Michigan Technological University

Human Research Protection Program and IRB

Policies and Procedures

Revised February 25, 2025

Table of Contents

1. Requirement for IRB Approval and IRB Authority 7
   1.1. Purpose 7
   1.2. Definitions 7
   1.3. Policy 9
   1.4. Procedures 11
2. Roles and Responsibilities 13
   2.1. Purpose 13
   2.2. Role of the Institutional Official 13
   2.3. IRB Responsibilities, Functions, and Duties 13
   2.4. IRB Chair Responsibilities 14
   2.5. IRB Member (and Alternate) Responsibilities 15
3. Institutional Review Board (IRB) Membership 17
   3.1. Purpose 17
   3.2. Definitions 17
   3.3. Policy 17
   3.4. Procedures 19
   3.5. New IRB Board Member Education and Training 20
   3.6. Visitors/Guests Who Can Attend the IRB Meeting 21
4. Review of Financial Disclosures in Research and Conflicts of Interest 22
   4.1. Purpose 22
   4.2. Definitions 22
   4.3. Investigator Conflict of Interest 23
   4.4. IRB Member Conflict of Interest 23
5. Procedures for Processing Submissions to the IRB and Triaging Reviews 25
   5.1. Purpose 25
   5.2. Definitions 25
   5.3. Procedures for Submission of New Studies for IRB Review 25
   5.4. Procedures for IRB Screening for Complete Submissions 27
   5.5. Procedures for Determination of Level of Review 27
6. Review of Exempt Research 29
   6.1. Purpose 29
   6.2. Procedure 29
   6.3. Policy 32
7. Expedited Review of Research 33
   7.1. Policy 33

7.2. Definitions 33
7.3. Procedures for Submission 33
7.4. Procedures for Expedited Review 34
7.5. Categories of Research that May be Reviewed Through an Expedited Review Procedure 34
7.6. Approving Expedited Review of Research 36
8. Convened IRB Review (Greater than Minimal Risk) 38
8.1. Policy 38
8.2. Procedure 38
8.3. Operational Details 39
8.4. Criteria for IRB Approval of Research 40
8.5. Approving Research at the Time of Initial Review 43
8.6. Effective Date of the Initial Review 43
8.7. Notification of IRBs Initial Review Determination to the Investigator 43
8.8. Appeal of IRB Decisions/Determinations 44
9. Recruitment of Subjects and Informed Consent 47
9.1. Purpose 47
9.2. Definitions 47
9.3. Recruitment 48
9.4. Screening, Recruiting, or Determining Eligibility 49
9.5. Payment/Compensation to Research Subjects 49
9.6. Procedures for Consent Process 50
9.7. Elements of the Informed Consent 51
9.8. Additional Considerations for Studies Collecting Protected Health Information (PHI) 54
9.9. Michigan Technological University (MTU) Requirements 55
9.10. Documentation of Informed Consent Process 55
9.11. Translation of Informed Consent for Non-English-Speaking Subjects 57
9.12. Approving Waivers or Alterations of Informed Consent 58
9.13. Assent by Children and Individuals without Decisional Capacity or Permission by Parent or Authorized Representative 58
9.14. Posting of IRB-approved consent on public website [45 CFR 16.116(h)] 60
9.15. Informed Consent at the Time of the Continuing Review – IRB Responsibilities 60
9.16. Responsibilities of Researchers 61
10. Research with Protected Health Information – IRB Review of HIPPA 63
10.1. Policy 63
10.2. Definitions 63

10.3. Procedures 64
11. IRB Review of Changes/Modifications in Approved Research 66
11.1. Policy 66
11.2. Definitions 66
11.3. Procedures for Submission of Modifications for IRB Review and Approval 66
11.4. Types of Modifications 67
11.5. Pre-Review of Modifications 69
11.6. Procedures for IRB Review of Modifications 69
11.7. Review of Informed Consent Form (s) 69
11.8. Changes Implemented in Order to Avoid Harm 70
11.9. IRB Determination to Approve or Disapprove the Proposed Changes / Modifications 70
11.10. IRB Notification / Communication with the Investigator 71
12. Reports of Unanticipated Problems Involving Risks to Subjects or Others 72
12.1. Purpose 72
12.2. Definitions 72
12.3. Reporting of Unanticipated Problems Involving Risks to the IRB 73
12.4. IRB Review of Unanticipated Problems and Reporting to Federal Agencies 75
12.5. Reporting Adverse Events and at the Time of Continuing Review 76
13. IRB Continuing Review of Research 78
13.1. Introduction 78
13.2. Definitions 78
13.3. Procedure 78
13.4. Expiration of IRB Approval (i.e., lapse in IRB Approval) 80
13.5. Criteria for IRB Approval of Research 82
13.6. IRB Continuing Review and Approval 82
13.7. Verification from Sources Other than the Investigator that no Material Changes Occurred 83
13.8. Approving Research at the Time of Continuing Review 84
13.9. Determining Frequency of Continuing Review 85
13.10. Effective Date of the Initial IRB Approval and the Dates for Continuing Review 86
13.11. Notification of IRBs Continuing Review Determination to the Investigator 86
14. Study Completion, Closure, or Expiration 87
14.1. Purpose 87
14.2. Definitions 87
14.3. Procedure 87

15. MTU Investigator Noncompliance 91
15.1. Policy 91
15.2. Definitions 91
15.3. Reporting of Noncompliance 92
15.4. Procedure for Reviewing the Allegation of Noncompliance 93
15.5. Procedure for Reviewing the Findings of Noncompliance 94
15.6. Procedure for Reporting to the IRB and IRB Review of the Noncompliance 95
15.7. Suspension and Termination of Approved Research 97
15.8. IRB Reporting Requirements 98
15.9. Managing Subject Complaints 98
16. Suspension or Termination of Institutional Review Board (IRB) Approved Research 101
16.1. Policy 101
16.2. Definitions 101
16.3. Procedures 102
17. MTU Reporting Requirements 105
17.1. Policy 105
17.2. Definitions 105
17.3. Procedures 106
18. IRB Review of Vulnerable Subjects 108
18.1. Purpose 108
18.2. Review of Research Involving Children (45 CFR 46, Subpart D) 108
18.3. Review of Research Involving Pregnant Women, Human Fetuses, or Neonates (45 CFR 46, Subpart B) 112
18.4. Review of Research Involving Prisoners (45 CFR 46, Subpart C) 113
19. Research at Schools or Educational Institutions 117
19.1. Purpose 117
19.2. Family Educational Rights and Privacy Act (FERPA (34 CFR Part 99) 117
19.3. Pupil Rights Amendment (PPRA) (34 CFR Part 98) 118
20. IRB Review of FDA Regulated Studies 121
20.1. Purpose 121
20.2. Definitions 121
20.3. Procedure 122
20.4. Human Research with Investigational or FDA-approved Drugs 124
20.5. Other Considerations Involving Clinical Investigations with Drugs 126
20.6. Investigational Devices 126
20.7. Compliance with Good Clinical Practices (GCP) 129

21. Single IRB Review of Cooperative Research/Multi-Center Studites 131
21.1. Purpose 131
21.2. Definitions 131
21.3. Process for Requesting Reliance on an External IRB 132
21.4. Responsibilities of the External IRB Include, but are not Limited to: 132
21.5. MTU Principal Investigator (PI) Responsibilities When Relying on an External IRB 133
21.6. Procedures 134
22. Retention of Institutional Review Board (IRB) Records 136
22.1. Policy 136
22.2. Definitions 136
22.3. Procedure 136
22.4. IRB Record Retention and Storage 137
22.5. Minutes of Convened IRB Meetings 138
23. Research Record Retention Requirements for Investigators 139
23.1. Purpose 139
23.2. Policy 139
24. Principal Investigator (PI) Responsibilities 141
24.1. Purpose 141
24.2. Definitions 141
24.3. Who May Serve as a Principal Investigator (PI) of a Research Study Involving Human Subjects? 142
24.4. Principal Investigator (PI) Responsibilities 142
24.5. Principal Investigator (PI) Leaving MTU 144
24.6. Sponsor Investigators 144
24.7. Protocol Personnel / Research Staff 145

1. Requirement for IRB Approval and IRB Authority

1.1. Purpose

To establish the institutional authority under which the Michigan Technological University (MTU) Institutional Review Board (IRB) is established and empowered and to define the purpose and authority of the IRB; and to establish the principles which govern the IRB in assuring that the rights and welfare of subjects are protected.

As an academic institution, MTU conducts human subjects research. It is the objective of MTU to ensure that the IRB review protocols and conduct of all human subjects research and/or that the use of investigational devices, drugs, biologics, and/or investigational diagnostic tests in human subjects is conducted in accordance with federal, state, and local laws and regulations and in compliance with the MTU IRB Policies and Procedures.

1.2. Definitions

Clinical trial (HHS, Common Rule definition) – a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Engaged in Research – an institution is engaged in non-exempt human subjects research when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.

Federalwide Assurance ("FWA") - A written commitment by an institution, filed with the Office for Human Research Protections ("OHRP"), to comply with the HHS' regulations for the protection of Human Subjects.

Human subject (FDA) – an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. May be either a healthy human or patient.

Human subject (HHS definition) - a living individual about whom an investigator (whether professional or student) conducting research obtains:

- Information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
- Uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Intervention includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and subject.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (i.e., a medical record).

Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

Institutional Official (IO) - The individual authorized to act for MTU and, on its behalf, obligates MTU to the terms of its FWA. The Associate Vice President for Research Development (AVPRD) serves as the IO for MTU.

Institutional Review Board (IRB) - any board, committee, or other group formally designated by an institution and established in accordance with federal regulations to review, to approve the initiation of, and to conduct periodic review of, human subjects research in accordance with federal regulations for the protection of human subjects in research and with these policies and procedures.

Investigational new drug (IND) - a drug not yet approved for marketing by the FDA and available only for use in experiments to determine its safety and effectiveness. An IND# allows the investigational drug to be used in a clinical study in order to collect safety and effectiveness data.

Investigational Device Exemption (IDE) - allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data. Clinical studies are most often conducted to support a Premarket Approval (PMA).

IRB approval - the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

Key Personnel - the National Institutes of Health (NIH) replaced the term “key personnel” with “senior/key personnel” in September 2010. In addition to the Program Director/Principal Investigator (PD/PI), senior/key personnel are defined as individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not salaries or compensation are requested. In addition, an NIH Funding Opportunity Announcement (e.g., RFA, PA) may instruct certain types of personnel to be identified as senior/key.

Minimal risk - the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Principal Investigator - an individual who actually conducts human subjects research or clinical investigation (e.g., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject; or whatever procedures

described in the protocol) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

Research - a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

1.3. Policy

1.3.1. All human subjects research whether or not the research qualifies for exemption under the federal regulations, conducted under the auspices of MTU, or at MTU, must obtain prospective approval from the MTU IRB before the initiation of research activities.

1.3.2. An investigator or sponsor may request that IRB review be conducted by an external IRB, however, that decision will be made by the Institutional Official or designee, and permission to utilize an external IRB will be managed through the MTU IRB Office after confirmation that an appropriate IRB Authorization Agreement has been executed. The MTU IRB Office will maintain documentation of all external IRB reviews and will ensure adherence of MTU policies/procedures in accordance with the MTU IRB Standard Operating Procedures (SOPs).

1.3.3. The Institutional Official (IO) as designated on the MTU Federalwide Assurance (FWA) reports to the MTU Vice President for Research. The IO has central oversight of the MTU Human Research Protection Program (HRPP) via the AVPRI, and responsibility for compliance oversight of the MTU research enterprise. The IO and AVPRI establish and administer the policies governing review and approval by the MTU IRB and the conduct of research by MTU. The MTU IRB Chair reports to the IO, and the HRPP Administrator reports to the AVPRI.

1.3.4. The IO will appoint the IRB Chair and IRB members in accordance with the MTU IRB SOPs. The roles and responsibilities for the IO, the IRB Chair, IRB members, the AVPRD, the HRPP Administrator, and the Principal Investigator are provided in the IRB SOPs.

1.3.5. MTU is committed to the ethical conduct of research. MTU will promote a culture that adheres to the following ethical principles articulated in the Belmont Report ("Ethical Principles and Guidelines for the Protection of Human Subjects in Biomedical and Behavioral Research", released in 1979) for both the IRB review of, and the conduct of research:

1.3.5.1. **Respect of Persons** – The IRB in their review of research and investigators in their conduct of research will respect the autonomy of research participants/subjects by obtaining legally-effective consent, unless the consent can be waived in accordance with 45 CFR 46 and/or 21 CFR 50.

1.3.5.2. **Beneficence** – The IRB in their review of research and investigators in their conduct of research will make efforts to enhance the benefits of research while minimizing potential risks of research.

1.3.5.3. **Justice** – The IRB in their review of research and investigators in their design of research studies will enhance the equitable selection of subjects whenever possible in a manner that distributes the burdens and benefits fairly in society (i.e., whereby the burdens and risks of research are not placed upon vulnerable populations for the benefit of non-vulnerable populations).

1.3.6. The review of research by the MTU IRB, or any external IRB to which MTU cedes review of research, will be conducted in compliance with the following regulatory requirements and institutional policies and procedures:

1.3.6.1. Department of Health and Human Services (HHS) (45 CFR Part 46, Subparts A, B, C, and D);

1.3.6.2. The regulations of any other Federal department supporting the study (e.g., Department of Defense, Department of Education, National Science Foundation, etc.);

1.3.6.3. Food and Drug Administration (FDA) (21 CFR Parts 50, 56, 312, 600, 812)

1.3.6.4. Health Insurance Portability and Accountability Act (HIPAA) (45 CFR Part 160, 162, and 16);

1.3.6.5. Michigan state law;

1.3.6.6. MTU IRB Policies and SOPs for the conduct and/or review of human subjects research.

1.3.7. The main purpose of the MTU IRB shall be the protection of the rights and welfare of persons participating as research subjects. The MTU IRB approval shall be required prior to the conduct of any research involving intervention with human subjects or the collection of identifiable private information about human subjects. These requirements are intended to protect the rights and welfare of human subjects involved in such research.

1.3.8. The IRB shall function and act to ensure that:

1.3.8.1. The rights and welfare of research subjects are protected.

1.3.8.2. Research design, methodology, analysis, and conclusions are in the best interests of the research subjects in terms of their rights and welfare and in accordance with the mission of MTU.

1.3.8.3. No conflict of interest exists between the conduct of research and IRB voting members or between the participating research investigators and the research sponsors that might serve to jeopardize the quality of the research or reduce the rights and/or welfare of the research subjects.

1.3.9. The IRB shall review and have authority to approve, require modifications in or disapprove all human subjects research activities conducted at, or by, MTU and covered by this policy.

1.3.10. The IRB shall review and approve prospectively any research that will identify MTU as his/her affiliation even if the research was not performed at MTU.

1.4. Procedures

1.4.1. The IRB will prepare and maintain a current IRB policies and procedures manual which contains IRB governing policy and procedures by which the scope of IRB authority is carried out in compliance with 21 CFR 50, 56 312, 600, 812 and 45 CFR 46, and other relevant State, local, and MTU regulations, guidelines, policies, and procedures. This Manual must include, but not be limited to, the following procedures for:

1.4.1.1. Conducting IRB initial and continuing review of research and for reporting IRB findings and actions to the investigator(s).

1.4.1.2. Describing the appointment and function of IRB members and alternate members (if any).

1.4.1.3. Determining which projects require review more often than every 12 months and which projects need verification from sources other than the investigator(s) that no material changes have occurred since previous IRB review.

1.4.1.4. Ensuring prompt reporting to the IRB of proposed changes in a research activity, and for assuring that changes in approved research, during the period for which IRB approval already has been given, may not be initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subjects.

1.4.1.5. Ensuring prompt reporting to the IRB of unanticipated problems involving risks to subjects or others.

1.4.1.6. When the research is subject to HHS or FDA reporting regulations, ensuring prompt reporting of unanticipated problems involving risks to subjects or others by filing reports with the appropriate federal agency.

1.4.1.7. Timely reporting to the appropriate institutional officials of any serious or continuing noncompliance by investigators with the requirements and determinations of the IRB. For research subject to HHS and FDA regulations, these reports also must be made to HHS, or the FDA, as appropriate.

1.4.1.8. Establishing whether an expedited review procedure may be used. If used, the IRB shall adopt a method for keeping all members advised of research proposals that have been approved under the procedure.

1.4.2. The IRB will prepare and maintain forms appropriate for use in carrying out the scope of authority of the IRB.

References

1. 21 CFR 56
2. 45 CFR 46

2. Roles and Responsibilities

2.1. Purpose

To establish the roles and responsibilities of the Institutional Official (IO), the MTU IRB, the IRB Chair, and IRB Members.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy"). All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

2.2. Role of the Institutional Official

The IO has overall responsibility for the MTU research enterprise and has the following responsibilities:

2.2.1. develops a culture of compliance with the Belmont Report and federal regulations for the protection of human subjects in research.

2.2.2. develops and administers all institutional policies governing MTU's research;

2.2.3. ensures that MTU complies with the terms of the FWA;

2.2.4. ensures adequate resources for the MTU IRB operation;

2.2.5. ensures that the MTU IRB can conduct its reviews without undue influence from investigators, MTU administrators, or any group of individuals;

2.2.6. is informed of IRB decisions and has the authority to review decisions of the IRB. In instances of disagreement, the IO works with the IRB to resolve certain issues/ concerns. The IO cannot approve a study for which the IRB has disapproved the research.

2.2.7. is responsible, together with the IRB, for reporting unanticipated problems involving risks to subjects or others, continuing noncompliance, and/or serious noncompliance to federal regulatory agencies.

2.3. IRB Responsibilities, Functions, and Duties

2.3.1. Protect the rights and welfare of human subjects participating in research.

2.3.1.1. Abide by the IRB governing ethical principles found in the Belmont Report.

2.3.1.2. Comply with federal regulations for the protection of human subjects participating in research.

2.3.2. Comply with MTU IRB policy under which the IRB is established and empowered.

2.3.3. Comply with MTU IRB standard operating procedures (SOPs).

2.3.4. Conducting initial and continuing review of research involving MTU subjects:

2.3.4.1. Notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of any required modifications needed prior to IRB approval.

2.3.4.2. If the IRB decides to disapprove a research activity, the IRB will include in its written notification a statement of the reasons for its decision and will give the investigator an opportunity to respond in person or in writing.

2.3.4.3. Determine which projects require review more often than every 12 months.

2.3.4.4. Determine which projects need verification from sources other than the investigators that no material changes have occurred since prior IRB review.

2.3.5. Ensure prompt reporting to the IRB of proposed changes in a research activity. Changes may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

2.3.5.1. Determine if a proposed device study involves a significant or non-significant risk to the subject(s).

2.3.6. Ensuring prompt reporting to the IRB, appropriate institutional officials and federal department or agency head of:

2.3.6.1. Any unanticipated problems involving risks to subjects or others;

2.3.6.2. Any serious or continuing noncompliance with Federal regulation or the requirements or determinations of the IRB;

2.3.6.3. Any suspension or termination of IRB approval.

2.4. IRB Chair Responsibilities

2.4.1. The IRB Chair reports directly to the IO and has the following responsibilities: (along with the HRPP Administrator and/or designee) determine the type of review appropriate for new protocols (exempt, expedited, full board);

2.4.2. serves as primary reviewer of protocols when appropriate or delegating this responsibility to another IRB member;

2.4.3. conducts the business of full board meetings following basic parliamentary rules;

2.4.4. reviews on behalf of the IRB, revisions to protocols/consent documents required as a condition of approval;

2.4.5. reviews unanticipated problems involving risks to subjects or others/serious adverse experience reports;

2.4.6. recommends to the IO new and/or replacement IRB members;

2.4.7. reviews report(s) of non-compliance in coordination with the HRPP Administrator and when appropriate, the IO;

2.4.8. assesses and recommends appropriate IRB training for the IRB, investigators, and support staff;

2.4.9. ensures that submitted protocols receive an efficient review;

2.4.10. complies with MTU IRB policies and procedures;

2.4.11. serves as a resource for investigators and IRB members regarding issues related to MTU and federal policies;

2.4.12. signs the MTU IRB Confidentiality and Conflict of Interest Agreement;

2.4.13. reports potential conflict of interests to the IRB Chair and/or HRPP Administrator before beginning review of an IRB submission; and

2.4.14. maintains the confidentiality of IRB meeting discussions.

2.5. IRB Member (and Alternate) Responsibilities

The IRB Member reports directly to the IRB Chair and HRPP Administrator, and has the following responsibilities:

2.5.1. Regularly attend IRB meetings promptly (at least 75% meetings) and notify the HRPP Administrator in advance when the member will not be able to attend a meeting;

a) Meeting minutes must clearly document attendance of IRB members and that quorum was achieved and maintained throughout an IRB meeting.

b) Member may vote and be counted as part of the quorum.

2.5.2. (along with the HRPP Administrator) determine the appropriate type of review for submitted protocols (exempt, expedited, full board);

2.5.3. review assigned materials and participate in discussions for submissions assigned to a convened IRB meeting, including new submissions, modifications/amendments, continuing review, unanticipated problems involving risks, and noncompliance cases;

2.5.4. be prepared to discuss issues related to human participants protections at IRB meetings;

2.5.5. serve as primary reviewer at IRB meetings or on expedited protocols when requested by the IRB Chair;

2.5.6. be informed about the specific requirements regulating the participation of human subjects in research;

2.5.7. comply with MTU IRB policies and procedures;

2.5.8. sign the MTU IRB Confidentiality and Conflict of Interest Agreement;

2.5.9. report potential conflict of interests to the IRB Chair and/or HRPP Administrator before beginning review of an IRB submission; and,

2.5.10. maintain the confidentiality of IRB meeting discussions.

2.5.11. complete required training associated with being an IRB Member as established in MTU policy and procedures.

References

1. 21 CFR 56
2. 45 CFR 46

3. Institutional Review Board (IRB) Membership

3.1. Purpose

To specify Michigan Technological University (MTU) Institutional Review Board (IRB) Committee membership in accordance with federal and state regulations and MTU procedures; and who may attend an IRB meeting.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy").

3.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

IRB Conflict of Interest – any situation where an IRB member has any significant personal or financial interest which has the potential to bias the design, conduct, report or review of research.

Non-institutional member – member who is not affiliated with MTU in any manner other than serving on the IRB and who is not part of the immediate family of a person who is affiliated with MTU.

Scientific member – member who's training, background, and occupation would incline them to view scientific activities from the standpoint of someone with a behavioral or biomedical research discipline.

Non-Scientific member - member who's training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral research discipline.

Quorum – is the minimum number (50% the IRB members on the roster plus one) and type of IRB members that must be present at a convened meeting for the IRB to conduct business.

3.3. Policy

3.3.1. The IRB shall be composed in a manner that meets the requirements of the Federal Department of Health and Human Services (HHS) 45 CFR 46, any other Federal Department sponsoring the research, the Food and Drug Administration (FDA) regulations 21 CFR 56, and any State or local laws or regulations that provide for the protection of human research subjects.

3.3.2. The IRB shall be sufficiently qualified to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

3.3.3. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations,

applicable law, and standards of professional conduct and practice. The IRB shall, therefore, include persons knowledgeable in these areas.

3.3.4. In accordance with the MTU IRB SOPs, the IRB membership shall be as follows:

3.3.4.1. Number of Members: The IRB shall have at least five (5) voting members, one of which serves as the Chair.

3.3.4.2. Qualifications of Members: The IRB Chair must be qualified with knowledge in federal regulations for the protection of human subjects, research practices and norms, and have leadership qualities. The remaining minimum number of members will have the following qualifications:

3.3.4.2.1. At least half of the voting members shall be primarily representative of the scientific disciplinary area, such as physicians or social, biological, engineering, or computational scientists, being professionally competent with experience in research.

3.3.4.2.2. At least one voting member shall be primarily representative of the non-scientific disciplinary area, such as a lawyer, ethicist, clergy person, law enforcement person, such as a sheriff or police person, or patient advocate.

3.3.4.2.3. At least one voting member shall have no affiliation with MTU, including having no immediate family affiliated with MTU. This may be a local community resident unrelated in any way with MTU other than voluntarily serving as an IRB voting member. This individual may have experience in research.

3.3.4.2.4. If the IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

3.3.4.2.5. One IRB voting member may satisfy more than one membership category. For example, one member may be otherwise unaffiliated with MTU and have a primary concern in a non-scientific area. This individual would satisfy two of the membership requirements of the regulations. The IRB should strive, however, for a membership that has a wide range of representative capacities and disciplines.

3.3.4.3. Alternate Voting Members: Each voting member may have one or more designated alternates approved by the IRB.

3.3.4.4. Ex-Officio Members: Any research administrative director may attend the IRB meetings as an ex-officio member, without voting privileges.

3.4. Procedures

3.4.1. Appointments: The Chair will be appointed by the Institutional Official (IO). The Chair or an IRB member may recommend to the IO other appointments for membership on the IRB, including designated alternates.

3.4.2. Membership Terms: Membership terms shall be for three years. Members can serve unlimited consecutive terms.

3.4.3. Ad Hoc Substitutes: Ad Hoc substitutes shall not be permissible as members of the IRB.

3.4.4. Use of Consultants: The IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

3.4.4.1. The consultant(s) may present a written report to the IRB of their findings in person or forward the report to the IRB Chair.

3.4.4.2. If a written report is presented to the IRB, it will be attached to the meeting minutes. The IRB cannot use the services of a consultant in the review of a research protocol in which the consultant has a conflict of interest.

3.4.4.3. Any consultant used by the IRB shall sign the MTU IRB's confidentiality agreement and a conflict-of-interest disclosure form.

3.4.5. Quorum Requirements: The majority of members must be present to have "quorum" at the convened meeting. The majority must include at least one (1) voting member that is considered to be non-scientific. Quorum must be maintained throughout the meeting.

3.4.5.1. Should the quorum fail during the meeting or if a non-scientific voting member is not present, the IRB may not take further official action or vote for approval of the review, unless quorum can be restored.

3.4.5.2. Quorum is determined by voting members only:

- Even number of voting members: half of the total IRB voting members plus one (e.g., 4 is half of 8 voting members plus 1 is 5. Five is the majority).
- Uneven number of voting members: half of the total IRB voting members and round up to the next whole number (e.g., 3.5 is half of seven voting members, rounded up to four. Four is the majority).

