans for Research and Regulatory Affairs, the Health System Legal Office, and the PI will be notified. A finding of serious and/or continuing noncompliance as determined by the convened IRB will be sent to the PI, the Department Chair and Associate Chair for Research (if applicable), the Medical School Associate Deans for Research and Regulatory Affairs, the Health System Legal Office, and the UMOR. If, at the request of the Medical School or the UMOR, there is additional information or investigation needed, UMOR may request the assistance of OHRCCR. Any request for additional information or investigation will be assessed by OHRCCR for the amount of staff resources, time required, and the depth of review. The outcome of this assessment will be reported to the requesting party.

#### F. Actions of the Institutional Official

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

#### G. Response to Determinations of Noncompliance

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

The IRBMED Co-Chairs will convey the board's decision by telephone or e-mail to the Principal Investigator at the conclusion of the board meeting and vote as to whether or not the noncompliance constitutes serious and/or continuing noncompliance. A formal letter will be sent to the Principal Investigator outlining the reasons for the board's decision and any requested remediation, e.g., attendance at a designated IRBMED educational workshop(s).

#### **Monitoring Activities**

##### 1. Special Requirements for Monitoring the Conduct of Human Research

The IRBMED may monitor studies both for-cause (e.g., suspected noncompliance) and not-for-cause (e.g., random or risk-based review for quality assurance purposes). Monitoring may include, but is not limited to, accessing and reviewing any or all of the following:

- Signed informed consent documents
- Study files (protocol, approval letters, advertisements, etc.)
- Drug dispensement log/IDS logs
- Patient records
- Lab tests
- 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 subjects
- Study personnel logs

##### 2. Considerations for Imposition of Special Monitoring Requirements

The IRBMED may impose special requirements or restrictions on either a PI or a particular study. These may be imposed because of risk level, safety issues, conflict of interest issues, or because of findings of noncompliance.

#### **Examples of Special Monitoring Requirements**

Requirements or restrictions imposed on a PI, study team member or project may include, but are not limited to, any or all of the following:

- Requirement for education, certification in the conduct of clinical research, i.e., the Association of Clinical Research Professionals (ACRP) or the Society of Clinical Research Associates (SoCRA), and re-certification of PEERRS
- Less than 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 subject participation (e.g., after every third subject completes the trial or after the first three doses of an 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, from obtaining informed consent from subjects
- Prohibition, permanently or for a period of time, from conducting certain types of research
- Prohibition, permanently or for a period of time, from serving as a PI or study team member

#### H. Institutional Notification and Reporting Requirements

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

### III. OTHER REPORTABLE EVENTS (ADVERSE EVENTS, UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS OR OTHERS) AND SUSPENSION OR TERMINATION OF IRB APPROVAL

Refer to [HRPP OM Part 12](#) and the information below.

#### A. Background

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

#### B. Roles and Responsibilities

Refer to [HRPP OM Part 12.III.A.1](#)

##### 1. Researchers

As noted in the OM, guidelines and reporting procedures for reporting Adverse Events (AEs), Other Reportable Information or Occurrences (ORIOs), including those AEs and ORIOs that are also unanticipated problems involving risks to subjects or others, 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 workshops that review the guidelines and will consult with study teams as needed in order to assist PIs in understanding the reporting requirements. Failure to follow these guidelines may require the IRBMED to halt the study and/or the institution to report the noncompliance 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](#), which applies the most stringent reporting required by the FDA (21 CFR 312 and 812), NCI and NIH. Researchers who initiate an approved study using a standard adverse event 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.

For studies that do not involve investigational agents, and particularly for studies that are minimal risk, a study-specific plan is recommended. [Guidance for developing a study-specific plan](#) can be found on the IRBMED website.

2. The IRBs (Members, Consultants, and Staff)

Refer to [HRPP OM Part 12.III.A.2](#)

a) AEs, ORIOs and Unanticipated Problem Involving Risks to Subjects or Others (UaPs/UPIRSOs) Review Decisions

An essential element of human subject protection is identifying, analyzing the causes of, and responding appropriately to expected and unexpected AEs, as well as to UaPs/UPIRSOs. Principal Investigators are required to identify and help analyze the events and to formulate responses.

Adverse Events are events that involve physiological, social, legal, financial, or psychological harm to subjects or risks of harm to additional subjects or others. Adverse Events include expected and unexpected harmful effects, as well as unexpected risks of an interaction or intervention.

