Institutional Review Board
(IRB-FLINT)
Standard Operating Procedures

May 2012
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PART 1 - GENERAL INTRODUCTION

Institutional Review Boards (IRBs) protect the rights and welfare of human subjects participating in research. The University of Michigan IRBs review and oversee research conducted by the University to assure that it meets ethical principles and complies with federal regulations that pertain to human subject protection at 45 CFR 46 and other pertinent regulations, policies and guidance.

The Vice President for Research (VPR) has developed and implemented a Human Research Protection Program (HRPP), an integrated system consisting of research leadership, administration, and oversight functions, including education, quality assurance and compliance; research review units, including institutional review boards (IRBs) and other organizations charged with responsibility for protecting human subjects, investigators, sponsors and research participants. Together these individuals and organizations promote excellence in all aspects of human research.

The purpose of the HRPP is to protect the rights and welfare of human subjects participating in biomedical and behavioral research conducted at the University of Michigan or elsewhere by University faculty, staff and trainees. Its goals are to promote compliance with relevant legal requirements and ethical standards at all levels, while addressing the needs and concerns of researchers and enhancing support of their endeavors.

The HRPP Operations Manual (OM) serves as a reference for investigators, IRBs, administrators, and others and the Standard Operating Procedures (SOPs) serves as the method by which the IRBs implement the policy.

The Office of the Vice President for Research maintains a research web site where extensive information concerning research conducted at the University and by its faculty may be found. All human subject research conducted by the University must be approved by an Institutional Review Board or granted an exemption by a University IRB (through its members or staff) or the VPR as specified in the IRBs Standard Operating Procedures. Research that has been reviewed and approved by a University IRB may be subject to further review and disapproval by other review bodies or officials (including the Vice President for Research); however, no person or organization may override an IRB’s disapproval determination.

Except for research that is specifically exempted in accordance with applicable laws and regulations and Part 4, Section IV of the OM, the University’s IRBs review and monitor all University research involving human subjects, regardless of funding source. In addition, certain types of research involving human subjects must be reviewed and approved by additional departments, division or units of the University. Depending on the nature and scope of a project, a University IRB may withhold its approval pending confirmation of approval by and/or receipt of additional information from any of these units and/or from review units at other performance sites.

The Institutional Review Board’s first and most important function is to protect the rights and welfare of human research subjects. Secondly, the IRBs seek to support the design and conduct of sound research by UM investigators in pursuit of the University’s mission to develop and disseminate new knowledge in the public interest. The safeguarding of subject rights and welfare must, at all times, take precedence over the goals and requirements of any research endeavor overseen by the IRB. IRB members and staff, as well as researchers submitting applications to the IRB, must be informed of and understand this obligation.
PART 2 - ORGANIZATION OF THE HRPP SUPPORTING IRB-FLINT

I. Administrative Structure for IRB-FLINT
IRB-FLINT consists of one separately constituted IRB registered with OHRP, supported by an administrative office and infrastructure. The IRB meets approximately once per month, but by agreement and collaboration via the chair and the core members, agrees to work collaboratively in order to facilitate the review of time-sensitive applications.

The Office of the Vice President for Research (OVPR) provides administrative and compliance support for IRB-FLINT with the Provost or designee on the Flint Campus assigned responsibility for oversight of the office.

The Provost or designee, the IRB-FLINT Chair, and the Director of the Flint Office of Research meet periodically to review IRB workflow, consider guideline/SOP/policy modifications, provide general direction for the IRB, and consider development of new initiatives and receive updates on progress for existing initiatives.

The day-to-day operation of the IRB is under the direction of the Director of Research and the IRB-FLINT Chair. The Director of Research is not involved in the day-to-day operations of the review process.

II. Organizational Entities That Support IRB-FLINT
Numerous additional organizational entities contribute to the operation of the University’s HRPP and IRB-FLINT. These include:

- The Division of Research Development and Administration (DRDA), and the Office for Human Research Compliance Review (OHRCR), and coordinating committees, such as the Human Research Coordinating Council (HRCC) and the IRB Council;
- The schools, colleges and other academic units to which faculty, staff and trainees engaged in human research are appointed;
- Other research review units with responsibility for monitoring specific categories of research;
- Other support units and committees, such as the Center for Statistical Consultation and Research (CSCAR), and the Research Administrators’ Network (RAN), and
- Key executive and administrative offices and functions including the Provost or designee’s Office and Office of General Counsel.

Refer to the OM Part 2, Section II for a detailed description of each of these entities.
PART 3 - HRPP POLICY

I. Introduction
The Bylaws of the Board of Regents of the University of Michigan assign to the Vice President for Research general executive responsibility for the research programs of the University, including maintenance of appropriate liaisons between the University and government agencies and other organizations supporting University research. The Vice President for Research, in turn, has established the HRPP. A detailed discussion of the HRPP and its institutional policy can be found in Part I of the OM.

II. The Operations Manual (OM)
The Operations Manual (OM) is the primary location for compiling, organizing, and integrating the rules, policies, practices, and guidance encompassing the University's HRPP. The VPR has approved the OM and approves each modification or amendment to it. Records of such approval are maintained in the Office of the Vice President for Research (OVPR).

At least once every three years, in conjunction with the AAHRPP accreditation cycle, OVPR 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. Nonsubstantive 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 Deputy Institutional Official with notice to the VPR.

III. IRB Standard Operating Procedures and Policies
A. General Provisions
IRB-FLINT, to which these SOPs refer, is mandated by and follows Federal regulations, is accountable to the Provost or designee, and operates under the authority of the University’s Vice President for Research. IRB-FLINT has oversight of human subject research conducted by all the schools, colleges, and units of the University of Michigan Flint. The following is a list of major schools and units served by IRB-FLINT:

- College of Arts and Sciences
- School of Education and Human Services
- School of Health Professions and Studies
- School of Management
- University Outreach

IRB-FLINT assures that where applicable, research will comply with state and local laws and regulations and University policies that relate to research involving human subjects. Additionally, IRB-FLINT complies with any other federal and state regulations and statutes which apply to research under its jurisdiction, including the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

The IRB may, in its discretion, consider other ethical guidelines as well, including those set forth in the Nuremberg Code, the Declaration of Helsinki, the International Conference on Harmonisation, professional society codes of ethics and reports and recommendations from national advisory bodies, such as the National Bioethics Advisory Commission (NBAC) and the Secretary’s Advisory Committee on Human Research Protections (SACHRP).

The IRB-FLINT cooperates with OVPR to establish, review, and revise these SOPs. These SOPs and any substantive revisions thereto, are subject to review and approval by OVPR.
Any changes made to maintain compliance with a new law, regulation, or order or formal
guidance of a governmental agency, 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 IRB-FLINT do not require further review or
approval by OVPR.

IV. IRB-FLINT Membership and Staff
The IRB-FLINT membership is selected so as to be sufficiently qualified through the experience,
expertise, and diversity of its members.

A. Qualification and Appointment of Chair and Reviewers
1. Chair
IRB-FLINT has one chair appointed by the Provost or designee. The chair serves at the
will of the Provost or designee and is a respected faculty member of, and has an
appointment in, one of the schools whose research is subject to IRB-FLINT jurisdiction.
The chair shall be qualified through experience and expertise, concerned about human
rights and ethical issues, and familiar with regulations relevant to the use of human
subjects in research.

The chair also may serve as a board representative of their respective school, college,
or unit. The appointment of a chair will, as practical, rotate among the major units under
IRB-FLINT jurisdiction.

One or more members of the IRB may be selected by the Chair as alternate chair in the
event that the chair is absent and not able to convene an IRB-FLINT meeting. An IRB
member or core staff member may be designated to fulfill an administrative function
associated with the chair’s role (e.g., attend IRB Council), but that designation does not
carry the full authority of the chair unless specifically authorized.

2. Expediting Reviewers
Expediting review is conducted by a single reviewer with relevant expertise. IRB-Flint
chair or IRB members appointed by the chair may conduct expedited reviews under the
regulations stated in 45 CFR 46.110. Expediting reviewers are selected based on their
knowledge of pertinent content areas and concern for human rights and ethical issues.

Expediting reviewers have authority to review and approve expedited and exempt
applications or refer them to the convened board, as necessary.

Staff members who are sufficiently qualified through experience and expertise and are
familiar with regulations relevant to the use of human subjects in research, may also
review and approve scheduled continuing renewals according to criteria set by IRB
guidelines. Designated staff members may also perform expedited review of other
selected projects, including initial applications or amendments, according to criteria set
by IRB guidelines.

3. Exempt Reviewers
Expediting reviewers and qualified members of the IRB staff may act as exempt
reviewers. Staff members acting as exempt reviewers must be qualified through
experience and expertise, and familiar with regulations relevant to the use of human
subjects in research. The Director of Research and the IRB chair will jointly assess the
readiness of staff to conduct autonomous exempt reviews based on previous education and experience and performance in their current role.

B. Qualifications and Appointment of IRB-FLINT Members

1. Regular Members
IRB-FLINT will consist of not fewer than five persons. Representatives from the primary academic units under IRB-FLINT jurisdiction (one of whom must be a scientist), plus at least one community member not affiliated with the University of Michigan, and one non-scientist will be appointed to serve.

Membership shall be sufficiently diverse in order to evaluate categories of research presented to the Board. IRB-FLINT must have members with knowledge of the specific scientific disciplines relevant to the research that it reviews. If the IRB regularly reviews research involving identified vulnerable populations, the IRB will secure members experienced in working with such populations. The IRB must also possess knowledge of the local research context to fulfill its review responsibilities under federal regulations and the OM. If the appointed membership is not sufficiently knowledgeable about the scientific discipline or research context, consultants or other information may be used to supplement IRB-FLINT review (refer to section D, below).

Scientist members are members whose training, background and occupations would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline.

Non-scientist members are members whose training, background, and occupation would incline them to review research activities form a standpoint outside of any biomedical or behavioral scientific discipline.

Community representatives may be scientists or non-scientists. Community members are individuals who are sensitive to community attitudes and mores in the promotion of respect regardless of race, gender and cultural background, and counsel to safeguard the rights and welfare of human subjects. To be eligible for participation on IRB-FLINT as a community representative, neither the member 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, volunteer at the institution on business unrelated to the IRB, 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.

A copy of the current membership roster is on file in the IRB-FLINT office. The roster is updated as required, at least quarterly, and provided to The Provost or designee. The Provost or designee is responsible for providing required updates of membership changes to OHRP.

Members are expected to attend, actively participate in, and vote at monthly meetings of the IRB-FLINT and to serve as reviewers of assigned applications. Issues regarding poor attendance of members will be addressed by the IRB-FLINT chair and administrative directors on a case-by-case basis.