3.4.6. IRB Conflict of Interest

3.4.6.1. Potential sources of conflict of interest.

- Individual conflict of interest:

- IRB member has a pre-existing relationship or affiliation with the researcher;
- IRB member was involved in the development of any materials or products affiliated with the research;
- IRB member will benefit from the research or commercialization of its findings.

- Financial conflict of interest - defined as anything of monetary value, including but not limited to:
  - Salary or other payments for services (e.g., consulting fees or honoraria);
  - Equity interests (e.g., stocks, stock options or other ownership interest, excluding any interest arising solely by reason of investment in a business by a mutual, pension or other institutional investment fund over which the IRB member or his/her immediate family does not exercise control).

3.4.6.2. An IRB member serving in the role as a convened full board member or serving as an expedited reviewer, with a declared conflict of interest may not participate in the review of the project, except to provide information requested by the IRB.

3.4.6.2.1. This includes review of any materials submitted over the course of the research project, such as:

- Initial IRB application;
- Continuing Review reports;
- Modifications to approve research;
- Reportable events;
- Allegations of non-compliance with regulations or requirements of the IRB.

3.4.6.2.1.1. If the IRB Chair has a conflict, he/she may not chair the meeting during the consideration of the item in which conflict resides.

3.4.6.3. Convened Full Board Review

- The IRB Chair begins each meeting with a reminder for the members that if conflict of interest with an agenda item(s) exists; it must be disclosed at that time.
- The member must leave the room (i.e., recuse) during the discussion and vote of the project.
  - Recused member is not counted towards quorum. If quorum fails, the IRB may not take further action or vote on the project.
  - The meeting minutes will reflect the name of the IRB member, and his/her absence during the vote due to conflict of interest

3.5. New IRB Board Member Education and Training

3.5.1. All new IRB members will receive an orientation from the HRPP Administrator before starting their service. During the orientation, new members will receive education and training on the purpose of the IRB, its authority, and its policies and procedures for protecting the rights and welfare of human subjects. Orientation includes review and discussion of the:

- IRB Orientation Training Materials;
- IRB policy and IRB Standard Operating Procedures (SOPs);
- Federal Regulations for the protection of human subjects in research;
- Belmont Report;
- Meeting agendas and minutes;

3.5.2. The IRB will ensure that all IRB members have completed the required Collaborative Institutional Training Initiative (CITI) module(s) as well as any required additional education and training.

3.5.3. IRB Members will receive continuing education and training of policies and procedures, regulations, and other relevant guidelines at the regularly scheduled IRB meetings. Such education and training may include handouts of educational materials, discussion of newly proposed policies and procedures, and/or guest presentations of educational matters at IRB meetings, etc.

3.6. Visitors/Guests Who Can Attend the IRB Meeting

MTU will permit visitors to attend Institutional Review Board (IRB) meetings. The following procedures must be in place to protect the privacy and confidentiality of deliberations:

3.6.1. IRB staff should be notified to allow screening of guests and obtaining signed confidentiality agreements;

3.6.2. The presence of the visitor should be noted in the Minutes;

3.6.3. Visitors will be asked to sign a confidentiality statement and will be asked to leave the room for discussions that should only occur in executive session.

References 45 CFR 46.107**,** 21 CFR 56.107

4. Review of Financial Disclosures in Research and Conflicts of Interest

4.1. Purpose

This standard operating procedure (SOP) describes potential Conflicts of Interest (COI) for investigators and research staff engaged in human subjects research, and the requirements and procedures for disclosure and managing COI.

It is the responsibility of the Institutional Review Board (IRB) and the Investigator(s) to ensure conflict of interest (COI) in research does not compromise the rights and welfare of human subjects and is consistent with regulatory requirements (42 CFR 50, Subpart F and 45 CFR 94).

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy").

4.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Clinical Investigator –A listed or identified Principal Investigator or sub-investigator (also commonly referred to as a co-investigator) who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the investigator or sub-investigator (21 CFR 54.2 (d)). (Note a Sub-investigation is the same as a co-investigator).

Conflict of Interest – involves any situation where a member of the research team or IRB has a significant interest which has the potential to bias the design, conduct, reporting or reviewing of the research. Conflicts of interest may be actual or perceived, and can occur in two basic categories:

i. Financial Conflict of Interest. A situation, real or perceived, in which an individual's relationships with the University may be exploited for financial or other gain, which may compromise or have the appearance of compromising professional judgment when making decisions or influencing the decisions of other employees.
ii. Conflict of Commitment. A situation where an individual's professional activities, especially the allocation of time and effort to the different institutions and organizations they serve as professionals, may take precedence over other professional responsibilities to the University.

Conflict of Interest Coordinator - Michigan Technological University's contact person and coordinator for handling conflicts of interest.

Significant financial interest - Any Financial Interest that separately or in the aggregate, equals or exceeds the threshold established by conflict-of-interest regulations by the U.S. Public Health Service (42 CFR Part 50, Subpart F and 45 CFR Part 94) as provided below:

a) Salary or other income, whether for consulting, lecturing, travel, service on an advisory board or for any other purpose paid by a Business that has in the prior twelve months exceeded the PHS Threshold (currently $5,000) or is expected to exceed such amount in the next twelve months;

b) For a publicly held Business, an equity interest that exceeds the PHS Threshold, currently: (i) $5,000 in value or (ii) representing 5% ownership in such Business;

c) For a privately held Business, any equity interest in such Business, regardless of the amount;

d) Royalty Payments, including those received under a University agreement, that in the aggregate have in the prior twelve months exceeded the PHS Threshold or are expected to exceed the PHS Threshold in the next twelve months;

e) Service as an officer, manager, member of a board of directors, or in any other fiduciary or managerial role for a Business, whether or not remunerated; or

f) Any intellectual property or other property right that would reasonably appear to be affected by the research at issue.

4.3. Investigator Conflict of Interest

4.3.1. Initial submissions on the electronic IRB system must identify any research team members who have a COI regarding the project.

4.3.2. The PI of the submission will be directed by the electronic IRB system to contact the Conflict of Interest Coordinator (COIC) with the same information.

4.3.3. The HRPP Administrator will also directly alert the COIC to the disclosed COIs.

4.3.4. PIs must promptly submit a modification to a study on the electronic IRB system if the COI status of any research team member changes. The modification must identify the researcher(s) whose COI status has changed. Sections 4.3.2 and 4.3.3 will also then apply.

4.3.5. Any modification to a study that adds new personnel must identify in the electronic IRB system any of the new personnel who have COIs regarding the study. Sections 4.3.2 and 4.3.3 will also then apply.

4.3.6. If the COIC confirms that a COI exists regarding a study, the HRPP administration will review the situation and determine whether the conflict can be managed/reduced through a management plan, or whether the relevant team member(s) must withdraw from involvement in the study.

4.4. IRB Member Conflict of Interest

4.4.1. An IRB member serving in the role of a convened full board member, or serving as an expedited reviewer, with a declared conflict of interest may not participate in the review of the project, except to provide information requested by the IRB.

4.4.2. This includes review of any materials submitted over the course of the research project, such as:

a) Initial IRB application;
b) Continuing Review reports;
c) Modifications to approve research;
d) Reportable events;
e) Allegations of non-compliance with regulations or requirements of the IRB.

4.4.3. If the IRB Chair has a conflict, he/she may not chair the meeting during the consideration of the item in which conflict resides.

4.4.4. Expedited Review.

4.4.4.1. An expedited reviewer, who recognizes a conflict of interest with an item under expedited review procedures must have the item reassigned by the Chair to a reviewer without conflict of interest.

4.4.5. Convened Full Board Review.

4.4.5.1. The IRB Chair begins each meeting with a reminder for the members that if conflict of interest with an agenda item(s) exists; it must be disclosed at that time.

4.4.5.2. The member must leave the room (i.e., recuse) during the discussion and vote of the project.

4.4.5.3. A recused member is not counted towards quorum. If the quorum fails, the IRB may not take further action or vote on the project.

4.4.5.4. The meeting minutes will reflect the name of the IRB member, and their absence during the vote due to conflict of interest.

References:

Financial Conflict of Interest: HHS Guidance (2004)
21 CFR 54.2
45 CFR 46.107 (e)
21 CFR 56.107 (e)

5. Procedures for Processing Submissions to the IRB and Triaging Reviews

5.1. Purpose

These Procedures outline the information that needs to be submitted to the Michigan Technological University (MTU) Institutional Review Board (IRB) in order to have the proposed research project approved by the IRB. and how the submissions are processed by the MTU IRB depending on the level of IRB review required.

The MTU IRB is responsible for conducting a review of human subjects research in accordance with federal regulatory requirements. There are different levels of review based on the potential risks that the research may pose for research subjects.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy").

5.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Key Personnel - the National Institutes of Health (NIH) replaced the term "key personnel" with "senior/key personnel" in September 2010. In addition to the Program Director/Principal Investigator (PD/PI), senior/key personnel are defined as individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not salaries or compensation are requested. In addition, an NIH Funding Opportunity Announcement (e.g., RFA, PA) may instruct certain types of personnel to be identified as senior/key.

Minimal Risk – the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

5.3. Procedures for Submission of New Studies for IRB Review

5.3.1. Qualifications

The investigator who plans to conduct the proposed research at MTU must submit to the IRB his/her professional qualifications to conduct the research for greater than minimal risk research. These qualifications should include, as applicable, a description of the necessary staffing, support services, equipment, and supplies that the investigator has or will provide to do the research.

5.3.2. Study Protocol

The investigator who plans to conduct the proposed research at MTU must submit to the IRB the originating protocol for the study. The study protocol shall include or address when applicable, but not be limited to, the following:

- Title of the study.
- Purpose and overall intention of the study (including the expected benefits obtained by doing the study).
- Sponsor of the study.
- Results of previous related research.
- Subject inclusion/exclusion criteria.
- Justification for use of any special/vulnerable subject populations (for example, the decisionally-impaired, children).
- Study design (including, as needed, a discussion of the appropriateness of research methods).
- Description of procedures to be performed.
- Provisions for managing unanticipated problems (e.g., harms to subjects).
- The circumstances surrounding consent procedure, including setting, subject autonomy concerns, language difficulties, vulnerable populations.
- The procedures for documentation of informed consent, including any procedures for obtaining assent from minors, using witnesses, translators and document storage.
- Compensation to subjects for their participation.
- Any compensation for injured research subjects.
- Provisions for protection of subject's privacy and confidentiality.
- Extra costs to subjects for their participation in the study.
- Extra costs to third party payers because of subject's participation.

5.3.3. Other Documents

The investigator who plans to conduct the proposed research at MTU may be required additional documents to the IRB as appropriate. These may include, but not be limited to, the following:

a) Grant application, or copy of the contract scope of work, if sponsored by the government or a foundation.

b) Any recruitment materials, including flyers, advertisements, and recruitment letters intended to be seen or heard by potential subjects;

c) The proposed informed consent documents (i.e., informed consent form, assent form, verbal consent script or justification for waiver of consent):

   - Containing all requirements of 21 CFR 50.25(a) and 45 CFR 46.116(a);
   - Containing requirements of 21 CFR 50.25(b) and 45 CFR 46.116(b) that are appropriate to the study;
   - Meeting all requirements of 21 CFR 50.20 and 45 CFR 46.116;
   - A clear plan for accurate translation of documents, considering likely subject populations;

d) COI Disclosure Forms;

e) Human subjects protection and Good Clinical Practice (GCP) training certificates, as required by IRB/MTU policies;

f) CVs for the Principal Investigator and Sub-Investigators.

For FDA-Regulated Research (items g to j are required, when applicable)

g) Clinical Investigator Brochure for studies involving an investigational drug. (Refer to 21CFR 56.111(a)(2), and 21CFR 312.55);

h) A drug package insert for studies involving an FDA-approved drug;

i) A device manual for studies involving an investigational device;

j) For studies involving an investigational drug, documentation from the sponsor and/or FDA that an Investigational New Drug (IND) # has been granted by FDA; for studies involving an investigational device that is determined to be a significant risk device, documentation from the sponsor and/or FDA that an Investigational Device Exemption (IDE) # has been granted by FDA.

5.4. Procedures for IRB Screening for Complete Submissions

5.4.1. The HRPP Administrator or designated staff will review each submission submitted to the IRB to ensure that the application is complete and that none of the required items in section 5.3 above are missing.

5.4.2. If essential information is missing from the submission, the HRPP Administrator or designated staff will notify the PI regarding any missing items and whether the IRB can proceed to review the submission.

5.4.3. If the study is sponsored, the HRPP Administrator will review the grant application and the protocol to conduct a congruency review to ensure that the protocol includes all relevant information that was included in the grant application.

5.5. Procedures for Determination of Level of Review

5.5.1. **Not Human Subjects Research**

The HRPP Administrator will make the preliminary decision as to whether the submission is human subjects research versus not human subjects research.

- Studies that are considered “not human subjects research” do not need to be submitted to the IRB for such a determination. However, sometimes some sponsors require written IRB approval for the study regardless of the level of review.
- For all submissions that are not human subjects research, the HRPP Administrator will draft a letter stating that the research is “not human subjects research in accordance with 45 CFR 46 informing the PI that the research may begin if there is no funding. If there is funding, the PI must obtain approval from the Office of Research after a contract or grant with the sponsor has been executed.

5.5.2. **Exempt Research**

Federal regulations recognize certain types of research involving human subjects as being exempt from requiring IRB review and approval.

- MTU requires that all “research” involving “human subjects” be submitted to the IRB for review.
- Upon review of initial applications, the HRPP Administrator or the IRB Chair will determine whether the proposed research meets the qualifications for exempt review.
- If necessary, the HRPP Administrator will consult with the IRB Chair whether a study qualifies for Exempt Review or should receive Expedited Review.
- The IRB can decide to review an Exempt study by Expedited Review.
- Studies that qualify for Exempt Review will be processed according to the Exempt Review SOP.

5.5.3. **Expedited Review (Minimal Risk)**

The expedited review process may be used by the IRB to review applications that present no more than minimal risk to human subjects and involve only procedures listed in one or more of the categories specified in either 45 CFR 46.110 (HHS) or 21 CFR 56.110 (FDA).

- Upon review of initial applications, the HRPP Administrator will determine whether the proposed research meets the qualifications for expedited review.
- If necessary, the HRPP Administrator will consult with the IRB Chair whether a study qualifies for Expedited Review or should receive review by the convened IRB.
- The IRB can decide to review a study that qualifies for Expedited Review by the convened IRB.
- Studies that qualify for Expedited Review will be processed according to the Expedited Review Procedures.

5.5.4. **Convened IRB Review (Greater than Minimal Risk)**

Depending on the level of required review, the submission will follow the procedures for Exempt Review, Expedited Review, or convened IRB review.

- Upon review of initial applications, the HRPP Administrator will determine whether the proposed research is greater than minimal risk and requires review by the convened IRB (also commonly referred to as “Full-Board Review”).
- If necessary, the HRPP Administrator will consult with the IRB Chair whether a study should receive review by the Convened IRB.
- The IRB Chair can decide to review a study that qualifies for Expedited Review by the convened IRB, if the study would benefit from additional expertise provided by the convened IRB.
- Studies that are reviewed by the Convened Board will be processed according to the convened IRB Review Procedures.

References 45 CFR 46 101, 102, 109, 111; 21 CFR 56 109, 111

6. Review of Exempt Research

6.1. Purpose

All human subjects research conducted under the auspices of the Michigan Technological University (MTU) must be submitted to the MTU Institutional Review Board (IRB) for review and approval prior to initiation of the research, including "Exempt Research." This Procedure outlines processes that the IRB performs for the review of research that qualifies for the exemptions offered in the Health and Human Services regulations for the protection of research subjects from research risks (45 CFR 46.101(b)).

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy"). All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

6.2. Procedure

MTU requires that all "research" involving humans, including exempt research, be submitted to the IRB for review and approval.

Upon review of initial applications, the HRPP Administrator will determine whether the submission is complete and that none of the required items in section 5.3 above are missing.

The HRPP Administrator will ensure that exempted research the research fits one or more of the following categories taken from 45 CFR 46.104(d).

NOTE: (Exemptions 7 and 8 of the revised New Common Rule will not be used by MTU; rather such activities will be reviewed under expedited review procedure)

1. Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research that only includes interactions, involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

   (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot be readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside of the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational achievement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through identifiers linked to the subjects and an IRB conducts a limited review to make the determination required by 45 CFR 46.111(a)(7) (i.e., that when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data).

3. (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subjects prospectively agrees to the intervention and information collection and at least one of the following is met:

   A. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
   B. Any disclosure of the human subjects' responses outside of the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational achievement, or reputation; or
   C. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through identifiers linked to the subjects and an IRB conducts a limited review to make the determination required by 45 CFR 46.111(a)(7) (i.e., that when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data).

   (ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play on online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of cash between themselves and someone else.

   (iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purpose of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify the subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of a Federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including 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. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements such as sections 1115 and 1115A of the Social Security Act, as amended.

   (i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

6. Taste and food quality evaluations and consumer acceptance studies;

(i) If wholesome foods without additives are consumed or

(ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

6.3. Policy

6.3.1. The study will be reviewed by the HRPP Administrator, the IRB Chair, or a designated IRB Member or designated IRB staff.

6.3.2. If necessary, the HRPP Administrator will consult with the IRB Chair whether a study qualifies for Exempt Review or should receive Expedited Review

6.3.3. The IRB can decide to review an Exempt study by Expedited Review.

6.3.4. Once the HRPP Administrator, IRB Chair, or designated IRB Member, or IRB staff determined that a study qualifies for Exempt Status, the IRB will release an IRB Exempt Approval Letter to the PI.

6.3.5. The IRB requires that any modification or amendment to an Exempt Study that would alter the exempt determination requires submission to the IRB for review.

6.3.6. The IRB, at its discretion, retains the right to require continuing review when warranted by the nature of the research and/or inclusion of vulnerable subject populations.

6.3.7. The HRPP Administrator will periodically verify with the PI the status of an exempt study to see whether it is continuing or has been completed.

6.3.8. Unless required by the IRB in its Exemption Approval Letter for an individual research project, Continuing Reviews will not be conducted for Exempt Research.

References:
45 CFR 46.101(b)

7. Expedited Review of Research

7.1. Policy

7.1.1. It is the policy of the Organization that the Institutional Review Board (IRB) may use an expedited review process. An expedited review process may be used only in accord with Department of Health and Human Services (HHS) and Food and Drug Administration (FDA) regulations. Therefore, only research that meets the regulatory definition of research involving no more than minimal risk, meets all applicability criteria in the document "Categories of Research That May Be Reviewed By The Institutional Review Board (IRB) Through An Expedited Review Procedure" published by HHS and FDA in the Federal Register and that involves procedures that are listed in one or more of the categories in this document are eligible for an expedited review process. An expedited review process may be conducted for initial new applications, continuing review applications, or proposed minor changes in previously approved research.

7.1.2. An expedited review may be conducted by any member on the designated IRB reviewer list, with the exception of research involving a drug, biologic, or Complementary Alternative Medicine (CAM), which must be reviewed by a physician. Members will be added to the designated member list when the IRB Chair determines the member has sufficient experience and training to conduct such reviews. A primary reviewer conducting an expedited review is not authorized to disapprove an application. New applications, continuing review applications, or proposed changes in already approved research that a reviewer finds at expedited review may not be approvable must be referred for discussion at a convened meeting.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy").

7.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Minimal risk - the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

7.3. Procedures for Submission

The following types of submissions may be considered under expedited review procedures to the IRB:

7.3.1. For a new protocol that qualifies for expedited review, submit all applicable documents and items as described in the IRB SOPs.

7.3.2. The IRB may approve, by expedited review, non-substantive changes or modifications in the informed consent process or consent forms, advertising and

recruitment materials, the protocol, survey instruments, the investigator's brochure or other items previously approved by the IRB. The instructions for submission of a modification and the IRB review of such changes/modifications are described in the IRB Review of Changes/Modifications in Approved Research SOP.

7.3.3. The IRB may conduct continuing review of certain research studies by expedited review. The instructions for submission of a continuing review and the review by the IRB are described in the IRB Continuing Review of Research SOP.

7.4. Procedures for Expedited Review

7.4.1. The HRPP Administrator will confirm the submission is complete, the study qualifies for expedited review using this SOP as guidance and notifies the IRB Chair that the submission is ready for review.

7.4.2. The review and approval may be conducted by the IRB Chair or by one or more experienced (i.e., qualified) IRB members designated by the Chair.

7.4.3. In order to consider the research for approval the reviewer shall determine that all the criteria outlined in 45 CFR 46.111 or 21 CFR 56.111 as articulated in the Convened IRB Review SOP are satisfied. All non-exempt human subjects research must have the same criteria applied when conducting expedited review, the only difference is that expedited review is conducted by one or two members rather than the convened board.

7.4.4. An IRB member must not review the research in which the member has a conflict of interest (COI), except to provide information requested by the chair or his/her designee.

7.4.5. Expedited review may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so those risks related to invasion of privacy and breach of confidentiality is no greater than minimal.

7.4.6. The expedited review procedure may not be used for classified research involving human subjects.

7.4.7. The standard requirements for informed consent (or its waiver, alteration, or exception) and HIPAA compliance applies even if expedited review is utilized.

7.5. Categories of Research that May be Reviewed Through an Expedited Review Procedure

The IRB Chair or designee will ensure that every new project approved by expedited review is minimal risk and meets one or more of the following criteria, as referenced in 45 CFR 46.110:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
b) from other adults and children [2], considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means. *Examples*: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) *Examples*: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4) </ohrp /regulations-and-policy/regulations/45-cfr-46/index.html>. This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) </ohrp/regulations-and-policy/regulations/45-cfr-46/index.html> and (b)(3). This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the convened IRB as follows:
    a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
    b. where no subjects have been enrolled and no additional risks have been identified; or
    c. where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

10. Minor administrative changes in previously approved research during the period for which approval is authorized and involves no more than minimal risk.

7.6. Approving Expedited Review of Research

7.6.1. Possible actions that can be taken by the IRB Chair or the IRB designated reviewer:

- approve the research without any conditions;
- require modification in (to secure approval of) research but may not disapprove research under expedited review;
- not approve if there are significant questions or concerns and refer the study to the full board for review.

7.6.2. The HRPP Administrator will prepare an IRB Approval Letter and forward it to the Principal Investigator.

7.6.3. A list of all actions taken through an expedited review process will be provided to the IRB at a convened meeting. Any member of the IRB may request re-review of research approved using an expedited process. If such a request is made, the project will be scheduled for a convened meeting discussion.

7.6.4. Minimal risk studies approved by expedited review do not require annual continuing review, unless the study involves an investigational drug, device, or diagnostic test, or is otherwise regulated by the FDA. All other studies approved by expedited review will not have a continuing review conducted, unless required by the IRB.

7.6.4.1. If the IRB requires a continuing review for non-FDA regulated studies, the IRB will document the justification or a rationale for conducting a continuing review.

7.6.5. For expedited review studies that will no longer require continuing review, the MTU IRB, will conduct a brief inquiry (called an “administrative check-in”), which will require the researcher to submit a status update to the IRB every 3 years so long as the study remains active, simply to determine whether the research has been completed and hence IRB approval is no longer needed.

7.6.5.1. This will allow the IRB to remove potential studies from unnecessary oversight by the IRB and keep more accurate metrics regarding the total number of active studies.

7.6.5.2. The IRB will distinguish in all approval documents and study records the requirements for either a complete continuing review (with the continuing review period) or an annual administrative review.

REFERENCES:

45 CFR 46.110
45 CFR 46.108(b)
22 FR 56.110
HHS.gov OHRP Expedited Review Categories (1998). Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure, located at: http://www.hhs.gov/ohrp/policy/expedited98.html

8. Convened IRB Review (Greater than Minimal Risk)

8.1. Policy

All research projects that have greater than minimal risk must be reviewed by the convened Institutional Review Board (IRB). This Standard Operating Procedure (SOP) outlines processes that the IRB performs for the review of research by the convened IRB in accordance with FDA regulations 21 CFR 56 and the Health and Human Services (HHS) regulations (45 CFR 46) and the Michigan Technological University (MTU) policies for the protection of research subjects from research risks.

The MTU IRB is responsible for conducting an Initial Review of research to ensure the rights and welfare of human subjects is protected. This SOP applies to all human subjects research falling under the purview of MTU IRB.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy"). All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

8.2. Procedure

Convened IRB - All initial and continuing review of studies that are greater than minimal risk or do not qualify for one of the expedited review categories, and any other study that the IRB Chair determines would benefit from additional expertise provided by the convened IRB, will be reviewed by the convened IRB. The convened IRB will also review certain modifications/amendments to research (i.e., substantive changes) and Unanticipated Problems Involving Risks to Subjects or Others (UPs) in accordance with the IRB Review of /Modifications in Approved Research and Unanticipated Problems Involving Risks to Subjects or Others SOPs, respectively.

8.2.1. The Chair will call the meeting to order once enough members are present to meet quorum requirements.

- Quorum must be maintained throughout the meeting.
- Should the quorum fail during the meeting or if a non-scientific member is not present, the IRB may not take further action or vote for approval of the review, unless quorum can be restored.

8.2.2. When an extra convened board meeting is scheduled to review any type of business and time, weather, or other extenuating circumstances do not allow for a convened board meeting, the entire meeting may be held by teleconference when all other requirements of these policies and procedures are upheld.

8.2.3. The Chair will announce at the beginning of the IRB meeting that anyone present with a conflict of interest must be excused from the meeting and leave the room for the portion of the meeting that reviews the study with which they have a conflict.

8.2.4. At the discretion of the IRB Chair, IRB Staff, and/or primary reviewer (if one is designated), investigator(s) may be invited to attend the IRB meeting to answer

questions, clarification of specific points, or discussion. Invited investigator(s) are required to leave the meeting for subsequent discussion and voting on their protocol.

8.2.5. The official meeting minutes document the number of votes for, against, or abstaining. A simple majority vote of the members present at the meeting is required for approval.

8.2.6. The meeting minutes must be in sufficient detail to show the actions taken by the IRB, the vote on the actions and a summary of the discussion of controversial issues and their resolution and include all items listed in the Retention of Institutional Review Board (IRB) Records SOP.

