

University of Michigan Medical School
Institutional Review Boards

Standard Operating Procedures

Working Version 1/15/2007

UNIVERSITY OF MICHIGAN MEDICAL SCHOOL INSTITUTIONAL REVIEW BOARD (IRBMED) STANDARD OPERATING PROCEDURES (SOPs)

1. INTRODUCTION

The purpose of the IRBMED is to promote the protection of human participants in research conducted at the Medical School and the University of Michigan Hospitals and Health Centers (UMHHC), including research conducted off-site by University faculty and staff as University employees or in connection with their University appointments. The IRBMED protects 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 a number of Review Boards, each of which complies with applicable regulations concerning membership and conduct.

The University's Human Research Protection Program (HRPP) Operations Manual (OM), maintained by the University's Office of the Vice President for Research (OVPR), is the primary location for compiling, organizing, integrating, and pointing to the rules, policies, practices, and guidance encompassing the UM HRPP. The IRBMED, designated by the University to review and monitor human research under its FWA, maintains written standard operating procedures (SOPs) and may issue additional guidance as necessary. These SOPs are consistent with and supplemental to the OM.

2. SOURCES OF INSTITUTIONAL AUTHORITY

2.1 HRPP OM and Referenced Sources

Refer to OM Part 1, Sections III, IV, and V.

The UM HRPP, of which the IRBMED is a part, operates under the authority of and in accordance with:

- *A Federalwide Assurance* (FWA) established by the University (through its Vice President for Research) and the United States Department of Health and Human Services (through OHRP) (“Assurances”).
- Applicable federal regulations, including (1) for federally funded research, the “Common Rule” (45 C.F.R. part 46, subpart A) and special rules for research involving pregnant women, fetuses, and neonates (45 C.F.R. part 46, subpart B), prisoners (45 C.F.R. part 46, subpart C), and

minors (45 C.F.R. part 46, subpart D); (2) parallel and additional rules for research regulated by the Food and Drug Administration, including human subjects protections (21 C.F.R. part 50), institutional review boards (21 C.F.R. part 56), investigational drugs (21 C.F.R. part 312), and investigational devices (21 C.F.R. part 812); (3) similar rules for research involving recombinant DNA or otherwise regulated by the National Institutes of Health Office of Biotechnology Activities; and (4) privacy regulations issued under the Health Insurance Portability and Accountability Act of 1996 (45 C.F.R. parts 160 and 164).

- Ethical principles set forth in the Belmont Report, as formally adopted by the United States Public Health Service. The IRBMED may, in its discretion, consider other ethical guidelines as well, such as those set forth in/by the Nuremberg Code, the Declaration of Helsinki, the International Conference on Harmonization (ICH), the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, the National Bioethics Advisory Commission (NBAC), the Secretary's Advisory Committee on Human Research Protection (SACHRP), and other professional society codes of ethics.
- Applicable University policies and procedures.

2.2 Local IRBMED Requirements

IRBMED jurisdiction is established by the OVPR and described in the OM. In general, protocols that fall into any of the categories listed below must be reviewed by and are subject to the oversight of the IRBMED:

- Research sponsored by the Medical School or UMHHC; that is, research funded by the Medical School or UMHHC or funded by third parties but administered through the Medical School, UMHHC, or DRDA on their behalf.
- Research that takes place on the premises of or uses the property or facilities of the Medical School or UMHHC.
- Research that takes place elsewhere but involves a faculty or staff member of the Medical School as an investigator in connection with his or her appointment (i.e., that is performed during the time or in the course of providing services for which the individual is compensated by any component of the UMHHC).
- Research that utilizes any non-public data collected or maintained by the Medical School or UMHHC concerning their patients, research subjects, faculty, staff, and students.

At its discretion, the IRBMED may accept for review and oversight research projects that do not fall into one of the above categories. In addition, the IRBMED may delegate the authority to review, approve, and oversee research to other University institutional review boards. Finally, the IRBMED may make alternative arrangements as permitted under the Common Rule. Any decision to accept for review a project that does not fall into one of the categories listed above, to delegate

authority to review a project to another University IRB, or to make alternative arrangements, shall be subject to OVPR approval consistent with applicable Assurances and University policy.

The IRBMED will ensure that all collaborating institutions and investigators engaged in federally supported human subject research operate under an appropriate OHRP or other federally approved Assurance for the protection of human subjects.

The IRBMED will ensure that engagement in human research activities of each independent investigator who is not an employee or agent of the University of Michigan, or organization for whom the IRBMED is the IRB of record, will be in accordance with a formal, written agreement of commitment to relevant human subject protections policies and IRBMED oversight as set forth in the OM.

The IRBMED may, in its discretion, accept additional responsibilities regarding certain non-research activities.

3. IRBMED MEMBERSHIP AND STAFF

The IRBMED conducts its business through multiple institutional review boards, each of which is a separately registered IRB for purposes of University policy and the Federalwide Assurance (FWA).

Board	Registration No.	FWA	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 facilitated review of cooperative group sponsored projects through an agreement with the National Cancer Institute (NCI) Central Institutional Review Board (CIRB).

3.1 Qualification and Appointment of Chair(s)

The IRBMED has at least one chair and may have one or more vice chairs (collectively referred to as the “chairs” throughout these SOPs). Each chair is a respected, active member of the University of Michigan faculty, who qualifies as a scientist member, is concerned 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.

Any scientist who is a regular member or alternate member of a review board may serve as a substitute chair of that review board in the absence of the appointed chair or vice chair.

When a vacancy arises, the Medical School Research Dean or his/her designee may solicit nominations for a new chair from the current and prior chair(s), IRBMED members, staff and

consultants, and the Medical School faculty. The Research Dean then makes a recommendation to the Medical School Compliance Committee, which may adopt or reject the Research Dean's recommendation and in turn communicates its position to the Dean of the Medical School. The Dean of the Medical School is responsible for the appointment and reappointment of a chair. An individual may serve a maximum of three complete three-year terms as Vice-Chair and three complete three-year terms as chair.

3.2 Qualification and Appointment of Members

The IRBMED membership is selected so as 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) to promote respect for its advice, counsel, and determinations in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRBMED is able to ascertain the acceptability of proposed research in terms of institutional commitments and policies, applicable law, and standards of professional conduct and practice.

Each Review Board will have at least five regular voting members, including the chair(s), with varying backgrounds to promote a thorough and responsible review of research activities commonly conducted at the Medical School and UMHC. At least one member will be a scientist, one a non-scientist, and one a non-affiliated community representative.

- Scientist members include physician scientists (MDs or DOs), non-physician scientists (e.g., nurses, geneticists, biomedical engineers), and social and behavioral scientists (e.g., psychologists, social workers, counselors). Scientist members have significant educational background (i.e., an advanced degree) and experience in scientific disciplines, and are generally recruited from among active and emeritus members of the University faculty and staff.
- Non-scientist members are individuals without significant scientific educational background who have expertise in human rights issues or ethical or legal issues considered to be relevant to human subject research. They generally are recruited from among active and emeritus members of the University faculty and staff and also from the community.
- Community representatives may be scientists or non-scientists. To be eligible for participation on the IRBMED as a community representative, neither the individual nor any member of his/her immediate family may otherwise have a direct affiliation (for example, as an employee, contractor, student in a degree program, or active emeritus faculty member) with the University. The fact that an individual is an alumnus or former faculty or staff member of the University, or contributes to University fundraising drives, does not necessarily constitute a direct affiliation.