2. Alternate Members
Alternate members may be chosen by, among other qualifications, their ability to expand the expertise and/or diversity of the IRB-FLINT. Alternate members will be appointed from the academic units whose research is subject to the jurisdiction of the IRB-FLINT and may also be appointed for community and non-scientist members.

Alternate members may attend all meetings of the IRB, but are not counted towards quorum and may not vote unless the regular member for whom they are appointed as an alternate is absent.

Alternate members may be assigned to replace full members in the event the full member is on leave from the University (e.g., for a sabbatical or medical leave).

Alternate members may serve as primary or secondary reviewers for expedited, exempt and full board reviews.

3. Appointment and Reappointment
Potential IRB-FLINT members affiliated with the University may self-nominate or be identified by the IRB-FLINT chair or representative of the academic unit under the jurisdiction of IRB-FLINT. Community and/or non-scientist members (not affiliated with the University) may self-nominate or be recommended for nomination by third parties.

The IRB-FLINT chair and designated staff will evaluate each identified candidate. Evaluations consist of a face-to-face meeting with each potential member to discuss their motivations and interests relative to human subject research. Special academic, professional, and/or personal experiences which may contribute to the expertise of the Board are also addressed. Where appropriate, candidates are asked to provide a curriculum vita. If one is not available, a brief summary of previous educational, professional, and/or personal experiences is requested.

The IRB-FLINT chair recommends appropriately qualified candidates to the Provost or designee for appointment. Upon agreement with the recommendation, the Provost or designee will sign a letter of appointment indicating the term and status of the candidate’s appointment as an alternate or full member. Changes in appointment status (i.e., status as a full member decreased to an alternate member during a leave from the university) can be approved. The letter of appointment may be issued by either the IRB-FLINT chair or the Associate Provost or designee.

C. Terms of Appointment
1. Term of Service
The IRB-FLINT chair serves a five-year term and may be reappointed based on recommendation of the Director of Research, and mutual agreement by the chair.

Regular or alternate members serve three year terms subject to reappointment based on recommendations of the IRB-FLINT chair, the Director of Research and staff, and mutual agreement by the member.

2. Termination of Appointment
The IRB-FLINT chair serves at the pleasure of the Associate Provost or designee and their appointment can be terminated by the Associate Provost or designee. If it becomes necessary to terminate a regular or alternate member before expiration of their
appointment, the Associate Provost or designee, on the advice of the IRB-FLINT chair will effect termination.

Reasons for early termination include: (i) failure to attend meetings, (ii) failure to participate at meetings, (iii) failure to uphold the central tenants of the Belmont Report or other applicable policies or ethical principles, (iv) engaging in activities deemed inappropriate or incompatible with IRB membership.

3. Compensation of Chairs and Members
The rates of compensation for the roles of chair and expediting reviewer are determined by the Provost or designee in consultation with the academic units, if necessary.

Rates of compensation for community members are determined by the Provost or designee in consultation with Director of Research and the IRB chair.

Representatives of the IRB (including committee members and chair) are invited to attend conferences each year on various human research protections topics; payment for travel and registration expenses is provided according to available budget.

4. Liability Coverage
Liability coverage is a matter of institutional policy and is further described in Part 3, Section III of the OM.

D. Consultants, Advisors and Ad-Hoc Reviewers
1. Selection
The IRB must possess sufficient knowledge of the local research context to fulfill its review responsibilities under federal regulations and the OM. To supplement this knowledge, the Director of Research, the IRB chair, IRB membership and IRB staff may, at their discretion, invite from among the faculty and staff of the University or the community at large, persons whose experience or expertise may aid the IRB in performing its responsibilities, whether during meetings or otherwise.

Consultants may include, but are not limited to, ad hoc reviewers for individual protocols, legal advisors, or others. Alternate members may serve as non-voting consultants to the IRB when their expertise would contribute to the evaluation of the research.

2. Participation
Consultants may participate in the deliberations concerning any 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. Information provided by consultants is documented in the minutes of the meeting at which the relevant protocol is reviewed.

A consultant, who is unable to attend the convened board meeting or meet directly with an expediting reviewer, will send a written communication for review and consideration. Information presented by the consultants will be added to the application file.

E. Periodic Review of Membership and Composition
1. Review of Membership
The membership and composition of the board is reviewed at least annually with the IRB-FLINT chair, IRB administrative staff, and the Director of Research. Changes are
made to the membership or composition of the board to meet regulatory or organizational requirements as needed.

2. Reappointment of Members

Members may be recommended for reappointment as full or alternate members, or their reappointment may be declined. Members are assessed based on their continuing interest and availability, preparation and participation at meetings, and the ongoing requirement for their special expertise.

3. Reappointment of the Chair

Prior to the end of their term, the chair is evaluated by the Provost or designee, with input from the Director of Research, IRB staff and IRB membership, as appropriate. The Chair is assessed based on their continuing interest and availability, preparation and participation at meetings, participation in policy efforts, and the ongoing requirement for their special expertise. Upon the recommendation of the Director of Research, the Provost or designee may choose to reappoint the chair. A Chair desiring to continue IRB-FLINT service at the end of their term as chair may be reappointed by the Provost or designee as a full or alternate member of the IRB.

4. Member and Chair Evaluation

The Associate Provost evaluates the IRB-FLINT chair each year, and feedback is provided.

IRB members are evaluated and given feedback every year by the IRB Chair. Criteria for evaluation include: attendance at meetings, level of participation at meetings, thoroughness of review and regulatory knowledge, use of eResearch, working relationship with IRB staff, and interactions with principal investigators (where indicated). Members may be evaluated more often if circumstances dictate. Members are informed of these expectations and the evaluation process at the time of their appointment(s).

F. IRB-FLINT Staff

1. Support and Supervision

The IRB-FLINT is supported by a professional staff who report to the Director of Research. Day-to-day supervision is provided by the Director of Research and the IRB Chair.

2. Hiring

Qualified personnel are hired according to the University policies and procedures. A summary of positions and job descriptions is kept on file in the IRB office.

3. Duties

IRB-FLINT staff are responsible for facilitating IRB operations (e.g., protocol review, documentation and record retention, fact-finding, creation of informational resource development and educational activities) in such a manner as to maintain compliance with applicable regulations and University policies. IRB staff may also participate in additional projects and assignments, as directed.

4. Staff Evaluation
Staff are evaluated yearly in a performance appraisal conducted by the Director of Research in consultation with the IRB Chair. If circumstances dictate, staff are evaluated more often.

**G. Orientation and Continuing Education of IRB-FLINT Members and Staff**

IRB-FLINT provides IRB administrative staff and IRB members with sufficient training and opportunities for continuing education in order for them to effectively discharge their duties.

1. **IRB-FLINT Membership**
   a. **New Member Orientation**
      New IRB-FLINT members are provided a detailed orientation designed to prepare them to effectively discharge their duties. The orientation includes a series of meetings with the chair and IRB staff. Most members attend one or more convened IRB-FLINT meetings as a non-voting guest prior to the initiation of their formal appointment.

      During the orientation process, IRB procedures are described and discussed, basic resource materials are distributed (including copies of pertinent federal regulations, the Belmont Report, OHRP information, guidelines, and policies and standard operating procedures) and paths for acquiring additional information are provided.

      Members review the relevant educational modules of the UM PEERRS program and complete the associated testing.

      IRB members are also encouraged to obtain membership in, and monitor the dialogue of, the IRB-Forum listserv.

   b. **Current Member Continuing Education**
      IRB-FLINT members are informed of opportunities for continuing education. As permitted by the number of agenda items at an individual convened meeting, time is devoted to educational activities. Current developments and the application of regulations in human subjects protection may be discussed. Invited speakers on special topics may be scheduled.

      IRB members are encouraged to attend local presentations from other units of the University or other locally available educational opportunities or courses such as those offered by IRBMED, Michigan State University or other local universities, societies, or organizations.

      As budget and availability permit, support is available for members to pursue other opportunities such as national meetings sponsored by PRIM&R or OHRP.

2. **IRB-FLINT Staff**
   a. **New Staff Orientation**
      New staff receive an orientation to IRB office policies, procedures, and practices.

      Staff receive specialized training of the eResearch system in order to conduct reviews of electronically submitted applications.
IRB staff are required to take and pass the Human Subjects module in PEERRS and it is strongly recommended that additional modules in research administration, conflict of interest, or other appropriate modules be completed.

b. Current Staff Continuing Education
As budget and availability permit, IRB staff are provided with opportunities to attend local and national conferences and encouraged to attend locally available educational opportunities or courses such as those offered by IRBMED, Michigan State University or other local universities, societies, or organizations.

IRB staff participate in learning activities within the office including, ‘lunch and learn’ presentations, and journal subscriptions.

IRB staff are also encouraged to monitor the dialogue of the IRB-Forum listserve.

PART 4 - IRB-FLINT FUNCTIONS AND OPERATIONS
IRB-FLINT has the authority to approve, disapprove, terminate, or require modifications to human research projects under its jurisdiction. This section details the procedures for making these determinations in addition to exempt or not regulated human research determinations.

I. Application Submissions
Research proposals requiring IRB-FLINT review must be submitted via the web-based eResearch Regulatory Management System (http://eresearch.umich.edu). The University developed eResearch to provide a unified system for the submission and review of research applications and the continuing management and oversight of research information. eResearch is designed to help the University meet its obligation to ensure that research is conducted in an ethical manner and in accordance with the laws and regulations governing the conduct of research. Any investigator intending to initiate a research study involving human subjects that is under IRB jurisdiction must submit an initial application for review and approval of the study. No aspect of the study (including testing performed solely to determine eligibility for the study) may begin until IRB has approved the application or issued an exemption determination via eResearch.

A. Application Types
1. Initial
Any investigator intending to initiate a research study involving human subjects that is under IRB-FLINT jurisdiction must submit an initial application for review and approval of the study. No aspect of the study (including testing performed solely to determine eligibility for the study) may begin until IRB-FLINT has approved the application or issued an exemption determination via eResearch.

The eResearch initial application offers customized application paths for a variety of research designs:
- Standard, non-exempt, research projects
- Secondary use of existing identifiable data/records/specimens
- Exempt human subjects research
- Activities not regulated as human subjects research
- Projects lacking immediate plans for involvement of human subjects, their data, and/or their specimens
- Request for review by a non-UM IRB.
2. **Scheduled Continuing Review**
Continuing review is required in accordance with 45 CFR 46 for all research studies under IRB oversight at intervals appropriate to the magnitude of risk of the project and other considerations. For research studies with federal sponsorship, IRB conducts a continuing review at least once each year. Some research may require continuing review at an interval of less than one year as assessed by the convened board or expediting reviewer.

The principal investigator of an active project is responsible for submitting an application for scheduled continuing review to the IRB with sufficient time allocated for the IRB to review and approve the study renewal prior to the expiration date.