**Adverse Events may be caused by:**

- The test article or test procedure
- Other aspects of the interaction or intervention
- The subject's underlying condition
- The subject's concurrent standard treatment

**IRBMED board members consider the following when reviewing an AE report:**

- Principal Investigator'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/UPIRSO
  - Whether urgent communication with the PI, IRBMED director, UM Office of General Counsel, UMOR, or other authority or unit (e.g., whether risk management is required)
  - Safety of subjects (including whether the study should be halted or modified)
  - Risk/benefit assessment of the study
  - Impact of AE on subjects' willingness to participate in the study

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

- Whether AE/SAE type should be added to the ICD
- Whether previously enrolled subjects should be notified and/or re-consented

**IRBMED board members consider the following when reviewing an ORIO report:**

- Principal Investigator'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 UaPs/UPIRSOs
  - 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, Co- or Vice-Chair, UMOR or other authority is required
- Whether the report indicates that serious or continuing noncompliance may have occurred
- Whether the report indicates that an UaP/UPIRSO has been identified
- Safety of subjects (including whether the study should be halted or modified)
- Risk/benefit assessment of the study
- Impact of ORIO on subjects' willingness to participate in the study

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

- Whether event or information should be added to the ICD
- Whether previously enrolled subjects should be notified and/or re-consented

**IRBMED Board Members consider the following when reviewing an UaP/UPIRSO. Is the event:**

- 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 subject 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 subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

**The list of problems that require reporting in accordance with the above definition. Include:**

- Internal AEs that are unexpected, involve new or increased risks, and are related to the research.
- External AEs that are UaPs/UPIRSOs.
- Changes made to the research without prior IRB approval in order to eliminate apparent immediate harm.
- Other unanticipated information that is related to the research and indicates that subjects 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 IRBMED.
    - A paper is published from another study that shows that the risks or potential benefits of your research may be different than initially presented to IRBMED.
    - A breach of confidentiality.
    - Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
    - Change to the protocol taken without prior IRBMED review to eliminate an apparent immediate hazard to a research subject.
    - Incarceration of a subject in a protocol not approved to enroll prisoners.
    - Event that requires prompt reporting to the sponsor.
    - Sponsor imposed suspension for risk.
    - Complaint of a subject 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 subjects or others or that indicates subjects or others may be at increased risk of harm.

The review of problems reported by investigators. In this description, specify the following:

- The individual or individuals (by position or title) who are responsible for making an initial determination about whether a reported event is an UaP/UPIRSO.
- The information that reviewers receive to determine whether a reported event is an UaP/UPIRSO.

**IRBMED staff will consider the following when reviewing an AE, ORIO or UaP/UPIRSO report:**

- Whether urgent notification of the IRBMED Director, Health System Legal Counsel, a Co- or Vice-Chair, the Medical School Associate Deans for Research and Regulatory Affairs, UMOR, or other authority is required (e.g., whether to notify Co- or Vice-Chair of subject incarceration report)
- Completeness
- Whether necessary supporting documents are included
- Whether submission occurred within the required timeframe
- Whether the event or information is described in the currently approved informed consent document (when applicable)

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 UaP/UPIRSO.

**b) AEs, ORIOs, and UaP/UPRISOs Triage, Timelines, and Type of Review**

The workflow for review of AEs and ORIOs is described [here](#).

The workflow for possible UaPs/UPRISOs is found [here](#).

**The timelines for completion of review are dependent upon:**

- Whether the report is a UaPs/UPIRSOs
- The seriousness of the report
- Completeness of the report
- Openings on IRBMED meeting agendas for full-board reviews or Single IRB Member review workload

Generally, IRBMED staff open submissions for initial assessment within three (3) but no more than ten (10), business days from their arrival in the staff in-box. Requests for incomplete reports to be completed by the study team should be sent in a timely manner from the date of the initial assessment. However, if an incomplete report raises serious concerns, it may be sent to a designated reviewer while the missing information is being collected. Serious reports identified as possible UaP/UPIRSO will receive full board review as soon as possible, usually at the next available full-board IRB meeting. Non-serious reports identified as possible UaP/UPIRSO will receive standard assignment of a full-board meeting based on the available members and open agenda slot of that reviewer. 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 based upon that report, or if the report is judged to include potential UaPs/UPIRSOs, the submission must be sent for convened full-board review. UaP/UPIRSO problems will be reported to UMOR as soon as possible, but not later than seven (7) days from IRBMED's Board determination.

All AEs and ORIOs review decisions for eResearch projects are documented electronically.

**3. University of Michigan Office of Research (UMOR)**

*Refer to [HRPP OM Part 12.III.A.3](#)*

**4. Office of Human Research Compliance Review (OHRCR)**

*Refer to [HRPP OM Part 12.III.A.4](#)*

**IV. QUESTIONS AND CONTACT INFORMATION**

Questions are answered by phone by the IRBMED Receptionist or staff designee. The receptionist or designee will take the pertinent information and route the message to the most appropriate person to answer the question.

Principal Investigators and study team members may request representatives from the IRBMED office to 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](mailto:irbmed@umich.edu)
- US Mail: IRBMED, 2800 Plymouth Rd., Building 200, Room 2086, Ann Arbor, MI 48109-2800

**B. Questions Concerning University Policies and Procedures**

- The Office of Research: (734) 615-1332
- The 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](#)

#### B. Educational Initiatives for the Research Community

The IRBMED provides researchers, board members, and IRBMED office staff with opportunities for the 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.
- 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

### 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
- Global e-mail to all researchers
- Directed e-mail or phone calls to particular researchers, units, or departments
- Announcements in UM communication venues such as, but not limited to, the UMHS Daily Bulletin, Biomedical News, or the University Record

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.