8.3. Operational Details

8.3.1. The MTU IRB usually meets whenever a full board review is required or minimally three times per year.

8.3.2. The IRB Meeting Agenda will be distributed to each board member prior to the meeting for their review and will include the following items, as applicable:

8.3.2.1. Copy of the IRB meeting minutes from the previous IRB meeting;

8.3.2.2. Meeting Agenda

- List of new studies to be reviewed by the full board;
- List of any modifications requiring full-board review;
- List of any continuing review requiring full-board review;
- List of any unanticipated problems requiring full-board review;
- Any incidents of noncompliance that needs full-board review;
- Any items or notices for continuing education of IRB members;
- List of studies that were approved by expedited review providing the IRB number, the title of the study, and the name of the Principal Investigator. This information will be sent to board members even if a meeting is canceled.

8.3.3. The full board review generally does not use a primary reviewer system of review. All members are expected to review each protocol and supporting documents for each study. If the agenda becomes large enough whereby reviewing all studies on the agenda may become a burden to the IRB members or when the IRB Chair determines that the quality of review may be enhanced by assigning a primary reviewer to one or more studies on the agenda, then the primary reviewer system will be utilized.

8.3.3.1. IRB Members must review all materials that were submitted to the IRB electronic system for any protocol they were assigned to serve as a primary reviewer. For all other studies, members are asked to review a summary of the study and the informed consent document(s) and recruitment materials.

8.4. Criteria for IRB Approval of Research

The HRPP Administrator or an IRB member will determine if all the following requirements are satisfied prior to approving the research:

8.4.1. **Risks** - Identify the risks associated with participating in the research study and differentiating them from the risks that the subjects would encounter if they were not in the study.

8.4.1.1. The risks will include physical, psychological, emotional, economical/financial risks, and those related to a loss of privacy or a breach of confidentiality.

8.4.1.2. The identification of risks is based on review of the protocol, supporting information submitted to the IRB for review, the IRB members' experience, and knowledge, and from external sources such as a review of the literature.

8.4.1.3. The IRB must be able to determine whether the potential risks are minimal risk or greater than minimal risks so that the appropriate level of review can be applied to the research.

8.4.2. **Minimization of Risks** - The study design and study procedures will be evaluated to determine whether risks have been minimized to the extent possible that will still permit the ethical conduct of the study and that study objectives can be met.

8.4.2.1. Whenever possible, procedures should be utilized that will otherwise be performed on subjects if they were not enrolled in the study (e.g., for biomedical research using diagnostic or treatment that would be conducted in standard practice).

8.4.2.2. The IRB may minimize risks by any of the following:

8.4.2.2.1. Removing the risk by removing the procedure, intervention, or interaction that will cause the risks;
8.4.2.2.2. Substituting an alternative procedure, intervention, or interaction that is associated with less risks;
8.4.2.2.3. Adding precautions, procedures, interventions, or interactions that will manage or remove the risks;
8.4.2.2.4. Adding safeguards such as additional monitoring or testing that will identify the risks earlier and allow intervention or removal of the risks before they are exacerbated.

8.4.3. **Risks to subjects are reasonable in relation to anticipated benefits**, if any, to subjects and the importance of the knowledge that may be expected to result.

8.4.3.1. Identify the probable benefits to be derived from the research and determine that the risks are reasonable in relation to the benefits.

8.4.3.2. The IRB should not consider the possible long-term effects of potential knowledge that may be gained from the study when considering whether to approve the study (e.g., the possible effects of the research on public policy).

8.4.4. **Selection of subjects is equitable** - Ensure that protocols have appropriate plans for the equitable selection of subjects by reviewing the purpose of the study, the setting in which the research will be conducted and inclusion and exclusion criteria for selection of subjects.

8.4.4.1. The IRB should also consider the settings and/or communities from which subjects will be recruited and review the recruitment plan, recruitment materials, and even the informed consent document(s) from this perspective (See the Recruitment of Subjects and Informed Consent SOP).

8.4.4.2. When reviewing these considerations, the IRB should be aware of issues related to the enrollment of vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. Decisions on whether vulnerable subjects should be included should be made with consideration of the justice principle of the Belmont Report.

8.4.5. **Informed consent** – Ensure that protocols have plans to obtain legally-effective informed consent from each prospective subject or the subject's legally authorized representative, and appropriately documented, unless the requirement for consent is waived by the IRB.

NOTE: Since informed consent is such an integral activity for the ethical conduct of research and there are many considerations for effectively obtaining consent from subjects, a separate section is devoted to the topic in *Recruitment and Informed Consent* SOP.

8.4.6. **Documentation of Informed Consent** – Ensure that the documentation of the informed consent process is documented appropriately to ensure legally-effective consent, unless the requirement is waived by the IRB.

8.4.7. **Monitoring the data** - Where appropriate, the research plan adequately provides for monitoring the data collected to ensure the safety of subjects and to protect their privacy and maintain confidentiality of the data.

8.4.7.1. All studies that are greater than minimal risk, the IRB should review a safety monitoring plan that details how the study will monitor the data to ensure safety of subjects.

8.4.7.2. If reviewed, the IRB will determine whether the safety monitoring plan can be managed by the investigator and research team or whether there should be an additional review of safety data by a separate committee (e.g., data monitoring committee/data safety monitoring board) and/or the sponsor. Some considerations for when a monitoring committee will be required include moderate to high-risk research

(especially studies that may include death as a risk), inclusion of vulnerable subjects, large number of subjects, and double-blind study designs.

8.4.7.3. When considering a separate monitoring committee, the IRB may determine that the monitoring board should be entirely independent from the research team(s) and/or the sponsor so as to remove all potential conflicts of interest. Additional considerations for when a monitoring committee will be necessary include requirements by the FDA or NIH or the sponsor for research regulated or supported by them.

8.4.7.4. The IRB shall also determine whether additional monitoring may be required by MTU when the PI is also the PI of a multicenter study. In such situations, the IRB may determine that the monitoring plan should provide details of how safety data will be collected in a timely manner from all performance sites and how the plan will ensure the safety and well-being of subjects at all sites.

8.4.8. Privacy and Confidentiality - Determine the adequacy of the provisions to protect subject privacy and maintain data confidentiality. If the research study involves greater than minimal risk as a result of a potential breach of confidentiality, a data protection plan will be required for review by the IRB.

8.4.9. Special Consideration for Projects Involving Vulnerable Populations - When some or all of the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, handicapped or mentally disabled persons, economically or educationally disadvantaged persons, additional safeguards have been included in the research project and in the IRB review process to protect the rights and welfare of these participants.

8.4.9.1. In reviewing these research projects, the IRB ascertains that the inclusion of the vulnerable population is adequately justified and that safeguards are implemented to minimize risks unique to each population.

8.4.9.2. For approval of research projects involving vulnerable populations, the IRB considers if one of the following conditions is met:

8.4.9.2.1. The research does not involve more than minimal risk to the subject;
8.4.9.2.2. The research is likely to benefit the subject directly, even if the risks are considered to before than minimal; or
8.4.9.2.3. The research involves greater than minimal risk with no prospect of direct benefit to individual participants but is likely to yield generalizable knowledge about the subject's disorder or condition.

8.4.10. The IRB has the authority to disapprove or require modifications in research activity.

8.4.11. A member or consultant with a conflict of interest may participate in the review by providing information but must leave the room during the vote.

8.5. Approving Research at the Time of Initial Review

The IRB can take any of the following actions:

8.5.1. Approve the research study;

8.5.1.1. Without any conditions or;

8.5.1.2. With conditions (also referred to as “conditional approval or contingent approval”);

8.5.1.2.1. IRB may require the investigator make specific changes to the protocol or informed consent;

8.5.1.2.2. IRB may require the investigator to submit additional documents;

- IRB Chair or other individuals (with expertise or qualifications) may review materials submitted from the investigator and determine that the conditions have been satisfied;
- Further review by the IRB at a subsequent convened meeting would not be necessary;

8.5.1.2.3. IRB should specify whether any conditions need to be satisfied before an investigator can initiate research activities.

8.5.2. Requiring Modifications – to secure IRB approval;

8.5.2.1. Defer or table the study for further review at a future date after the required modifications are submitted by the investigator;

8.5.3. Disapprove the research;

8.5.3.1. FDA recommends the IRB notify the sponsor of any decision to disapprove the research and the reason(s) for the disapproval determination.

8.6. Effective Date of the Initial Review

8.6.1. The effective date of the initial approval is the date of the IRB meeting.

8.6.2. Unless the IRB designates a shorter approval period based on potential risks of the study or other concerns, the expiration date of the initial approval is the day before the one-year anniversary after the effective date.

8.7. Notification of IRBs Initial Review Determination to the Investigator

After the review, the investigator will receive a letter with the IRB decision:

8.7.1. For studies approved – an approval letter with the date of approval and expiration date of IRB approval will be sent to the PI.

8.7.2. For studies approved with conditions – IRB conditional approval indicates that the IRB has approved the protocol pending submission and approval of minor revisions.

8.7.3. For studies tabled/deferred - (Convened IRB only) indicates that the IRB withholds approval pending submission of major revisions/additional information that must be re-reviewed by the IRB.

8.7.3.1. The HRPP Administrator will send the investigator a letter listing the reasons for deferring the study for re-review by the convened IRB and include a description of the revisions or clarifications requested.

8.7.4. For disapproved research – (Convened IRB only) A vote to disapprove research indicates that the IRB will not allow the research to be conducted.

8.7.4.1. Disapproval of a protocol usually occurs when the IRB determines that the risk of the procedure outweighs any benefit to be gained or if the proposed research does not meet the federal criteria for IRB approval.

8.7.4.2. Disapproval generally indicates that even with major revisions to the application the issues preventing approval will not be resolved.

8.7.4.3. The HRPP Administrator will send the investigator a letter describing the reasons for disapproving the protocol.

8.7.4.4. The investigator will be given an opportunity to respond to the IRB decision to disapprove the research.

8.7.4.4.1. The investigators' responses will be reviewed at a subsequent convened meeting of the IRB.

8.7.5. A copy of the notification letter will be kept in the IRB study file.

8.8. Appeal of IRB Decisions/Determinations

8.8.1. Investigators may appeal the IRB’s approval, deferral of approval (i.e., requests for changes for a submission), or disapproval decision for the review of any new study, modification or continuing review of an existing study, or review and determinations regarding allegations of noncompliance/review of noncompliance.

8.8.2. An investigator may appeal to the IRB for a formal re-review of a decision whenever there has been more than two unsuccessful efforts by the investigator and the IRB to resolve the investigator’s concerns and the investigator believes

that the IRB's decision is due to: inadequate or inaccurate information; or, IRB non-compliance with MTU IRB SOPs, state law, or federal regulation.

8.8.3. At the discretion of the IRB Chair, the investigator may make such an appeal in person and/or in writing to the IRB.

8.8.3.1. The appeal request consists of sending the HRPP Administrator a cover letter outlining the basis for the appeal and documents that support the appeal.

8.8.3.2. The HRPP Administrator reviews the appeal request to determine whether an appeal is appropriate. This may include consultation with the investigator, the IRB Chair, select members of the IRB, the HRPP Administrator, or the Institutional Official, as needed. The HRPP Administrator informs the investigator by email of whether the request has been accepted for review.

8.8.4. If the decision being appealed was made by the convened IRB, the appeal is heard and considered by the convened IRB. This may be a regularly scheduled IRB meeting, or it may be a meeting convened for this specific purpose. If the decision being appealed was made by the Expedited or Exempt (both minimal risk) process: the IRB Chair will hear the appeal.

8.8.5. The following outlines the process for appeals heard by the convened IRB.

8.8.5.1. The IRB Chair may hold a closed session of the IRB without the researcher, prior to the appeal portion of the meeting, to establish the key issues and questions to consider.

8.8.5.2. The researcher is invited to present information and rationale to the IRB.

8.8.5.3. There is a question-and-answer session with the researcher.

8.8.5.4. The research leaves the meeting room.

8.8.5.5. The IRB members and other meeting attendees discuss the appeal.

8.8.5.6. The HRPP Administrator or designee prepares anonymous written ballots to distribute to the members for voting when the discussion has ended. After voting, the ballots are read by the IRB Chair. The IRB moves and then votes whether to take one of the following actions:

8.8.5.6.1. Approve the appeal and modify the original decision;
8.8.5.6.2. Disapprove the appeal and uphold the original determination; or,
8.8.5.6.3. Defer the appeal and obtain additional information or consultation in order to make a final decision.

8.8.5.7. The IRB's appeal determination, and any other considerations or requirements associated with it, are communicated to the researcher in

a letter within 10 business days of the IRB's determination. If appropriate, the determination may also be communicated by email or telephone call with follow-up email by the HRPP Administrator or IRB Chair.

8.8.5.8. A decision by the IRB to disapprove, suspend, or terminate a project is not subject to reversal by the MTU Institutional Official or any other officer of MTU, state, or federal government.

8.8.5.9. Only one appeal will be allowed on a given matter. The concluding IRB decision of an appeal is final and cannot be appealed.

References:

Guidance for IRBs, Clinical Investigators, and Sponsors; IRB Continuing Review after Clinical Investigation Approval; February 2012
45 CFR 46.108; 46.109
21 CFR 56.111; 56.108(a)(1); 56.108(a)(2-4); 56.109(f)
45 FR 46.110(b)(2); 46.111; 46.116; 46.117

9. Recruitment of Subjects and Informed Consent

9.1. Purpose

9.1.1. It is the policy of Michigan Technological University (MTU) that no one may involve a human being as a participant in research or in a clinical investigation unless the investigator has obtained Institutional Review Board (IRB) approval and, when required by the IRB, that person's legally effective informed consent. The MTU IRB may alter or waive the requirement of informed consent under the Department of Health and Human Services (DHHS) regulations governing human subject research [46.116(f)] but may not waive consent for studies regulated by the Food and Drug Administration (FDA) unless the subject is in a life-threatening condition and criteria under 21 CFR 50.23 or 50.24 are met. If the participant is an adult who is unable to consent for him/herself, the investigator must describe the process of evaluating the individual's capacity to provide consent, and if that capacity is lacking in a subject, must obtain informed consent from a legally authorized representative in accordance with State law. If the participant is a minor, the investigator must describe the consent/assent process in accordance with federal and state law.

9.1.2. The Principal Investigator (PI) is responsible for ensuring that legally effective informed consent is obtained from each subject, unless waived by the IRB and for compliance with the investigator requirements of this SOP.

These procedures supplement the REQUIREMENT FOR IRB APPROVAL AND IRB AUTHORITY policy.

9.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Legally authorized representative - an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Family member - any one of the following legally competent persons: spouse; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

Exculpatory language - Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) consider exculpatory language to be language which has the general effect of freeing or appearing to free an individual or an entity from malpractice, negligence, blame, fault, or guilt.

Minor – persons who have not attained the legal age of consent to treatment or procedures involved in research in the state of Wisconsin, a minor is less than 18 years of age.

Assent – an affirmation, verbally or non-verbally, to participate in research by an individual who cannot provide consent, i.e., children and incompetent participants.

Dissent –an expressed desire, verbally or non-verbally, not to participate in the research by an individual who cannot provide consent, i.e., children and incompetent participants.

Permission – the agreement of parent(s) or guardian to the participation of their child or ward in research.

Parent – a child's biological or adoptive parent.

Guardian – an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

Ward – a child whose welfare is the responsibility of the State or other agency, institution or entity.

9.3. Recruitment

9.3.1. Since the informed consent process is considered to start with the recruitment process, the IRB also considers recruitment materials during its review of informed consent.

9.3.1.1. The IRB will review proposed methods of recruitment and recruitment materials, to ensure that the process will be conducted in a manner that is ethical.

9.3.1.2. Recruitment material may include flyers, recruitment letters, advertisements, television, or radio ads, and posting on social media, among other strategies.

9.3.1.3. The IRB review of recruitment materials will ensure that benefits are not overstated or presented in a manner that may be coercive or pose undue influence over a subject's decision-making process.

9.3.1.4. For these reasons, the information provided in recruitment materials should be limited to information that will generate interest from the subject, determine their eligibility, and provide contact information for the research team. As relevant, the recruitment material may include following:

9.3.1.4.1. an explanation of the purpose of the study;
9.3.1.4.2. eligibility information (e.g., brief summary of the main inclusion/ exclusion criteria);
9.3.1.4.3. a summary or brief list of the benefits;

9.3.1.4.4. the name of the researcher and/or research institution or facility;
9.3.1.4.5. time or other commitments needed from the subjects;
9.3.1.4.6. contact information for the research team.

9.3.2. Advertisements must not:

9.3.2.1. State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol;

9.3.2.2. Include exculpatory language;

9.3.2.3. Promise “free treatment” when the intent is only to say subjects will not be charged for taking part in the investigation.

9.3.3. If the recruitment material presents the amount of compensation offered for participation, the amount should not stand out more than the rest of the content in the recruitment material by increasing the font size, bold font, or brighter color.

9.3.4. Only recruitment material that is presented directly to subjects needs review by the IRB. Materials or media coverage about the research that is intended for scientists, educators, health professionals or other individuals not targeted as subjects for the study do not need to be reviewed by the IRB.

9.4. Screening, Recruiting, or Determining Eligibility

In accordance with 45 CFR 46.116(g), an IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject’s legally authorize representative, if either of the following conditions are met:

9.4.1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or

9.4.2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

9.5. Payment/Compensation to Research Subjects

9.5.1. Payment to research subjects may be an incentive for participation or a way to reimburse a participant for travel and other experiences incurred due to participation. However, payment for participation is not considered a research benefit.

9.5.2. Regardless of the form of remuneration, PIs must consider the degree of risk and must exercise care to avoid undue influence for subjects to accept risks that they would not otherwise accept if there was no payment and must also avoid coercion of subjects. Payments should reflect the costs, inconvenience, or discomfort associated with participation or may be used to encourage

participation in a study that is not generating interest as long as the payment, as previously stated, would not cause undue influence.

9.5.3. The IRB will review both the amount of payment and the proposed method of disbursement to assure that neither entails problems of coercion or undue influence. PIs may allow payment accrual as the study progresses. Payment can be contingent upon the participant completing the entire study, but this fact needs to be made known to the participant at the beginning of the study. If a bonus is given for completion of the study, the bonus must be reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn; this also must be disclosed at the beginning of the study.

9.5.4. The PI may not offer a “finder’s fee” to individuals such as professors or supervisors to refer prospective subjects when those individuals have a power relationship over the prospective participant. “Bonus payments” used to accelerate recruitment that is tied to the rate or timing of enrollment may not be paid to or accepted by PIs or research staff.

9.5.5. The consent form must describe the terms of payment and the conditions under which subjects would receive partial payment or no payment (e.g., if they withdraw from the study before their participation is completed).

9.5.6. If compensation in any form (e.g., cash, coupons, gift cards or certificates, vouchers) for payment is administered through MTU, the expenditure of funds for this purpose must fall within all applicable Federal, State, and institutional requirements.

9.6. Procedures for Consent Process

Informed Consent Process. The MTU IRB must review the proposed consent process. Investigators must seek consent under such circumstances that provide the prospective participant with sufficient time and opportunity to consider whether or not to participate.

The MTU IRB’s evaluation of the investigator’s proposed participant selection/ recruitment process and informed consent process will include the following key features:

9.6.1. completely disclosing all critical information needed for the potential research subjects to make an informed decision;

9.6.2. ensure the subjects or their legally authorized representatives adequately understand what has been disclosed to them so they can make informed choices;

9.6.3. promote the voluntariness of the decision about whether or not to participate in the research; and,

9.6.4. consent with subjects is seen as an ongoing process, and not the reading of a stagnant document.

9.6.5. Considering the capacity of the participant to make an independent and voluntary informed decision whether or not to participate in a study.

9.6.6. Reviewing who will obtain consent and under what circumstances.

9.6.7. Deciding whether and how consent will be documented.

9.7. Elements of the Informed Consent

9.7.1. General Requirements

9.7.1.1. The investigator must obtain a legally effective informed consent from the subject or the subject's legally authorized representative prior to (prospectively) involving the human subject in research unless the IRB finds and documents that the informed consent can be waived in accordance with 45 CFR 46.116 (e) or (f).

9.7.1.2. Investigator shall seek such consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

9.7.1.3. The information that is given to the subject or the legally authorized representative shall be in a language understandable to the subject or the representative. If this involves a language other than English, the IRB will require a clear plan for accurate translation, and may require that translated versions be approved prior to use (see section 9.11). Regardless of the language in which the consent document is written, the document should be written at a reading level that would be understood by subjects (i.e., an 8th grade reading level).

9.7.1.4. The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate and an opportunity to discuss that information.

9.7.1.5. (Except for broad consent obtained in accordance with the 45 CFR 46), informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension. The concise and focused presentation of key information is not required for minimal risk studies with relatively short consent forms.

9.7.1.6. Informed consent as a whole must present information in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

9.7.1.7. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

9.7.2. **Basic Elements of Informed Consent**

The following information must be provided to each subject:

9.7.2.1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed and identification of any procedures which are experimental;

9.7.2.2. A description of any reasonably foreseeable risks or discomforts to the subject;

9.7.2.3. A description of any benefits to the subject or to others which may reasonably be expected from the research;

9.7.2.4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

9.7.2.5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

9.7.2.5.1. Statement(s) should be included to explain who has access to review the research records for inspection purposes [e.g., MTU, Food and Drug Administration (FDA) for FDA-regulated research and the Office for Human Research Protections (OHRP) for HHS-supported research];

9.7.2.5.2. Additionally, for NIH-supported grants or contracts, language should be included to explain the protections provided by the Certificate of Confidentiality, which are automatically provided for all NIH grants (as of October 1, 2017). For non-NIH-supported grants, an explanation of the protections provided by a Certificate of Confidentiality should be included whenever one has been obtained for the study;

9.7.2.6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any

medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

9.7.2.7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and,

9.7.2.8. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

9.7.2.9. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

9.7.2.9.1. A statement that the identifiers might be removed from the identifiable private information or identifiable private biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative if this might be a possibility; or

9.7.2.9.2. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

9.7.3. **Additional Elements of Informed Consent**

When appropriate, the following elements of information shall also be provided to each subject:

9.7.3.1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

9.7.3.2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent;

9.7.3.3. Any additional costs to the subject that may result from participation in the research;

9.7.3.4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

9.7.3.5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;

9.7.3.6. The approximate number of subjects involved in the study;

9.7.3.7. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

9.7.3.8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and

9.7.3.9. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome of that specimen).

9.7.3.10. For all clinical trials, the following statement will be included: "A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time." These statements are usually placed towards the beginning of the consent document after the Purpose section.

9.7.3.11. An explanation of any payments or compensation to subjects as a result of participation, including any reporting to the Internal Revenue Service (IRS) as a result of the payment (e.g., $600 or more in total payments will result in a Form 1099 be filed to IRS along with the subject's social security number, name, and address);

9.7.3.12. For studies involving audio and/or video recordings an explanation of the use and storage of such recordings and how confidentiality will be protected.

9.8. Additional Considerations for Studies Collecting Protected Health Information (PHI)

9.8.1. Studies that involve the collection of Protected Health Information (PHI), or access to PHI, within the covered entities of MTU must comply with the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.8.2. Any study that will involve PHI should have its review comply with the "Research with Protected Health Information – IRB Review of HIPAA" SOP.

9.8.3. For studies involving collection or access to PHI, the Privacy Board of the covered entity providing the PHI to the MTU researcher(s) must determine one of the following:

9.8.4. Appropriate authorization is obtained from all subjects in the study in accordance with 45 CFR 164.508(a); or

9.8.5. The study qualifies for a waiver of such authorization in accordance with 45 CFR 164.512(i); or

9.8.6. The PHI will be de-identified consistent with the definitions in 45 CFR 164.514(a); or

9.8.7. The PHI will be obtained or accessed from a limited data set with the necessary safeguards to protect confidentiality of the data in accordance with 45 CFR 164.514(e) and a data use agreement approved by MTU has been executed.

9.9. Michigan Technological University (MTU) Requirements

9.9.1. The written consent form should identify the association with MTU either in a letterhead or within the text of the informed consent.

9.9.2. Generally, use Times New Roman font with a minimum font size 12.

9.10. Documentation of Informed Consent Process

9.10.1. Informed consent will be documented by the use of a written consent form, except as provided in 21 CFR 56.109(c) and 45 CFR 46.117(c) (as specified in section 9.10.3. below).

9.10.1.1. The Informed consent process and documentation must be approved by the IRB before use.

9.10.1.1.1. The date of the IRB approval and the date of expiration of IRB approval will be documented on the bottom of each page of the informed consent, as applicable.

9.10.1.1.2. The consent form will be signed (including in an electronic format) and dated by the subject or the subject's legally authorized representative at the time of consent, as applicable.

9.10.1.1.3. A copy will be placed in the study file.

9.10.2. Informed consent process and form may be either of the following:

9.10.2.1. A written consent form that contains all the elements of informed consent.

9.10.2.1.1. The form may be read to the subject or the subject’s legally authorized representative.

9.10.2.1.2. Either the subject or the representative will be given adequate opportunity to read it before it is signed.

9.10.2.1.3. For greater than minimal risk research, in addition to having the signed consent form serve as documentation that the consent was obtained, the PI, or delegate, may also be required to document a summary of the consent process. The summary should include details of how

others may have participated in the consent process or if there were any controverted issues discussed (e.g., include details of who translated the discussion into another language if the subject is a non-English speaking subject, or who served as a legally authorized representative if the subject was a minor or lacked capacity, etc.).

9.10.2.2. A short form written consent document stating that all the elements of the informed consent have been presented orally to the subject or the subject's legally authorized representative, and that the key informed consent information was presented first to the subject, before other information, if any, was provided. The IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Only the short form itself is to be signed by the subject or the subject's legally authorized representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the subject's legally authorized representative, in addition to a copy of the short form.

9.10.2.2.1. For non-English-speaking subjects, the short form may only be used when the enrollment of a subject speaking the particular language was not expected at the time of the last review of the study by the IRB and time does not permit for the review and approval of a translated ("long-form") version of the consent. See next section on "Translation of Informed Consent for Non-English-Speaking Subjects."

9.10.3. The IRB may waive the requirement for the investigator to obtain a signed consent form (i.e., waiver of the documentation of consent) for some or all subjects if it finds any of the following (taken from 45 CFR 46.117(c)(1)):

i. That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. This waiver criteria cannot be applied to FDA significant risk regulated studies; or

ii. That the research presents no more than minimal risk of harm to subjects, and involves no procedures, for which written consent is normally required outside of the research context; or

iii. If the Subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and

provided there is an appropriate mechanism for documenting that informed consent was obtained.

9.10.4. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research.