The IRBMED may, in its discretion, recruit 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 or alternate voting member of any IRBMED may serve as a primary reviewer at another convened IRBMED meeting. When serving in this capacity, they are classified as an ad hoc reviewer and are not counted towards

quorum. The IRBMED chair(s) may reassign a voting member of one review board as a voting member of another review board, or may reclassify a regular voting member as an alternate voting member or vice versa, by notifying the member, the Medical School Research Dean, and OVPR. At the chair's discretion, an individual member may serve concurrently on more than one review board.

In addition to voting members, the membership of each review board may be augmented as necessary by consultants (such as ad hoc reviewers and legal advisors).

The Medical School Research Dean may solicit nominations (including self-nominations) from members of the Medical School faculty and staff and the University community. Community representatives may be recruited by the Research Dean or solicited through advertisements in local news media or other means. Solicitations may, as necessary, include information concerning the background, qualifications, and experience desired to promote diversity of experience and presence of necessary expertise on the IRBMED.

The Research Dean will consult with the IRBMED chair(s) on potential new members and then make a recommendation to the Medical School Compliance Committee based on each individual's qualifications, past participation (in the case of a reappointment), and other relevant criteria. The Compliance Committee will adopt or reject the Research Dean's recommendations and will communicate its determinations to the Dean or his designee, who has final authority to make each appointment or reappointment.

The IRBMED will revise its roster(s) when new members are approved by the Medical School Compliance Committee, and when members resign or are no longer eligible for membership. Upon its approval, OVPR will submit the updated roster to OHRP.

3.3 Term of Service, and Termination of Appointment

Each member is appointed to an initial three-year term, which may be renewed at the discretion of the Medical School Dean. A scientist member shall serve no more than ten consecutive years of service, after which s/he will be ineligible for membership for three years. A non-scientist member or community representative may be invited to serve for an unlimited number of consecutive terms.

In the case of a member who is chosen to become a chair, the duration of his/her membership is extended automatically to permit completion of his or her tenure as chair, after which he/she will be ineligible for membership for a period of three years.

Periodically the IRBMED chair(s) will evaluate the members of the board to ensure that their expertise 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. If necessary, the chair(s) may recommend that individuals, because of repeated non-attendance or lack of participation in continuing education, be relieved of their service on the IRBMED.

3.4 Compensation of Chairs and Members

The IRBMED chair(s) are compensated for the portion of their effort required to perform their duties as chair. Community members of the IRBMED receive compensation to offset the time and expense of attending IRBMED meetings and reviewing protocols. This may include, but is not limited to, parking expenses, computer support, and a modest per-meeting stipend. Regular, affiliated IRBMED members do not generally receive compensation for their service. However, representative members of each IRBMED Committee are encouraged and receive financial support to attend a national conference each year.

3.5 Consultants, Advisors, and Ad-Hoc Reviewers

The IRBMED, the Medical School Research Dean, or the Vice President for Research 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 ad hoc reviewers, legal advisors, 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 deliberations 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 will be recorded in the minutes. Any individual asked to serve the IRBMED in this manner will be required to sign the standard IRBMED confidentiality agreement and follow the standard IRBMED member conflict of interest procedures.

3.6 Periodic Review of Membership and Composition

To ensure that the IRBMED is sufficiently diverse in experience, expertise, education, ethnicity, gender, cultural background, and sensitivity to such issues as community attitudes, the chair(s) will periodically review the membership composition. Additional members will be recruited to ensure sufficient breadth of board composition, to fill vacancies when members' terms expire or members leave the board, to increase the size of standing boards or to form additional boards, and to meet review needs based on the number of incoming applications based on area of review.

The IRBMED will track and manage membership information including, but not limited to: membership role (physician scientist, non-physician scientist, social-behavioral scientist, and non-scientist); areas of expertise, conflicts of interest; university affiliation; and advocates for minority populations; prisoners; disabled communities; and children/minors.

3.7 Staff

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The IRBMED is supported by a professional staff hired, supervised, and supported by the Medical School Research Dean or his/her designee. The staff is responsible for facilitating IRBMED operations (protocol review, documentation and record retention, fact-finding, informational resources and educational activities, etc.) in such a manner as to maintain compliance with applicable laws, regulations, and policies, and for performing related activities as designated by the Research Dean.

4. IRBMED FUNCTIONS AND OPERATIONS

4.1 Applications

The IRBMED staff, in consultation with the IRBMED chairs, the Medical School Research Dean, and OVPR, has developed, utilizes, and updates as necessary forms and electronic systems to facilitate application by principal investigators for IRBMED review and approval of new projects and continuing oversight of established projects.

4.2 Staff Review and Determinations

Applications are submitted to the IRBMED by the principal investigator (PI), and triaged to a designated IRBMED staff review team. The IRBMED staff review team assesses and reviews the application and any other supporting documentation (e.g., informed consent document(s), data collection forms, etc.) for completeness and adherence to regulatory requirements. Either concurrent with or following the staff team assessment/review, the application is reviewed by an IRBMED primary reviewer.

4.2.1 Review of Applications for Completeness and Special Considerations

Generally, applications undergo administrative review by IRBMED staff where they are checked for completeness and compliance with the regulations. If applications meet preliminary standards, they are entered into the review process. If incomplete, the investigator is notified of the actions necessary to complete the application before it is submitted for review.

4.2.1.1 Generally

IRBMED staff, following regulatory criteria and, as necessary, in consultation with IRBMED chair(s) or director(s), make the preliminary determination as to whether or not an application should be considered for a non-human subject research determination, for exemption, for expedited review, or should be scheduled for a convened board review.

4.2.1.2 Human Research vs. Not Human Research

Refer to the OM, Part 4, Section I.

The IRBMED does not require investigators to seek a determination of Not Human Subject Research from the IRBMED when the activity falls outside the DHHS and FDA definitions of human subject research. Investigators may consult informally with IRBMED staff or members in order to facilitate a self-determination, but must submit a new electronic (eResearch) application if a written determination from the IRBMED is desired. Determination letters of Not Human Subject Research are released within eResearch.

Research that lacks definite plans regarding human involvement, even if undertaken with knowledge that human subjects may someday be involved, need not be reviewed in advance by the IRBMED. However, IRBMED review and approval must be secured before any human involvement actually begins, unless the research is otherwise exempt from IRBMED oversight.

4.2.1.3 Engaged vs. Not Engaged

Refer to OM Part 5, Section II.A.

4.2.1.4 Exempt vs. Not Exempt

Refer to OM, Part 4, Section IV.

The authority to determine whether a project qualifies for exemption rests solely with the IRBMED or other University officials, as specified in the OM and applicable Assurance, and not with the investigators performing the study.