As a courtesy to principal investigators, reminder notices are sent 90, 60 and 30 days prior to the expiration date of the project. If a scheduled continuing review application is not submitted by the expiration date, the eResearch system triggers an expiration notice for the project. The notice informs that investigator that all research activity on the project, including data analysis, must stop until a scheduled continuing review application is approved by the IRB. If IRB approval does lapse, the PI will also be required to submit an ORIO (Other Reportable Information and Occurrences) report disclosing the reason for the lapse and reporting any project activity that has taken place during the lapse of approval.

The principal investigator is responsible for notifying the IRB of the completion and closure of a study. The investigator must notify the IRB immediately if the study is suspended by an outside entity (i.e., FDA, OHRP, etc.) or if the principal investigator terminates the study for the safety of the human subjects. The Scheduled Continuing Review (SCR) application is used to submit the investigator's study completion (Termination) report.

At the time of continuing review, research qualifying for exemption under 45 CFR 46.101 or UM and IRB-FLINT policies and will receive an exempt determination, if appropriate.

3. **Amendment**
A principal investigator may not implement any changes to an approved study subject to IRB oversight (including to the protocol or informed consent document) without prior IRB review and approval, unless the change is necessary to eliminate apparent immediate hazards to the subjects. A change made to eliminate an immediate hazard must be reported promptly to IRB. An eResearch amendment application is submitted to request a modification to an approved study.

Modifications to a study that require an eResearch amendment include, but are not limited to:
- Changes to the study protocol, including changes to eligibility criteria or to study materials such as recruitment materials and advertisements, questionnaires, surveys, and scripts, including the addition of new materials.
- Changes to previously approved informed consent documents
- Changes in study team members (including principal investigator, co-investigators or study staff) or performance sites(s).
- Changes in funding or project support.
- Changes in any other aspect of the research.
The IRB may use the expedited review procedure to review minor changes in research previously approved by the convened board. Examples of changes that may be reviewed by the expedited procedure include:
- Addition of survey questions that do not impact the risk to subjects
- Minor alterations to recruitment materials
- Minor administrative changes to the informed consent.

The IRB may authorize its staff to acknowledge amendments containing non-material changes to protocols and informed consent without submission of the amendment application to the convened board or by an expedited reviewer. These may include:
- Correction of typographical or grammatical errors
- Changes in investigator or IRB contact information

The date of IRB approval of a modification to an application does not change the date by which a regularly scheduled continuing review must be completed.

For projects in exempt status, an amendment may be required for significant modifications to the study that would move the project outside the definition of the exemption granted for the study.

4. Adverse Event Notification and Other Reportable Information and Occurrences Report

The application form for reporting adverse events (AEs) or other reportable information and occurrences (ORIOs) is also found in eResearch. IRB-FLINT has adopted reporting guidelines and timeframes for studies under its jurisdiction.

**Adverse Events (AEs) include:**
- Death
- A life threatening experience
- Severe social, psychiatric/psychological/familial or financial harm related to the research
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/incapacity
- A congenital anomaly/birth defect
- Events that jeopardize the patient or subject and may require medical/psychiatric, dental or surgical intervention to prevent one of the outcomes listed above

**Other Reportable Information Occurrences include:**
- Audits
- Other Reports
- Protocol deviations
- Protocol violations
- Facility/data accidents
- Complaints

II. General Review and Approval Procedures

The eResearch application is designed as a comprehensive application for investigators and a review tool for IRB members and office staff. The eResearch application is designed to gather information and materials including research protocols, informed consent documents,
recruitment materials, grant applications, survey instruments and audio/visual materials necessary for the IRB to evaluate and approve research in accordance with relevant regulations: 45 CFR 46.109, 46.110, and 46.111. IRB staff, IRB reviewers and board members, and study team members all have access to the same application materials via the eResearch system. IRB staff and reviewers utilize regulatory checklists imbedded in the eResearch system to guide their review of application materials.

III. Determining Whether and Under What Authority Research is Regulated

As part of the process, the IRB Research Compliance Specialist in consultation with IRB-FLINT chair, as necessary, assesses whether: 1) the activity described in the application is research as defined by the Common Rule; 2) the research is exempt from IRB oversight; 3) the University of Michigan is engaged in the research.

Only non-exempt, human subjects research where UM is engaged requires IRB oversight.

A. Projects Not Regulated under the Common Rule

The IRB-FLINT Research Compliance Specialist will review all applications to determine whether they meet the definition of human subjects research regulated under the Common Rule, using guidance found in the UM HRPP OM Part 4.V.B and Part 3.III.C, the Decision Trees posted on the UM HRPP website, and the OHRP Decision Charts found at http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm. He/she will consult the chair, as needed.

By using the tools available within eResearch, PIs can self-assess a proposed project to determine whether it meets the definition of IRB-regulated human-subjects research. Submission of an eResearch application is not required for those activities deemed outside of IRB regulatory authority. PIs may, however, submit a brief eResearch application to self-generate a determination letter for support or publication purposes, or may consult with the IRB Research Compliance Specialist or chair to confirm the ‘not regulated’ status of the project.

Some types of projects that are not regulated under the Common Rule may require initial IRB review only for the purpose of assessing compliance with HIPAA or other regulations or institutional policies.

Once a ‘not regulated’ determination has been issued, the IRB is no longer involved in the oversight or monitoring of that activity.

B. Exempt Projects

As per the University HRPP Operations Manual, in order be deemed to be exempt, human research activities must be reviewed and determined to fall within one or more of the explicit exemption categories listed in the federal regulations or, for non-federally supported research, fall under exemption categories described in UM policy (see HRPP Innovation and Demonstration Initiative web site).

With the exception of research involving certain vulnerable populations and of FDA-regulated research, research may be granted exempt status if all proposed research activities involve procedures listed in one or more of the specific categories listed below:

Federal Exemption Categories under 45 CFR 46.101(b):
1. Research conducted in established or commonly accepted educational settings involving normal educational practices, such as research on regular and special education instructional strategies, or research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observations of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects outside of the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, or reputation. This exemption does not apply to research with children when the investigator will participate in the observation of public behavior.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior not exempt under the previous category but if the human subjects are elected or appointed public officials or candidates for public office; or federal statutes require without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available; or the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

5. Research and demonstration projects that are conducted by or subject to the approval of federal department or agency heads, and that are designed to study, evaluate, or otherwise examine: public benefit or service programs; procedures for obtaining benefits or services under those programs; possible changes in or alternatives to those programs or procedures; or possible changes in methods or levels of payment for benefits or services under those programs. This exemption is for federally-supported projects and is most appropriately invoked with authorization or concurrence by the supporting agency. The following criteria must be satisfied to invoke this exemption:

   o The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutritional services under the Older Americans Act);
   o It must be conducted pursuant to specific federal statutory authority;
   o There must be no statutory requirements that the project be reviewed by an IRB;
   o The project must not involve significant physical invasions or intrusions upon the privacy of participants.

Non-federally supported research and demonstration projects conducted by or subject to the approval of state department or agency heads, and that otherwise meet the above requirements, are also eligible for exemption.

The University has already departed from federal regulations by creating a new "exemption" parallel to existing Exemption 5 for projects sponsored by the State of
Michigan. Additional exemptions may be considered, or additional flexibility in applying exemption categories may be considered, for non-federally sponsored research that poses little or no risk to subjects or for which another institutional oversight mechanism is better designed.

6. *Taste and food quality evaluation and consumer acceptance studies* if wholesome foods without additives are consumed; or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, by the Food and Drug Administration or approved by the Environmental Protections Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

In addition to the six federal exemption categories above, the U-M grants exemptions under the following category 7 conditions:

7. *Research in which study activity is limited to analysis of identifiable data.* For purposes of this research study, all research subject interactions and interventions have been completed and the data continues to contain subject identifiers or links. Research which is federally supported, FDA regulated or was issued a Certificate of Confidentiality may not select this category.

The eResearch application provides an exempt application pathway to assist PIs and the IRB-FLINT in identifying exempt research, but under UM policy, only the IRB has the authority to issue an exempt determination. Designated IRB-FLINT staff, IRB chair(s), or expediting reviewers, 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 Institutional Official or their designee.

The IRB 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 IRB oversight, unless the scope of the project changes such that it no longer meets the criteria required for exemption.

The exempt determination is issued to the investigator via eResearch. The notification letter includes the exemption category assigned to the study as well as instructions to amend the eResearch application for IRB for review if the scope of the project changes beyond the criteria for exemption.

C. UM Engagement in Research

IRB-FLINT staff, in consultation with IRB chair(s) and/or the Director of Research, as necessary, determine whether UM is “engaged” in a non-exempt research project. A performance site becomes engaged in human-subjects research when its employees or agents intervene or interact with living individuals for research purposes, or obtain individually identifiable private information for those purposes. A site is always deemed to be engaged when it receives a direct federal grant or other award to support non-exempt human-subjects research. See the OHRP guidance on “Engagement of Institutions in Research” and the OM Part 4.

IRB-FLINT has oversight only for research in which UM Flint is engaged or has completed an IRB Authorization Agreement (IAA) or Individual Investigator Agreement (IIA) and accepted additional responsibility for oversight of a research project or personnel. All such agreements are authorized by OVPR.
IV. Standard Review Procedures for Non-Exempt Research

For projects that are subject to IRB-FLINT oversight, the IRB staff, in consultation with IRB chair(s) and IRB administration, as necessary, makes a preliminary assessment as to whether the proposed research qualifies for expedited review or must be scheduled for convened board review. Non-exempt research projects involving human subjects must be reviewed by an expediting reviewer or by the convened IRB. The expedited and convened board review procedures are used for initial applications, amendments, scheduled continuing review applications, and adverse event/ORIO reports.

A. Expedited Review

1. Criteria for Expedited Review
   a. Projects qualifying for expedited review include: Research involving no more than minimal risk to subjects that meets the expedited review categories identified in 63 FR 60364-60367, November 9, 1998. ([http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm](http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm))
   b. Minor changes to approved research previously reviewed by the convened board. See OM Part 3, Section III C.3.

2. Expedited Review Process

   eResearch submissions qualifying for expedited review are accepted and reviewed by the IRB on a continuing basis, during University business hours, except during seasonal holidays when University administrative offices are closed. The IRB-FLINT staff and reviewers make every attempt to review expedited applications without undue delay.

   IRB staff conducts an administrative review of each application for completeness and adherence to regulatory requirements. An application that is not complete is returned to the PI via eResearch with instructions regarding necessary changes before the application can be submitted for regulatory review. Once the administrative review process is complete, the IRB staff assigns the application to the expediting reviewer.

   Expedited review is conducted by a single reviewer. The IRB-FLINT chair(s) or IRB members appointed by the chair(s), may conduct expedited reviews under the regulations stated in 45 CFR 46.110.