9.11. Translation of Informed Consent for Non-English-Speaking Subjects

9.11.1. The informed consent should be obtained in a language understandable to the subject or the authorized representative. It is expected that the PIs will assess the comprehension and capacity of the subjects to understand the consent language.

9.11.1.1. Whenever the investigator anticipates that non-English speaking subjects may be enrolled in a given study, plans should be included in the submission for a translated consent form(s) in that language.

9.11.1.2. If the IRB, during its review of the submission, determines that it is likely that non-English speaking subjects will be enrolled, the IRB will request a plan for translation.

9.11.1.3. Once the IRB approves an English version of the consent form(s), it may request that a translated version is submitted to the IRB for each language that is anticipated.

9.11.1.4. The investigator, IRB, and MTU are all responsible for ensuring legally effective consent. Therefore, the translation of the IRB-approved English version of the consent must be translated in a manner that the investigator and IRB have confidence that the translation effectively communicated the content and tone of the English version of the consent form. Options for obtaining a reliable translation include the following:

9.11.1.4.1. A company or organization that provides translations as a service to the public;

9.11.1.4.2. An individual who is fluent in both English and the anticipated language of the Non-English-speaking subject; for greater than minimal risk studies, the IRB may require a back-translation from another individual who is fluent in both languages to help ensure the accuracy of the translation.

9.11.1.4.3. A sponsor, such as NIH or a medical device manufacturer.

9.11.2. For greater than minimal risk studies, the consent process must involve a witness.

9.11.2.1. If required by the IRB, the consent process must include a certified translator.

9.11.2.2. Documentation of the consent process must include both versions of the consent form and translator information.

9.12. Approving Waivers or Alterations of Informed Consent

9.12.1. Waiver of Informed Consent: The IRB may approve a consent procedure, which does not include, or which alters, some or all the elements of informed consent, in accordance with CFR 46.116 (f).

9.12.2. The Investigator will assess the proposed research to determine if it meets regulatory requirements for a waiver of informed consent procedures. The IRB may waive or alter the requirement of informed consent provided that either (a) the study is determined to be Exempt in accordance with section 6.2, or (b) the study meets all five of the following conditions from 45 CFR 46.116(f)(3):

i. The research involves no more than minimal risk to the subjects;

ii. The research could not practicably be carried out without the waiver or alteration;

iii. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;

iv. The waiver or alteration will not adversely affect the rights and welfare of the subjects;

v. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

9.12.3. The IRB, or in the case of expedited review the IRB Chair or Designated Reviewer(s) will consider the request for a waiver of informed consent and the Investigator's justification is appropriate for the proposed research activity.

9.12.3.1. If the IRB/IRB Chair/Designated Reviewer(s) agrees with the Investigator's justification for waiver of consent, such determination will be documented in the IRB records.

9.12.3.2. If the IRB/IRB Chair/Designated Reviewer(s) do not agree with the Investigator's justification or if they do not agree that waiver or alteration of the consent is allowable and appropriate, the IRB will not approve the request for waiver, document its determination, and inform the investigator accordingly.

9.13. Assent by Children and Individuals without Decisional Capacity or Permission by Parent or Authorized Representative

9.13.1. Minors and individuals who lack decisional capacity to provide consent should be given the opportunity to assent (affirmational agreement) to participate in the research study.

9.13.1.1. In determining whether children are capable of assenting, the ages, maturity and psychological state of the children should be considered.

9.13.1.2. Assent for a minor must be obtained in a language that is understandable to the child.

9.13.1.3. Assent guidelines for children by age:

9.13.1.3.1. No assent is required for children under the age of 7.

9.13.1.3.2. Unless otherwise approved by the IRB, verbal or documented assent must be obtained for children ages 7 to 12:

9.13.1.3.3. Unless otherwise approved by the IRB, documented assent must be obtained for children ages 13 to 17.

9.13.1.4. The permission/informed consent of a parent or legally authorized representative (LAR) must be obtained in conjunction with the assent of a child:

9.13.1.5. If the study participation is critical to the health of the child, the child's dissent may be overruled by the parents:

9.13.2. Obtaining permission from parents or guardians:

NOTE: If there are two parents available but they disagree about allowing their child to participate in the study, the child may NOT be enrolled unless that disagreement can be resolved (even if only one parent signature is required).

9.13.2.1. Permission of one parent is sufficient for:

9.13.2.1.1. Research not involving greater than minimal risk (45 CFR 46.404; for FDA regulated research: 21 CFR 50.51); 13.2.1.2 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405, 21 CFR 50.52).

9.13.2.2. Permission of both parents is required for:

9.13.2.2.1. Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition (45 CFR 46.406, 21 CFR 50.53);

9.13.2.2.2. Research not otherwise approvable which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children (21 CFR 50.54, 45 CFR 46.407).

9.13.2.3. Exception for permission of both parents:

9.13.2.3.1. One parent is deceased, unknown, lacks capacity or is not reasonably available or when only one parent has legal responsibility for the care and custody of the child.

9.13.2.3.2. In order to establish that only one parent has legal responsibility for the care and custody of a child, an order issued by a court from the state in which such parent resides must grant sole custody of the child to such parent.

9.13.2.3.3. A copy of the court order should be retained with the documentation with the parent's permission.

9.13.2.4. Permission by parents or guardians will be documented using the procedures found in section 9.10.

9.14. Posting of IRB-approved consent on public website [45 CFR 16.116(h)]

9.14.1. For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Website that will be established as a repository for such informed consent forms.

9.14.2. If the Federal Department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Website (e.g., confidential commercial information), such Federal Department may permit or require redactions of the information.

9.14.3. The consent must be posted after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

9.15. Informed Consent at the Time of the Continuing Review – IRB Responsibilities

9.15.1. The primary reviewer will complete the Continuing Review form.

9.15.1.1. The completed form will be placed in the study file.

9.15.2. The IRB will assess the adequacy of Informed Consent:

9.15.2.1. Review informed consent to verify that the site is using the most recently approved version;

9.15.2.2. Evaluate whether the consent contains accurate, up-to-date information about the research;

9.15.2.3. Assess whether the currently approved consent adequately addresses the required Elements of Informed Consent;

9.15.2.4. Assess if the consent provides an accurate and up-to-date description of the reasonably foreseeable risks and discomforts of the research to the subject;

9.15.2.5. Assess whether any new appropriate alternative procedures or courses of treatment that might be advantageous to the subject;

9.15.2.6. Assess whether any new information presented by the investigator or others that raises concerns about the circumstances under which the consent is obtained (e.g., subject not provided with sufficient opportunity to consider whether or not to participate, possible coercion or undue influence; and,

9.15.2.7. Consider if any new findings should be communicated to the subjects who are already enrolled in research which could relate to the subjects willingness to continue to participate (e.g., newly identified risk information, new adverse events).

9.16. Responsibilities of Researchers

9.16.1. Researchers are responsible for:

9.16.1.1. ensuring that legally-effective informed consent is obtained, unless waived by the IRB, from all participants, in accordance with the IRB-approved process, prior to initiating any research activities, including screening procedures;

9.16.1.2. ensuring that all individuals who will obtain consent are qualified and appropriately trained to explain the research and to answer questions;

9.16.1.3. obtaining IRB approval for any revisions to the consent process, before implementation;

9.16.1.4. reporting deviations in the informed consent process to the IRB in accordance with the reporting requirements in IRB SOPs.

References:
45 CFR 46.103; 46.116; 46.117
45 CFR 46.401-409 (Subpart D)
21 CFR 50
21 CFR 56.111(b)
45 CFR 164.512(i)
HHS.gov; Informed Consent FAQs

Guidance on Exculpatory Language in Informed Consent, August 19, 2011
FDA guidance: IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects, July 2017

10. Research with Protected Health Information – IRB Review of HIPPA

10.1. Policy

The federal Health Insurance Portability and Accountability Act (HIPAA) applies only to covered entities who provide health care services, process health information, or administer health plans. The HIPAA Privacy Rule requires a Privacy Board (often the IRB at an academic medical center or health care facility) to evaluate patient privacy and grant waivers of research authorization.

Michigan Technological University (MTU) is not a covered entity, therefore HIPAA does not directly apply to the university. However, when MTU researchers are collecting, receiving, or utilizing PHI from covered entities, MTU researchers may be asked to sign a Business Associates Agreement (BAA) with the covered entity. The BAA will clarify that the MTU researchers must comply with HIPAA and the covered entities' policies.

HIPAA required the creation of regulations for the protection of health information. The resulting regulations are known as the Privacy Rule (45 CFR Part 160, 162, 164) and became effective in April 2003. MTU must ensure that research involving PHI complies with HIPAA and BAA requirements including obtaining authorization for the use or disclosure of PHI in the research, unless the requirement has been waived by the Privacy Board/IRB of the covered entity, and appropriate protections are implemented to ensure the confidentiality of such information.

10.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Business Associate - a person (other than an employee of a covered entity) who on behalf of such covered entity or of an organized health care arrangement (as defined in Part 160.103) in which the covered entity participates, creates, receives, maintains, or transmits protected health information for a function or activity regulated by Part 160.103, including claims processing or administration, data analysis, processing or administration, utilization review, quality assurance, patient safety activities listed at 42 CFR 3.20, billing, benefit management, practice management, repricing, consultation, research, or other services as described in Part 160.103. A Business Associate can be a person, business/organization, or another covered entity.

Covered Entity - a (1) health plan, (2) health care clearinghouse or (3) a Covered Health Care Provider, as more particularly described in Section 160.103.

Disclosure - the release, transfer, provision of access to, or divulging in any manner of information outside the entity holding the information.

Individually Identifiable Health Information (IIHI) - any information (including demographic and genetic information) created or received by a covered entity that relates to (1) the past, present or future physical or mental health or condition of an individual, (2) the provision of Health Care to an individual or (3) the past, present or

future payment for the provision of Health Care to an individual and either (a) identifies the individual or (b) with respect to which there is a reasonable basis to believe that the information can be used to identify the individual, as further defined in Section 160.103.

Limited Data Set – A limited data set protected health information (PHI) that excludes the following direct identifiers of an individual or relatives, employers or household members of the individual:

- Names (including initials);
- Postal address information, other than town or city, state and zip code;
- Telephone numbers;
- Fax numbers;
- Email addresses;
- Social security numbers (including partial social security numbers;
- Medical record numbers;
- Health plan beneficiary numbers;
- Account numbers;
- Certificate/license numbers;
- Vehicle identifiers and serial numbers, including license plate numbers;
- Device identifiers and serial numbers;
- Web Universal Resource Locators (URLs);
- Internet Protocol (IP) address numbers;
- Biometric identifiers, including finger and voice prints; and
- Full-face photographic images and any comparable images,

A covered entity may use or disclose a limited data set only for the purposes of research, public health, or health care operations.

Principal Investigator (PI) - the individual who is responsible for the conduct of the human research study.

Protected Health Information (PHI) – individually identifiable health information that is maintained or transmitted in or by electronic media or maintained/transmitted in any other form or media. PHI excludes IIHI: (i) in educational records covered by the Family Educational Rights and Privacy Act (FERPA); (ii) in records described at 20 U.S.C. 1232g(a)(4)(B)(iv); (iii) in employment records held by a covered entity in its role as employer; and (iv) regarding a person who has been deceased for more than 50 years.

10.3. Procedures

For submissions for IRB review that involve PHI, the IRB will require documentation of a Privacy Officer approval (or IRB approval, if the IRB also serves as a Privacy Board at a given institution) from the institution that is releasing PHI. The approval may involve a HIPAA authorization for disclosure or release of PHI, waiver of authorization, or use of a limited data set (with appropriate safeguards in accordance with 45 CFR 164.514(e) and a data use agreement has been executed).

The MTU IRB will review the plan for protection of confidentiality and ensure that the plan adequately protects the PHI from potential breach of confidentiality in accordance

with the BAA and Criteria for IRB Approval. The review of the plan to protect confidentiality will be conducted within the IRB's review to minimize risks.

Whenever MTU research will collect PHI, the IRB will also review the informed consent document to ensure that the use of PHI and efforts to minimize risks and protect confidentiality are appropriately described in the informed consent document, unless informed consent can be waived in accordance with 45 CFR 46.116(d). When appropriate, the IRB will also review the HIPAA authorization for release of PHI from the institution that is releasing PHI for consistency with the informed consent document.

11. IRB Review of Changes/Modifications in Approved Research

11.1. Policy

The Organization requires Institutional Review Board (IRB) review and approval of proposed changes in approved research prior to initiation of any changes.

The exception is a change in research necessary to eliminate apparent immediate hazards to a research participant. In cases where changes were made to eliminate apparent immediate hazards, it is the responsibility of the Principal Investigator (PI) to inform the IRB promptly of the change and the IRB must determine if the modified research is consistent with ensuring participants' continued welfare.

These procedures supplement the "Convened IRB Review (Greater Than Minimal Risk)" Policy.

11.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Minor Modification, Change, or Amendment - a change in research related activities that do not significantly affect the risk/benefit ratio of the study and/or does not substantially change the specific aims or design of the study.

Modification, Change, or Amendment – any change or amendment to the IRB approved study protocol.

Substantive Modification, Change, or Amendment - a change in research related activities that affects the risk/benefit ratio of the study in a manner that may elevate the risk so that it is greater than minimal risk or substantially changes the specific aims or design of the study.

Qualified IRB member -a voting member or alternate voting member who has received training relative to the expedited review categories and possesses the scientific or regulatory expertise needed to review the proposed research.

11.3. Procedures for Submission of Modifications for IRB Review and Approval

Changes in research may encompass amendments, addenda, deletions, or revisions to either the protocol or consent document associated with a protocol. The PI must submit information to allow the IRB to determine if the proposed change may be approved.

11.3.1. Investigators must report planned changes in the conduct of a study and receive approval from the IRB prior to implementing these changes except when necessary to avoid an apparent immediate hazard to a subject.

11.3.2. The approval letters sent to investigators of expedited and full board studies notify them of the need for submitting any changes in their research projects to the IRB for review and approval. Likewise, the approval letters for exempt studies inform investigators that any changes in the research that affect the exempt status of the research must be submitted for IRB approval.

11.3.3. Modifications may only be initiated without IRB review and approval when necessary to eliminate apparent immediate hazard to the subject(s).

11.3.4. Complete a modifications in research form with an explanation of changes that are being requested.

11.3.4.1. Submit informed consent document(s) with tracked changes (if applicable);

11.3.4.2. Submit clean copy (no redline or tracked changes) of the final version of consent document(s);

11.3.4.3. Recruitment materials (i.e., advertising, flyers, etc.) with tracked changes (if applicable) and clean copy of the advertisement(s);

11.3.4.4. Submit the protocol with tracked changes (if applicable);

11.3.4.5. Submit final copy of protocol.

11.4. Types of Modifications

11.4.1. Minor modifications/amendments

Examples of minor changes in most situations:

11.4.1.1. A modest increase or decrease in proposed enrollment target;

11.4.1.2. Narrowing the range of the inclusion criteria;

11.4.1.3. Broadening the range of the exclusion criteria;

11.4.1.4. Alteration in the dosage form of a drug (e.g., tablet or capsule or oral liquid), provided the dose and route of administration remains constant;

11.4.1.5. Decreasing the number or volume of biological samples collections, provided that such a change does not affect the collection of information related to safety evaluations;

11.4.1.6. A decrease in the number of study visits, provided that such a decrease does not affect the collection of information related to safety evaluations;

11.4.1.7. Reduction or minor changes in participant payment or liberalization of the payment schedule with proper justification;

11.4.1.8. Changes to improve the clarity of statements or to correct typographical errors, provided that such a change does not alter the content or intent of the statement;

11.4.1.9. The addition or deletion of qualified investigators or study personnel;

11.4.1.10. The addition of study sites (which may require a Federal Wide Assurance (FWA) and appropriate IRB approval) or the deletion of study sites.

11.4.2. Significant modifications/amendments

Examples of significant changes in most situations:

11.4.2.1. Broadening the range of inclusion criteria;

11.4.2.2. Narrowing the range of exclusion criteria;

11.4.2.3. Addition of a new subject population (e.g., control group, additional cohort, etc.). However, such a modification/amendment may require review as a new submission if it substantively changes the design of the study;

11.4.2.4. Addition of research procedures that involve greater than minimal risk to subjects (e.g., collection of sensitive, confidential information such as criminal activity or substance abuse with potential breach of confidentiality; addition of a new drug to a treatment regimen; addition of invasive procedures; change in route or frequency of drug administration, etc.);

11.4.2.5. Extending substantially the duration of exposure to the test material or invention;

11.4.2.6. The deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations;

11.4.2.7. Addition of new significant risks to the protocol and/ or the Informed Consent Document(s);

11.4.2.8. Changes, which, in the opinion of the IRB Chair or his/her designee, do not meet the criteria or intent of a minor modification;

11.4.2.9. The addition of a qualified investigator with a disclosable conflict of interest.

11.5. Pre-Review of Modifications

11.5.1. The HRPP Administrator will make the initial review of modifications to determine if the submission is complete and whether the modification is a minor or substantive change.

11.5.2. The HRPP Administrator will contact the investigator if any information is missing from the submission necessary to complete IRB review of the modification.

11.5.3. The HRPP Administrator will then inform the IRB Chair that the submission is ready for review.

11.6. Procedures for IRB Review of Modifications

11.6.1. Materials submitted in support of changes will be distributed to IRB members in accord with the IRB SOPs. IRBs delegated responsibility for review of changes in research are authorized to conduct the process in accord with federal regulations using either:

11.6.1.1. An expedited review process (see Expedited Review of Research SOP), which is restricted to review of changes in previously exempted studies, changes in previously approved expedited studies, and minor changes in studies previously approved by convened review; or

11.6.1.2. A convened review process [see Convened IRB Review (Greater than Minimal Risk) SOP].

11.6.2. If study modifications reviewed by the expedited review are approved, then information regarding the approval will be presented at the next full board meeting and documented in the meeting minutes.

11.6.3. Substantive changes in research involving drugs, biologics, or Complementary Alternative Medicines (CAMs) must be reviewed by an appropriately qualified IRB member [e.g., a physician or appropriate health professional serving as an IRB member or consultant] for either an expedited review or a convened review. Changes or modifications reviewed through an expedited review process will be reported to the IRB members on a list as noted in Expedited Review SOP, and complete files of the research project will be made available to any member upon request for further review.

11.6.4. IRBs conducting review of changes in research are authorized to alter the approval period for the research based on the degree of risk posed by the change in research or to retain the original approval period granted at initial review. IRBs have the authority to require revisions to consent documents and require notification to enrolled participants of approved changes in research that may affect the participants' decision to continue in the research.

11.7. Review of Informed Consent Form (s)

11.7.1. Every modification reviewed will include consideration of whether the changes in the research will affect the informed consent form(s)/document(s).

11.7.2. The IRB must determine whether new and/or current subjects must be informed of information related to the study modifications.

11.7.2.1. Investigators must provide new information to current subjects if it may alter their study participation, if the new information relates to safety or risks, or if the new information could otherwise impact subjects' willingness to continue in the study.

11.7.2.2. Former subjects must be notified if the study modifications or new information impact their safety and welfare.

11.7.2.3. The new information will be given to subjects in a revised consent document (for active participants) or a notification letter (for participants in follow-up).

11.7.3. IRB review of a proposed modification/change during the period for which approval is authorized (not during a continuing review) does not constitute a continuing review.

11.7.4. The review does not extend the date by which the continuing review must occur (e.g., beyond one year from the effective date of the initial approval or the most recent continuing review approval).

11.8. Changes Implemented in Order to Avoid Harm

If a change was temporarily implemented without prior IRB approval in order to avoid immediate harm to subjects, the investigator must notify the IRB within five (5) working days, with submission of a modification in research form, or minimally by email or letter.

11.8.1. Supply all relevant information concerning the modification and potential risks/harms to subjects.

11.8.2. Submit any Unanticipated Problems Involving Risks to Subjects or Others that may have occurred.

11.8.3. The investigator also must submit a modification in research form if long-term implementation of the change is needed, along with revised study documents, as applicable.

11.9. IRB Determination to Approve or Disapprove the Proposed Changes / Modifications

Possible actions that can be taken the IRB:

11.9.1. Approve the research without any conditions;

11.9.2. Require modification in (to secure approval of);

11.9.3. Disapprove the research - there are significant questions or concerns.

11.10. IRB Notification / Communication with the Investigator

For each of the possible actions listed in Section 9.0 above, the corresponding letter will be sent to the PI.

11.10.1. A letter of approval will be sent to the PI.

11.10.1.1. A copy of the approval letter will be kept in the IRB study file in the IRB electronic submission system. NOTE: Approved modifications do NOT extend the approval period of the protocol.

11.10.2. A letter will be sent to the PI requesting modifications in the research in order to secure approval.

11.10.3. A letter with the reason for disapproving of the changes in the research will be sent to the PI.

11.10.3.1. Disapproval of a study may only be approved by the convened board.

References:

45 CFR 46.110(b)(2)
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117
22 FR 50.25

12. Reports of Unanticipated Problems Involving Risks to Subjects or Others

12.1. Purpose

Michigan Technological University (MTU) requires researchers to comply with all applicable local, state, and federal regulations in the conduct of research studies. As part of this requirement, researchers are required to submit written reports of events promptly (within five working days) that meet the definition of "Unanticipated Problems Involving Risks to Subjects or Others" (UPs) to the Institutional Research Board (IRB) as defined in this Standard Operating Procedure (SOP). The PI must also report UPs and/or adverse events to applicable regulatory agencies or sponsors as required in the Responsibilities of Principal Investigators Policy.

These procedures supplement the "Convened IRB Review (Greater Than Minimal Risk) Policy.

12.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Adverse Event (AE) – any untoward or unfavorable medical occurrence in a human subject; including any abnormal sign, symptoms or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

Serious Adverse Event (SAE) – any adverse event that:

- results in death;
- is life-threatening (places the subject at immediate risk of death from the event as it occurred);
- results in inpatient hospitalization or prolongation of existing hospitalization;
- results in a persistent or significant disability/incapacity;
- results in a congenital anomaly/birth defect; or
- based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

External Site – a site at which a non-MTU investigator is conducting the research.

Monitoring Entity – the group that is responsible for overseeing the safety of all subjects enrolled in the study in accordance with the protocol (e.g., a Data Safety Monitoring Board (DSMB), a Data Monitoring Committee (DMC), a coordinating or statistical center, or a sponsor). Usually pertains to biomedical research or behavioral clinical trials.

Internal Site – a site at which a MTU investigator is conducting the research.

Suspension – a temporary cessation of IRB approval includes a stop to the enrollment of new subjects, activities involving previously enrolled subjects and other research activities.

Termination – a permanent cessation of IRB approval prior to study expiration that includes permanent halt in the enrollment of new subjects, approved activities involving previously enrolled subjects and other research activities.

Unanticipated Problems (UP) involving risks to participants or others – any incident, experience or outcome involving risk to subjects or others in any human subjects research that meets all of the following criteria:

- unexpected (in terms of nature, severity or frequency) given the research procedures that are described in the IRB-approval protocol and other study documents, and the characteristics of the subject population being studied;

- related or possibly related to or caused by participation in such research (i.e., there is a reasonable possibility that the incident, experience or outcome may have been caused by the procedures involved in such research); and

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

Prompt Reporting – reporting of unanticipated problems/events as soon as possible after the PI learns of the event, but in all cases within five (5) working days.

12.3. Reporting of Unanticipated Problems Involving Risks to the IRB

12.3.1. UPs must be reported by the PI (or designee) to the designated IRB that approved the study within five working days of the research team's discovery of the event or incident.

12.3.2. Some AEs or SAEs meet the definition of a UP. Only those AEs/SAEs that were unexpected, possibly related, and place subjects/others (e.g., family member) at greater risk are UPs and need to be reported under this SOP.

- If a researcher is told by a sponsor or external entity that they need to report an SAE or AE to the IRB (that the PI does not determine to meet the definition of a UP), the PI can direct the sponsor/external entity to this SOP and inform them that the designated IRB will not accept the report.

12.3.3. It is important to note that UPs also include non-physical risks/harms such as potential or real breach of confidentiality of sensitive information (e.g., loss of a laptop with Protected Health Information (PHI), social security number, etc.), psychological stress (e.g., anxiety, embarrassment), financial loss, loss of employment, etc.

12.3.4. Each Unanticipated Problem should be reported to the designated IRB, whether:

12.3.4.1. It is serious or non-serious.

12.3.4.2. It occurs at an “Internal Site” or an “External Site”.

12.3.4.3. For research conducted at an Internal Site, the MTU investigator should make the determination as to whether an incident, experience, or outcome constitutes an Unanticipated Problem.

12.3.4.4. For research conducted at an External Site, an incident, experience, or outcome generally should be reported to the IRB only if a Monitoring Entity or an External Site investigator has determined that it constitutes an Unanticipated Problem, which is subsequently reported to the MTU investigator.

12.3.5. When reporting a UP, the PI or study staff will provide the following information:

12.3.5.1. The protocol title, protocol number, PI’s name, and the date of the occurrence;

12.3.5.2. PI, or appropriate designee, must determine whether or not the event is an unanticipated problem based on the definition and explain the basis for determining whether or not the event was unexpected, related, or possibly related to the research study, and places subjects or others at a greater risk of harm;

12.3.5.3. Date, location, and a detailed description of the adverse event, incident, experience, or outcome;

12.3.5.4. Date and means by which the PI became aware of the incident, experience, or outcome;

12.3.5.5. Location of occurrence;

12.3.5.6. Subject ID number and initials;

12.3.5.7. A description of any changes to the protocol and/or informed consent document(s) or other corrective actions that has been taken or is proposed in response to the unanticipated problem to minimize risks/harms or reoccurrence of the event;

12.3.5.8. Entities to which the incident, experience, or outcome was reported;

12.3.5.9. For multicenter research protocol proposed changes in response to the unanticipated problem the investigator should consult with the sponsor or the coordinating center in addition to designated IRB.

12.4. IRB Review of Unanticipated Problems and Reporting to Federal Agencies

12.4.1. Upon receipt of the report, the HRPP Administrator will begin an evaluation to determine if the unanticipated problem indicates a new or increased risk to study subjects or an urgent safety issue.

12.4.1.1. Notify IRB Chair, or designee, of the UPs.

12.4.1.2. Any serious adverse event or harm that raises potential concerns regarding the safety and well-being of subjects and/or the integrity of the study, and meets the criteria of an unanticipated problem, will be reviewed by the next convened full board meeting.