The IRBMED may determine that a research project is exempt from IRBMED review and oversight if it meets the exemption requirements set forth at 45 CFR 46.101 and is not subject to regulation by the FDA or federal Office of Biotechnology Activities (OBA).

The IRBMED will not exempt research involving prisoners. Likewise, the IRBMED will not exempt research involving survey or interview procedures or observation of public behavior that involves children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

4.2.1.5 Expeditable vs. Not Expeditable

Refer to OM, Part 3, Section III.C.3.

Certain categories of research projects submitted to the IRBMED for review are eligible for “expedited review” according to federal regulatory criteria. These criteria are described in a guidance document available at <http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm>

4.2.1.6 Adverse Events and Other Reportable Information and Occurrences

Investigators responsible for the conduct of approved projects are required to report to the IRBMED adverse effects (AEs) of study interventions, unanticipated problems involving risks to subjects or others, certain other adverse events, and new information about a project that adversely influences the risk-benefit ratio previously assessed by IRBMED (“Other Reportable Information and Occurrences” – “ORIOs”).

The required reporting frequency is specified in the IRBMED-approved protocol or in guidance developed and posted by IRBMED, and depends on the seriousness of the event, whether it is expected or unexpected, and whether it is considered definitely, probably, possibly, not likely, or definitely not related to the research intervention.

AEs may include, but are not necessarily limited to, the following:

- Expected or unexpected harmful effects of an intervention, such as an investigational or FDA-approved drug, biologic or device, observed in the approved project or in other research settings similar to that of the approved project.
- A protocol deviation or other procedural error involving a human subject enrolled in the study, such as failure to properly obtain or document informed consent, or dosage or medication errors.
- Physical, social, or emotional harm suffered by a subject or affecting the subject’s rights or welfare during the execution of or otherwise in connection with the investigational protocol.
- A breach of privacy or confidentiality.
- An event or accident occurring on the premises of the institution where the project takes place that affected one or more subjects of the project, even if not a direct result of the research intervention.

ORIOs may include, but are not necessarily limited to, the following:

- Subject incarceration
- Protocol Deviations
- Accidents/Incidents that involves Subjects (if harm occurred report as an AE)
 - Data Specimen
 - Facility
- Complaints about the research
- Enrollment of a state ward in a project approved under 45 CFR 406 or 407 and/or 21 CFR 50.53 or 54
- Other Information and Progress Reports
- Audits and Inspections conducted by outside entities
- General Summary or Annual Reports to Oversight Bodies
- Reports/letters from oversight bodies

Expected AEs and ORIOs are those that have been identified (including nature, frequency, and

severity) in the protocol, investigator's brochure, informed consent document, scientific literature, or other appropriate document. For research involving more than minimal risk to participants, an appropriately detailed plan for minimizing the likelihood of, monitoring the occurrence of, and reporting expected and unexpected adverse events to the IRBMED is required in the initial application or protocol. If a specific reporting plan is not included in these documents, the standard IRBMED reporting requirements apply.

The IRBMED scrutinizes reports of AEs and ORIOs to determine the degree to which risks to human subjects may have changed and whether there is any need to modify the protocol to minimize the risk or to notify existing subjects or revise the consent document for future participants.

Events or information that are serious, unexpected, and related to the research will be flagged for the reviewer to assess whether or not they represent an unanticipated problem. Unanticipated problems involving risks to subjects or others are reported to OVPR in accordance with OM Part 12.

4.2.1.7 Facilitated Review

The University maintains an IRB Authorization Agreement with the National Cancer Institute (NCI) Central Institutional Review Boards (CIRBs).

Principal investigators participating in cooperative group studies that are under the oversight of the NCI CIRB may submit the CIRB-approved documents (protocol, consent form, CIRB application, etc.) from the CIRB website (www.ncicirb.com) to the IRBMED for "Facilitated Review". The facilitating reviewer will review the materials for local context and decide whether to accept the CIRB review.

The facilitating reviewer may propose/approve minor additions and/or changes to the protocol or informed consent document in order to facilitate improved comprehension by the local population and/or accommodate local requirements, but he/she may not delete or contradict any CIRB-approved protocol or informed consent document content.

Should the facilitating review decide not to accept the CIRB review, the investigator may resubmit the cooperative group protocol to the IRBMED through the regular application process.

4.2.1.8 Other Special Considerations

Special Applications, Agreements, and Certifications

a) Application and Approval for Waiver of HIPAA Authorization

A qualified investigator may request Privacy Review Board approval of a waiver of patient authorization of the use and disclosure of PHI for research purposes, which may include a database

or registry, or other human subject research project not otherwise subject to IRBMED oversight in which PHI may be used or disclosed without patient authorization. The Privacy Review Board may approve a Waiver only if all 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;
- The use or disclosure of PHI for the project involves no more than minimal harm to the privacy of individuals. This criteria may be met where the following elements are present:
 - An adequate plan is in place to protect patient identifiers and PHI from improper use and disclosure;
 - An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a Privacy Review 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.
 - The research could not practicably be conducted without the Waiver or alteration of authorization; and
 - The research could not practicably be conducted without access to and use of the PHI.
- Where the investigator anticipates the disclosure of PHI outside the Covered Entity (as that may be determined from time to time), the investigator must account for each disclosure and retain records of such disclosures.

b) Certification for Review Preparatory to Research

A researcher may access and use PHI without patient authorization in preparation for an anticipated research project by filing in advance a Certification for Review Preparatory to Research with the Privacy Review Board. The Certification must include the following information:

- The PHI for which use of or access to is sought is necessary for the research purposes;
- The use or disclosure is sought solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research; and
- No PHI will be removed from the University by the researcher in the course of the review.
- No PHI obtained under the authority of a Certification may be used in subsequent research without the permission of the IRBMED.

The researcher may commence his or her review of PHI upon receipt from the Privacy Review Board of a signed Certification.

c) Certification for Research Involving Decedents Information

A researcher may use or disclose PHI for research involving decedents' information by filing, in advance, a Certification with the Privacy Review Board that includes the following representations:

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- That the use or disclosure is solely for research on the PHI of decedents;
- The requesting investigator can provide any documentation requested by the Privacy Review Board, IRBMED, or other oversight/regulatory body confirming the deaths of the individuals whose PHI will be used or disclosed; and
- The PHI for which the use or disclosure of is sought is necessary for research purpose described in the Certification

d) Internal and External Data Use Agreements

Data Use Agreements will be evaluated by the UMHS Privacy Officer, or delegate, and will be retained with the UMHS Privacy Office, not the IRBMED.

e) Lapses in Approval

Refer to OM Part 3, section III.C.2.e.

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 administratively terminate that protocol. An administrative termination under this provision does not constitute a suspension or termination of IRBMED approval reportable to OVPR and federal regulators under 45 C.F.R. § 46.113 or these SOPs.

f) Study Withdrawal

A principal investigator may withdraw a submitted application at any point prior to an IRBMED approval/disapproval determination. In addition the IRBMED may act to administratively withdraw an incomplete application after providing the investigator with a notice of intent to withdraw and a final opportunity to respond.