   If relevant expertise to review an application does not exist among the expediting reviewers, then the reviewer may request, via the IRB office, that an ad hoc consultant review the application and supporting materials. The outcome of this review is documented for the review and consideration by the expediting reviewer.

   The application and supporting documents including informed consent documents, study protocols, survey instruments, and recruitment materials are forwarded to the reviewer via eResearch. Materials that cannot be provided via eResearch are set aside for review within the IRB Office. A regulatory checklist is also generated for the reviewer at the time of assignment, including comments provided by the IRB staff. In addition, the reviewer has access to all eResearch correspondence between the IRB staff and the study team. The assigned expedited reviewer examines the application and supporting materials for compliance with regulations and documents the review and determination using the reviewer checklist in eResearch.

3. Expedited Review Determinations
All expedited determinations, decisions, and contingencies issued by the IRB are recorded in eResearch and are available for review by the members of the IRB, the IRB staff, the investigator and study team. Investigators receive extensive detail regarding any changes required in order to achieve approval of the application.

a. Approve
The expediting reviewer may issue a determination to approve an application without imposing changes to the study or informed consent process if it meets all regulatory requirements for approval (refer to Section D, below). The reviewer must also identify the expedited review category used to approve the study.

The approval period begins on the date of the submission of expedited reviewer’s approval with contingencies regardless of when the specified changes are resubmitted to IRB.

For federally-supported research, the approval period shall not extend beyond one year (364 days).

b. Approve with Contingencies
The expediting reviewer may make approval contingent on the principal investigator making specified changes to the protocol, informed consent document(s), or other supporting materials. The investigator is notified of the study outcome via eResearch and is provided with detailed instructions regarding required changes to the application or study materials that must be completed before the application can receive final approval. The expediting reviewer may indicate whether they wish to review and approve the response to contingencies or whether the IRB staff can perform that activity.

The IRB 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 and may be administratively terminated.

c. Changes or Clarification Requested
For projects that require significant revision before approval can be granted, the expediting reviewer will request that the application be returned to the investigator using the Changes or Clarification Requested activity. The investigator will be provided with detailed instructions, via eResearch, of the materials needed or revisions to the application or study materials that must be submitted before reconsideration of the application by the expediting reviewer.

The Board 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 and may be administratively terminated.

d. Request Review by Convened Board or Other Review Path
An expediting reviewer may return an application to the IRB-FLINT staff with a request that the chair place the study on the agenda for the convened board, if the reviewer finds that the study does not meet the criteria for expedited review, or if the reviewer feels that the expertise of the full board would prove useful in the review. Only the convened IRB can disapprove a study.
An expediting reviewer can also recommend that a study receive an exempt or not regulated determination.

e. Reporting of Expedited Reviews to the Convened Board
Expedited approvals for the time period between meetings are reported to the board at the next meeting of the convened IRB.

B. Convened (Full) Board Review
1. Criteria for Convened Board Review
Projects requiring IRB-FLINT oversight that do not meet the criteria for expedited review are assigned to the convened IRB for review. Such projects include:
   - Research involving more than minimal risk to subjects
   - Research involving vulnerable populations, sensitive topics, or complex design elements that would benefit from review by the breadth of expertise represented at the convened board.
   - Projects referred to the convened board by the IRB chairs or at the request of an expediting reviewer.

2. Convened Board Review Process
IRB-FLINT meets monthly, according to a published schedule, to review assigned applications. The IRB staff, in consultation with the IRB chair assigns a primary and secondary reviewer from the IRB membership for each initial application. Scheduled Continuing Reviews and Amendments may be assigned only a primary reviewer, or a primary and secondary reviewer, depending on the complexity of the application. The primary reviewer typically has relevant expertise or knowledge of the subject matter. The secondary reviewer may represent a different field of expertise or experience, and will be chosen from the membership at-large, including the non-scientific and community members.

   If relevant expertise to review the application does not exist among the IRB membership, then the IRB chair, the primary or secondary reviewer, or the IRB staff, may select an ad hoc consultant to review the application and supporting materials and present the outcome of their review at the convened meeting. IRB staff facilitates contact with the consultant and provides them with a copy of relevant application materials and confidentiality statement. Consultants are typically used to provide expertise in a specific subject area or about a particular subject population.

   The application and supporting documents including informed consent documents, study protocols, survey instruments, and recruitment materials are forwarded to the primary and secondary reviewers via eResearch. Materials that cannot be provided via eResearch are set aside for review within the IRB Office. A regulatory checklist is also generated for each reviewer at the time of assignment, including comments from the IRB staff. In addition to the assigned reviewers, IRB board members have access to the full application and supporting materials for review prior to the meeting, including all eResearch correspondence between the IRB staff and the study team.

3. IRB-FLINT Determinations
All convened board determinations, decisions, and contingencies issued by the IRB are recorded in eResearch and are available for review by the members of the IRB, the IRB
staff, the investigator and study team. Investigators receive extensive detail regarding any modifications required in order to achieve approval of the application.

a. **Approve**
The convened board may vote to approve an application without imposing changes to the study or informed consent process if it meets all regulatory requirements for approval (refer to Section D, below).

The approval period begins on the date the submission is approved by the IRB and generally expires 364 days later unless the IRB issues a shorter approval period.

b. **Approve with Contingencies Pending**
The IRB may vote to make approval contingent on specified changes to the protocol, informed consent document(s), or other supporting materials. The principal investigator is notified of the study outcome via eResearch and is provided with detailed instructions regarding required changes to the application or study materials that must be completed to the satisfaction of the IRB before the application can receive final approval. Such changes must require no more than the simple concurrence of the investigator. The IRB, in its vote, must indicate whether the response to contingencies can be reviewed and approved by the chair, a primary reviewer, or returned for review and approval by the convened board.

The date of the vote to approve with contingencies pending shall be deemed the date of approval by the convened IRB regardless of when the specified changes are submitted to IRB for final review and release of the contingent approval. Approval periods are issued according to the standards outlined in the preceding section.

The Board 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 and may be administratively terminated.

c. **Action Deferred**
The IRB-FLINT may vote to defer action on an application when a significant action on the part of the investigator or the convened board is required before the IRB can consider approval or disapproval. If the action involves the principal investigator, notification is provided via eResearch and includes detailed instructions regarding required changes to the application or study materials that must be completed to the satisfaction of the IRB before the application can receive additional consideration and possibly, final approval. If the required action involves the IRB, appropriate, designated individuals will undertake the necessary actions.

The Board 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 and may be administratively terminated.

d. **Disapproval**
The IRB-FLINT may vote to disapprove an application to conduct human subjects research when it determines that the study design does not provide, and is unlikely to be modified to provide, adequate protection to subjects. Disapproval of an application usually follows several attempts by the investigator, in conjunction with the efforts of the IRB, to modify the study design to afford protection to the subjects.
If the IRB disapproves a research activity, the PI will be notified of the decision in writing. The notification will include a statement of the reasons for disapproval and will provide instructions to the investigator regarding his/her right to respond to the IRB in person or in writing.

Only the convened IRB can disapprove a study and this study-specific decision may not be modified by any other agency or entity at the University of Michigan. A principal investigator may submit a new study on the same research topic, without prejudice, if the IRB’s reasons for disapproval in the first instance are fully addressed.

e. Appeal of Disapproval
An investigator may submit an appeal to the IRB via the eResearch system and may appear before the convened IRB to respond to the disapproval.

f. Appeal of a Decision Other than Disapproval
If an investigator wishes to appeal any other decision issued in conjunction with the review of a study, the investigator may contact the IRB for a full and considered discussion of the concern. Examples of these decisions include the transfer of an application to a different UM IRB for review and oversight or objection to a contingency or change request within the application. Concerns will be addressed by the IRB chair in consultation with the reviewing entity (convened board or expediting reviewer).

C. Criteria for IRB Approval
All applications for research with human subjects, reviewed by a single expediting reviewer or by the convened board, are reviewed and approved in accordance with the requirements of 45 CFR 46.111. The IRB considers the following elements when evaluating and approving a research proposal:

1. Scientific Merit and Feasibility
The IRB considers whether research procedures are consistent with sound research design in order to yield the expected knowledge. Scientific merit is examined in relationship to the risks and benefits of the research.

For projects that have undergone a peer review process, the eResearch application asks the researcher to identify the organization that conducted the scientific review. All studies that receive federal support are subject to scientific review before award. The grant application and related materials are uploaded into the eResearch system or accessed via a link into the UM proposal management system and are considered as part of the IRB review. For student applications, it is expected that the faculty advisor has reviewed the study for scientific merit before it is submitted to the IRB.

2. Assessment of Risks and Benefits
The Belmont principle of beneficence directs that studies involving human subjects should be designed so as to minimize possible harms and maximize possible benefits. The Belmont Report defines “risk” as the possibility that harm may occur, both in the chance (probability) of experiencing harm and the severity (magnitude) of the envisioned harm. Potential harms from research can include physical, psychological, reputational,
financial, civil or criminal risks. The term “benefit” is used in the research context to refer to something of positive value related to health or welfare.

A risk/benefit assessment is concerned with assessing probability and magnitude of possible harms in relation to anticipated benefits. Risks can extend beyond individual participants to include their families or to segments of society. Benefits of the research include those that may accrue to the individual subject or their family, or to society at large (or to certain subsets of society). While many studies do not offer the hope of any direct benefit to their participants, the risk/benefit calculus properly includes benefits that may be realized by others.

In assessing the risks and benefits arising from a research proposal, the IRB only considers the risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). In addition, the possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) should not be assessed as a potential research risk by the IRB.

To approve research, IRB-FLINT verifies that the research plan, including research design, methodology, and allocation of resources will not place participants at unnecessary risk. In order to make this determination, IRB-FLINT must determine that risks to participants are minimized by evaluating the following:

- Procedures are consistent with sound research design and do not expose participants to unnecessary risk
- When appropriate, the research uses procedures already being performed on the participants for diagnostic or treatment purposes
- The time for the investigators to conduct and complete the research is adequate
- There are an adequate number of qualified staff and
- The facilities where the research will be conducted are adequate
- The investigators have access to a population that will allow recruitment of the necessary number of subjects
- Medical or psychosocial resources that subjects may need as a consequence of the research are available.

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

The IRB will review the eResearch application to evaluate the risk/benefit balance of the study, using supporting documents and scientific references, as well as staff and reviewer checklists and opinions provided by consultants (as needed).

The initial step in evaluating a study for risk is to determine if the study meets the federal regulatory definition of minimal risk [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 minimizes risk to the subjects, the IRB considers the following:

- The principal investigator’s assessment of the subjects’ risk level as presented in the eResearch application
• 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 harms
• An evaluation of whether the subjects are vulnerable in some way
• An evaluation of the steps taken, or planned, by the investigator to alleviate the potential harms (including the quality of the data safety monitoring plan (DSMP), if appropriate)
• The investigator’s history of compliance with research protocols and IRB procedures.