12.4.2. When reviewing the report of an unanticipated problem at the convened full board meeting, the IRB should consider the following:

12.4.2.1. Informing enrolled participants of the UP;

12.4.2.2. The research protocol still satisfies the requirements of the IRB approval, in particular whether the risks to subjects are still minimized and reasonable in relation to the anticipated benefits, if any, to the subjects and the importance that may reasonably be expected to result;

12.4.2.3. Revising the informed consent document(s);

12.4.2.4. Other corrective actions by the institutions (e.g., addressing a data security policy).

12.4.2.5. Any proposed changes to the research study in response to the UP must be reviewed and approved by the designated IRB before being implemented, except when necessary to eliminate apparent immediate hazards to subjects.

12.4.3. The IRB may take/recommend the following actions:

12.4.3.1. If the report describes a serious increased risk or safety issue, the protocol may be suspended until the issue has been addressed;

12.4.3.1.1. Suspension of enrollment of new subjects;
12.4.3.1.2. Suspension of research procedures in currently enrolled subjects;
12.4.3.1.3. The PI may be required to re-obtain consent from previously enrolled subjects or minimally be required

to notify research subjects about the unanticipated problem and the newly recognized risks or be required;

12.4.3.2. The PI may be required to submit a Modification In Research Form with the changes to the protocol to eliminate apparent immediate hazards to subjects;

12.4.3.3. The PI may need to modify the informed consent documents to include a description of newly recognized risks;

12.4.3.4. The PI may be required to submit a corrective action plan (CAPA) to address the rights, safety and welfare of the research subjects;

12.4.3.5. All project team may be required to complete further education;

12.4.3.6. PI may be required to submit more frequent continuing reviews to the IRB.

12.4.4. If the IRB proposes changes to the protocol or informed consent in addition to those proposed by the study sponsor, coordinating center, or local investigator, the IRB should request in writing that the local investigator discusses the proposed modifications with the study sponsor or coordinating center, if applicable, and submit a response or necessary modifications for review by the IRB.

12.4.5. Reporting of UP Reports to Institutional Officials and Regulatory Agencies - All UPs that result in a change in the protocol and/or the consent documents (either by the IRB, the investigator, or the sponsor) shall be reported to appropriate institutional officials, the supporting agency head (or designee), and for federally supported or conducted research to OHRP within one month of the IRB's receipt of the report. If the research is FDA-regulated, then the IRB will report the UP to the FDA (CDER for UPs resulting from drugs; CDRH for UPs resulting from devices; CBER for UPs resulting from biologics).

12.4.5.1. If the IRB suspends or terminates a study due to reported UP report(s), MTU notifies federal regulatory agencies in accordance with MTU IRB SOPs.

12.5. Reporting Adverse Events and at the Time of Continuing Review

12.5.1. A submission for continuing review must include a summary of all adverse events not qualifying as unanticipated problems since the last IRB review.

12.5.2. If the study is a multi-center study and is subject to oversight by a Monitoring Entity, a current report from the Monitoring Entity may be submitted in lieu of the summary of AEs described above. The current monitoring report must indicate the date of the review and the Monitoring Entity's assessment of the data reviewed. If not described in the data safety monitoring plan submitted to the IRB, the report should also identify what information was reviewed.

12.5.3. Any Monitoring Entity reports that have not been previously submitted to the IRB should also be included with the continuing review submission.

13. IRB Continuing Review of Research

13.1. Introduction

Michigan Technological University (MTU) Institutional Review Board (IRB) is responsible for conducting a Continuing Review of previously approved research to ensure the protection of the rights and welfare of human subjects are maintained as originally planned during the initial IRB review, as well as to review the progress of the study. The IRB must conduct a substantive and meaningful continuing review of research, as outlined in this Standard Operating Procedure (SOP), at intervals appropriate to the level of risk, but not less than once per year and prior to the expiration of the one-year approval date, as applicable.

13.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Modification – any change or amendment to the IRB approved study protocol. 2.2

Expedited Review - review conducted by the IRB Chair or by one or more qualified reviewers designated by the chairperson from among members of the IRB.

Qualified IRB Member -a voting member or alternate voting member who has received training relative to the expedited review categories and possesses the scientific, clinical, or regulatory expertise needed to review the proposed research.

Accrual - the number of subjects enrolled in the study/trial that have passed a screening phase and are deemed eligible for the study.

Enrolled – the number of subjects who have provided consent and joined the study and have participated in some portion of the study regardless if they have been deemed eligible for the study. Therefore, the number of enrolled subjects is at least the number of accrued subjects as it includes screen failures.

13.3. Procedure

13.3.1. Process for Conducting Continued Review

13.3.1.1. Continuing Review for all research that is greater than minimal risk (or any study that is minimal risk, but the IRB Chair determines would benefit from convened IRB review) takes place during a convened meeting with the majority of IRB members present. Otherwise, minimal risk research for which the IRB required Continuing Review made be conducted by the expedited review process.

13.3.1.2. The IRB will conduct a Continuing Review of research prior to the expiration date of the last IRB approval for studies that the IRB required Continuing Review.

13.3.1.3. The Principal Investigator (PI) is responsible for submitting required materials in an adequate time frame as defined in this SOP.

13.3.1.4. The meeting minutes will be in sufficient detail to show the actions taken by the IRB, the vote on the actions and a summary of the discussion of controversial issues and their resolution.

13.3.1.5. Unless an IRB determines otherwise, continuing review is not required in the following circumstances:

13.3.1.5.1. Research eligible for expedited review in accordance with the MTU policies and procedures and HHS regulations (45 CFR 46). Minimal risk research governed by FDA regulations (21 CFR 56) must have continuing review at least by expedited review at least once per year;

13.3.1.5.2. Research reviewed by the IRB in accordance with the limited IRB review described in the Exempt Research SOP;

13.3.1.5.3. Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

- Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
- Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

13.3.1.5.4. If the IRB determines that a continuing review will be required for any of the above situations, the IRB will document the rationale/ justification for the requirement of continuing review.

13.3.2. Submission of Documents to the IRB

13.3.2.1. To ensure that the continuing review and re-approval occur prior to the expiration date of the current IRB approval, the HRPP Administrator will provide an advanced written notice to the Investigator. Submission of the required documents to the IRB is the responsibility of the PI regardless of a courtesy notice from the HRPP Administrator.

13.3.2.2. The investigator must submit the following information for continuing review through the IRB electronic system, providing ample time for review before the expiration date. For full board / convened review studies this could mean 30 days before the next convened board meeting.

13.3.2.3. The following data concerning enrollment:

- The number of subjects enrolled (i.e., had informed consent obtained);
- The number of subjects accrued (e.g., met the eligibility criteria and would be counted as an evaluable subject in the data analysis);
- A summary of any subjects who were withdrawn from the research by the PI since the last IRB review and the reason(s) for withdrawal;
- A summary of any subjects who dropped out from the research on their own accord since the last IRB review and the reason(s) for dropping out.

13.3.2.4. Any new and relevant information, published or unpublished, since the last IRB review, especially information about risks associated with the research;

13.3.2.5. A summary of any adverse events that did not constitute unanticipated problems;

13.3.2.6. A summary of any complaints about the research from the subjects enrolled at the local site since the last IRB review;

13.3.2.7. If applicable (usually only for clinical trials), a copy of all Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) reports and any communications to and from the DSMB/DMC during the past approval period, if a DSMB or DMC exists for the study.

13.4. Expiration of IRB Approval (i.e., lapse in IRB Approval)

13.4.1. Whenever for any reason, the IRB has not conducted a continuing review and re-approved the research before the expiration date of IRB approval, the IRB approval expires automatically.

13.4.1.1. HHS and FDA regulations offer no provisions for any grace period which permits the conduct of research beyond the expiration date of IRB approval.

13.4.1.2. All research activities must immediately stop after IRB approval expires, including screening, recruitment, or enrollment of new subjects; collection or analysis of private identifiable research data, including questionnaires, surveys; any interventions or interactions with subjects, including treatments or therapies that may provide benefit; any monitoring of subjects; or any other research activity for the study.

13.4.1.3. In its review of the research upon receipt of a continuing review submission or request for closure of the study, the IRB should also determine the reason(s) for the lapse in IRB approval occurred, whether any research activities were conducted during the lapse,

and if appropriate, any corrective actions that the investigator or the IRB should implement to prevent any future lapse of approval or noncompliance.

13.4.1.4. The above determinations will be documented in the IRB meeting minutes.

13.4.1.5. OHRP and FDA do not consider an expiration of IRB approval to be a suspension or termination of IRB approval and such event does not need to be reported to OHRP or FDA.

13.4.1.6. If the IRB notes a pattern of noncompliance with the requirements for the continuing review the IRB should determine whether such a pattern represents serious or continuing noncompliance that needs to be reported to FDA and/or OHRP (e.g., an investigator repeatedly neglects to submit materials for continuing review in a timely fashion or the IRB itself is not meeting the continuing review dates).

13.4.2. If a stopping all research activities would cause potential harm to subjects and the investigator determines that it would be unethical to stop/withhold treatment/ interventions (or withdrawing safety monitoring) because it would pose increased risks/harm to subjects, the investigator should:

13.4.2.1. immediately notify the IRB Chair or HRPP Administrator;

13.4.2.2. submit a written request to continue those research activities that are deemed unethical to interrupt;

13.4.2.3. include a justification why stopping such activities would cause harm and request approval to continue those activities.

13.4.3. The written request for approval along with the justification should be submitted to the IRB electronic system. The investigator should follow-up with the IRB Chair/HRPP Administrator to ensure receipt and response to the request.

13.4.4. The IRB Chair may approve the request by the simplest and quickest written means (e.g., email, fax, etc.) that permits a printed copy of the approval for the IRB records.

13.4.5. If an investigator wants to continue the study, he/she needs to submit a complete continuing review submission for the study, if not already done. The IRB will complete the continuing review as soon as possible. No new screening or enrollment of subjects or continuation of other non-essential research procedures (other than the treatment/intervention and/or safety monitoring) can occur until the full board has approved the Continuing Review. The PI may resume human subjects research once the continuing review approval has been granted by the IRB.

13.5. Criteria for IRB Approval of Research

13.5.1. The IRB will review the continuing review submission to determine if all the following requirements continue to be satisfied prior to recommending approval of the research:

13.5.1.1. Risks to subjects are minimized;

13.5.1.2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects; and the importance of the knowledge that may be expected to result;

13.5.1.3. Selection of subjects is equitable;

13.5.1.4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative and appropriately documented;

13.5.1.5. Where appropriate, the research plan adequately provides for monitoring the data collected to ensure the safety of subjects;

13.5.1.6. Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data;

13.5.1.7. Appropriate additional safeguards are included to protect vulnerable subjects; and,

13.5.1.8. Where the study involves vulnerable subjects, the research complies with the MTU-MC IRB Policies and SOPs.

13.5.2. The IRB reviewer or the HRPP Administrator will enter the notes of their review in the IRB electronic submission system.

13.5.2.1. The contents of the continuing review submission and the IRB reviewer's notes will be discussed at the convened meeting, unless the study qualifies for expedited review. If the study is reviewed by expedited review, the same considerations and review will be conducted by the IRB Chair or designee(s).

13.6. IRB Continuing Review and Approval

The IRB has the authority to disapprove or require modifications in research activity that does not meet the Criteria for IRB Approval of Research.

13.6.1. The IRB should focus on whether there is any new information provided by the investigator or information available to the IRB that would alter the IRB's prior determination, especially the IRB's prior determination of the potential benefits or risks to the subjects.

13.6.2. The IRB should assess whether any new information (since the initial approval or last continuing review, whichever occurred last) would necessitate revision of the protocol and/or the informed consent.

13.6.3. The IRB should pay particular attention to the following areas:

13.6.3.1. Risk assessment;

13.6.3.2. Adequacy of informed consent;

13.6.3.3. Local issues for all sites at which research is conducted under the auspices of MTU; and,

13.6.3.4. Progress of the study from the perspective of protection of human subjects from research risks, the ethical conduct of the research, and based on available information to the IRB, the integrity of the study is maintained.

13.7. Verification from Sources Other than the Investigator that no Material Changes Occurred

13.7.1. When concerns are raised regarding the conduct of the study or potential risks to subjects that may have changed that the IRB cannot satisfactorily resolve with the investigator, the IRB may verify whether or not material changes may have occurred in the conduct of the research since the last review by the IRB.

13.7.2. The IRB may verify such concerns by reviewing the audit report that may have been conducted by an external entity or requesting additional information from sources other than the investigator (e.g., the sponsor) that may address the concerns.

13.7.3. The IRB may request an audit of the research. The reason(s) for on-site review may include, for example:

13.7.3.1. Random selection;

13.7.3.2. Complex projects involving unusual levels or types of risks to participants;

13.7.3.3. Projects conducted by an investigator who previously failed to comply with IRB determinations, or

13.7.3.4. Projects where continuing review or reports from other sources have indicated that changes without IRB approval may have occurred.

13.7.4. The IRB may decide to conduct an on-site review that may include:

13.7.4.1. Requests for progress reports from investigators;

13.7.4.2. Examinations of research records, including signed informed consent documents, protocol amendments, and serious and/or unexpected adverse experience report(s); or,

13.7.4.3. Contacts with research participants.

13.7.5. The IRB has the authority to observe the informed consent process. Examples of when observation of the consent process could occur include:

13.7.5.1. The full board IRB determines during review of a project that a conflict of interest, potential noncompliance, or other concerns that may affect the consent process exists such that the informed consent process should be observed by a neutral party;

13.7.5.2. The IRB is made aware of a complaint or concern with regards to the informed consent process; or

13.7.5.3. The IRB determines as a result of the monitoring process or an audit that the consent process is insufficient, and education/training is required for conduct of consent.

13.7.6. A written record of any monitoring activities performed by the IRB is maintained in the IRB records.

13.8. Approving Research at the Time of Continuing Review

The IRB can take any of the follow actions:

13.8.1. Approve the research study without any conditions or with conditions (also referred to as “conditional approval or contingent approval”);

13.8.1.1. The IRB may require an investigator make specific changes to the protocol or informed consent;

13.8.1.2. IRB may require an investigator to submit additional documents, after which:

13.8.1.2.1. the IRB Chair or other designated IRB members (with expertise or qualifications) may review materials submitted from the investigator and determine that the conditions have been satisfied;
13.8.1.2.2. further review by the IRB at a subsequent convened meeting would not be necessary;

The IRB should specify whether any conditions need to be satisfied before an investigator can continue particular research activities (e.g., research activities involving currently enrolled subjects may continue, but no new subjects may be enrolled until a designated IRB member reviews a revised protocol).

Halting all research activities, especially subject enrollment due to a lapse in IRB approval would not be considered a suspension of IRB approval that needs to be reported to OHRP or FDA.

13.8.2. Requiring modifications for re-review by the full board to secure IRB approval - Defer or Table the study for further review at a future date after the required modifications are submitted by the investigator.

Note: this may cause a lapse in IRB approval (see above and below sections).

13.8.3. Suspension or termination of IRB approval - The IRB has the authority to suspend or terminate approval of research involving human participants that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants.

13.9. Determining Frequency of Continuing Review

The IRB must determine the frequency of the continuing review for each clinical investigation to ensure the continued protection of the rights and welfare of the subjects.

13.9.1. IRB must conduct continuing review of research at intervals appropriate to the degree of risk posed to subjects, but not less than once a year.

13.9.2. Continuing review more frequently than once a year is appropriate when the risks to subjects warrants more frequent assessment.

13.9.3. Factors the IRB should consider when deciding on an appropriate interval for continuing review:

13.9.3.1. The nature of any risks posed by the research;

13.9.3.2. The degree of uncertainty regarding the risks involved;

13.9.3.3. The vulnerability of the subject population;

13.9.3.4. The experience of the investigator conducting the research;

13.9.3.5. The IRB's previous experience with the investigator (e.g., compliance history, prior complaints from subjects about the investigator, previous problems with the investigator obtaining informed consent);

13.9.3.6. The projected rate of enrollment; and,

13.9.3.7. Whether the research project involves novel interventions (new or unusual approach of treatment).

13.9.4. The approval period will be documented in the meeting minutes.

13.10. Effective Date of the Initial IRB Approval and the Dates for Continuing Review

13.10.1. When the IRB reviews and initially approves research for one year without requiring changes to the protocol or informed consent or submission of clarification or additional documents, the effective date of the initial approval is the date of the IRB meeting. The expiration date of the initial approval and the date by which the first continuing review must occur may be as late as one day before the one-year anniversary after the date of the IRB meeting.

13.10.2. When the IRB reviews and initially approves research with conditions without requiring further review at a subsequent convened meeting, the effective date of the initial approval is the date on which the IRB Chair or designee has reviewed and accepted as satisfactory all changes to the protocol and/or the informed consent document(s) or any other material required by the IRB from the investigator. The expiration date of the initial approval is one day before the one-year anniversary date of the effective date.

13.11. Notification of IRBs Continuing Review Determination to the Investigator

After the IRB completes the continuing review, the IRB must provide a written notification informing the investigator of the IRB's determination.

13.11.1. For studies approved to continue – a clear statement will be provided when the approval is effective, the period of time for which the study is approved and the next continuing review date.

13.11.2. For studies approved with conditions – notification should state whether any conditions need to be satisfied before an investigator can continue particular research activities.

13.11.3. For suspended or terminated research – provide a written statement of the reason(s) for the IRB decision and give the investigator an opportunity to respond in person or in writing.

13.11.4. A copy of the notification letter will be kept in the IRB electronic system.

14. Study Completion, Closure, or Expiration

14.1. Purpose

The completion or termination of the study is a change in activity and must be reported to the IRB. IRB oversight of a research protocol is required as long as the activities conducted involve human subjects.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy").

14.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Identifiable private information (or specimens) are considered to be individually identifiable when they can be linked to specific individuals (i.e., the identity of the subject is or may readily be ascertained) by the investigator(s) either directly or indirectly through coding systems.

Screened refers to all procedures performed to determine whether a potential participant is eligible to take part in the study.

Accrual - the number of subjects enrolled in the study/trial that have passed a screening phase and are deemed eligible for the study.

Enrolled participants are individuals who are eligible for participation (i.e., meet the inclusion criteria for the study), have given informed consent and participated in some or all the study procedures.

14.3. Procedure

A study closure report is required for all human research studies. The closure report updates the IRB on the conduct and outcomes of the study, any new risks, safety issues or problems that may have arisen since the last study renewal and informs the IRB of the final disposition of research records and data.

14.3.1. **Completion or Permanent Closure**

14.3.1.1. When a study is closed or permanently discontinued for any reason, a closure form should be completed by the Principal Investigator (PI) and submitted to the IRB within thirty (30) days.

14.3.1.2. The Closure Form serves as notification to the IRB that all research activities for the given study have been completed and the continuing review of the study is no longer required.

14.3.1.3. The IRB will review all reports of study completion and, if needed, request additional information from the PI when necessary.

14.3.1.4. Once a Closure Form has been submitted, no further data collection may occur.

14.3.1.4.1. Therefore, if an investigator is still collecting follow-up data about participants (either directly from participants or indirectly from existing records), the project must remain open until all data have been collected, even if new participants are no longer being enrolled.

14.3.1.5. Once the IRB approves study closure, the study is considered to be closed on the day the IRB approved closure of the study.

14.3.1.5.1. The IRB determination will be documented in the meeting minutes.
14.3.1.5.2. A letter confirming IRB approval for permanently closing the study will be sent to the PI. The letter will be kept in the PI's study folder.
14.3.1.5.3. A copy of the letter will be placed in the IRB's study file.
14.3.1.5.4. Records shall be retained for at least three years after completion of the research and the records shall be accessible for inspection.
14.3.1.5.5. Identifiable private data may be maintained without continuing IRB approval if there will be no further use, research or analysis involving the data and the storage of such data was approved by the IRB.

14.3.2. **Criteria for Closing a Study**

14.3.2.1. The research was not conducted OR

14.3.2.2. Project completion is when ALL the following has occurred:

14.3.2.2.1. Enrollment/accrual is permanently closed, AND
14.3.2.2.2. Research related interventions, procedures, and interactions with human subjects have ended, including follow-up care, AND
14.3.2.2.3. No individually identifiable private information (data), including follow-up data is being collected or used, AND
14.3.2.2.4. Data analysis involving the use of PHI is completed (protected health information that is directly or indirectly identifiable).

14.3.3. **Administrative Closure for Lapse in IRB Approval**

14.3.3.1. A study is considered expired after IRB approval has lapsed due to the PI's failure to submit for continuing review.

14.3.3.2. No research activity may take place during a period of expiration (e.g., enrollment, follow up, data collection, etc.).

14.3.3.3. If study approval has expired for more than thirty (30) days, the PI must submit either an Initial Review submission or a closure form to close the study. IRB will consider this study closed after 30 days.

14.3.4. **Principal Investigator Responsibilities**

14.3.4.1. Ensure that all research-related activities, interventions or interactions with human subjects have been completed prior to submitting the Closure Form to the IRB.

14.3.4.2. Investigator responsibility after study closure:

14.3.4.2.1. Records retention;

14.3.4.2.1.1. Research records must be retained for at least three years after completion of the research and the records shall be accessible for inspection. For research that includes Protected Health Information (PHI), the records must be maintained for at least six years after completion of the study.

14.3.4.2.2. Maintain confidentiality and data security for identifiable private data;

14.3.4.2.3. If the investigator seeks to use previously collected data after the IRB has approved permanent closure, the PI must submit a new application for IRB review and approval.

14.3.5. **Principal Investigator (PI) Leaving MTU**

14.3.5.1. The PI is responsible for ensuring that their research-related duties are appropriately transitioned or completed before officially exiting their position.

14.3.5.2. The PI must contact the MTU IRB within 60 days of leaving MTU.

14.3.5.3. PI must submit an amendment/modification transferring the study to another PI or a Closure of Study submission.

14.3.5.3.1. If the subjects are still participating in the research study, the IRB recommends the PI provide the subjects with a letter to update them of the change in PI and to update them regarding changes in relevant telephone numbers (e.g., for study-related questions) and addresses e.g., to withdraw authorization).

14.3.5.4. If Criteria for Closing a Study are met, a Closure Form may be submitted instead of an amendment/modification for transfer.

14.3.5.5. All changes must be reviewed and approved by the IRB prior to the change being implemented (except to eliminate hazards to subjects).

14.3.5.6. If the study is funded, the PI must notify the Sponsor of the change in status.

14.3.5.7. All study related records will remain at MTU, unless specifically approved by MTU.

15. MTU Investigator Noncompliance

15.1. Policy

Michigan Technological University (MTU) has granted the responsibility for review of all human subject research to MTU Institutional Review Board (IRB). MTU IRB may approve applications that meet the criteria set forth in government regulations, MTU policies, and other federal, state, and local law and regulations.

The PI is responsible for conducting the approved research in accordance with the IRB-approved protocol, IRB's requirements, as well as in accordance with all ethical standards, MTU policies, federal or state laws or regulations applicable to the research study. However, all investigators and members of the research team involved in human subjects research are required to comply with the ethical standards of the Belmont Report, federal regulations and other laws governing research activities as well as MTU IRB policy, SOPs and the IRB determinations.

It is the obligation of the PI and study team to submit a written report to the IRB of any alleged or potential noncompliance (which include protocol violations), as defined below, must be reported to the MTU IRB in accordance with this SOP, even when the study is relying on external IRB. The IRB will investigate, manage, and report to applicable federal regulatory agencies any noncompliance in accordance with these procedures.

15.2. Definitions

Continuing Noncompliance – any noncompliance that has been previously identified during an audit or investigation, confirmed by the IRB or an external authority (e.g., OHRP, FDA, sponsor, etc.), and the findings of noncompliance have been communicated in writing to the investigator or research team and those incidents of noncompliance occur again.

Minor noncompliance - includes minor or technical violations which result from inadvertent errors, inattention to detail, or failure to follow operational procedures which do not pose immediate risk to subjects, the environment, or researchers, and/or violate research subject's rights and/or welfare.

Noncompliance - a failure to comply with the IRB-approved protocol, MTU policies governing research (including requirements imposed by the IRB during review of a research study), or applicable federal and state laws, regulations and policies governing the protection of human subjects in research.

Principal Investigator - the individual who is responsible for the conduct of the human research study.

Protocol violation - a protocol change or modification (commonly referred to as a protocol deviation) that was not approved by the IRB and is identified by the research team after the change was implemented.

Research misconduct – any fabrication, falsification, or plagiarism of research or research results.

Serious noncompliance - is a failure to adhere to the laws, regulations, or policies governing research or the IRB approved protocol that may reasonably be determined to:

- Pose an actual or potential increased risk to the subject(s);
- Affect the integrity of data;
- Violates the safety, rights or welfare of human research subject(s), research staff or others;
- Affect the subjects' willingness to participate in the study.

Examples of serious noncompliance may include, but are not limited to:

- the failure to obtain or maintain prospective IRB approval before conducting human subjects research;
- the enrollment of subjects in a study without obtaining legally effective informed consent;
- implementing a substantive modification to the research without IRB approval, or
- the failure to report or failure to report promptly serious unanticipated problems involving risks to subjects or others.

Suspension (of research) – a temporary or permanent halt to some or all research procedures short of a termination until the IRB determines whether the research may recommence (with or without modifications to the research) or whether the research must be terminated.

Termination (of research) – a permanent cessation of IRB approval prior to study expiration that includes permanent halt in the enrollment of new subjects, approved activities for previously enrolled subjects and all research activities.

15.3. Reporting of Noncompliance

Any protocol violation and/or alleged noncompliance must be reported by the PI, research staff, or any employee aware of the alleged noncompliance.

15.3.1. The alleged noncompliance must be reported promptly to the IRB Chair or HRPP Administrator, but no later than five working days, after learning about the noncompliance.

15.3.2. The report of the alleged noncompliance should include all known details of the alleged noncompliance including all individuals involved and the location where the alleged noncompliance occurred.

15.3.3. The report should be preferably in writing. If the individual(s) reporting the alleged noncompliance is not able or comfortable reporting the alleged noncompliance in writing, then the report may be made verbally to the HRPP Chair and/or the HRPP Administrator.

15.3.4. MTU, the MTU IRB, the IRB Chair, the HRPP Administrator, and all IRB members and staff will protect the confidentiality of the person submitting the allegation to the extent allowed by law and the MTU policies/SOPs.

15.4. Procedure for Reviewing the Allegation of Noncompliance

15.4.1. The IRB Chair will be notified of all reported noncompliance within two business days of the accepted allegation(s) of noncompliance.