4.2.1.9 Administrative Modifications

Refer to IRBMED SOPs Section 4.3.5 below.

4.2.2 Assignment of Applications for Review to Qualified Members or Consultants

Upon receipt of an application, the staff will identify an IRBMED member to function as the “primary reviewer,” based on the member’s expertise, experience, and/or representation of pertinent subject population, as indicated on the member’s Curriculum Vitae, documentation of community experience, response to the IRBMED expertise survey form, and/or other methods. The IRBMED staff will forward a complete set of documents (in electronic and/or printed form) directly relevant to the application to that member.

Scientific review of a study is one criterion to make an effective determination of the risks and benefits of the study. A reviewer assigned by the IRBMED office staff and/or chair will have the ability to evaluate study methodology; the qualifications of the investigator(s) to perform and complete the project; and assess the scientific value of the proposed aims in relation to current scientific knowledge. In the event that the assigned reviewer requires additional information to make and present a determination concerning the scientific validity of the study, a consultant with expertise in the field will be invited to provide additional review.

All of the project documents also shall be made available to all other IRBMED members and authorized consultants for advance review.

4.3 Standard Review Procedures for Applications Requiring Board or Member Action

All initial applications, applications for continuing review, and applications for protocol amendments require review by a convened review board, unless eligible for expedited review.

4.3.1 Reviewer System

Upon receipt of an application, the staff will identify an IRBMED member to function as the “primary reviewer.” The staff, in its discretion or at the direction of the chair or primary reviewer, may also assign a secondary reviewer and/or a consultant. All of the project documents also are made available to all other IRBMED members and authorized consultants for advance review. Prior to any meeting convened to discuss an application, the primary reviewer may request from the investigator additional information or documents, or explore proposed revisions that may be required as a condition of IRBMED approval of the project. After completing his/her review, a reviewer (or other IRBMED member on the reviewer’s behalf) presents the project to the board at a convened meeting for discussion, deliberation, and vote, unless approval is expeditable. The chair or staff may require the reviewer to return an application for re-assignment if he/she is not able to present it to a review board for discussion or vote within a reasonable period of time after the reviewer’s original receipt.

4.3.2 Distribution of Materials for Review

The staff provides each primary reviewer and, as applicable, any secondary or ad hoc reviewer assigned to an application, with the application and all supplemental materials (including, if applicable, the grant application, informed consent document(s), protocol, investigator’s brochure, data collection sheet, advertisement, etc.), as well as a worksheet/checklist to help ensure that all criteria necessary for approval of the application have been met in accordance with applicable regulations and these procedures.

In addition, for continuing review applications, the primary reviewer receives for consideration the complete project file, which includes all amendments and other reports, including adverse events, unanticipated problems involving risks to subjects, and other reportable information and

occurrences.

Applications requiring full board review will be listed on an agenda sent to members sufficiently prior to the meeting to provide time for review of materials. Access to materials is web-based and available to all members via either eResearch or the IRBMED members-only website.

4.3.3 Initial Review

Refer to OM, Part 3, Section III.3.C and Part 4, Section IV.

Any investigator who intends to initiate a research project involving human subjects that is subject to IRBMED jurisdiction must submit an initial application for IRBMED review and approval of the project. No aspect of the project (including testing performed solely to determine eligibility for the project) may begin until the application has been approved in writing by IRBMED.

An application will not be deemed complete, and may not be accepted for review, unless it includes at least the following items:

- The research protocol, including, as applicable, any questionnaires, surveys, or scripts used by investigators or research support staff to communicate with research subjects or their representatives.
- The investigator's brochure or equivalent documentation if the project involves use of an investigational drug, biologic, or device.
- Sample informed consent document(s), or a request for IRBMED approval of a waiver of written informed consent.
- Copies of advertisements and any other recruiting materials (including, but not limited to, posters, websites, videotapes, scripts for telephonic communications, etc.), if used.
- Documentation of approval from other University departments or divisions from which the IRBMED 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 performing the research, if the University (directly or through the principal investigator) has ultimate responsibility for the conduct of the protocol or performs any coordinating functions including, without limitation, study coordination, data management, monitoring, or otherwise; or certification that such approval will be obtained before the study begins.
- Any relevant federal grant applications and, for multi-center trials supported by the Department of Health and Human Services, the approved sample informed consent document and complete HHS-approved protocol (if any).
- Any other supporting documentation that the IRBMED, in its discretion, requests in order to facilitate a complete and meaningful review of the project, such as sponsor or contract research organization contracts governing the conduct of the research, conflict of interest management plans (if applicable to the project), FDA documents (if applicable to the project), and so forth.

A new application will be eligible for approval only if the following criteria (per 45 C.F.R. § 46.111) are met:

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- Risks to subjects are minimized (i) by using procedures that are consistent with sound research design and do not unnecessarily expose subjects to risk; (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes; and (iii) adequate resources are available to protect and minimize harm to participants.
- 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 benefit as well as societal benefit. In evaluating risks and benefits, the IRBMED will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits subjects would receive even if not participating in the research). The IRBMED does not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as 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.
- Informed consent (unless waived) will be documented on a form approved by IRBMED.
- 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 (see Section 5.3 below), additional safeguards have been included in the study to protect the rights and welfare of these subjects (e.g., minimize risks peculiar to these groups and the possibility of coercion or undue influence).

The primary reviewers receive sufficient information (as described above) prior to review of applications to prepare their recommendations for approval of the research. To facilitate the review process, a reviewer may request clarifications or revisions to any or all of the application documents prior to board presentation.

Prior to the meeting all members of the Board receive a complete agenda, which provides a link to the complete application materials for their review. The primary reviewer presents the application and his/her recommendation to the review board, including any suggested changes.. Following the primary reviewer's presentation, board members discuss the application, deliberate, and arrive at a decision by majority vote of the quorum present. The primary reviewer must complete a reviewer worksheet/checklist prior to issuance of the final approval to the PI.

If an application is determined to be approved with specified minor contingencies, the office staff will notify the principal investigator of the changes and/or clarifications that the IRBMED has required. The principal investigator will revise the application accordingly, and the IRBMED

reviewer will verify the changes/clarification prior to release of the approval by the IRBMED staff. If the contingencies are of an administrative nature (e.g., correction of typographical errors), the reviewer may request that the IRBMED staff team verify those changes before releasing the approval. If the principal investigator disagrees with the IRBMED request, or proposes an alternate change, the approval status of the application will revert to “deferred”, and the application must be re-presented to the board in order to obtain approval.

4.3.4 Continuing Review

Refer to OM Part 3, Section III.C.2.a.

The IRBMED conducts continuing review of any research project subject to its oversight at intervals appropriate to the magnitude of risk of the project and other considerations, but not less than once each year.

The principal investigator of an active project is responsible for submitting an application for continuing review and approval sufficiently in advance of the expiration date of the current approval period to permit IRBMED review within that period. The IRBMED sends reminder notices in advance of the expiration date of the current approval period. If approval for continuation is not issued prior to the expiration date, the investigator 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 the subject.