Generally, studies with a low probability of harm are considered minimal risk.

If the study does not meet the federal definition of minimal risk, then IRB evaluates the design of a proposed study to ensure that, 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.

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

4. Qualifications of the Principal Investigator

By University policy, the IRB recognizes only one principal investigator (PI) for each application. This policy ensures that the PI assumes full responsibility for the project and for compliance with applicable laws, regulations and institutional policy. Only the PI can execute the command to submit an eResearch application (initial, continuing review, or amendment) to the IRB and by doing so, must attest to full knowledge and approval of the content of the submission and supporting documentation. Part 6, Section I of the OM describes who may serve as principal investigator on an IRB application.

The PI must be qualified by training and experience to oversee all aspects of the proposed research. The PI, as well as key study personnel (co-investigators, faculty advisors, study coordinators), must complete PEERRS human subjects research training before their research can be granted IRB approval.

As an academic institution, the University of Michigan trains students to design, develop, and implement research studies. The IRB permits student trainees (undergraduate and graduate) to act as principal investigators, but requires that all such studies involve oversight from a Faculty Advisor with appropriate knowledge, training and expertise to oversee the conduct of the study and serve as a Study Team co-investigator. Faculty advisors attest to their oversight of and responsibility for the student researcher via acceptance of their role in the eResearch application. Students may not submit an application unless the faculty advisor has accepted their role. Undergraduate students are generally not permitted to conduct research involving more than minimal risk to the subjects.

5. Recruitment, Selection, and Enrollment of Subjects
The process of inviting a person to participate in a research project involves presenting clear information that allows a knowledgeable decision to enter a study. Recruitment into a study must be free of coercion.

The IRB will evaluate each submission to ensure that the project provides for “equitable selection” of research subjects, paying particular attention to the subject inclusion and exclusion criteria and recruitment methodology.

Among the points IRB-FLINT may consider in making its determination are whether:
- The research is grounded in appropriate current science; is of value to the subject, researcher or the field; and the setting is appropriate
- The burdens of participating in the research fall on those most likely to benefit
- The recruitment of subjects will avoid placing a disproportionate share of the burdens of research on any single group
- The nature of the research requires or justifies using the proposed population
- Any groups who might be more susceptible to the risks presented by the study ought to be excluded and whether procedures for identifying those groups are adequate
- The benefits and burdens are fairly distributed
- If it is more appropriate to conduct the study with other, less vulnerable subjects
- The selection process, by design, will overprotect potential subjects who may be vulnerable so that they are denied appropriate opportunities to participate
- Vulnerable subjects will be adequately protected during recruitment

The IRB reviews all materials or methods intended to recruit prospective subjects. Recruitment materials are submitted as part of the eResearch application and are reviewed as part of the initial review or submitted as an amendment and must be approved prior to implementation. When recruitment materials are submitted as part of an amendment and can easily be compared to the approved informed consent, the IRB chair, or other designated IRB member, may review and approve the material by expedited review.

The IRB reviews both the information contained in the recruitment material, as well as the format of the material to ensure that the procedure for recruiting subjects is: 1) not coercive; and 2) does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.

In the review of advertisements, the IRB will evaluate the following:
- The mode of its communication
- The final copy of printed advertisements
- The final audio or video taped advertisements

As part of their review, the IRB will ensure that these advertisements do not include exculpatory language, and do not promise “free treatment” when the intent is only to say that subjects will not be charged for taking part in the investigation.

Recruitment materials should be limited to the information the prospective subjects need to determine their eligibility and interest. The following may also be included, though are not required:
• The name and address of the investigator and/or research facility;
• The condition under study and/or the purpose of the research;
• In summary form, the criteria that will be used to determine eligibility for the study;
• A brief list of participation benefits, if any;
• The time or other commitment required of the subjects;
• The location of the research and the person or office to contact for further information and
• Information about payment to subjects. As a practice, recruitment materials should not emphasize the amount to be paid, by such means as larger or bold type when studies involve greater than minimal risk. Payment may be coercive in specific settings.

6. Review of Payment Arrangements to Subjects
The IRB will review the arrangement for payments or other participation incentives offered to subjects. The IRB will assess:
• Whether the payments appear to be appropriate for the proposed research, particularly whether the payment might be coercive or provide undue incentive based on the risk level of the study.
• Whether all information concerning payment, including the amount and schedule of payments, is set forth in the consent document.
• Whether the payment is considered sufficient to take into account other costs to the subject for participating in the research (e.g., travel, lodging).
• Whether credit for payment accrues as the study progresses and is not contingent upon the subject completing the entire study.
• The schedule for prorating payments in the event that a subject withdraws from the study prior to its conclusion.

Where subject pool credit is offered as an incentive for participation, the IRB will ensure that students are offered an option for extra credit if they choose not to participate in research.

There are four types of payment options available to pay human subject incentives; cash, check, coupon, and visa card. The type of payment for a study must be authorized by the IRB unless the study is exempt. The Principal Investigator is responsible for knowing which incentives types may be provided to subjects. Details on the Human Subjects Incentives Program are available on-line at: http://www.treasury.umich.edu/hsiptrainingresources.htm

7. Data Monitoring
Detailed information about Data and Safety Monitoring Plans can be found in the OM Part 7, Section II. With respect to any research project or class of research projects, the IRB 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 IRB such additional conditions are necessary or appropriate for the protection of human subjects.

a. Considerations for the Imposition of Special Monitoring Requirements
The IRB-FLINT may, at its discretion, perform monitoring or request monitoring (via OVPR) of a project in addition to that accomplished through initial, amendment, and annual continuing reviews, and analyses of interim reports such as adverse event
and audit reports. For example, the IRB may choose to undertake extra monitoring for research which presents greater than minimal risk or to gauge the progress of recruitment for vulnerable subjects or to follow the research progress on controversial subject matter. The IRB may also consider the frequency and nature of adverse events reported to-date.

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

b. Examples of Special Monitoring Requirements
Monitoring may include, but is not limited to:

- Shortened approval periods and/or interim, scheduled reports from the investigator during the approval period
- Site visits to research locations
- Interviews of subjects
- Third party witness to the informed consent process
- Review of research records
- Independent, third-party monitoring that no material changes in the study have occurred
- Independent Data Safety and Monitoring Board (DSMB)

The IRB shall communicate with investigators, as appropriate, regarding the outcomes of these additional monitoring efforts.

8. Protection of Subject Privacy and Data Confidentiality
The IRB will ensure that the research plan contains adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. See OM Part 3, C.4.(f) for a detailed description of points the IRB should consider in determining whether a protocol includes plans sufficient to address privacy and confidentiality concerns. For more on privacy and confidentiality, see the OPRR IRB Guidebook Chapter III (D).

9. Review of Informed Consent Process
IRB-FLINT will review the informed consent process, including consent documents, for each submitted application to assure that subjects provide legally effective, voluntary, informed consent. Informed consent materials (including oral scripts), requests for waiver of informed consent, and waiver of documentation of informed consent are submitted to the IRB as part of the eResearch application. The IRB will assess applications and issue waivers of documentation or waivers of some or all of the elements of informed consent, where appropriate under regulatory guidance.

Except as otherwise approved by the IRB, no investigator may involve a human subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative.

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

- The consent process is facilitated by a person knowledgeable about the study, its enrollment criteria, and its risks, benefits, and alternatives (usually a principal
investigator or co-investigator, though other study team members may also be qualified).

- The prospective subject will be provided with the 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 investigators will give the subject (or representative) 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 is presented in a neutral, non-coercive manner and in a language readily understandable by the subject.

- The discussion may be supplemented with additional information (e.g., video tape, written material), provided that the materials are approved in advance by the IRB.

**a. Elements of Informed Consent**

Except as otherwise approved by the IRB, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject’s legally authorized representative. A copy shall be given to the person signing the form. A consent document is valid only after its approval by the convened board or expediting reviewers.

In its review of informed consent documents, IRB will ensure that all of the basic elements of informed consent are included (45 CFR 46.116) and the materials do not contain any exculpatory statements suggesting that any of the subject’s legal rights are being waived, or that the investigator, sponsor, or the University of Michigan is being released from liability for negligence.

A detailed explanation of the elements of informed consent, including templates and suggested wording is posted at the IRB website.

**b. Waivers of Documentation of Informed Consent**

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all of the subjects if the requirements of 45 CFR 46.117(c) are satisfied.

Situations justifying a waiver of documentation of informed consent may include:

- Telephone surveys
- Web-based surveys
- Research involving deviant or illegal behavior
- Research involving socially sensitive issues such as HIV status
- Research involving socially sensitive situations such as abused or battered women

When the IRB waives the requirement for documentation of informed consent, it will determine whether investigators should provide subjects with a written or oral (e.g., in cases of phone interviews) statement explaining the nature, benefits, and risks of the research. The text of any written or oral script or statement must be reviewed and approved by the IRB before its use.
c. Waivers of Informed Consent
The IRB may approve a consent procedure which does not include or which alters some or all of the basic elements of informed consent or waives the requirement to obtain informed consent if the IRB finds that appropriate conditions of 45 CFR 46.116(c) or (d) are satisfied. Projects involving the use of deception in the consent process must meet the criteria for waiver of informed consent.

d. Short form, comprehensive oral script, and witness
The IRB may approve a short form consent process that documents that the elements of informed consent required by HHS have been presented orally to the subject or the subject’s legally authorized representative and must be signed by a witness. This consent process is used in populations that cannot read the consent document. See 45 CFR 46.117(2) and OM Part 2, Section C. This consent process is rarely used in projects overseen by IRB-FLINT.

10. Institutional Approval
Research approved by IRB-FLINT is still subject to disapproval by the Vice President for Research and, as applicable, other institutional officials. However, no institutional official, including the Vice President, is empowered to approve research previously disapproved by an IRB.

D. Special Review Considerations for Projects Involving Vulnerable Populations
Research may, by design or by random recruitment, involve subject populations that may be vulnerable to coercion or undue influence. In order to protect the rights and welfare of these subjects, the IRB will consider additional safeguards to protect these individuals.

Subparts B, C and D of 45 CFR 46 include additional IRB review requirements which apply to research supported by HHS involving the following vulnerable populations:
- Pregnant women, human fetuses and neonates (Subpart B)
- Prisoners (Subpart C)
- Children (Subpart D) (In Michigan, the legal age to consent to the treatments or procedures involved in the research is 18.)

When individuals from these populations participate in research, the IRB shall require investigators to specify what additional protections, if any, will be provided to protect their rights and welfare and minimize risks unique to these participants.