15.4.2. The HRPP Administrator and/or the IRB Chair or designee appointed by the Administrator/IRB Chair, will conduct a preliminary brief inquiry to determine whether the allegation involves a current approved study, whether the study is sponsored and if yes, by whom, and whether the study involves other research involves other research oversight committees/units.

15.4.2.1. Initial findings will be communicated to the HRPP Administrator and the IRB Chair.

15.4.3. The IRB Chair, or designee will make the determination as to whether the allegation of non-compliance has enough information to make findings, whether additional information is needed, or whether to open an investigation.

15.4.3.1. Self-reported noncompliance with details of the noncompliance may not need investigation to conclude the accuracy of the noncompliance (e.g., informed consent was obtained after research was initiated with submission of a copy of the signed consent form and a copy of research datum/data on a subsequent date).

15.4.3.2. When additional information is needed to determine that a protocol violation or noncompliance with regulations or policies occurred, the Chair, or designee, will determine what information is needed, who should obtain the information, and from what source(s) the information should be obtained.

15.4.3.3. When the HRPP Administrator and/or the IRB Chair, or designee, determine(s) that an investigation should be opened, a determination will be made whether the investigation would be conducted by an HRPP Administrator, another individual(s), or because special expertise is needed an ad-hoc committee.

15.4.3.3.1. A target date for completion of the audit will be determined by the IRB Chair or designee and the composition of the committee.
15.4.3.3.2. If an ad-hoc committee is needed, the IRB Chair or designee, will determine in writing who shall serve on the ad-hoc committee.
15.4.3.3.3. All members serving on the ad-hoc committee must sign the IRB's Conflict of Interest and Confidentiality agreement.

15.4.3.3.4. Whenever an investigation for an allegation of noncompliance is initiated, the allegation and the method for investigating the allegation will be reported to the convened IRB at the next available meeting in accordance with Section 15.6.

15.4.4. The IRB Chair will determine, based on the information collected to date, whether the safety, rights and welfare of subjects are at immediate harm.

15.4.4.1. In this case the IRB Chair, or designee, will contact the PI in order to establish an appropriate interim measure (e.g. suspend all new subject enrollment) to be taken to protect subjects until such a time that the full committee can review the study.

15.4.4.2. If the PI refuses to cooperate with the interim measure, the matter is referred to the IO.

15.4.4.3. If the study is suspended or any interim action is taken to mitigate or eliminate any risk or harm to subjects, the suspension/interim action will be reported to the IRB at the next available convened meeting in accordance with Section 6.

15.5. Procedure for Reviewing the Findings of Noncompliance

15.5.1. The person, persons, or ad-hoc committee designated to review an allegation of noncompliance will provide a written report/summary of their review or investigation with conclusions of whether the allegation of noncompliance was determined to be serious or continuing noncompliance, minor noncompliance, or no noncompliance.

15.5.2. **Finding of No Noncompliance**: If the IRB Chair or designee determines that noncompliance with the IRB-approved protocol, regulations, or MTU policies did not occur, the HRPP Administrator will prepare a letter for signature by the IRB Chair/designee and forward the letter to the PI, copied to any individuals who were notified of the allegation/initial report of potential noncompliance.

15.5.2.1. If the allegation of noncompliance was reported by an individual(s), a separate communication will be made to inform them of the outcome. The communication will be made separately in order to protect their confidentiality.

15.5.2.2. The Chair or designee will determine whether the communication to the individual reporting the allegation should be in writing or verbal. If the communication is made verbally, the communication will be documented in writing and included in the IRB records.

15.5.3. **Finding of Minor Noncompliance**: If the IRB Chair or designee determines that minor noncompliance with the IRB-approved protocol, regulations, or MTU policies did occur, the IRB Chair/designee will discuss appropriate corrective actions first with the HRPP Administrator, and then with the PI. If the IRB

Chair/designee and the HRPP Administrator do not agree on appropriate corrective actions, details of the minor noncompliance and corrective actions will be reviewed by the convened IRB in accordance with Section 6.

15.5.3.1. The HRPP Administrator or designee will prepare a letter for signature by the IRB Chair/designee and forward the letter to the PI, copied to any individuals who were notified of the allegation.

15.5.3.2. The Chair or designee will determine whether the communication to the individual reporting the allegation should be in writing or verbal. If the communication is made verbally, the communication will be documented in writing and included in the IRB records.

15.5.4. **Finding of Serious or Continuing Noncompliance**: If the IRB Chair/ designee/ad-hoc committee determines that serious or continuing noncompliance with the IRB-approved protocol, regulations, or MTU policies did occur, the HRPP Administrator will forward the draft report to the PI, copied to any research staff who were determined to all be in noncompliance.

15.5.4.1. The PI and any research staff who were determined to all be in noncompliance will be given three working days to review the report and its findings and given an opportunity to respond with any additional information or comments that may improve the accuracy of the report.

15.5.4.2. The IRB Chair/designee/ad-hoc committee will then review the PI/research staff's response(s) and determine whether the report should be revised. The IRB Chair/designee/ad-hoc Committee should discuss any revision of the report with the HRPP Administrator if he/she was not involved in the review/investigation.

15.5.4.3. A final report will be completed as soon as possible so that the noncompliance case can be forwarded to the convened IRB for review in accordance with Section 6.

15.6. Procedure for Reporting to the IRB and IRB Review of the Noncompliance

15.6.1. The reported noncompliance or allegation of suspected noncompliance and appropriate review materials will be distributed to the IRB Committee members approximately one week prior to the meeting.

15.6.1.1. Appropriate review materials may include but are not limited to the following: the written report, inquiry correspondence (to and from investigator), study protocol (if relevant), current approved informed consent, Investigator's Drug/Device Brochure (if applicable), and other pertinent documents.

15.6.2. The IRB will make one of the following determinations:

15.6.2.1. There is no noncompliance;

15.6.2.2. The noncompliance is minor; or

15.6.2.3. The noncompliance is serious and/or continuing noncompliance.

15.6.3. Possible board actions for noncompliance include, but are not limited to:

15.6.3.1. Place an administrative hold on the research;

15.6.3.2. Initiate audits of all or some of the investigator's active protocols;

15.6.3.3. Suspend any or all components of the research (i.e., new enrollment, treatment, follow-up and data analysis) until a Corrective Action/ Prevention Plan (CAPA) can be developed and implemented or until additional review can occur;

15.6.3.4. Require that the PI modify the protocol to minimize risk;

15.6.3.5. Require the interval at which continuing review is conducted to be modified to less than one year as appropriate to the degree of risk;

15.6.3.6. Require that the PI modify the informed consent;

15.6.3.7. Require observation of the research or the consent process and modify the information disclosed during the consent process;

15.6.3.8. Require notification of current and previously enrolled subjects of new information that may relate to a subject’s willingness to continue participation in the research;

15.6.3.9. Require submission of status reports on a defined set schedule to the IRB;

15.6.3.10. Require additional education and training for the investigators and support staff;

15.6.3.11. Accept and approve the PI’s proposed Corrective Action/Prevention Plan (CAPA) or changes;

15.6.3.12. Require a directed for-cause investigation by an outside consultant;

15.6.3.13. Terminate the research.

15.6.4. IRB discussion, action(s), the final determination, and vote will be documented in the meeting minutes.

15.6.5. An IRB written letter with the results of the review will be sent to the investigator by the HRPP Administrator.

15.6.5.1. If it is determined by the IRB that the finding of noncompliance is not serious and not continuing, the investigator will be notified in writing with any board action(s).

15.6.5.1.1. A copy of the letter will be placed in the study file.

15.6.5.2. If it is determined by the IRB that the finding of noncompliance is serious and/or continuing:

15.6.5.2.1. The Investigator will be informed in a written letter with the IRB determination and the basis for the determination in writing and is given a chance to respond.

15.7. Suspension and Termination of Approved Research

15.7.1. The MTU IRB has the authority to suspend or terminate previously approved research if:

15.7.1.1. The conduct of the research is not compliant with the IRB requirements, Federal regulations, state, or local laws or MTU policy and SOPs applicable to human subject research.

15.7.1.2. Has been associated with actual or potential unexpected serious harm to the subject(s).

15.7.2. In some instances, study suspension or early termination may have an adverse effect on currently enrolled or past subjects, or others.

15.7.2.1. Every effort will be made to reduce the risk of harm to subjects or others resulting from suspension or termination.

15.7.2.2. This may include corrective action directed to the PI by the convened IRB that requires study-related activity for the protection of human subjects or others during the suspension, or after termination.

15.7.3. If the study is suspended, the incidence will be placed on the next full board meeting agenda.

15.7.3.1. IRB may request additional information.

15.7.3.2. Request corrective action such as, but not limited to, study modification, remove study suspension, or terminate study approval.

15.7.3.3. All determinations made by the convened IRB will be documented in the IRB meeting minutes.

15.7.3.4. A formal notification will be sent to the PI and a copy will be included with the study file.

15.7.4. When a study is suspended, the convened IRB may remove study suspension and reinstate IRB approval.

15.7.4.1. The IRB must have sufficient documented information that the raised concerns and issues have been rectified.

15.7.4.2. All determinations made by the convened IRB will be clearly documented in the IRB meeting minutes.

15.7.4.3. A formal notification from the IRB office will be made to the PI and a copy will be included with the study file.

15.7.5. The fully convened IRB may terminate the IRB approval of research if:

15.7.5.1. Termination is the most favorable response to help prevent or reduce the likelihood of serious harm to subjects (i.e., it is unlikely that suspension of the study and modification of the protocol/research can reduce the harm to subjects) or the study is confirmed to be in serious and/or continuing noncompliance with applicable rules, procedures, and/or policies and corrective actions would not be sufficient to resolve compliance concerns.

15.7.5.2. There must be sufficient evidence or just cause before a decision to terminate a study is made.

15.7.5.3. The determination to terminate study approval will be clearly documented in the convened IRB meeting minutes.

15.7.5.4. A formal notification will be sent to the PI, and a copy will be included with the study file. Formal notification should include:

15.7.5.4.1. the reason(s) for the termination.
15.7.5.4.2. the effective date, notification of the sponsor (if applicable), any restrictions or further actions imposed by the IRB or institution (if applicable) and copying need-to-know officials.
15.7.5.4.3. notice that the investigator may make an appeal. An appeal will be considered by the convened IRB.

15.8. IRB Reporting Requirements

Any serious and/or continuing noncompliance must be reported promptly to the MTU IO, the appropriate regulatory agency (e.g., OHRP if federally supported or conducted and the FDA if FDA-regulated), and the federal department if federally supported (e.g., program official) in accordance with the "MTU Reporting Requirements” SOP.

15.9. Managing Subject Complaints

15.9.1. Most subject complaints do not involve noncompliance; rather they usually provide information about a subject's dissatisfaction with a process related to the research (e.g., slow payment of a stipend for a survey or reimbursement of travel expenses; concern with not having a phone call returned, etc.). However, some subject complaints may involve noncompliance with the study protocol.

15.9.2. All calls or written correspondence from subjects that involve a complaint or express a concern about the conduct of the study or the performance of the research team should be responded as soon as possible, preferably within the same day by an appropriate member of the research team.

15.9.2.1. The PI should designate the appropriate staff member who will respond to the subject complaint. Such an individual should be knowledgeable about the study protocol and the processes of the research team for the conduct of the study. Additionally, the person should have strong listening and communication skills and the ability to diffuse adversarial situations.

15.9.2.2. All subject complaints should be recorded by the research team and if the complaint involves potential noncompliance or a serious concern, it should be reported to the MTU IRB promptly, in addition to any reporting requirement of a central or designated IRB other than the MTU IRB.

15.9.2.3. All other subject complaints should be reported to the MTU IRB at the time of continuing review.

15.9.2.4. When the IRB receives a report of a subject complaint that is determined to involve potential noncompliance or a concern of the conduct of the study or performance of the research team, the HRPP Administrator or IRB Chair shall call the subject as promptly as possible. The first call should involve listening to and recording details of the subject's concerns.

15.9.2.4.1. The HRPP Administrator or Chair who called the subject shall document information about the call and provide a preliminary determination of whether the subject complaint is considered as potential noncompliance. If a potential noncompliance determination is made, then the IRB SOPs for managing and investigating potential noncompliance should be followed as outlined above.

15.9.2.4.2. Otherwise, the HRPP Administrator or Chair should work with the PI/research team and the subject to resolve the subject's concerns.

References:

45 CFR 46.103 (b)(5)(i)
21 CFR 56.108 (b)(2)
21 CFR 56.113

45 CFR 46.113
Regulations and Guidance: OHRP Guidance on Reporting Incidents to OHRP.
Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs (Draft Guidance) November 2015

16. Suspension or Termination of Institutional Review Board (IRB) Approved Research

16.1. Policy

Michigan Technological University 9MTU) authorizes the Institutional Review Boards (IRB), the IRB Chair, or the Institutional Official (IO) to suspend or terminate human subjects' research projects. The IRBs may determine that a project should be suspended or terminated due to:

16.1.1. Unanticipated problems involving risk to subjects or others under in accordance with the MTU IRB SOPs.

16.1.2. Serious or continuing non-compliance.

16.1.3. Findings presented in the continuing review process or change in research review process.

16.1.4. Problems identified in a monitoring process.

16.2. Definitions

Continuing Noncompliance – any noncompliance that has been previously identified during an audit or investigation, confirmed by the IRB or an external authority (e.g., OHRP, FDA, sponsor, etc.), and the findings of noncompliance have been communicated in writing to the investigator or research team and those incidents of noncompliance occur again.

Noncompliance - a failure to comply with the IRB-approved protocol, MTU policies governing research (including requirements imposed by the IRB during review of a research study), or applicable federal and state laws, regulations and policies governing the protection of human subjects in research.

Principal Investigator - the individual who is responsible for the conduct of the human research study.

Serious noncompliance - is a failure to adhere to the laws, regulations, or policies governing research or the IRB approved protocol that may reasonably be determined to:

- Pose an actual or potential increased risk to the subject(s);
- Affect the integrity of data;
- Violates the safety, rights or welfare of human research subject(s), research staff or others;
- Affect the subjects' willingness to participate in the study.

Examples of serious noncompliance may include, but are not limited to:

- the failure to obtain or maintain prospective IRB approval before conducting human subjects research;

- the enrollment of subjects in a study without obtaining legally effective informed consent;
- implementing a substantive modification to the research without IRB approval; or
- the failure to report or failure to report promptly serious unanticipated problems involving risks to subjects or others.

Suspension (of research) – a temporary or permanent halt to some or all research procedures short of a termination until the IRB determines whether the research may recommence (with or without modifications to the research) or whether the research must be terminated.

Termination (of research) – a permanent cessation of IRB approval prior to study expiration that includes permanent halt in the enrollment of new subjects, approved activities for previously enrolled subjects and all research activities.

16.3. Procedures

16.3.1. The MTU IRB has the authority to suspend or terminate previously approved research if:

16.3.1.1. The conduct of the research is not compliant with the IRB requirements, federal regulations, state, or local laws or MTU policy and SOPs applicable to human subject research.

16.3.1.2. Has been associated with actual or potential unexpected serious harm to the subject(s).

16.3.2. The Organization also authorizes the IO, or an IRB Chair, or the HRPP Administrator, to suspend human subjects research when an event occurs and, in their judgment, taking such action cannot wait until a convened IRB meeting in order to protect the rights and welfare of participants. An action taken by the IO, an IRB Chair, or the HRRP Administrator to suspend research will be reported to the IRB at the next convened meeting.

16.3.3. In some instances, study suspension or early termination may have an adverse effect on currently enrolled or past subjects, or others.

16.3.3.1. Every effort will be made to reduce the risk of harm to subjects or others resulting from suspension or termination. Consideration should be given to not suspend intervention or treatment for currently enrolled subjects unless it is done to remove immediate potential harm to subjects. Likewise, every effort should be made to not remove safety monitoring of subjects during a suspension.

16.3.3.2. This may include corrective action directed to the PI by the convened IRB that requires study-related activity for the protection of human subjects or others during the suspension, or after termination.

16.3.4. If the study is suspended, the incidence will be placed on the next full board meeting agenda.

16.3.4.1. IRB may request additional information.

16.3.4.2. Request corrective action such as, but not limited to, study modification, remove study suspension, or terminate study approval. The IRB will determine and inform the PI of steps to be taken as a result of suspension or termination of the research. Steps could include:

16.3.4.2.1. Notification of currently enrolled participants that the study has been terminated by a written communication approved by the IRB. In this case, communication to participants will explain the rationale for the action taken;
16.3.4.2.2. Withdrawal of participants, considering the rights and welfare of those individuals before such a step is taken;
16.3.4.2.3. Informing the participants of any follow-up procedures permitted or required by the IRB for participant safety; and
16.3.4.2.4. Submission of reports to the IRB and the sponsor of any adverse events/outcomes that occurred during the period when suspension or termination occurred.

16.3.4.3. All determinations made by the convened IRB will be documented in the IRB meeting minutes.

16.3.4.4. A formal written notification will be sent to the PI and a copy will be included with the study file.

16.3.4.4.1. The notice of suspension or termination of IRB approved research must include a statement of the reasons for the action.
16.3.4.4.2. The communication to the PI will offer the PI an opportunity to respond to the decision.
16.3.4.4.3. The communication will ask the PI to provide a plan for ensuring that the rights and welfare of all currently and previously enrolled (if appropriate) participants are protected.

16.3.4.5. When a study is suspended, the convened IRB may remove study suspension and reinstate IRB approval.

16.3.4.5.1. The IRB must have sufficient documented information that the raised concerns and issues have been rectified.
16.3.4.5.2. All determinations made by the convened IRB will be clearly documented in the IRB meeting minutes.
16.3.4.5.3. A formal notification from the IRB office will be made to the PI and a copy will be included with the study file.

16.3.4.6. The fully convened IRB may terminate the IRB approval of research if:

16.3.4.6.1. Termination is the most favorable response to help prevent or reduce the likelihood of serious harm to subjects (i.e., it is unlikely that suspension of the study and modification of the protocol/research can reduce the harm to subjects) or the study is confirmed to be in serious and/or continuing noncompliance with applicable rules, procedures, and/or policies and corrective actions would not be sufficient to resolve compliance concerns.

16.3.4.6.2. There must be sufficient evidence or just cause before a decision to terminate a study is made.

16.3.4.6.3. The determination to terminate study approval will be clearly documented in the convened IRB meeting minutes.

16.3.4.6.4. A formal notification will be sent to the PI, and a copy will be included within the study file. Formal notification should include:

16.3.4.6.4.1. the reason(s) for the termination.

16.3.4.6.4.2. the effective date, notification of the sponsor (if applicable), any restrictions or further actions imposed by the IRB or institution (if applicable), and copying need-to-know officials.

16.3.4.6.4.3. notice that the investigator may make an appeal. An appeal will be considered by the convened IRB.

References

45 CFR 46

21 FR 56

17. MTU Reporting Requirements

17.1. Policy

Michigan Technological University (MTU) has the responsibility to report Unanticipated Problems involving risk to subjects or others ("UP"), serious or continuing non-compliance, and suspension or termination of approved research, to the MTU IRB, the MTU Institutional Official (IO) and appropriate agencies.

The Institutional Official (IO) is authorized as the individual who will submit reports to federal regulatory agencies when an Institutional Review Board (IRB) has confirmed that any of the above three reportable events for federally-supported human subjects research. In cases where the IRB and IO determine that additional information is required before submitting a final report, a preliminary report may be made to the appropriate officials, supporting federal agency (as applicable), Office for Human Research Protection (OHRP), and Food and Drug Administration (FDA), as applicable, within one month of the IRB's determination.

17.2. Definitions

Continuing Noncompliance – any noncompliance that has been previously identified during an audit or investigation, confirmed by the IRB or an external authority (e.g., OHRP, FDA, sponsor, etc.), and the findings of noncompliance have been communicated in writing to the investigator or research team and those incidents of noncompliance occur again.

Noncompliance - a failure to comply with the IRB-approved protocol, MTU policies governing research (including requirements imposed by the IRB during review of a research study), or applicable federal and state laws, regulations and policies governing the protection of human subjects in research.

Principal Investigator - the individual who is responsible for the conduct of the human research study.

Serious noncompliance - is a failure to adhere to the laws, regulations, or policies governing research or the IRB approved protocol that may reasonably be determined to:

- Pose an actual or potential increased risk to the subject(s);
- Affect the integrity of data;
- Violates the safety, rights or welfare of human research subject(s), research staff or others;
- Affect the subjects' willingness to participate in the study.

  Examples of serious noncompliance may include, but are not limited to:

  - the failure to obtain or maintain prospective IRB approval before conducting human subjects research;
  - the enrollment of subjects in a study without obtaining legally effective informed consent;

- implementing a substantive modification to the research without IRB approval, or
- the failure to report or failure to report promptly serious unanticipated problems involving risks to subjects or others.

Suspension (of research) – a temporary or permanent halt to some or all research procedures short of a termination until the IRB determines whether the research may recommence (with or without modifications to the research) or whether the research must be terminated.

Termination (of research) – a permanent cessation of IRB approval prior to study expiration that includes permanent halt in the enrollment of new subjects, approved activities for previously enrolled subjects and all research activities.

17.3. Procedures

17.3.1. Whenever the IRB terminates approval of human subjects research, a draft preliminary or final summary or report (depending on the amount of details; e.g., a serious noncompliance case resulting in termination of IRB approval is more likely to require a report) will be prepared for review by the IO, and when appropriate the General Counsel (GC). The draft summary or report will contain the following information:

17.3.1.1. The nature of the event.

17.3.1.2. The finding of the organization.

17.3.1.3. The actions taken by the organization and IRB, including plans to protect the rights and welfare of the participants.

17.3.1.4. The reasons for the organization's and IRB's actions.

17.3.1.5. The plans for continued oversight or investigation or action.

17.3.2. The draft report will be finalized by the HRPP Administration, the IO, and, when appropriate, the General Counsel. The IO will sign the report within 20 days of the agreed upon final revision of the report.

17.3.3. The final report will be submitted promptly (but no later than 30 days of reporting of the event/incident to the MTU IRB) to the OHRP if the research is conducted, funded, or overseen by Department of Health and Human Services (DHHS); to FDA, if the research is regulated by FDA; and to other agencies that are signatories to the Common Rule [1], if the research is conducted, funded or overseen by that agency. A copy of the report will be sent to the reviewing IRB, Office of Regulatory Affairs (ORA) if the project is funded by an outside sponsor, Risk Management (if applicable), and the Principal Investigator (PI). The IO may determine the report should be provided to the Director of the department in which the PI is appointed as Staff. If the event involves unauthorized use, loss, or disclosure of PHI, a copy will be sent to the Health Insurance Portability and Accountability Act (HIPAA) Privacy Officer.

17.3.3.1. If it is not possible to complete an investigation and report of the alleged noncompliance within 30 days, then an initial report outlining the allegation and explaining that an investigation has begun must be reported to the federal regulatory agency as soon as possible, but no later than 30 days.

17.3.3.2. The final report will be sent to the federal regulatory agency as soon as possible after the investigation has been completed.

17.3.4. A copy of all correspondence related to the report will be maintained in the IRB records.

[1] These are Department of Agriculture, Department of Energy, National Aeronautics and Space Administration, Commerce Department, Consumer Product Safety Commission, Housing and Urban Development, Department of Justice, Department of Defense, Department of Educations, Veterans Administration, National Science Foundation, Department of Transportation, Environmental Protection Agency, Agency for International Development, Office of Science and Technology Policy, Department of Homeland Security, Social Security Administration, and the Central Intelligence Agency. Note: The Department of Justice (DOJ) has signed on to the 1991 Common Rule, but not the 2017 Revised Rule. Nevertheless, reporting of noncompliance should still be submitted to DOJ for DOJ-supported or conducted research.

18. IRB Review of Vulnerable Subjects

18.1. Purpose

Whenever the IRB identifies that a research subject may enroll vulnerable subjects (such as children, prisoners, pregnant women, neonates, elderly, subjects who lack capacity or are mentally ill or disadvantaged, students, employees, economically disadvantaged, etc.), the IRB will consider additional protections to ensure that the research is conducted ethically.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy").

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

18.2. Review of Research Involving Children (45 CFR 46, Subpart D)

Children, like other potential vulnerable populations, require additional protections when they are research subjects. At the same time, children should not be denied the opportunity to enroll or the prospective benefits of participating in research. There are federal regulations in 45 CFR 46 Subpart D that provide additional protections for children when they are research subjects.

Federal guidelines require that children be included in certain research activities unless there is a justification for excluding them, while federal regulations require that additional precautions be taken when children are research subjects, depending on the degree of risk involved in the research. NIH policy, which guides the conduct of much human research due to funding relationships, has similar requirements.

The regulations also set forth requirements for obtaining parental permission and, where appropriate, assent by the children themselves. The IRB will review research that involves children in consideration of Subpart D of the applicable HHS and FDA regulations, Michigan state law, and institutional policy. When appropriate, requirements for involvement of minors in research postulated by the Michigan Department of Children's Protective Services (DCPS), and/or Department of Education, are also considered.

Information provided by the investigator regarding level of risk, prospect of direct benefit (when applicable), assent and parental permission, and inclusion of wards/foster children is evaluated by the IRB, which may concur with the investigator's determinations, make alternative determinations, or impose additional requirements.

18.2.1. Determination of Risk/Benefit Category

When the IRB (or qualified reviewer for research that is eligible for expedited review) reviews research involving children, it will be determined which of the risk/benefit categories described in 45 CFR 46 (Subpart D) and 21 CFR 56 (Subpart D) the research fits into, whether assent will be required, the manner in which assent will be obtained, if required, the requirements for parental permission or approval of waiver thereof, and the

appropriateness of the inclusion of wards/foster children if their involvement is proposed for research that involves greater than minimal risk with no prospect of direct benefit. The IRB will consider information provided by the research team in the submission. The IRB's (or reviewer's, for research that is eligible for expedited review) determinations will be entered into the minutes for the meeting at which the research was reviewed, if full Board review is indicated, or in the IRB record, in the case of expedited reviews. Any concern with the information provided by the researchers should be included in the documentation of Subpart D findings.

The IRB may approve research involving children only if it meets the criteria in one of the four following categories:

18.2.1.1. 45 CFR 46.404; 21 CFR 50.51: Research not involving greater than minimal risk.

"Minimal Risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

The IRB, or designated expedited reviewer, will provide the basis for the determination of minimal risk.