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 administratively terminate that protocol.

Note that neither expiration of approval nor administrative termination constitutes a “suspension” of IRBMED approval reportable to OVPR and federal regulators under 45 C.F.R. § 46.113 or these SOPs.

See also OM Part 3, section III.C.3.a.

An application for continuing review 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.
- A summary or tabulation of any:
 - Continuing reviews
 - Amendments
 - Adverse events (AEs) or other reportable information or occurrences (ORIOs), such as:
 - Subject withdrawals from the study

- Subject complaints and their resolutions
 - Protocol deviations/violations
 - Accidents/incidents involving data, specimens, or facilities
 - Pertinent publications/public announcements
 - Potential unanticipated problems involving risks to subjects or others
 - Pertinent reports from or to a sponsor or oversight entity
 - documentation of any findings made by external inspectors, reviewers, or auditors and the investigators' response to the findings
- Copies of or links to the informed consent document(s) approved by the IRBMED and currently in use.

The criteria applied to review of any application for continuing review are similar to those applied to an application for initial review.

4.3.5 Review of Amendments to Previously Approved Research

Refer to OM Part 3, section III.C.2.d.

Once a project has been approved, an investigator may not make any material changes to the project (including to the protocol or informed consent document) 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.

Regardless of whether a change to the project is “material,” any change to information provided in a previous application to IRBMED must be reported to IRBMED in a timely fashion. Reportable changes may include, but are not limited to:

- Amendments to the study protocol, including changes to the eligibility criteria, recruiting materials and advertisements, questionnaires, surveys, and scripts.
- Amendments to the investigator's brochure or equivalent documentation.
- Amendments to previously approved informed consent documents.
- Changes in investigatorship (including principal investigator, co-investigator, sub-investigator) or performance site(s).
- Changes in any other aspect of the research.

At its discretion, the IRBMED may authorize its staff to acknowledge non-material changes to protocols and informed consent documents such as corrections of typographical or grammatical errors and changes in contact information (but not investigatorship) without submission of the application to a review board or chair.

Different types of amendments may be requested individually or in combination. For example, a change in a study protocol or investigator's brochure may require a corresponding change in the informed consent document. 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 informed consent document or process, whether proposed changes in the informed consent document are appropriate, and/or whether there is any need to notify previously enrolled subjects of the changes.

The date of IRBMED approval of an amendment does *not* change the date by which a regularly scheduled continuing review must be completed.

4.3.6 Review of Applications for Study Closure

The principal investigator of an approved project must notify the IRBMED upon completion of the project. A project termination report should include at least the following information:

- Affirmation that the involvement of human subjects and use of identifiable human data or specimens has concluded
- Description of the plan for secure storage of data and specify whether or not data will be de-identified
- Number of subjects involved
- Ethnic, racial, and gender breakdown of subjects
- Number of subjects withdrawing from the project and the reasons
- Number of subject complaints about the project and description/resolution of those complaints
- Number of adverse events reported to IRBMED during the project (including any reported concurrently with submission of the termination application)
- For research governed by the federal Food and Drug Administration, the final report is submitted to the FDA

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 administratively terminate that protocol. An administrative termination under this provision does not constitute a suspension or termination of IRBMED approval reportable to OVPR and federal regulators under 45 C.F.R. § 46.113 or these SOPs.

4.3.7 Adverse Events and Other Reportable Information or Occurrences (ORIO) Review Decisions

IRBMED board reviewers will consider the following when reviewing an adverse event report:

- Investigator's assessment of the AE and concurrence or disagreement with that assessment (e.g. non-serious, unrelated, expected)
- Safety of subjects (including if 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 adverse events not described in the currently approved informed consent document (ICD) the review will consider:

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

Events that are serious, unexpected, and related to the research will be assessed to determine whether or not the event represents an unanticipated problem.

IRBMED board reviewers will consider the following when reviewing an ORIO report:

- If urgent communication with the investigators, IRBMED director, UM Office of General Counsel, co- or vice-chair or other authority is required
- Safety of subjects (including if the study should be halted or modified)
- Risk/benefit assessment of the study
- Impact of ORIO on subjects' willingness to participate in the study

When applicable, for ORIOs not described in the currently approved informed consent document (ICD) the review will consider:

- If ICD should be modified
- If previously enrolled subjects should be notified and/or re-consented

Events that are serious, unexpected, and related to the research will be assessed to determine whether or not the event represents an unanticipated problem.

4.3.8. Review of Emergency Use of Investigational Agents

Refer to OM Part 8, and IRBMED SOPs Section 10.1 below.

4.3.9 Expedited Review Procedures

Initial assignment of an incoming application for consideration for expedited review will be made by the IRBMED staff. Expedited reviews are performed by an IRBMED chair, or experienced IRBMED member approved by a chair according to their experience and service as an IRBMED Member.

Expediting reviewers may exercise all of the authorities of the full board except that the reviewers may not disapprove the research. The research may only be disapproved after review in accordance with the non-expedited review procedure. When applicable, questions and/or requirements pertaining to an expedited application will be communicated to the PI in writing and must be addressed to the expediting reviewer's satisfaction prior to approval. An expediting reviewer may choose to consult a review board on some aspect(s) of an expeditable application, in which case the application shall remain routed for expedited review unless a motion is made and carried to require full board approval. At his/her discretion, an expediting reviewer may refer an application for full board review. The expediting reviewer will document findings, determination, or recommendations

on a reviewer worksheet/checklist.

All protocols approved by expedited review, together with a description of each and the reason(s) they qualify for expedited review, are available electronically to IRBMED members, the Medical School Research Dean, OVPR, and authorized consultants on an ongoing basis. A list of recently conducted expedited reviews will be presented to IRBMED board members at a convened meeting at least monthly.

4.4 Procedures for Appeal of IRBMED Requirements or Determinations

A principal investigator may appeal an IRBMED requirement or determination. At the discretion of the chair, the investigator may make such an appeal in person and/or in writing to the IRBMED.

4.5 MEETINGS

4.5.1 Standard Schedule

Each Review Board convenes regularly to fulfill the mandate to oversee research involving human subjects subject to IRBMED jurisdiction. The IRBMED is comprised of five boards. Two of four boards meet every other week (i.e., two boards meet every other week on the odd weeks, and two boards meet on the even weeks), and one board meets weekly. As necessary, additional meetings may be convened throughout the year. The boards meet in a convened board fashion and by conference call when necessary.

4.5.2 Agendas

The IRBMED staff assigns incoming applications to upcoming meeting agendas based generally on the board assignment and availability of the designated primary reviewer.

The staff maintains an agenda that includes general discussion topics (e.g., educational, announcements, etc.) and a list of all research project applications and reports scheduled for review at a given meeting. Updated working agendas are available at all times to IRBMED members, the Medical School Research Dean, OVPR, and authorized consultants. The planned meeting agenda is distributed to all voting members sufficiently in advance of each meeting (generally three days) to allow review of application materials of interest. At the beginning of each meeting, all voting IRBMED members are alerted to any changes that may have been made in the planned agenda. In the event an application is discussed that does not appear on the planned meeting agenda (e.g., emergency use, time-sensitive submission), a narrative summary of the protocol and sample informed consent form(s), 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 vote is taken.