If available, an IRB reviewer with expertise in the vulnerable population will review the application. If appropriate expertise is not represented by the IRB membership, a consultant will be engaged and invited to review the application and present a report. The IRB Research Compliance Specialist will ensure that at least one member knowledgeable about or experienced in working with such subjects will be present for the IRB meeting at which this research is reviewed, or if necessary, that the input of a non-member consultant is solicited before the meeting.

The University of Michigan’s Federalwide Assurance (FWA) does not obligate IRB to apply these specific regulatory subparts to research that is not supported by HHS. However, it is the position of the University that the subparts are applied to applicable research, regardless of the support source. Refer to the OM Part 1 Section II, Part 7 Section IV and Part 11 Section III for specific references related to University policy regarding the use of vulnerable populations as research subjects.
1. **Application of Regulations for Pregnant Women, Human Fetuses and Neonates**
   *(Subpart B: 45 CFR 46.201-207)*
   When reviewing research involving pregnant women, human fetuses, and neonates, the IRB considers additional assessments in order to ascertain whether the subjects are vulnerable to coercion or undue influence and whether these risks have been minimized.

   The IRB will, as it deems necessary, seek the additional expertise of consultants to assist in fully evaluating the research proposal. The IRB may also choose to refer these applications to another University of Michigan IRB according to the policies outlined in the OM Part 5 Section I.

   In order to approve HHS-supported research involving pregnant women, fetuses, and neonates, IRB must apply the regulatory components of subpart B and satisfy the conditions of 45 CFR 46.201-207. For research not supported by HHS, the IRB considers the substantive elements of Subpart B in its deliberations, but may also utilize other comparable ethical guidelines, polices or procedures. Refer OM Part 7, Section IV for further details.

2. **Application of Regulations for Prisoners**
   *(Subpart C: 45 CFR 46.301-306)*
   A “prisoner” means any individual involuntarily confined or detained in a penal institution such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. The term is also intended to encompass individuals sentenced to such an institution under a criminal or civil statute, detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution and individuals detained pending arraignment, trial or sentencing. The OM Part 7, Section IV (page 6) includes several examples of individuals who are considered to be prisoners.

   Federal regulations provide a slightly modified definition of “minimal risk” for prisoner research that IRBs and PIs must be mindful of in considering the assignment of subject risk: “Minimal risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.” 45 CFR 46.303(c)

   By practice, research involving prisoners is reviewed by the IRB-FLINT convened board or another University of Michigan IRB. The convened IRB will include, as a member of the voting quorum, a prisoner representative.

   When reviewing research involving prisoners, the IRB considers additional assessments in order to ascertain the voluntariness of the process and whether coercion or undue incentives have been minimized.

   a. **Voluntariness of the informed consent process**
      Due to the nature of institutionalization, inmates may not have sufficient autonomy to provide true, informed consent. The IRB will carefully examine the procedure for approaching and recruiting an inmate including any limitations placed on the process by the prison system.

   b. **Coercion during recruitment and consent**
The effect of the research on the living conditions and/or critical consequences for the inmates must be considered. The IRB will carefully examine whether participation in the research affects the inmates’ living arrangements or provides early release options.

c. Undue incentives during recruitment and consent process
For inmates living in a closed system, with controlled wages, participation in a research project with a financial incentive may be considered an undue incentive. The IRB will consider the impact of financial incentives on the consent process and whether alternate incentives are appropriate. For example, the inmate could be offered a smaller incentive with the balance going into a general fund to benefit all inmates.

In order to approve HHS supported research, IRB must apply the regulatory components of subpart C. The IRB will submit all required materials to OHRP, including those pertaining to the informed consent process, as provided for in 45 CFR 46.306. For research not supported by HHS, the IRB considers the substantive elements of Subpart C in its deliberations, but may also utilize other comparable ethical guidelines, polices or procedures. For prisoner research not requiring review by OHRP, the IRB will submit all required materials to OVPR, including those pertaining to the informed consent process, as provided for in OM Section.

3. Application of Regulations for Children (Subpart D: 45 CFR 46.401-409)
For research involving children, the IRB will, as it deems necessary, seek the additional expertise of consultants to assist in fully evaluating the research proposal. The IRB may also choose to refer these applications to another University of Michigan IRB according to the policies outlined in the OM Part 5 Section I.

In order to approve HHS-supported research involving children as subjects, the IRB must apply the regulatory components of Subpart D. For research not supported by HHS, the IRB complies with Subpart D in its deliberations, but may also utilize other comparable ethical guidelines, polices or procedures.

The IRB will determine whether the investigator has outlined adequate provisions for obtaining assent for the children and permission from parents/guardians according to 45 CFR 46.408. When research is supported by the U.S. Department of Education and conducted in public schools, additional regulatory requirements such as PPRA (Protection of Pupil Rights Amendment) and FERPA (Family Educational Rights and Privacy Act) may need to be considered. When research supported by the National Institute on Disability and Rehabilitation Research (NIDDR) targets children with disabilities or individuals with mental disabilities as subjects of the research, the IRB includes at least one member who is primarily concerned with the welfare of the research subjects.

The IRB will assess the investigator’s recruitment strategies, the environment for assenting, the additional resources to assist in the process (e.g., videos, books, pictures, etc.), and the age of the subjects in assessing the capacity of the child to understand the nature of the research.

The IRB will assess the adequacy of plans to obtain the permission of the parent(s)/guardian according to 45 CFR 46.408(b) and (c), 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.

a. 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.”

The IRB 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 4, assent is not generally sought
- Ages 4-7, verbal assent
- 8-12, simple written assent
- Full written assent, mirroring the parental permission document may be appropriate for children older than 12.

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

The IRB evaluates the procedures for obtaining assent, including the individual who will conduct the assent process. The IRB is granted wide discretion in determining whether a child is capable of assenting and can waive the requirement for assent if the child is not capable of providing it. Federal regulations do not specify any specific elements of assent or an age above which assent should be possible.

The IRB can grant waivers of child assent or documentation of assent if the research meets the regulatory criteria set forth in 45 CFR 46.116 and 46.117.

b. 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.

IRB-FLINT assesses the procedures and appropriateness of the parental permission process. The IRB can grant waivers of parental permission or documentation of parental permission if the research meets the regulatory criteria set forth in 45 CFR 46.116 and 46.117. 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 specific requirements for obtaining parental permission for HHS conducted or supported studies are found at 45 CFR 46.406 and 46.407.

c. Wards
Special requirements exist for research involving children who are wards of the state or another agency if that research falls under 45 CFR 46.406 or 407. Wards may participate in such research only if it meets the provisions of 45 CFR 46.409 (a). In such cases, the IRB will require an advocate to be appointed for each child and will ask the principal investigator for verification of the appointment.
4. Research Involving Other Vulnerable Populations

IRB-FLINT considers certain other individuals or groups to be vulnerable to the possibility of coercion or undue influence. When a member of any vulnerable population participates in research, the IRB shall require investigators to specify what additional protections, if any, will be provided to protect their rights and welfare and minimize risks unique to these groups or an individual. Some additional vulnerable populations include, but are not limited to:

- Cognitively impaired adults
- Economically or educationally disadvantaged persons
- Employees or students of investigators conducting the study
- Patients of physician/dentist-investigators
- College students
- Individuals who are illiterate
- Individuals who are not fluent in English

a. Informed Consent in Special, Vulnerable Populations

The IRB applies additional scrutiny in reviewing the informed consent process for vulnerable populations. Emphasis is directed toward assessing the autonomy, cognitive capacity, and/or potential coercion of the prospective subjects during the informed consent process. The informed consent process assumes special importance in certain populations, including children, pregnant women, prisoners, students, and persons with diminished decision-making capacity. The principle of autonomy, or respect for persons, includes those unable to make fully autonomous decisions. In the case of a research subject with diminished autonomy, beneficence is enhanced through protections proportional to risks. It is the responsibility of the person obtaining the subject’s consent, with the oversight of the IRB, to determine that the person has sufficient capacity to give it.

Unless the requirement is waived by the IRB, each prospective subject or a legally authorized representative must provide a legally effective informed consent to participate in the project.

When the IRB regularly reviews research conducted with human subjects representing specific populations, the IRB will add representation to the board to represent that specific population, when possible. The representative will guide the IRB through a focused assessment of the informed consent process as outlined by the investigator and offer input as to any special considerations or circumstances which may contribute to a potential alteration or waiver of the consent process.

When the IRB reviews research for subject populations not otherwise covered in policies, procedures, or represented by a member of the IRB, the IRB will utilize a consultant to assist in providing a focused evaluation of the informed consent process and any other special considerations for the vulnerable population.

b. Informed Consent Involving Adults with Decisional Impairment

When reviewing the informed consent process for research involving decisionally-impaired adults, the IRB 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 impairments may be transient, others 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 a more severe degree of impairment are not competent to consent. Before these individuals are allowed to participate in any study consent must be secured from competent and legally sanctioned guardians. In these circumstances, the impaired individual must routinely provide assent even if they are unable to provide consent.

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

- The informed consent documents accurately and fairly represent the actual nature and potential risks of the proposed study.
- 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 IRB 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 investigator should outline a plan to obtain assent from the subject and informed consent from a legally authorized representative.
- Using open-ended questions to assess the individual’s understanding of the goals of the study and its risks and benefits.

c. 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 legally authorized representative while the subjects are capable. Once the legally authorized representative’s appointment becomes legally effective, the representative will reconsent to continued participation, amendments to the study, or may decide to end the subject’s participation in the research. The subject always has the right to discontinue participation in the research.

The IRB will review the study procedures to assure that the investigator has a plan to inform the legally authorized representative about the study, its implications for the
subject, and the legally authorized representative’s 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 Part 11 Section III of the University’s Operations Manual.

5. Other Special Review Considerations - Research in Schools and Universities
Research conducted in schools receiving U.S. Department of Education (DOEd) funds may be subject to additional regulations. The IRB will advise researchers when these regulations may apply to a research proposal. In addition, schools granting access to researchers may impose additional requirements of researchers, such as particular consent processes or district approval processes that would not be required by the IRB.

   a. The Family Educational Rights and Privacy Act (FERPA) (34 CFR Part 99)
   FERPA applies to research involving student education records for any institution receiving Department of Education support, meaning that it applies to most public and private K-12 schools as well as public and private universities. Access to identifiable student records requires written permission from the parent (for children) or the adult student unless certain exceptions apply. Questions regarding FERPA applicability and exceptions may be referred to the Office of General Counsel.

   b. The Protection of Pupil Rights Amendment (PPRA) (34 CFR Part 98)
The PPRA was created by the No Child Left Behind Act and applies to survey research conducted in elementary and secondary schools receiving funds under Department of Education programs. The provisions of PPRA apply to surveys that involve specific sensitive topics. The PPRA includes requirements for parental permission as well as for making the survey questions available for review. The PPRA also applies to DOEd conducted or supported research that is exempt from the Common Rule. Questions regarding PPRA applicability and exceptions may be referred to the Office of General Counsel.

   c. Research conducted or supported, in whole or part, by the DOEd
   Much of the research conducted by the DOEd will qualify for exemption from the Common Rule because many programs (e.g., National Center for Educational Statistics) are covered under federal confidentiality statutes [46.101(b)(3)(ii)].