If consent cannot be waived in accordance with 45 CFR 46.116, the IRB, or designated expedited reviewer, will almost always require that the permission of only one parent is necessary for research in this category, and will determine whether assent is required for some or all minors. However, the IRB has the discretion to require that the permission of both parents must be obtained.

18.2.1.2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405; 21 CFR 50.52):

For research to be approved under this category, the convened IRB must find that:

- the risk is justified by the anticipated benefits to the subjects; and
- the relation of the anticipated benefit to the risk must be at least as favorable to the subjects as that presented by available alternative approaches.

The IRB, at a convened meeting, will provide the basis for the determinations of greater than minimal risk and prospect of direct benefit.

The IRB may determine that the permission of one or both parents is required for research in this category and will determine whether assent for some or all minors is required.

18.2.1.3. Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition (45 CFR 46.406; 21 CFR 50.53):

For research to be approved under this category, the Board must find that it meets the requirements of 45 CFR 46.406 and 21 CFR 50.53, as follows:

18.2.1.3.1. The risk represents a minor increase over minimal risk;
18.2.1.3.2. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
18.2.1.3.3. The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition;
18.2.1.3.4. Adequate provisions are made for soliciting and documenting assent of the children; and
18.2.1.3.5. Adequate provisions are made for soliciting the permission of both parents of each child unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. (45 CFR 46.407 and 408).

The IRB, at a convened meeting, will provide the basis for the determinations of greater than minimal risk and no prospect of direct benefit.

The permission of both parents is required for research in this category, unless one parent cannot reasonably provide permission, as allowed per Subpart D. The assent of the minors involved is required unless the Board determines that some or all are not capable of providing assent.

18.2.1.4. Research not fitting into the aforementioned categories which presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407; 21 CFR 50.54):

The IRB, at a convened meeting, will provide the basis for its determinations regarding risk level and potential for direct benefit.

If the research is supported by HHS jurisdiction, and falls in this category, it cannot be performed without review by the Secretary of the HHS as outlined in 45 CFR 46.407.

Research under FDA jurisdiction that falls in this category cannot be performed without review by the Commissioner of Food and Drugs as outlined in 21 CFR 50.54.

If the research is HHS-supported or under FDA jurisdiction, the IRB staff will prepare a request for panel review promptly after the IRB review, and will provide such to the HRPP Administrator. The Administrator, or designee, will prepare a report for submission to OHRP to request a panel review as described in 45 CFR 46.407 or 21 CFR 50.54, as applicable.

Research in this category that is not federally funded and does not involve FDA-regulated products will be reviewed by a special panel convened by the MTU IRB office to make the determinations that would otherwise be made by HHS or FDA when evaluating research in this category.

The permission of both parents is required for research in this category, unless one parent cannot reasonably provide permission, as allowed per Subpart D. The assent of the minors involved is required unless the Board determines that some or all are not capable of providing assent.

18.2.2. Assent Determination

After the Board makes the risk/benefit determination, they must consider the issue of child assent, as described in 45 CFR 46.408(a) (Subpart D). The Board must decide whether assent is necessary, and also whether and how it will be documented if it is necessary.

Among the formats the Board may consider are the following:

- waiver of assent;
- determination that the children lack the ability to provide assent;
- verbal assent, without documentation;
- verbal assent, with documentation by the investigator and/or the legally authorized representative(s);
- written assent form, with subject signature; or
- subject signature block on consent form (for older children only).

The federal regulations do not require that assent be sought from children starting at a specific age, but that their assent should be sought when, in the judgment of the IRB, the children are capable of providing their assent. IRBs are to take into account the ages, maturity, and psychological state of the children involved (see 45 CFR 46.408(a)).

When the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary (45 CFR 46.408(a)).

18.2.3. Inclusion of Wards in Research

Special protections must be considered whenever children who are wards of the state or any other institution, agency, or entity are considered for inclusion in research that is greater than minimal risk with no prospect of direct benefit. Of primary concern are consent issues, i.e., who has authority to enroll a child who is a ward in research. Responsibility for ensuring that appropriate individuals provide permission rests with the PI and must be in compliance with applicable statutes and the process described in the protocol that was approved by the IRB.

Federal regulations do not require special provisions for wards enrolled in research that is either minimal risk or greater than minimal risk with the prospect of direct benefit. However, the IRB may impose additional requirements if the research and/or status of the child(ren) warrant additional safeguards. Michigan state laws and the Michigan DCPS policies will be considered during review of research that involves wards.

Wards may only be included in research that is greater than minimal risk and does not offer the prospect of direct benefit (45 CFR 46.406 or 45 CFR 46.406) when such research is either related to their status as wards or conducted in a facility at which most of the children are not wards.

If it is proposed that wards will be enrolled in research that is greater than minimal risk and does not offer the prospect of direct benefit, an advocate or advocates who will serve to ensure the best interests of each child are being upheld must be appointed, in addition to obtaining permission from any other individual acting on behalf of the child, e.g., as guardian or in loco parentis. One individual may serve as an advocate for more than one child.

18.3. Review of Research Involving Pregnant Women, Human Fetuses, or Neonates (45 CFR 46, Subpart B)

Pregnant women/fetuses/neonates like other potential vulnerable populations require additional protections when they are research subjects. At the same time, they should not be denied the opportunity to enroll or the prospective benefits of participating in research. There are federal regulations in 45 CFR 46 Subpart B that provide additional protections for pregnant women/fetuses/ neonates when they are research subjects.

Distinction should be made between studies that are designed to study pregnant women or the characteristics of the pregnant woman and/or fetuses/ neonates (i.e., the inclusion criteria is geared to enroll pregnant women, fetuses, and/or neonates in the research), and studies for which pregnant women may enroll by chance. With regards to the latter, Subpart B requirements need not be met although when studies pose potential risks to pregnant women, neonates, or fetuses appropriate safeguards should be considered for women of child-bearing potential.

The IRB will ensure that the requirements of Subpart B are appropriately satisfied prior to granting approval of any study designed to study pregnant women, fetuses, or neonates. In addition to the considerations made by the IRB in the scope of its review (in accordance with Section VIII.A), the IRB will also consider the following:

- that there is adequate expertise on the IRB to evaluate the risks and benefits related to the inclusion of pregnant women, fetuses and neonates. When additional expertise is needed the IRB will consider adding an appropriate consultant(s);

- the determinations required by Subpart B are documented appropriately in the IRB records (in the IRB minutes for reviews conducted by the convened IRB or in the documentation for review for expedited reviews); any involvement of pregnant women or fetuses meets all requirements as stated in 45 CFR 46.204;

- any involvement of neonates meets all requirements as stated in 45 CFR 46.205;

- any research involving, after delivery, the placenta, the dead, macerated fetal material, or organs excised from a dead fetus will be conducted in accordance with 45 CFR 46.206, federal, state, or local laws and regulations;

- proposals that are supported by HHS and for which the inclusion of pregnant women, neonates, or fetuses is not approvable per Subpart B will be referred to the HHS Secretary for review. For other such proposals, the IRB will establish a separate panel composed of individuals with appropriate expertise to determine whether the research meets ethical and regulatory standards and whether the research should be approved. If the research is supported by another federal agency or sponsor, their requirements must be considered during this process;

- informed consent is obtained per provisions of Subpart B for pregnant women who have reached the age of majority or are legally emancipated;

- informed consent is obtained per provisions of Subparts B and D for pregnant minors (where research is related to prenatal care, consent of the pregnant minor may be acceptable);

- consent documents contain information regarding risks of breastfeeding, when risks to the pregnant woman or neonate is determined to be greater than minimal;

- consideration is given to excluding women of child-bearing potential when the woman's reproductive status is not relevant to the research and risks to the pregnant woman or fetus is determined to be greater than minimal.

18.4. Review of Research Involving Prisoners (45 CFR 46, Subpart C)

Prisoners like other potential vulnerable populations require additional protections when they are research subjects. Although prisoners should not be denied the opportunity to enroll in research that provides potential benefits, the submission for IRB review and approval should include a justification for the inclusion of prisoners as subjects in the study, particularly if the research will be conducted solely on prisoners. There are federal regulations in 45 CFR 46 Subpart C that provide additional protections for prisoners when they are research subjects.

A prisoner is defined by the federal regulations as any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals 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.

No federally-supported or -conducted research involving prisoners is eligible for exemption. Therefore, all research protocols that involve prisoners must receive at least expedited review. However, care must be given to applying the expedited review criteria because the definition of minimal risk under Subpart C is different from the definition of minimal risk for research not involving prisoners. For prisoner research, minimal risk is compared to "healthy persons" rather than what is experienced in "daily lives, or in the routine medical…examination of healthy persons", thereby raising the threshold of what may be permitted under expedited review. The following definition of minimal risk will be applied to research involving prisoners:

Minimal Risk - 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.

For prisoner studies requiring review by the convened IRB, a prisoner representative will be involved in the review of the study.

In addition to other considerations in these IRB Operating Procedures, the IRB will only approve federally-supported or -conducted research involving prisoners if it finds that the study meets all the requirements of 45 CFR 46.300 (Subpart C).

The IRB may proceed and approve the study if it determines that the research under review represents one of the following minimal risk categories in category 1 or 2 below. If the IRB determines that the research falls under category 3 or 4 below and the research is federally supported or conducted, the research must be submitted to OHRP for review by a panel.

18.4.1. Study of the possible causes, effects, or processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to subjects; or,

18.4.2. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risks, and no more than inconvenience to the subjects. If the IRB finds that the study involves one of the following categories and it is federally supported or conducted, then the IRB must forward the protocol (along with documentation of its review) to OHRP:

18.4.3. Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction and sexual assaults) provided that the study may proceed only after the Secretary (i.e., HHS) has consulted with appropriate experts including experts in penology medicine and ethics, and

published notice in the Federal Register, of its intent to approve such research; or

18.4.4. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary (i.e., HHS) has consulted with appropriate experts including experts in penology medicine and ethics, and published notice in the Federal Register, of its intent to approve such research.

The IRB shall ensure that the Michigan Penal Code limitations on experiments involving prisoners in Michigan are met for research conducted at MTU.

18.4.5. Legal Counsel

18.4.5.1. MTU IRB will consult General Counsel (not to suggest that legal counsel serves as an IRB member) regarding the details and status of the applicable federal and state regulations in regard to biomedical and behavioral research proposals submitted to the IRB in which the study subjects are prisoners, fetuses, children, or pregnant women, and to require the principal and participating investigators to comply with the applicable provisions for proposed studies involving any of the aforementioned special subjects. Additionally, procedures found in Attachment I, Protections Pertaining to Research Involving Fetuses, Pregnant Women, and Human In-Vitro Fertilization; Attachment II, Prisoners as Research Subjects; and Attachment III, Children as Research Subjects shall be followed.

18.4.6. Selection of Subjects

18.4.6.1. In compliance with 45 CFR 46, the IRB shall determine that adequate consideration has been given to the manner in which potential subjects who are prisoners, fetuses, children, or pregnant women will be selected and that adequate provision has been made by the applicant/investigator(s) for monitoring the actual informed consent process. In this regard, the IRB may elect a member or an advocate to participate in:

18.4.6.1.1. Overseeing the actual process by which individual consents required by federal and State regulations are secured either by approving induction of each individual into the activity or verifying, perhaps through sampling, that approved procedures for induction of individuals into the research study are being followed, and

18.4.6.1.2. Monitoring the progress of the research and intervening as necessary through such steps as visits to the study site and continuing evaluation to determine if any unanticipated risks have arisen.

References
21 CFR 56
45 CFR 46

Attachments
- Protections Pertaining to Research Involving Fetuses, Pregnant Women, and Human In-Vitro Fertilization
- Prisoners as Research Subjects
- Children as Research Subjects

19. Research at Schools or Educational Institutions

19.1. Purpose

Any research that is supported by the Department of Education or conducted in public schools must adhere to Family Educational Rights and Privacy Act (FERPA; 34 CFR Part 99) and Protection of Pupil Rights Amendment (PPRA; 34 CFR Part 98).

19.2. Family Educational Rights and Privacy Act (FERPA (34 CFR Part 99)

FERPA is designed to protect the privacy of a student's education records at all public elementary and secondary schools and virtually all public and private postsecondary institutions.

19.2.1. An educational agency or institution may disclose personally identifiable information from an education record of a student without consent if the disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to:

- Develop, validate, or administer predictive tests.
- Administer student aid programs.
- Improve instruction.

19.2.2. The IRB will determine, after consultation with, when necessary, General Counsel and the Provost's Office for research involving MTU student records conducted by or on behalf of the university, and/or the IO, when exceptions to parental/student consent to release student records for research are acceptable.

19.2.3. A school district or postsecondary institution that uses this exception is required to enter into a written agreement with the university or researcher conducting the research that specifies:

- The determination of the exception.
- The purpose, scope, and duration of the study.
- The information to be disclosed.
- That information from education records may only be used to meet the purposes of the study stated in the written agreement and must contain the current requirements in 34 CFR 99.31(a) (6) on re-disclosure and destruction of information.
- That the study will be conducted in a manner that does not permit personal identification of parents and students by anyone other than representatives of university with legitimate reasons to access the information as part of their work.
- That the university is required to destroy or return all personally identifiable information when no longer needed for the purposes of the study.
- The time period during which the university must either destroy or return the information.

19.2.4. Education records may be released without consent under FERPA if all personally identifiable information has been removed including:

- Student's name and other direct personal identifiers, such as the student's social security number or student number.
- Indirect identifiers, such as the name of the student's parent or other family members; the student's or family's address, and personal characteristics or other information that would make the student's identity easily traceable; date and place of birth and mother's maiden name.
- Biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting.
- Other information that, alone or in combination, is linked or linkable to a specific student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify the student with reasonable certainty.

19.3. Pupil Rights Amendment (PPRA) (34 CFR Part 98)

PPRA is designed to protect the rights of parents and students in programs that receive funding from the Department. These regulations apply to any research that is funded by the DOE, with the exception of the following funded programs:

- High School Equivalency Program and College Assistance Migrant Program (Section 418A of the Higher Education Act of 1965 as amended by the Education Amendments of 1980 (Pub. L. 96–374) 20 U.S.C. 1070d–2)
- Programs administered by the Commissioner of the Rehabilitative Services Administration (The Rehabilitation Act of 1973 as amended by Pub. L. 95–602 (29 U.S.C. 700, et seq.)
- College Housing (Title IV of the Housing Act of 1950 as amended (12 U.S.C. 1749, et seq.)

19.3.1. No student shall be required, as part of any research project, to submit without prior consent to surveys, psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:

- Political affiliations.
- Mental and psychological problems potentially embarrassing to the student or his or her family.
- Sex behavior and attitudes.
- Illegal, anti-social, self-incriminating and demeaning behavior.
- Critical appraisals of other individuals with whom the student has close family relationships.
- Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers.
- Religious practices, affiliations, or beliefs of the student or student's parent.
- Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.

Prior consent means:

- Prior consent of the student if the student is an adult or emancipated minor; or
- Prior written consent of the parent or guardian, if the student is an non-emancipated minor. Schools and contractors obtain prior written parental consent before minor students are required to participate in any ED-funded survey, analysis, or evaluation.

19.3.2. For research not funded by the US Department of Education (DOEd, the IRB must verify compliance with DOEd regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:

- The right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student.
- Any applicable procedures for granting a request by a parent for reasonable access to such a survey within a reasonable period of time after the request is received.
- Arrangements to protect student privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items):
  - Political affiliations or beliefs of the student or the student's parent.
  - Mental or psychological problems of the student or the student's family.
  - Sex behavior or attitudes.
  - Illegal, anti-social, self-incriminating, or demeaning behavior.
  - Critical appraisals of other individuals with whom respondents have close family relationships - Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers.
  - Religious practices, affiliations, or beliefs of the student or the student's parent.
  - Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program).
- The right of a parent of a student to inspect, upon the request of the parent, any instructional material used as part of the educational curriculum for the student.
- Any applicable procedures for granting a request by a parent for reasonable access to instructional material received.
- The administration of physical examinations or screenings that the school or agency may administer to a student.
- The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use.

- The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student.
- Any applicable procedures for granting a request by a parent for reasonable access to such a survey instrument within a reasonable period of time after the request is received.

19.3.3. In addition to federal requirements for school-based research, the study must comply with local requirements. Researchers should ensure that their research meets the requirements of the local school district or local independent school district.

20. IRB Review of FDA Regulated Studies

20.1. Purpose

The IRB must ensure that research studies involving drugs, vaccines, and other biological products and medical devices intended for human use are safe and effective and designed to be in compliance with FDA regulations.

The IRB must ensure that any FDA-regulated study it reviews is planned in a manner that it will comply with 21 CFR Parts 50, 54, 56, 312, 600, and 812.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy").

20.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Clinical investigation - An experiment in which a drug (approved or unapproved) is administered or dispensed to, or used involving, one or more humans.

Premarket approval (PMA) – a review of safety and effectiveness by FDA before a product can be marketed

Humanitarian Device Exemption (HDE) – a marketing application for a HUD. A HDE is exempt from the effectiveness requirements of a premarket approval (PMA).

Humanitarian Use Device (HUD) – a device intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year.

Immediately life-threatening disease or condition - a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

Investigational new drug (IND) - a new or biological drug used in a clinical investigation.

Investigational new device (IDE) – a device, including transitional device, is the object of investigation

Medical Device - an instrument, apparatus, implement, machine, contrivance (the thing that causes something to happen), implant, in vitro reagent, or other similar or related article, including a component part, or accessory. Examples of medical devices include:

- Simple items - tongue depressors and bedpans
- Complex technologies – pacemakers
- Dental devices
- Surgical implants and prosthetics

- Diagnostic products - in vitro diagnostic reagents, pregnancy test kits, imaging systems such as magnetic resonance imaging (MRI)

Serious disease or condition - a disease or condition associated with morbidity that has substantial impact on day-to-day functioning.

Significant Risk (SR) – investigational device that:

- is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety or welfare of a subject;
- is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject;
- otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Transitional device – devices that were regulated by FDA as new drugs before May 28, 1976.

20.3. Procedure

20.3.1. Review of Initial Submission

20.3.1.1. The HRPP Administrator will conduct a pre-review of all submissions to determine that the IRB receives the necessary information to make all determinations required by FDA regulations and these and other IRB SOPs. Any submission that involves a clinical investigation with one or more human subjects with a test article (e.g., investigational or FDA-approved drugs, investigational or FDA-approved devices, investigational or FDA-approved biologics, or investigational diagnostic tests) will be documented as an FDA-regulated study by the HRPP Administrator or designee.

20.3.1.2. The following categories of clinical investigations are exempt from the requirements for prior IRB review and approval:

20.3.1.2.1. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article is subject to IRB review.

20.3.1.2.2. Taste and food quality evaluations 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, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the

Food Safety and Inspection Service of the U.S. Department of Agriculture.

20.3.1.3. During the IRB pre-review process, the HRPP Administrator will ensure that the appropriate regulatory status of any drug or device used in the proposed research is clearly documented in the materials submitted for IRB review.

20.3.1.4. For FDA-approved drugs (that will be used for an off-label or new use), the package insert will be required.

20.3.1.5. For an investigational drug, one of the following will be required:

20.3.1.5.1. An approved IND#, appearing on the sponsor's protocol, the Investigator's Brochure, and/or the IND letter from FDA.

20.3.1.5.2. The sponsor's or investigator's (in an investigator-initiated study) letter to the FDA for submission of an IND application. Regarding this option, final approval of a study cannot be granted by the IRB until 30 days have passed from the date of submission to the FDA, and there has been no notice from FDA of a hold placed on the drug.

20.3.1.5.3. An explanation and justification from the sponsor/investigator that an IND is not required (investigators are strongly encouraged to consult with FDA for an official determination).

20.3.1.5.4. An explanation and justification from the sponsor/investigator as to why the drug may be exempt from the IND requirements in accordance with 21 CFR 312.2(b). If the drug is indicated for oncology, the IRB may rely on the FDA Guidance titled, "IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer."

20.3.1.6. For FDA-approved devices or investigational devices, the device manual will be required.

20.3.1.7. For investigational device, one of the following will be required:

20.3.1.7.1. An approved IDE#, appearing on the sponsor's protocol, the Device Manual, and/or the IDE letter from FDA.

20.3.1.7.2. The sponsor's or investigator's (in an investigator-initiated study) letter to the FDA for submission of an IDE application. Regarding this option, final approval of a study cannot be granted by the IRB until 30 days have passed from the date of submission to the FDA, and there has been no notice from FDA of a hold placed on the device.

20.3.1.7.3. An explanation and justification from the sponsor/investigator that the device is a Not-Significant Risk device and an IDE is not required (investigators are strongly encouraged to consult with FDA for an official determination).

20.4. Human Research with Investigational or FDA-approved Drugs

20.4.1. The IRB must determine whether the human research study requires an Investigational New Drug (IND). An IND is needed if ALL the following exist:

20.4.1.1. The research involves a drug;

20.4.1.1.1. The therapeutic purpose of drugs is intended for diagnosis, cure, mitigation, treatment, or prevention of disease;
20.4.1.1.2. Drugs are also compounds that affect the structure or any function of the body (i.e., a dietary supplement intended only to affect the structure or function of the body and not intended for a therapeutic purpose is not a drug);
20.4.1.1.3. Drugs can be prescription or non-prescription (OTC);
20.4.1.1.4. Biological products may also be considered drugs; (i.e., virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component, or derivative, allergenic product, protein applicable to the prevention, treatment, or cure of a disease condition of human beings);

20.4.1.2. The clinical investigation is not otherwise exempt from the IND requirements.

20.4.2. Categories of clinical investigations that are exempt from the IND requirements:

20.4.2.1. Certain research involving marketed drug products;

20.4.2.2. A clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the IND requirements if ALL the following apply:

20.4.2.2.1. The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication and there is no intent to use it to support any other significant change in the labeling of the drug;
20.4.2.2.2. In the case of a prescription drug, the investigation is not intended to support a significant change in the advertising for the drug.
20.4.2.2.3. The investigation does not involve a route of administration, dose, and patient population or other factors that significantly increase the risk associated with the use of the drug product.

20.4.3. Investigators should carefully consider the risk implications of any conditions of use in the study that deviate from the conditions of use described in the drug's labeling, with particular attention to the following:

20.4.3.1. Route of administration- a change in route can introduce a significant new risk (i.e., oral to IV or injection or inhaled);

20.4.3.2. Dose –increase dose, frequency, or duration can significantly increase risk; a decrease dose could significantly increase risk;

20.4.3.3. Patient population –could increase risk due to increased age, different disease or stage of disease, decreased renal or hepatic function.

20.4.4. The IRB must determine that a Clinical Investigation is conducted in compliance with the requirements for IRB review and the informed consent.

20.4.5. The IRB must determine that a Clinical Investigation is not intended to promote or commercialize the drug product.

20.4.6. Bioavailability (BA) or bioequivalence (BE) studies in humans do not require an IND if **ALL** the following conditions are met:

20.4.6.1. The drug product does not contain a new chemical entity, is not radioactively labeled and is not cytotoxic.

20.4.6.2. The dose (single dose or total daily dose) does not exceed the dose specified in the labeling of the approved version of the drug product.

20.4.6.3. The investigation is conducted in compliance with the requirements for review by an IRB and with the requirements for informed consent.

20.4.6.4. The sponsor meets the requirements for retention of test article samples and safety reporting.

20.4.7. Lack of documentation of FDA approval of an IND.

20.4.7.1. If adequate documentation has not been obtained that an investigational drug has an IND # or that a determination has been made by FDA that an IND is not needed for the study, the IRB will determine in a convened meeting whether an IND is needed and document its determination in the minutes.

20.4.7.2. The IRB or an investigator can find information regarding drug approvals and the drug approval process at http://www.fda.gov/Drugs/default.htm.

20.4.7.3. Alternatively, one can submit questions regarding whether an IND is needed by contacting the FDA's Center for Drug Evaluation (CDER)

(Human Drug Information, Division of Drug Information) by sending an email to druginfo@fda.hhs.gov or by calling (855) 543-3784 or (301) 796-3400.

20.5. Other Considerations Involving Clinical Investigations with Drugs

20.5.1. The IRB will review the Investigator's Brochure and/or the package inserts to determine the risks of the drug(s) used as test articles in the study.

20.5.2. The IRB will also review the investigator's plan on how the drug (whether investigational or FDA-approved) will be supplied, stored, dispensed, and administered to subjects, and whether any special handling of the drug is required. The plan must ensure that the integrity and quality of the drug will not be compromised during the storage process. For example, if temperature controls are needed to maintain the stability of the drug, the plan must document how the drug will be stored accordingly. The plan should also describe how drug accountability will be maintained (who will be responsible for the storage, distribution and record-keeping of the drug; e.g., research pharmacy or research team, and if the latter which member of the research team).

20.5.3. If there is a known antidote for the drug in case of overdose or over-administration resulting in toxicity, the investigator's plan for management and storage of the drug should also include that of the antidote, its availability and potential use, will be clearly communicated to research staff members.

20.5.4. If there is specific information regarding birth control measures that should be taken by subjects with reproductive capacity, the IRB will ensure during its review of the informed consent document(s) that that information is included in the Risks section.

20.5.5. If the research involves gene transfer with a biologic or drug (i.e., transfer of DNA or RNA derived from recombinant RNA), MTU Institutional Biological Committee (IBC) review and approval is required before the IRB can complete its review and grant its approval.

20.5.6. For such studies, the investigator must comply with the reporting requirements of Appendix M to the NIH Office of Science Policy (OSP) [which in March 2016 replaced Office of Biotechnology Assessment (OBA)]. As a result, the investigator must submit serious adverse events to the IBC.

20.6. Investigational Devices

20.6.1. The HRPP Administrator will help the IRB confirm the regulatory status of the device, the potential risks to subjects, and determine if review by the convened IRB is required.

20.6.2. The IRB will determine and document that the use of the device in the study falls into one of the following categories:

20.6.2.1. Significant Risk (SR) – The sponsor is responsible for making the initial risk determination. The PI should submit a copy of the sponsor's risk assessment and the rationale used for making the SR/NSR determination.
The determination must also be made by the convened IRB, if not previously made by FDA for the indication of the device used in the proposed study.

20.6.2.2. Non-Significant Risk (NSR) - an investigational device that does not meet the definition of a significant risk device.