4.5.3 Meeting Procedures

Each review board meets as often as is necessary to review, without undue delay, non-expedient applications awaiting disposition. The chair or, in his or her absence, a vice chair or senior scientist member of the review board, leads each meeting. The IRBMED staff monitors attendance to ensure that the quorum, composition, and diversity are present for each meeting as defined by federal regulations. A quorum (defined as more than half the number of regular voting members of a review board, including at least one non-scientist) must be present for each formal vote. An initial, amendment, or continuation application may be approved or disapproved only upon a majority vote of the voting members present.

Guests may be in attendance for all or part of an IRBMED meeting. These guests are usually staff or trainees of the UMHS, or student trainees from neighboring institutions. Guests are invited by an IRBMED member or chair, and are required to sign the UMHS Statement of Confidentiality. The statement indicates that it is the expectation of UMHS that all individuals exercise due care in any discussion, access, storage, interpretation, release, or handling of confidential patient/student/M-CARE member/employee specific information. This includes the sensitive or confidential information that may be shared in the course of an IRBMED meeting.

4.5.4 Board Actions

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

- Approve the application as presented to the review board.
- Approve the application contingent on specified changes to the protocol, informed consent document(s), or other items being made by the principal investigator.
 - Approved Pending Office (APO) - approve the application contingent on specified administrative changes (e.g., correction of typographical or grammatical errors) requested by the board and to be verified by the IRBMED staff prior to release of approval.
 - Approved Pending Reviewer (APR) - approve the application contingent on specified minor changes requested by the board to be verified by the reviewer,

The date of the vote to “approve pending” shall be deemed the date of approval, regardless of when the specified changes are made by the PI and verified by the IRBMED. The IRBMED may, in its discretion, require that the investigator 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.

- Board Action Deferred (BAD) - In the event that the needed changes are significant or require more than simple concurrence of the PI, action on the application shall be deferred.

Action may be deferred on any application 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 investigator may be instructed to submit additional information or revisions required by IRBMED before reconsideration of the application. The IRBMED may, in its discretion, require that the investigator respond within a specified period and instruct that if the response is not received, the application will be considered withdrawn.

- Disapprove the application – The principal investigator will be notified of the reasons for disapproval and afforded the opportunity to appeal the decision. IRBMED disapproval of an application does not constitute a suspension.
- Voluntary Hold – At the request of the principal investigator, the IRBMED will consider acknowledgment of a voluntary hold on subject enrollment or any other portion of the research activities in order to facilitate ongoing IRBMED review or oversight of a currently approved protocol or its conduct by allowing for the opportunity to clarify or change the protocol. IRBMED acknowledgement of an investigator-proposed voluntary hold does not constitute a suspension.
- Suspension or Termination of IRBMED Approval – The IRBMED also may suspend or terminate approval of research that it determines, after appropriate review and deliberation, (1) is not being conducted in accordance with IRBMED requirements; (2) has been associated with unexpected harm to subjects; or (3) cannot minimize risks to subjects or maintain a favorable risk-benefit ratio. Any suspension or termination of approval under this provision shall include a statement of the reasons for the action and inform the principal investigator of an opportunity to respond.
 - *Suspension of Research Activity* is the temporary closing of a human subject project or discontinuation of an investigator’s privilege to conduct human subject research except for the continuation of follow-up activities necessary to protect human subject safety. The suspension may be partial in that certain activities may continue while others may not, or it may be complete in that no activity related to the research may proceed.
 - *Termination of Approval* is the ending of all activities related to a human research project or an investigator’s privilege of conducting human subject research at the University of Michigan except for the continuation of follow-up activities necessary to protect human subject safety.

4.5.5 Minutes

Following a Review Board meeting, the staff shall prepare minutes consisting of at least the following information:

- Attendance
- Acknowledgement of reviews approved by the expedited procedure

Approved _____
Effective _____

- For each protocol reviewed, any votes or other actions taken, and the vote on that action (including the number of members voting for, against, abstaining, the names of any abstaining members, and the names of conflicted members who left the room for the deliberation and vote)
- Protocol-specific information supporting any waiver of informed consent or documentation of consent; or the inclusion of vulnerable subjects in the research
- The basis for requiring changes in or disapproving research
- A written summary of controverted issues and their resolution
- Summary of any continuing education provided to Review Board members

Typically, within two (but not more than eight) weeks of the meeting date, a review board's minutes are distributed for review by its members, who require corrections if needed and vote to ratify them at a subsequent meeting. The ratified minutes are maintained by staff in accordance with applicable legal requirements and University policy.

4.5.6 Notification of Decisions to IRB members and Researchers

Following a review board meeting, the staff prepares written or electronic notification to inform the principal investigator of each submission upon which a vote was taken, and on the outcome of the vote. The staff also prepares notification of any expedited determinations. The notification includes at least the following information:

- The review board's decision and date it was reached
- For an approved project, the approval expiration date of the approval and notification of any interim reporting requirements
- For a project that has been approved contingent on specified changes to the protocol, informed consent documents, or otherwise, a description of the specific modifications necessary to comply with the terms of the approval.
- For a disapproved, suspended, or terminated project, the reason(s) for the Review Board's decision and notification of the investigator's opportunity to respond in person or in writing

The IRBMED may, in its discretion, require that the investigator 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. An investigator may appeal IRBMED required changes. At the discretion of the chair, the investigator may make such an appeal in person or in writing to the IRBMED

Documentation of all IRBMED determinations shall be available for review by the Medical School Research Dean, OVPR, IRBMED members, and authorized consultants. A copy of any notification of suspension or termination of a project shall be delivered under cover letter to OVPR for further disposition and notification to other interested parties, as necessary, such as government authorities with jurisdiction and, in the case of a sponsored project, the Division of Research Development and Administration (DRDA).

4.6. RECORDKEEPING

Approved _____
Effective _____

Refer to OM Part 3, Section III.F.

IRBMED paper or electronic records are maintained by the IRBMED for a minimum of three years after conclusion of the activity. Records related to HIPAA are kept a minimum of six years. Records are kept in a secure manner either in the IRBMED Office or off-site in secure commercial storage (retrieval time is generally next day).

5. CONFLICTS OF INTEREST

5.1 OM Definition

Refer to OM Part 9.