E. Additional Review Considerations for DOD, DOJ, and EPA Research
Research involving the Department of Defense, Department of Justice, and the EPA requires special consideration in during IRB review. The IRB-FLINT will conduct its review following the policies described in Part 11 of the University HRPP Operations Manual when reviewing research sponsored by these agencies.

F. International Research
Generally, the IRB-FLINT reviews all international human subject research projects conducted by U-M investigators under its jurisdiction, rather than deferring review to a collaborating international institution. When an international site is engaged in the conduct of a U-M research project and the research is federally supported by a Common Rule agency, the regulatory requirements of the Common Rule are applied and local IRB or ethics committee review is required. An FWA may be required by the supporting agency. 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. The IRB may require local IRB review, particularly for those involving more than minimal risk to participants. Where the international research site is not engaged in the conduct of the research, the IRB may request a letter of collaboration from an appropriate official agreeing to the conduct of the research.

The IRB-FLINT 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, and 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 IRB members do not possess the appropriate cultural knowledge to review research in a particular country or region, the IRB will seek guidance from consultants with cultural expertise to assist with the review. The IRB 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, the IRB does not require documentation of IRB review or other approvals from international sites.

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 modifications as projects conducted domestically. A key element of the review process is the assessment of the informed consent process and documents. The IRB evaluates the 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. Consent documents and other study materials must be provided to the IRB in the languages in which they will be offered, as well as in English.

Post approval monitoring, such as project reports to the IRB by the PI, may be imposed when necessary. As with domestic projects, investigators are obligated to report subject complaints, unanticipated problems involving risk to subjects or others and other reports of potential non-compliance to the IRB-FLINT. Research participants are provided with the IRB email address and international phone number as part of the consent process.

V. IRB Meetings
A. Standard Schedule
Convened IRB-FLINT meetings are scheduled once each month throughout the Academic year. The schedule, including the deadline date for submission of applications for each meeting, is published on the human subjects webpage. Any scheduled meeting may be canceled if there are no agenda items for consideration.

IRB members are reminded of a scheduled meeting approximately 10-14 days prior to the meeting in order to determine the ability to meet quorum. Approximately one week before the scheduled meeting, IRB members are provided, via eResearch, the agenda and copies of all applications referred to the full board for review.

B. Agendas
Agendas are prepared by IRB-FLINT staff via eResearch. In order to assure timely review, applications are assigned to scheduled meetings according to a triage scheme which takes into account the expiration dates of renewing studies, the need for review to meet funding obligations, application submission prior to the published deadline, the availability of
reviewer expertise and the volume of applications awaiting review. IRB-FLINT does not limit the number of items that may be reviewed at a meeting.

The IRB makes every effort to facilitate timely review of applications. IRB staff communicates with the investigator to inform them of the date their application is scheduled for full board review.

C. Meeting Procedures

1. Meeting Chair
The appointed IRB chair will preside over each meeting.

2. Quorum
A quorum is defined as more than half the number of regular or alternate voting members of the IRB and must include at least one non-scientist. A quorum must be present for each formal vote. Alternate members are included in the quorum vote only if they are replacing a regular member at the meeting. Initial applications, modifications, or scheduled continuing review applications may be approved or disapproved by a majority vote of the voting members present.

3. Alternate Meeting Format (Electronically Assisted)
In the event that not all necessary IRB members are able to be physically present to convene a scheduled meeting, the IRB may utilize electronic technology (e.g., teleconference, videoconference) to facilitate the participation of the members. All application materials are available, via eResearch or if required hard copies, to the remote member in advance of the meeting 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.

4. Review of conflict of interest for committee members, consultants and guests
The chair of the IRB or designee will ask whether any committee members, consultants or guests have any conflicts of interest for studies that will be reviewed at that meeting.

5. Review of studies dealt with out of full committee since the previous meeting
A list of the expedited reviews completed in the period between convened meetings is generated in eResearch by IRB Flint staff and a link to the list is located with the materials for members under the eResearch tab for each meeting. At the convened meeting the list is displayed for members and is reviewed. Members have the opportunity to comment and ask questions.

6. Presentation of Reviews
Assigned primary and secondary reviewers present their reviews at the convened meeting. If a reviewer is unexpectedly absent, their written reviews may be presented by another board member.

Primary reviewers are expected to provide a summary overview of the project and detail specific concerns relative to the conduct of the study or the human subjects involved.

Secondary reviewers are expected to present concerns or discuss elements of the application, especially where there may be a difference of opinion with regard to information presented by the primary reviewer.
An ad hoc consultant may attend a meeting to present his/her review or may submit a written review that is assigned to an IRB member (usually another reviewer or the chair) for presentation.

D. Board Action
The convened IRB-FLINT may vote to take any of the actions described in IRB Determinations with respect to an application for initial review, scheduled continuing review, or an application for modification. All determinations, decisions, and contingencies issued by the IRB are recorded in eResearch and are available for review by the members of the IRB, the IRB staff, the investigator and study team. Investigators receive extensive detail regarding any changes required in order to achieve approval of the application.

E. Minutes
IRB-FLINT will prepare and retain minutes of IRB meetings which shall be in sufficient detail to show:
- Attendance for each action, including verification that quorum was met and maintained throughout the meeting (majority and nonscientist present).
- Summary of any continuing education provided to board members.
- For each protocol reviewed, any votes or other actions taken and the vote on that action (including the number of members voting for, against, or abstaining, and the names of any abstaining members).
- Verification and summary showing the IRB considered and found all required determinations present (45 CFR 46.111) for protocol and informed consent approvals.
- Protocol-specific information supporting any waiver of informed consent or documentation of consent [45 CFR 46.116(c), (d)]; or the inclusion of vulnerable subjects in the research [45 CFR 46 subparts B, C, D].
- The basis for requiring changes in or disapproving research.
- A written summary of controversial issues and their resolution.
- Documentation that the IRB was informed of all expedited, exempt and not regulated review activity since the last IRB meeting as required by 45 CFR 46.110(c).

Following a convened IRB meeting, the IRB staff shall prepare minutes consisting of the information described above. The minutes will be distributed for review by IRB members, who will vote to approve or modify them, normally at the next convened meeting. The ratified minutes will be maintained by the IRB in accordance with applicable legal requirements and the data storage policies of the University and the IRB. Within eResearch, the approved Word document is considered the official version of the minutes.

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 deferred review.

I. Which University of Michigan IRB Should Oversee the Research
The University has nine IRBs registered under its Federalwide Assurance (FWA) with the U.S. Department of Health and Human Services. IRB-FLINT reviews research from the UM-Flint campus. IRB-HSBS reviews health, behavioral, and social science research occurring at the Ann Arbor campus except for that under the oversight of the University of Michigan Health System and the University of Michigan Medical School. IRB-Dearborn reviews research from
the UM-Dearborn campus. Five IRBs (collectively referred to as IRBMED) review research from the University of Michigan Health System and the Medical School.

The IRBs serve the institution as a whole. Approval by one IRB constitutes approval under the University’s HRPP. The IRBs are specialized to reflect the types of studies each regularly reviews. The membership of each committee is diverse and promotes a complete, adequate, fair and balanced review of research activities commonly conducted within its associated segment or discipline of the University.

The OM provides guidance to PIs to determine which IRB has jurisdiction over their research project (Refer to OM Part 5, Section 1).

II. Cooperative Research
Researchers at the University of Michigan frequently interact with entities or individuals outside the University. The University and its researchers have differing regulatory obligations and alternatives for addressing these interactions depending on if the outside entity or individual is “engaged” in human subjects research. The VPR has implemented the policies described in OM Part 5, Section II to ensure that the University can fulfill its obligation to assure appropriate oversight of research in which the University is “engaged” and also, under certain circumstances, of other “engaged” entities associated with University research.

If in its review of an eResearch application, IRB-FLINT staff or chair, determine that an outside entity or individual is engaged in research, the Office of Human Research Protection Administrative staff should be contacted to determine the appropriate review mechanism for the outside entities (Refer to section III and IV, below).

III. Coordinated or Joint Review
For federally supported research, an institution with an FWA that is participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangement for avoiding duplication of effort. The University permits similar arrangements for non-federally-supported research. In either case, the VPR or designee must approve the arrangement for either individual studies or categorically (e.g., facilitated review). Any coordinated or joint review effort requires a written agreement among the involved institutions, regardless of whether they maintain FWAs. Refer to the OM Part III, Section 5 for a detailed discussion of the types of agreements. IRB-FLINT administrative staff will coordinate with the Flint Provost or designee and the OVPR to determine the best type of agreement for coordinated review.

IV. Unaffiliated Investigators
Researchers engaged in federally-supported UM-initiated or UM-centered research who are not employees of the University (unaffiliated) and not agents of an outside entity able to provide IRB review, must sign an “Individual Investigator Agreement” (IIA) to assure that they understand obligations associated with conducting human research. The IRB may choose to employ different formats for an IIA depending on literacy or technology constraints of the investigator.

The requirements are generally the same for non-federally-supported research and the IRB may choose different formats depending on literacy or technology constraints for the investigator.

Unaffiliated investigators may obtain certification of human subjects education through the university on-line research education system: Program for Education and Evaluation in Responsible Research and Scholarship (PEERRS). PEERRS is a web-based instruction and
certification program offering modules and certification tests to improve the knowledge and awareness of responsible research practices. Certification in a module is granted for three years from the last date the user passes a certification test.

IRB-FLINT staff will alert the Provost or designee and the Director of Research to the potential need for an IIA and to begin coordinating with OVPR to determine the type of agreement that will be executed for the unaffiliated investigator.

PART 6 - CONFLICTS OF INTEREST

I. Conflict of Interest Policies
Operations Manual Part 9 contains detailed information regarding the University’s conflict of interest policies.

II. Additional Local Considerations
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. The IRB-FLINT strives to avoid conflicts of interest in performing its obligations. A conflict of interest may take many forms, but arises when an IRB member, staff member, or consultant, in relationship to an outside organization, is in a position to influence the university’s business, research, or other decisions in ways that could lead directly or indirectly to financial or other gain for the IRB member, IRB staff, or consultant (or their families) or give improper advantage to others, to the detriment of the University.

III. Local Rules for Identification and Management of Conflicts Among IRB Members, Consultants and Staff
   A. IRB Members
No IRB member, including the chair, shall be assigned to review an eResearch application if the member, or a member of his or her immediate family has a conflict of interest as detailed in OM Part 9, Section III.