20.6.3. Exempt studies (exempt from requirements of 21 CFR 812).

20.6.3.1. A legally marketed device used in accordance with its labeling.

20.6.3.2. Diagnostic device studies (e.g. in vitro diagnostic study) if the testing:

20.6.3.2.1. Is noninvasive;
20.6.3.2.2. Does not require an invasive sampling procedure that presents significant risk;
20.6.3.2.3. Does not by design or intention introduce energy into a subject;
20.6.3.2.4. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;
20.6.3.2.5. Consumer preference testing, testing of a modification, or testing of a combination of devices, if all are legally marketed devices;
20.6.3.2.6. Device intended solely for veterinary use;
20.6.3.2.7. Device shipped solely for research with laboratory animals and contains the label "CAUTION - Device for investigational use in laboratory animals or other tests that do not involve human subjects.

20.6.4. The IRB will complete an IRB investigational device risk determination checklist during the initial review.

20.6.4.1. The risk determination checklist will be filed in the IRB electronic system.

20.6.4.2. The risk determination will be documented in the IRB meeting minutes.

20.6.4.2.1. Document the IRB's reason for its SR or NSR determination.
20.6.4.2.2. Document that a copy of the SR IDE approval or conditional approval letter from the FDA was submitted to the IRB or a copy of the NSR letter from FDA or sponsor was provided, as applicable.

20.6.5. If the IRB finds that the device poses an NSR, the sponsor does not need to submit an IDE to the FDA. The FDA considers an NSR study to have an approved IDE after IRB approval and when the sponsor meets the abbreviated requirements at 21 CFR 812.2 (b) and informed consent requirements.

20.6.6. Review by the Convened IRB.

20.6.6.1. If the investigational device is determined to not meet the exemption criteria (and again the research involves the evaluation of the safety and effectiveness of the device) and FDA has not already made a NSR determination, the convened IRB must review the study and determine whether the device is considered to be a SR or a NSR device in accordance with 21 CFR 812 and FDA's guidance, "Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Significant Risk and Nonsignificant Risk Medical Device Studies."

20.6.6.2. If the convened IRB determines that the device is a significant risk (SR) device, then an IDE must be approved by the FDA before the IRB may proceed with approval of the study (or at least approval of the portion of the study that will involve the device).

20.6.6.3. If an IDE must be approved by the FDA, the PI will be informed in writing and instructed to inform the sponsor of the SR determination (if applicable).

20.6.6.4. The review of the device by the convened IRB and the determination of either a SR or NSR device will be documented in the minutes.

20.6.6.5. These determinations will be made in addition to the overall risk determination of the protocol of minimal risk or greater than minimal risk.

20.6.6.6. If the IRB determines the device to be an NSR device and the overall risk in the study to be minimal risk, the convened IRB may determine whether the continuing review may be done by expedited review. If such a determination is made, it will be documented in the meeting minutes.

20.6.6.7. If the FDA has not made the risk determination or the IRB disagrees with the NSR determination made by the sponsor; the IRB will notify the investigator and where appropriate, the sponsor in writing that the study involves a significant risk device (SR).

20.6.6.8. If the sponsor or the IRB needs assistance with making the SR/NSR determination, a written determination from the FDA may be obtained.

20.6.7. Other Considerations Involving Clinical Investigations with Devices

20.6.7.1. The IRB will also review the investigator's plan on how the device (whether investigational or FDA-approved) will be supplied, stored, utilized in the study, and whether any special handling of the device is required.

20.6.7.1.1. The plan must ensure that the integrity, quality, and sterility of the device will not be compromised during the storage process. For example, if temperature controls are needed to maintain the stability of the device, the plan must document how the device will be stored accordingly.

20.6.7.1.2. The plan should also describe how device accountability will be maintained (who will be responsible for the storage, distribution, and record-keeping of the device).

20.6.7.2. If the device is implanted, or otherwise requires sterilization, and does not come in a sterilized package, the autoclaving of the device (or other sterilization technique that will be used) should be described in the plan.

20.7. Compliance with Good Clinical Practices (GCP)

All FDA regulated research and NIH-supported clinical trials involving investigational drugs, devices, or biologics must comply with the International Conference for Harmonization (ICH) E-6 R2 Good Clinical Practice (GCP) Guidelines, to the extent that the GCP standards apply to the research study.

Additionally, it is recommended that all biomedical research complies with these GCP standards to the extent that the standards apply to the research.

In accordance with this guidance, the IRB should obtain the following documents:

- Trial protocol(s)/amendment(s);
- Written informed consent form(s);
- Informed consent form;
- Updates that the investigator proposes for use in the trial;
- Subject recruitment procedures (e.g., advertisements);
- Written information to be provided to subjects;
- Investigator's Brochure (IB);
- Available safety information;
- Information about payments and compensation available to subjects;

- The investigator's current curriculum vitae and/or other documentation evidencing qualifications, and any other documents that the IRB may require to fulfil its responsibilities.

Any investigator conducting an NIH-supported clinical trial must complete GCP-training and provide a copy of the certificate to the IRB.

References:

21 CFR 312.305
21 CFR 312.310
21 CFR 312.315
21 CFR 312.320
21 CFR 56.108 (c)
21 CFR 56.105
21 CFR 50

Drugs 21 CFR 312.2; 21 CFR 312.7
Devices 21 CFR 812.2
Biologic 21 CFR 601.2
21 CFR 814

Guidance for IRBs, Clinical Investigators, and Sponsors; IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites and the Determination of Whether an IND/IDE is Needed, August 2013

Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Frequently Asked Questions about Medical Devices, January 2006

Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Significant Risk and Nonsignificant Risk Medical Device Studies, January 2006

Decisions for Investigational Device Exemption Clinical Investigations
Guidance for Sponsors, Clinical Investigators, Institutional Review Boards, and Food and Drug Administration Staff; August 19, 2014

21. Single IRB Review of Cooperative Research/Multi-Center Studites

21.1. Purpose

With the approval of the Institutional Official (IO), the Michigan Technological University (MTU) IRB may rely upon the review of another qualified IRB, enter into joint IRB review arrangements, or make similar arrangements for avoiding duplication of effort.

A written agreement called an IRB Reliance Agreement or IRB Authorization Agreement (IAA) or individual investigator agreement (IIA), or memorandum of understanding (MOU) between MTU IRB and an external IRB will delineate the roles and responsibilities of the involved parties to ensure the rights and welfare of human research subjects are protected. The agreement can be for a single research study or for multiple studies.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the “Policy”).

21.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Local IRB or internal IRB – an IRB that provides review only for the researchers of its organization (i.e., MTU Multi-Center [MTU-MC] IRB).

External IRB - any IRB outside of MTU-MC.

Independent IRB (or Commercial IRB) – a review board that is not owned or operated by the research organization for which it provides review services; independent IRB may or may not charge for these services; an independent IRB may act as a central IRB for multisite trials.

Central IRB – the IRB is a single board that conducts reviews for multiple sites (i.e., NCI CIRB- National Cancer Institute Central IRB).

Accredited IRB - Accreditation uses a set of objective standards to evaluate the quality and level of protection that an organization provides research participants. Through accreditation, an organization can demonstrate the overall excellence of its research program by providing the most comprehensive protections for research participants. The Association for Accreditation of Human Research Protection Programs (AAHRPP) is the main accrediting entity for human research. AAHRPP accreditation is voluntary and currently granted for three years, after which the organization must repeat the process.

Ceding or deferring IRB review – MTU may agree to use an outside/external IRB to oversee a research study or studies.

21.3. Process for Requesting Reliance on an External IRB

MTU may rely on an external IRB for review and approval of human research if such reliance is:

- a requirement of the research or
- if it benefits MTU, MTU investigators and/or MTU research subjects.

All reliance requests must be described/outlined/explained to the MTU IRB in the IRB electronic system, for consideration and approval by the IO or designee.

Principal Investigators (PIs) who wish to open a study using an external IRB's review, must request reliance on the review of an external IRB. The request and the requested documents will be submitted to the MTU IRB Office via the IRB electronic system.

The IRB Office will review the information and determine if an external IRB is qualified to serve as the IRB of Record, using criteria such as the following:

- the external IRB is located within the U.S;
- the external IRB is currently registered and has an active Federalwide Assurance (FWA) on file with Federal Office for Human Research Protection (OHRP);
- the external IRB has not received any recent FDA warning letters or OHRP determination letters within the last year;
- the external IRB's Human Research Protection Program is accredited by AAHRPP;
- the Board membership satisfy the requirements of 45 CFR 46.107 and 21 CFR 56.107;
- the external IRB has an adequate process in place to notify the MTU IRB and researcher(s) of its approval, determinations, reportable events, suspensions and terminations.

The MTU IO or designee has the ultimate authority regarding whether or not to rely on external IRB. If it is determined that the external IRB is qualified to serve as the IRB of record, a written IRB Authorization Agreement (IAA) will be initiated either by the external IRB or MTU. The agreement must outline the responsibilities of the external IRB and the MTU IRB and the researcher(s). The agreement may be written to cover one research project or to cover research projects on a case-by-case basis. By delegating the responsibilities for review to an external IRB, MTU agrees to abide by the external IRBs' decision for the review process. The authorization agreement will be kept in the IRB files and will be made available upon official request.

21.4. Responsibilities of the External IRB Include, but are not Limited to:

21.4.1. Serve as the IRB of Record;

21.4.2. Conduct review of research according to the IRB Reliance Agreement, all applicable regulations, and laws, including initial review, informed consent, continuing reviews, and reviews of modification to previously approved research;

21.4.3. Be sensitive to factors such as community attitudes such as the community from which the subjects are drawn and the consent process is appropriate for the subject population involved;

21.4.4. Include the contact information for the MTU IRB Office in the consent;

21.4.5. Review potential unanticipated problems involving risk to subjects or others and/or serious or continuing non-compliance;

21.4.6. Notify the researcher and the MTU IRB in writing of its determinations and decisions;

21.4.7. Report to the MTU IRB, regulatory agencies, and sponsors of serious or continuing non-compliance, unanticipated problems involving risks to subjects or others, suspensions, or terminations of IRB approval;

21.4.8. Make available recent IRB minutes, IRB membership rosters and standard operating procedures to the MTU IRB upon request;

21.4.9. When appropriate, conduct on-site or remote post-approval monitoring or audits, unless delegated by MTU;

21.4.10. Ensure there are processes for data protection, conflict of interest management, and confirmation of human subject's protection training;

21.4.11. Maintain appropriate documentation per record retention policy/procedure to include an OHRP-approved Federalwide Assurance (FWA) for human subjects research;

21.4.12. Notify the MTU IRB Office of any changes to the IRB's FWA;

21.4.13. Maintain an IRB membership that satisfies the requirements of 45 CFR 46.107 and 21 CFR 56.107 and which provides special expertise as needed to adequately assess all aspects of each study.

21.5. MTU Principal Investigator (PI) Responsibilities When Relying on an External IRB

In addition to the PI responsibilities stated in the MTU PI Responsibilities policy, the PI must comply with the following additional responsibilities when their research is relying on external IRB:

21.5.1. Must submit an initial submission to the MTU IRB for permission to utilize an external IRB of Record. The submission must include the protocol, informed consent form, a list of all research staff for the study, documentation of education training certificates;

21.5.2. Must comply with the determinations and requirements of the IRB of Record (external IRB);

21.5.3. Must NOT enroll subjects in research prior to review and approval by the external IRB and initial approval is also granted by the MTU IRB;

21.5.4. Provide the external IRB with any local context issues relevant to the protocol;

21.5.5. Disclose financial conflicts of interest in accordance with the external IRB's policies and comply with any additional conflict of interest management plans required by the external IRB;

21.5.6. In addition to reporting to the external IRB of Record any item/incidents as required by their policies (i.e., unanticipated problems, serious or continuing noncompliance, subject complaints, suspension of the research, etc.), report the following to the MTU IRB:

21.5.6.1. any serious or continuing non-compliance or protocol deviations;

21.5.6.2. any complaints from a subject or other person regarding the research;

21.5.6.3. any request for an audit from a federal regulatory agency (e.g., FDA) or a sponsor;

21.5.6.4. any suspension in the research, whether by the external IRB, sponsor, or federal regulatory agency; and,

21.5.6.5. when the PI will no longer be the responsible party for a research project (e.g., no longer serve as PI).

21.5.7. Submit to the MTU IRB every continuing review approval and newly approved consent form during continuing review by the external IRB.

21.6. Procedures

The MTU IRB will ask investigators to specify who is responsible for coordinating communication among the multiple sites, especially communication about human subject protection issues. If MTU is not a lead site or coordinating center, the MTU IRB will ask the MTU PI to explain how important human subjects' protection issues will be communicated to the MTU site. When MTU leads the multi-site study or serves as the coordinating center, the IRB should confirm that the application indicates how the following issues are addressed:

21.6.1. Central review of each site's local IRB approval documents and consent forms.

21.6.2. For federally funded research, confirmation that each participating site has on file a Federal-Wide Assurance (FWA) with Office for Human Research Protection (OHRP).

21.6.3. Method for assuring all sites have the most current version of the protocol.

21.6.4. System to confirm that amendments to the protocol will be communicated to all sites.

21.6.5. Plan for collection and management of data from all sites.

21.6.6. Process for reporting and evaluating protocol events and deviations from participating sites.

22. Retention of Institutional Review Board (IRB) Records

22.1. Policy

It is the policy of Michigan Technological University (MTU) IRB to maintain documentation of all IRB activities in accordance with federal regulations 45 CFR 46.115 and 21 CFR 56.115.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the "Policy").

22.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Study completion date – day when all research-related interventions or interactions with participants have been completed and collection and analysis of identifiable private data are finished.

22.3. Procedure

22.3.1. Prepare and maintain documentation of IRB activities and regulatory requirements to include:

- Copies of all research proposals reviewed;
- Scientific evaluations, if any, that were conducted for review of the research proposals;
- Approved consent document(s);
- Statements of significant new findings that developed during the course of research in which may relate to the subject's willingness to continue participation that were provided to subjects as required by 45 CFR 116(b)(5), 21 CFR 50.25(b)(5);
- IRB review whether conducted by expedited review or the convened IRB (e.g., in Notes, correspondence, IRB reviewer form), including actions taken by reviewer or Board, approval and expiration dates), determinations (e.g., waiver of informed consent, waiver of documentation of informed consent, Subpart-specific determinations), restrictions (e.g., suspensions, contingencies), and reviewers;
- Amendments or modifications to protocols;
- Reportable events, such as unanticipated problems involving risks to subjects;
- Recruitment and advertisement materials;
- Investigator Brochure, drug package inserts and Device Manuals (if applicable);
- Data and Safety Monitoring reports (if applicable);
- Noncompliance findings/reports and documentation of outcomes;
- Reporting to federal regulatory agencies and any interactions with agencies regarding compliance matters;
- Progress reports submitted by the Principal Investigator (PI).

22.3.2. Records of continuing review activities.

22.3.3. Copies of all correspondence between the IRB and the PIs including approval letters and exemption determinations.

22.3.4. IRB Membership.

22.3.4.1. IRB Roster identified by:

- Name;
- Earned degree;
- Representative capacity;
- Experience - each member's experience described sufficiently to identify their anticipated contributions to IRB deliberations (e.g., board certification, licenses);
- Any employment or other relationship between each member and the institution (e.g., full-time employee, part-time employee, paid or unpaid consultant).

22.3.4.2. Curriculum vitae/Resume of each IRB member and appointment letters, and other relevant correspondence involving membership service (e.g., Confidentiality and COI Agreement);

22.3.4.3. Changes in IRB membership that were reported to Office for Human Research Protections (OHRP).

22.3.5. Versions of written IRB SOPs and IRB policies.

22.4. IRB Record Retention and Storage

The IRB records will be retained for at least three (3) years after completion of the research. For federally-supported research, the IRB records will be maintained for at least three years after the end date of the grant or contract.

22.4.1. Paper records for the previous three years are maintained and stored in the IRB office at MTU.

22.4.2. Electronic files and correspondence are on the MTU secure servers.

22.4.2.1. Electronic files are only accessible by the HRPP Administrator, IRB Staff, and MTU administrators responsible for oversight of the MTU IRB.

22.4.2.2. Records will be accessible for inspection and copying by authorized representatives of the Food and Drug Administration (FDA), Office of Research Protection (OHRP) or any other authorized agency at reasonable times and in a reasonable manner.

22.4.2.3. The HRPP Administrator will obtain and/or make copies of requested records.

22.4.3. Meeting minutes must be retained until all of the studies that were reviewed at that meeting have been completed for at least three years.

22.5. Minutes of Convened IRB Meetings

Meeting minutes provide a summary of what occurred during a convened meeting.

22.5.1. Minutes will be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions, including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research and a written summary of the discussion of controverted issues and their resolution.

22.5.2. Meeting minutes are electronically prepared after each meeting by the HRPP Administrator.

22.5.3. Minutes are reviewed and signed by the IRB Chair and the HRPP Administrator.

22.5.4. Minutes will be reviewed and approved by the board members at the next convened meeting.

22.5.5. Meeting minutes are stored electronically on the MTU secure server in the IRB file and a paper copy is kept in a binder in the HRPP Administrator's office.

23. Research Record Retention Requirements for Investigators

23.1. Purpose

Michigan Technological University (MTU) requires that investigators maintain research records for approved human subject protocols in accordance with federal and institutional requirements. The data stored must be kept in a secure, protected manner in accordance with MTU Institutional Review Board (IRB) guidance as posted on the MTU web site, or in accord with other MTU policies. Requirements for specific types of research are noted below.

This requirement to retain study records and to account for disclosures also applies to research that involves the secondary use of medical records or other identifiable health information.

23.2. Policy

23.2.1. Retention of Records Collected During the Conduct of Human Subjects Research:

Unless otherwise required by this SOP, MTU requires study records to be retained (at a minimum) of three years after the completion of the research or the end of the grant - whichever comes last.

23.2.1.1. Exceptions: Where questions have been raised regarding the validity of published data, the Principal Investigator (PI) must preserve original data until such questions have been resolved to the satisfaction of the Institution and any involved government agencies. The PI, unless otherwise required by the Dean of a School or the Department Chair, must decide whether to preserve original data beyond the three-year requirement.

23.2.2. Food and Drug Administration (FDA) Regulations:

23.2.2.1. For Investigational New Drug (IND) research involving drugs, biologics, and other “test articles,” the FDA requirements must be met. Sponsors and investigators must retain “records and reports required by this part for 2 years after a marketing application is approved for the drug; or if an application is not approved for the drug, until 2 years after shipment and delivery of the drug for investigational use is discontinued and the FDA so notified” [21 CFR 312.61(c)].

23.2.2.2. For Investigational Device Exemption (IDE) research, the FDA requires the investigator or sponsor to maintain the records “for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a

premarket approval application or a notice of completion of a product development protocol".

24. Principal Investigator (PI) Responsibilities

24.1. Purpose

All Principal Investigators, co-investigators, research staff, and employees who have any responsibility for the conduct of human subjects research conducted under the auspices of the Michigan Technological University (MTU) must comply with this policy.

This Policy defines who can serve as a Principal Investigator of a study at MTU and the responsibilities of PIs and Research Personnel.

These procedures supplement the Requirement for IRB Approval and IRB Authority Policy (the “Policy”).

24.2. Definitions

All terms used in these procedures have the same meaning set forth in the Policy, unless otherwise defined in these procedures.

Human subject - a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.

Identifiable information - the identity of the subject is or may be readily ascertained by the investigator or is associated with the information.

Interaction - includes communication or interpersonal contact between investigator and subject.

Intervention - includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Principal Investigator - the individual who is responsible for the conduct of the human research study.

Private Information - information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taken place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Research - a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Research Personnel - any co-investigators, research nurses, research managers, research coordinators, technicians, lab personnel, data coordinators, or any other employee assigned responsibilities for the conduct, oversight, or analysis and publication of research data.

Sponsor-Investigator - an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug, device, or biologic is administered or dispensed. The term does not include any other person other than an individual. The requirements applicable to a sponsor-investigator under 21 CFR 312 for drugs or biologics or 21 CFR 812 for devices include both those applicable to an investigator and a sponsor.

24.3. Who May Serve as a Principal Investigator (PI) of a Research Study Involving Human Subjects?

The right to serve as Principal Investigator (PI) on research involving human subjects is granted to any staff or faculty member specified in MTU's eligibility policy whom the IRB determines has the appropriate expertise to conduct the study.

24.4. Principal Investigator (PI) Responsibilities

The Principal Investigator (PI) directs a research project or program and is responsible for the design, conduct, fulfilling safety and regulatory reporting requirements and publication of research findings.

The PI is responsible for:

24.4.1. The protection of human subjects and the ethical conduct of research;

24.4.2. Ensuring that the research is conducted in compliance with MTU policies and procedures, and all state and federal regulatory requirements;

24.4.3. Obtaining IRB approval prior to initiation of any research involving human subjects;

24.4.4. Oversights of the research study and research personnel staff to ensure that the study is conducted in accordance with the IRB-approved protocol;

24.4.5. Appropriate delegation of responsibilities of the study to co-investigators and research staff and for ensuring that responsibilities are delegated to individuals who are qualified and appropriately trained to conduct those responsibilities;

24.4.6. Obtaining informed consent and data from human subjects in a manner consistent with federal regulations and in accordance with an IRB-approved protocol;

24.4.7. Ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject;

24.4.7.1. If a change was temporarily implemented without prior IRB approval in order to avoid immediate harm to subjects, the investigator must

notify the IRB within five (5) working days, with submission of a Modification in Research Form, or minimally by email or letter.

24.4.8. Safety monitoring of human subjects to ensure that potential risks to subjects are eliminated or minimized to the extent possible;

24.4.9. Submitting prompt reports of any unanticipated problems involving risks to subjects or others to the designated IRB;

24.4.10. Submitting prompt reports of non-compliance with federal regulations, protocol violations, research misconduct to the MTU IRB regardless of whether the investigator is relying on an internal or external IRB (i.e., non-MTU IRB); in addition, submitting prompt reports of non-compliance with the external IRB's policies, when relying on an external IRB.

24.4.11. When conducting a clinical trial, for providing reasonable medical care to ameliorate medical problems that arise during or at the end of a study that appear to be potentially related to the research, or referring to another provider when a consult is appropriate (the compensation of such care will be provided in accordance with the plan in the contract, IRB-approved protocol, or informed consent form);

24.4.12. Maintaining confidentiality of human subject data in accordance with the IRB-approved protocol. When the research involves Protected Health Information (PHI) or highly sensitive data (e.g., social security numbers, illicit drug use or other criminal activity, etc.), ensuring data security of the information to prevent a breach of confidentiality;

24.4.13. Submitting continuing review reports to the IRB in a timely manner; and,

24.4.14. The integrity of the analysis of data and the publication of results/findings.

24.4.15. Ensure that all research-related activities, interventions, or interactions with human subjects have been completed prior to submitting the Closure Form to the IRB.

24.4.16. Investigator responsibility after study closure:

24.4.16.1. Research records must be retained for at least three years after completion of the research and the records shall be accessible for inspection.

24.4.16.2. For federally supported research, three years after the end date of the grant or contract.

24.4.16.3. For research that includes Protected Health Information (PHI), the records must be maintained for at least six years after completion of the study.

24.4.16.4. Continue to maintain confidentiality and data security for identifiable private data after completion.

24.4.16.5. If the investigator seeks to use previously collected identifiable data after the IRB has approved permanent closure, the PI must submit a new application for IRB review and approval.

24.5. Principal Investigator (PI) Leaving MTU

24.5.1. The PI is responsible for ensuring that their research-related duties are appropriately transitioned or completed before officially exiting their position.

24.5.2. The PI must contact the MTU IRB within 60 days of leaving MTU.

24.5.3. PI must submit an amendment/modification transferring the study to another PI or a Closure of Study submission.

24.5.4. If the subjects are still participating in the research study, the IRB recommends the PI provide the subjects with a letter to update them of the change in PI and to update them regarding changes in relevant telephone numbers (e.g., for study-related questions) and addresses e.g., to withdraw authorization).

24.5.5. If Criteria for Closing a Study are met, a Closure Form may be submitted instead of an amendment/modification for transfer.

24.5.6. All changes must be reviewed and approved by the IRB prior to the change being implemented (except to eliminate hazards to subjects).

24.5.7. If the study is funded, the PI must notify the Sponsor of the change in status.

24.5.8. All study related records will remain at MTU, unless specifically approved by MTU.

24.6. Sponsor Investigators

The PI has additional responsibilities if she/he serves as a sponsor-investigator. In such situations, the PI must adhere to all FDA regulatory requirements (i.e., 21 CFR 50, 54, 56, 312, 600, and 812), state regulations, and MTU policies and compliance with ICH-E6 (R2) version of Good Clinical Practice (GCP) Guidelines, and:

24.6.1. If the study is sponsored/supported by the National Institutes of Health, the PI must complete a Good Clinical Practice course that includes ICH-E6 (R2) GCP guidelines.

24.6.2. Must submit an Investigational New Drug (IND) application for any new investigational drug or biologic in accordance with 21 CFR 312 or 21 CFR 600, respectively; or an Investigational Drug Exemption (IDE) for investigational devices in accordance with 21 CFR 812.

24.6.3. The investigator must comply with the investigator agreement and any Clinical Trial Agreement (CTA) between MTU and the sponsor;

24.6.4. Must comply with the sponsor and investigator responsibilities of 21 CFR 312 when conducting a clinical trial involving an investigational drug and 21 CFR 812 when conducting a clinical trial involving a significant risk device;

24.6.5. Must maintain an Investigator Site File (commonly called a Regulatory Binder) that includes all regulatory documentation for the study.

24.6.6. Must maintain appropriate drug/device/biologic accountability records to ensure accurate documentation of all dispensations and receipt of investigational product. It is recommended that all investigational drugs are managed and stored by a research pharmacy. If kept by the investigator, the PI must ensure appropriate storage and security of the investigational product to ensure its integrity and safety.

24.7. Protocol Personnel / Research Staff

Research Personnel (i.e., co-investigators, research nurses, research managers, research coordinators, technicians, lab personnel, data coordinators, etc., or any other partner assigned responsibilities for the conduct, oversight, or analysis and publication of research data) that will interact with human subjects during the course of research, or will have access to identifiable human subject data, must be listed on the Notification of New Research Study form.

Research Personnel are responsible for the ethical conduct of research and for adhering to the procedures in an IRB-approved protocol that were delegated to them by the PI. Research Personnel are also responsible for complying with federal regulations and MTU policies and procedures pertaining to human subject's research. Research Personnel are responsible for reporting any adverse events or unanticipated problems to the PI.