5.2 Additional Local Considerations

The primary responsibility of IRBMED members, staff, and consultants is to support the academic mission of the University of Michigan Medical School. No contract, consultancy, or outside endeavor should interfere with or compromise this primary obligation. A research award (contract, grant, or gift) should not result in any tangible personal profit other than direct compensation for actual effort committed to the project under University salary guidelines. Award-related research on potentially marketable products must be avoided by individuals who will benefit financially from the outcome. This includes stock holdings, options, bonuses, or other equity positions held by the individual or immediate family members in the sponsoring agent or its competitors. Consultancies that are independent of award-related research represent no conflict of interest. Awards to an investigator, a department or the Medical School from commercial sources can be accepted only if there is no reciprocation expected or demanded. Conflict of interest may arise not only in issues related to personal financial gain, but also those involving professional gain, such as in the biased review of manuscripts and grants. In some instances, the appearance of conflict of interest constitutes as great a potential hazard for the individual and the institution as actual conflict of interest. Therefore, it is incumbent upon individuals involved with research at the Medical School to disclose the conditions of all consultancies and awards according to existing University policy. Furthermore, adherence to existing University documents referring to conflict of interest, including the Medical School's Guidelines for the Ethical Conduct of Research and University guidelines for consultancy, is expected.

5.3 Local Rules for Identification and Management of Conflicts among IRBMED members, Consultants, and Staff

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 and Medical School

Conflict of Interest Boards to coordinate awareness of actual and perceived conflicts of interest of both IRBMED members and researchers.

5.3.1 IRBMED Members

At the beginning of their service, each new IRBMED member completes a questionnaire by listing their individual areas of expertise for reviewing applications, as well as their financial disclosures. The financial disclosure sections indicate disclosure of a significant financial interest in a sponsored project or technology transfer agreement. This information is also on file in other areas and offices of the University, including the Medical School Dean's Office, and the Office of Technology Transfer within the Division of Research and to the Development Administration (DRDA). Conflict of interest information associated with IRBMED members is also obtained from OVPR and the Medical School Conflict of Interest Boards. This information is considered during review assignment in order to ensure a member is not assigned to review an application for which they are identified as a conflicted member. It is the responsibility of IRBMED members to disclose both actual and perceived conflict of interests throughout their membership term.

An IRBMED member (including the chair) is not assigned to review an application if the member:

- Is an investigator on the study or the investigator's immediate relative; or
- Has a significant financial interest in the research (as defined by University and Medical School policies on conflicts of interest); or
- Has other conflicts that the member, review board, Dean, Conflict of Interest Committee, or OVPR believes might hamper the member's ability to perform an impartial review of the application.

A member (including the chair) shall not be present for, count for quorum, participate in deliberations, nor vote on the disposition of an application in which the member has a conflict as described above. The member may, however, be invited by the review board to provide information relevant to the board's consideration of the application. The member must be absent from the room during both relevant deliberation and voting.

A member (including the chair) shall not participate in the investigation of actual or alleged noncompliance or other misconduct (other than to cooperate with the investigation) if the member has a conflict as described above.

5.3.2 IRBMED Consultants

An individual cannot participate in the review of a research protocol in the role of IRBMED consultant when the individual has an actual or perceived conflict of interest related to the research protocol. An actual or perceived conflict of interest is defined as a significant personal or financial interest in the research protocol as noted above. The IRBMED staff will confirm whether an actual or perceived conflict of interest exists prior to contacting a consultant. The Conflict of Interest Committee or OVPR will be consulted, if needed. An individual shall not be identified as a

consultant to participate in the investigation of actual or alleged noncompliance or other misconduct investigation in a research protocol if a conflict of interest exists.

5.3.3 IRBMED Staff

An IRBMED staff person would be recognized as having a conflict of interest with research which he/she has a significant personal or financial interest in the research as defined above. When a conflict is identified either by OVPR, the University or Medical School Conflict of Interest Board, and/or by self-disclosure, the staff person must excuse him/herself from administrative handling of the research application and from the IRBMED meeting where there is deliberation and vote of the research protocol. IRBMED staff documents all conflicts of interest in the meeting minutes.

5.4 Local Rules for identification and Management of Conflicts Among Members of the Study Team

The IRBMED coordinates with the appropriate University Conflict of Interest Board to ensure that any relevant imposed terms of conflict management are considered in the review of applications submitted by the personnel in question. Staff will document all occurrences.

6. MONITORING ACTIVITIES

6.1 Special Requirements for Monitoring the Conduct of Human Research

The IRBMED may monitor studies both for-cause (e.g., suspected non-compliance) and not-for-cause (e.g., random or risk-based review for quality assurance purposes). Monitoring 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/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

6.1.1 Considerations for Imposition of Special Monitoring Requirements

The IRBMED may impose special requirements or restrictions on either an investigator or on a particular study. These may be imposed because of risk level, safety issues, conflict of interest issues, or because of findings of non-compliance.

6.1.2 Examples of Special Monitoring Requirements

Requirements or restrictions imposed on an investigator or study may include, but are not limited to, any or all of the following:

- Require education
- Submission of reports to the IRBMED at specific time intervals (in addition to the study's continuing review submission for renewal of IRB approval)
- Submission of reports to the IRBMED at specific increments of subject participation (i.e. after every third subject completes the trial or after the first three doses of an agent)
- Restriction on location of study activities
- Require additional supervision of overall study or aspects/activities of the study
- Prohibition from obtaining informed consent from subjects
- Prohibition from conducting certain types of research
- Prohibition from serving as a principal investigator

6.2 Investigation of Complaints and Allegations of Non-Compliance

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 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 appears necessary. In support of this effort, the IRBMED may acknowledge a request from the principal investigator to voluntarily "hold" 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 course of treatment.

IRBMED fact-finding is conducted by IRBMED staff, members, and consultants, and 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/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

7. RESPONSE TO COMPLAINTS OR ALLEGATIONS OF NONCOMPLIANCE

Upon completion of the fact-finding, an IRBMED staff member documents and compiles the information. The IRBMED director evaluates the credibility and potential seriousness of the case, and determines whether the complaint or allegation of noncompliance is reportable (1) immediately to the IRBMED chairs for a determination of serious or continuing noncompliance, or suspension or termination; or (2) quarterly to the IRBMED chairs and OVPR, in accordance with the reporting procedures outlined in the OM.

Under institutional authority and federal regulations, the IRBMED is responsible to oversee 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 requirements or (2) has been associated with unexpected serious harm to subjects.

In the event that a credible suspicion of scientific misconduct is discovered in the course of routine IRBMED fact-finding activities, the matter will be handled in accordance with University policies including, the University Policy Statement on the Integrity of Scholarship and Procedures for Investigating Allegations of Misconduct in the Pursuit of Scholarship and Research (SPG 303.3).

7.1 Roles and Responsibilities

The IRBMED shall notify the Medical School Research Dean and OVPR of any complaints or allegations of noncompliance as required in OM Part 12. OVPR shall notify any other applicable Federal Agency.

7.2 Board Considerations and Determinations

If, according to the results of the IRBMED fact-finding, the alleged noncompliance is determined by the IRBMED director to be credible and potentially serious, the case is presented to the IRBMED chairs, collectively. 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 non-compliance with IRBMED determinations or federal regulations.

In reviewing the alleged noncompliance the chair(s) may request a meeting with the principal investigator and others to discuss the concern(s) and provide an opportunity for the study team to correct or clarify the fact-finding information.