   No member, including the chair, shall 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.

UM legal counsel is available to IRB-FLINT to discuss a conflict of interest situation.

1. Convened Board Procedures
At the start of each convened IRB-FLINT meeting, the IRB administrative staff in consultation with the Director of Research will determine if any conflicts of interest exist on any applications that are to be reviewed and will note the conflict on the agenda. No IRB member, including the chair, shall be present for, nor participate in, the deliberations or 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 IRB to provide information relevant to the board’s consideration of the application.

IRB chair and staff will ensure that all identified, conflicted IRB members are:
- Excused from discussion except to provide information requested by the IRB
- Excused (absent from the room) during voting
- Not counted towards quorum
- Documented appropriately in the meeting minutes
To facilitate the identification of any previously unreported conflicts, the IRB staff or chair shall, at each meeting, inquire as to whether any member should excuse themselves from discussion and voting as outlined above.

2. Expedited and Exempt Review Procedures
Prior to assignment, the IRB staff also makes an assessment to ensure that an application is not assigned to a conflicted expediting or exempting reviewer. If a previously unreported conflict is identified in the course of reviewing an application, a new reviewer will be assigned to the application.

B. IRB Consultants
When a consultant is identified as a potential reviewer, they will be asked to verify that they have no conflict with the research content of application or the principal investigator.

Conflicts of interest involving consultants will be evaluated according to the same definition as IRB members (section III,A.).

If a conflict is identified by the consultant, but review of the application by the consultant is deemed necessary because of their special, qualified expertise, the IRB-FLINT chair will contact the consultant. Through an examination of the application content and the nature of the conflict, the chair will evaluate whether it is possible for the consultant to provide an objective assessment of the research study. If the chair believes the conflict does not preclude an objective review, the conflict will be disclosed to the board at the convened meeting or to the expediting reviewer and the consultant may present their review.

C. IRB Staff
Prior to administrative review of an eResearch application, IRB-FLINT staff will conduct a preliminary assessment to determine if they have an actual or potential conflict of interest with any aspect of the application including: research content, principal investigator or study team member. IRB staff should notify the IRB chair to discuss the potential or actual conflict. If a conflict is identified, the staff member will be excused from any IRB duties directly relating to the processing, review, or outcome determination of the application, as applicable.
PART 7 - INVESTIGATION OF COMPLAINTS, ALLEGATIONS OF NON-COMPLIANCE, AND UNANTICIPATED PROBLEMS

The HRPP promotes an organizational culture that encourages a commitment to compliance with the legal, regulatory, and ethical principles that govern human subjects research. The program relies on a system of self-regulation and integrated oversight to accomplish this objective. The OM Part 12, Section 1 describes the circumstances under which allegations of noncompliance and complaints may and must be reported and the process for reporting, protection for individuals who make reports, and the process for investigating and responding to reports. Although all complaints and concerns related to the HRPP or conduct of individual studies are reviewed, not all of them involve noncompliance.

The IRB shall promptly report the following to the Provost or designee or other appropriate institutional officials:

1. Any unanticipated problems involving risks to subjects or others (See below for detailed procedures on reporting unanticipated problems)
2. Any serious or continuing noncompliance with federal regulations, institutional policy, or IRB requirements
3. Any suspension or termination of IRB approval

I. Investigation of Complaints or Allegations of Non Compliance

If information brought to the attention of the IRB, through any source, indicates the possibility that research subjects or others are exposed to unnecessary or excessive risks, or the requirements of the IRB are not being met, the IRB 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 investigator and/or investigator’s research staff and/or suspension or termination of the project) appears necessary.

II. Investigation of Unanticipated Problems

Unanticipated Problems involving risks to subjects or others (UaPs) include events that:

- Are 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;
- Are 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); and
- Suggest 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.

Problems that require reporting in accordance with the above definition include:

- Internal adverse events that are unexpected, involve new or increased risks, and are related to the research.
- External adverse events that are unanticipated problems involving risks to subjects or others.
- 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, or which indicates a change to the risks or potential benefits of the research, including:
o An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB.

o 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 the IRB.

o A breach of confidentiality.

o Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.

o Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research subject.

o Incarceration of a subject in a protocol not approved to enroll prisoners.

o Event that requires prompt reporting to the sponsor.

o Sponsor imposed suspension for risk.

o Complaint of a subject when the complaint indicates unexpected risks or cannot be resolved by the research team.

o 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.

Investigators must report serious and non-serious unanticipated problems occurring in or related to studies under the direction of University faculty, staff or students. Serious unanticipated problems must be reported to the IRB within seven (7) days and non-serious unanticipated problems within fourteen (14) days of their occurrence or notice to the investigator.

IRB-FLINT staff reviews the eResearch inbox each business day to monitor if any UaPs have been submitted. IRB staff conducts an initial review of the submission for completeness; assesses the submissions to determine if they represent an unanticipated problem, and routes serious unanticipated problems and serious, unexpected, and related adverse events for prompt review.

If the Chair determines the report is serious, it will be placed on the agenda of the next IRB meeting for review. Non-urgent reports will receive a standard assignment to a full board meeting based on availability on the agenda. Information about the report will be presented to the convened board by a primary reviewer (usually the IRB Chair). All documents related to the review of the unanticipated problem (approved research application, approved informed consent, AE/ORIO report, any other supplemental material) are made available to the primary reviewer and the convened IRB members.

The IRB Chair is authorized to take immediate action to protect the health and safety of research subjects. Such action may take the form of:

- Asking the investigator to voluntarily impose a hold on the recruitment of subjects to facilitate additional inquiry by the IRB and/or institutional officials
- Asking the investigator to voluntarily impose a hold on the recruitment and research intervention to facilitate additional inquiry by the IRB and/or institutional officials
- Suspending recruitment or enrollment
- Altering or suspending current interventions
- Suspending the project
Any such action by the IRB Chair will be documented in the eResearch record immediately. If the IRB Chair imposes a partial or complete suspension, the IRB Chair will immediately report the suspension to OVPR. The IRB Chair shall report any such action taken to the convened IRB at its next regularly scheduled meeting.

If subjects are not at immediate risk of harm, a convened board will review serious and non-serious unanticipated problems occurring on studies under the direct oversight of IRB-FLINT, and external serious unanticipated problems. The IRB may endorse interim action by the Chair, if any, or may take a different action or additional actions.

If a majority of IRB-FLINT members vote that a submitted report is an unanticipated problem, the following steps will be taken:

- The Chair or chair’s designee will notify the Provost or designee
- The board will vote on additional actions. Possible actions to be considered include:
  - Suspension of the research
  - Termination of the research
  - Notification of current participants when such information may relate to participants’ willingness to continue to take part in the research
  - Modification of the protocol
  - Modification of the information disclosed during the consent process
  - Providing additional information to past participants
  - Requiring current participants to re-consent to participation
  - Modification of the continuing review schedule
  - Monitoring of the research
  - Monitoring of the consent process
  - Referral to other organization entities.
- The investigator will be notified
- The study records and IRB-FLINT minutes will document the findings and actions of the board

The Provost or designee shall receive notification of any research suspended or terminated for cause and shall make or direct any necessary reports to the Institutional Official or designee, who will make outside reports as needed.

III. Board Considerations and Determinations Regarding Noncompliance and UaPs
   A. Voluntary Hold
   In order to initiate a period of fact-finding and evaluation, the IRB may approve a request by an investigator to place a voluntarily “hold” whereby the investigator may not accrue new subjects and/or conduct research-related interventions during the fact-finding period.

   A voluntary hold does not constitute a suspension for purposes of these procedures.

   B. Suspension or Termination
   The convened IRB-FLINT may suspend or terminate approval of research that it determines (after appropriate review and deliberation):
   1. Is not being conducted in accordance with IRB requirements,
   2. Has been associated with unexpected serious harm to subjects, OR
   3. Cannot minimize risks to subjects or maintain a favorable risk-benefit ratio.

   • Suspension of Research Activity – Suspension is the temporary closing of a human subject
research project or discontinuing a Principal Investigator’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 Approval** – Termination is the ending of all activities related to a human research project or a Principal Investigators 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.

Only the convened board is authorized to suspend or terminate a research study, unless subjects are immediately at risk and the study must be suspended immediately. In such cases, the IRB Chair may suspend the research study and the action is then reported to the convened board at the next meeting.

When study approval is suspended or terminated, the IRB (or Chair in the case of urgent suspensions) should:

- Consider actions to protect the rights and welfare of currently enrolled subjects.
- Consider whether procedures for withdrawal of enrolled subject take into account their rights and welfare (e.g., making arrangements for medical care outside of a research study, transfer to another investigator, or continuation in the research under independent monitoring).
- Consider informing current subjects of the termination or suspension.
- Have any adverse event or outcome reported to the IRBs.

Any suspension or termination of approval under this provision shall include a written statement of the reasons for the action and inform the principal investigator of an opportunity to respond to the IRB. The Provost or designee shall receive notification of any research suspended or terminated for cause and shall make or direct any necessary reports to the Institutional Official or designee.

**C. Notification of Participants on a Terminated Study**

If study approval is terminated by IRB-FLINT, any subjects currently participating should be notified of the termination. The principal investigator will provide the notification unless otherwise directed by the IRB or institutional officials.

Any withdrawal of subjects currently enrolled in the study should take into account the rights and welfare of the subjects.

If follow-up of subjects for safety reasons is permitted/required by the IRB, the subjects should be so informed and any adverse events/outcomes should be reported to the IRB and the sponsor.

**IV. Reporting Requirements**

**A. IRB Reporting**

If an examination of the issues leads to a potential finding of serious or continuing non-compliance, the findings to-date will be presented to the convened board. If the convened board agrees (by majority vote) with the preliminary finding of serious or continuing non-compliance, they will affirm the finding and request that the materials associated with the investigation and the outcome of their assessment be forwarded to the Provost or designee for further examination and investigation, as necessary. If the incident of non-compliance
requires termination or suspension of research, the IRB must report this to the Provost or designee immediately, so that the Provost or designee may make the required external reports. In certain cases, the IRB may choose to provide an ‘early report’ of a case to the Provost or designee. Upon evaluation of the IRB’s report, the Provost or designee may choose to investigate the matter with additional University resources, including the Office for Human Research Compliance Review (OHRCR). For situations reported to the Provost or designee for additional review and/or reporting, the Provost or designee makes and reports the institutional conclusions to the Vice President for Research and imposes any institutional sanctions or remediation requirements.

Summaries of non-serious concerns are reported by IRBs to the Provost or designee on a quarterly basis as a way of monitoring the need for attention to policy or to education.

B. Institutional Reports
The UM HRPP Operations Manual Part 12 fully describes the obligations of the University to make additional reports outside the institution to sponsors and government authorities with jurisdiction.