If the IRBMED chairs consider the noncompliance to be possibly serious or continuing, the case will be presented at an upcoming convened meeting of the relevant IRBMED board. At that

meeting, a quorum of IRBMED members will review the case, discuss the findings, and vote on whether the non-compliance is continuing and/or serious, constitutes an unanticipated risk to subjects or others, and/or the research should be suspended or terminated.

7.3 Recordkeeping and Reporting Requirements

7.3.1 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 principal investigator and relevant study personnel.

The IRBMED chairs and Medical School Research Dean are provided with any copies of case reports or quarterly summary reports that are prepared for submission to the OVPR.

The IRBMED shall promptly notify OVPR of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with institutional policy and (ii) any suspension or termination of IRB approval. In certain instances of alleged or apparent noncompliance, the IRB may choose to provide an early report to OVPR prior to a determination of serious or continuing noncompliance. As described in the OM, Part 12, OVPR may choose to further investigate the reports of serious or continuing noncompliance or ask for additional review by the Office for Human Research Compliance Review (OHRCCR). For situations reported to OVPR 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 OVPR on a quarterly basis as a way of monitoring the need for attention to policy or to education.

7.3.2 Institutional Reports

The OM Part 12 fully describes the obligations of the University to make additional reports outside the institution to sponsors and government authorities with jurisdiction.

8. ORIENTATION AND CONTINUING EDUCATION OF IRBMED MEMBERS AND STAFF

The IRBMED orientation and continuing education program for members includes workshops, mock protocol reviews, and completion of the Program for Education and Evaluation in

Responsible Research and Scholarship (PEERRS) human research modules and the UMHS HIPAA training for researchers. New member workshops consist of five weekly two hour sessions. Topics covered include:

- Human Subject Protections Overview
- Federal Regulations—How They Affect the IRBMED Review Process
- Federal Regulations—Special Populations
- Reviewing and Communications
- Mock Review with an IRBMED Chair

All PEERRS human subject modules are required. New members are initially considered alternate members. The orientation period is followed by a practicum period during which new members attend meetings and review protocols as a primary reviewer. IRBMED chairs determine when each new member's status changes from alternate to regular, and also when a new member may serve as an expediting reviewer. This usually occurs after about six months, but can vary depending upon completion of workshops, attendance, performance, and scheduling.

Depending upon the role of the new staff, 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.

The University of Michigan provides the opportunity for IRBMED members and staff to attend a national or regional conference (such as PRIM&R) as resources permit. The IRBMED will notify its members of additional educational opportunities, as appropriate.

Continuing education on ethics, regulations, federal guidance, university policies, and eResearch are provided to staff and members in the form of workshops, presentations at meetings, and written or electronic materials is provided on an on-going basis.

9. RELATIONSHIP WITH THE RESEARCH COMMUNITY

As part of the HRPP community, the IRBMED welcomes comments and concerns from other HRPP committees to foster a comprehensive review of 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:

- General Clinical Research Center (GCRC)
- Investigational Drug Service (IDS)
- Radioactive Drug Research Committee/Subcommittee on the Human Use of Radioisotopes (RDRC/SHUR)
- Institutional Biosafety Committee (IBC)

- Hospital Biomedical Engineering Unit (BEU)
- Tissue Procurement Core (TPC)
- Medical School or OVPR Conflict of Interest Committee (CoI)
- IRBs at other performance sites or coordinating centers
- Other committees, including peer review committees (e.g., Cancer Center Protocol Review Committee, GCRC Advisory Committee) and core service groups (e.g., Human Applications Laboratory).

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

10. DISCRETIONARY REVIEW OF NON-RESEARCH ACTIVITIES

The IRBMED is responsible for oversight of certain activities that do not constitute “research” under the Common Rule. These activities and IRBMED policies concerning the activities are described below.

10.1 Non-Research Use of Investigational Products Regulated by the FDA

The Department of Health and Human Services and the Food and Drug Administration have recognized circumstances under which a test article (an investigational drug, biologic, or device) may be made available for use in patients with life-threatening or other serious illnesses for which no satisfactory alternative treatments exist. Guidelines for the use of test articles are available on the FDA website.

An initial application may be submitted for a sponsor-initiated treatment protocol, clinician-initiated single patient or small group access, or for use of those devices designated by FDA as humanitarian use devices. In urgent care situations, the investigator should advise the IRBMED of patient status at the time of application. When necessary, the IRBMED will conduct prospective full board review at its next scheduled meeting. When patient care demands do not permit time for prospective review, use of a test article for non-trial clinical treatment may be reported to the IRBMED through an Emergency Use Report.

The FDA requires notification of the IRBMED of a non-research emergency use of a test article before or within five (5) days after the use. A chair or designee of the chair reviews the notification and evaluates the appropriateness of the request and the nature of the informed consent, if any. The IRBMED staff then issues a letter acknowledging receipt of the notification and reminding the investigator that the emergency care may not be claimed as research, nor may any data collected in connection with such care be included in the clinical trial data analyses as a report of a prospectively conceived research activity. This restriction of data use does not apply when an initial application receives prospective review as described in the preceding paragraph.

If an investigator believes that there may be a need for more than one emergency use, he/she must submit a formal protocol (using a new project application) to the IRBMED before proceeding

with any additional administrations or interventions. The IRBMED may require the investigator to submit a formal protocol, regardless of the investigator's beliefs, if the IRBMED anticipates repeated emergency use.

10.2 Ethical Review of Non-Research Activities at the Request of a Faculty or Staff Member

On a case-by-case basis, and at the discretion of the IRBMED chairs, the IRBMED will accept a non-human-subjects-research activity for which a faculty or staff members has requested an ethical review.

10.3 Use of Protected Health Information for Other UMHS Projects

The IRBMED may, subject to relevant University policies, review requests for waiver of authorization pursuant to the Health Insurance Portability and Accountability Act of 1996 and relevant regulations (collectively HIPAA), even if the requests involve projects that do not qualify as "research" under the Common Rule.

11. APPROVAL, REVIEW, AND REVISION OF IRBMED SOPS

The IRBMED cooperates with the Medical School Research Dean and 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 Dean and Compliance Committee, and the Vice President for Research. For purposes of this section, any changes made to maintain compliance with a new law, regulation, or order or formal guidance of a governmental agency (including, but not limited to, the International Conference on Harmonization), or to add or change administrative information (contact, resource, etc.), is not considered a substantive revision. Standard forms, guidance documents, and similar information developed by the IRBMED in consultation with the Medical School Research Dean and OVPR do not require further review or approval.

12. QUESTIONS/CONTACT INFORMATION

Questions concerning IRBMED or related University policies and procedures may be directed to:

- The IRBMED Chair(s): (734) 763-4768
- The IRBMED Staff: (734) 763-4768 or irbmed@umich.edu
- The Medical School Research Dean: (734) 615-4199
- The Associate Vice President for Research: (734) 763-1289

Legal questions may be directed to the Health System Legal Office: (734) 764-2178.

The IRBMED office can also be contacted by mail at IRBMED, Argus I, 517 W. William Ann Arbor, MI 48103-4943.