1 Human Research Protection Program (HRPP)

Central Michigan University (CMU) fosters a research environment that promotes respect for the rights and welfare of individuals participating in research conducted at or under the auspices of CMU. In reviewing and conducting research, CMU will be guided by the principles of respect for persons, beneficence, and justice set forth in the ***Ethical Principles and Guidelines for the Protection of Human Subjects of Research***. In addition, CMU will be guided by the idea of respect for community as well. The actions of CMU will also conform to all applicable federal, state, and local laws and regulations. CMU has established a Human Research Protections Program (HRPP) to fulfill this commitment.

1.1 Mission

The mission of the HRPP is to:

1. safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected;
2. provide timely and high-quality education, review and monitoring of human research projects; and
3. facilitate excellence in human subjects research.

The HRPP includes mechanisms to:

1. Establish a formal process to monitor, evaluate, and continually improve the protection of human research participants.
2. Dedicate resources sufficient to do so.
3. Exercise oversight of research protection.
4. Educate investigators and research staff about their ethical responsibility to protect research participants.
5. When appropriate, intervene in research and respond directly to concerns of research participants.

1.2 Institutional Authority

The CMU HRPP operates under the authority of the Central Michigan University policy "Human Subject Research (HSR)" adopted on July 1, 2011. Human subject research is defined as a systematic, scientific investigation that can be either interventional (a trial) or observational (no test article) and involves human beings as the research subjects. As stated in that policy, the operating procedures in this document "serve as the governing procedures for the conduct and review of all human research conducted under the auspices of CMU." The HSR Policy and these operating procedures are made available to all CMU investigators and research staff and are posted on the HRPP website.

1.3 Definitions

Common Rule –The Common Rule refers to the "Federal Policy for the Protection of Human Subjects" adopted by a number of federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

The provisions of the revised Common Rule, which were is scheduled to be implemented in January 2018 but delayed until July 2018, have been adopted by the CMU. Until the revised Common Rule is formally implemented by the Common Rule agencies, CMU IRB will apply revised Common Rule provisions only to research not funded by or subject to regulation by federal agencies.

Engagement – Institutions are considered "engaged" in a research project when the involvement of their employees or agents in that project includes any of the following:

1. Intervention for research purposes with any human subjects of the research by performing invasive or noninvasive procedures.
2. Intervention for research purposes with any human subject of the research by manipulating the environment.
3. Interaction for research purposes with any human subject of the research.
4. Obtaining the informed consent of human subjects for the research.
5. Obtaining for research purposes identifiable private information or identifiable biological specimens from any source for the research. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to
   a. observing or recording private behavior;
   b. using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and
   c. using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

Human subject means a living individual about whom an investigator (whether professional or student) is conducting research:

1. Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
2 Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

For research covered by FDA regulations (21 CFR 50 and 56), "human subject" means an individual who is or becomes a participant in a clinical investigation (as defined below), either as a recipient of the test article or as a control. A subject may be in normal health or may have a medical condition or disease. In the case of a medical device, a human subject/participant also includes any individual on whose tissue specimen an investigational device is used or tested.

Note: The terms "subject" and "participant" are used interchangeably in this document and have the same meaning.

Human Subjects Research means any activity that meets the definition of "research" and involves "human subjects" as defined by either the Common Rule or FDA regulations.

Research – The Common Rule defines research as a systematic investigation, including research development, testing, and evaluation that is designed to develop or contribute to generalized knowledge.

For the purposes of this policy, a "systematic investigation" is an activity that involves a prospective study plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a study question. Investigations designed to develop or contribute to generalizable knowledge are those designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.

Additional Definitions: Sec 18.

1.4 Ethical Principles

Central Michigan University is committed to conducting research with the highest regard for the welfare of human subjects. It upholds and adheres to the principles of *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research* by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (1979). These principles include:

Respect for Persons, which is ensured by obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations.

Beneficence, which is assured by ensuring that possible benefits are maximized and possible risks are minimized.

Justice, which is the equitable selection of subjects.

1.5 Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law, and institutional policies. All human subjects research at CMU is conducted in accordance with federal regulations 45 CFR 46 and 21 CFR 50 and 56. The actions of CMU will also conform to all other applicable federal, state, and local laws and regulations.

CMU voluntarily applies the International Conference on Harmonization (ICH) Good Clinical Practices (GCP) Guidelines (sometimes referred to as ICH-GCP or E6) to certain types of human subject's research conducted under its HRPP only to the extent that they are compatible with FDA and DHHS regulations.

1.6 Federalwide Assurance (FWA)

Federal regulations require that federally-funded human subjects research only be conducted at facilities covered by a Federalwide Assurance (FWA) approved by the DHHS Office for Human Research Protections (OHRP). CMU has an OHRP-approved Federalwide Assurance. The FWA designates the Institutional Review Board that will review and oversee the research, specifies the ethical principles under which the research will be conducted, and names the individuals who will be responsible for the proper conduct of the research.

In its FWA, CMU has opted to limit the application of the FWA to research funded by DHHS or federal agencies that have adopted the Common Rule.

CMU reserves the right to apply "equivalent protections" to research that is not funded or otherwise subject to oversight by an agency that has adopted the Common Rule.

1.7 Research Covered by the HRPP

The CMU Human Research Protection Program Human covers all research involving human subjects that is conducted by agents of CMU or conducted under the auspices of CMU, regardless of funding.

1.8 Written Policies and Procedures

The "CMU Standard Operating Procedures for Human Research Protection" details the policies and regulations governing research with human subjects and the requirements for submitting research proposals for review by the CMU IRB. The Director of the Office of Research Compliance (DRC) is responsible for implementing changes in procedures necessary to comply with changes in federal regulations as well as other changes dictated by the IRB. The policies and procedures are reviewed every 3 years or as needed to respond to regulatory changes. The Institutional Official (IO) will approve all revisions of the policies and procedures.

The DRC will keep the Central Michigan University research community apprised on the IRB website and through campus electronic newsletters of new information that may affect the HRPP, including laws, regulations, policies, procedures, and emerging ethical and scientific issues. The policies and procedures will be available on the CMU IRB website.

1.9 HRPP Organization

The HRPP is a comprehensive system to ensure the protection of human subjects participating in research. It consists of various individuals and committees, such as the IO, the DRC, the IRB, other committees or subcommittees addressing human subject protection (e.g., Biosafety, Radiation Safety, Conflict of Interest), investigators, IRB staff, research staff, and health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer). The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

The following officials, administrative units, and individuals have primary responsibilities for implementing the HRPP.

1.9.1 Institutional Official

The ultimate responsibility of the HRPP resides with the Vice President for Research and Dean of Graduate Studies (VPR/DGS), who serves as the Institutional Official (IO) of the HRPP. The IO is responsible for ensuring the CMU HRPP has the resources and support necessary to comply with all institutional policies, federal regulations, and state laws that govern human subjects research. The IO is legally authorized to represent CMU, is the signatory of the FWA, and assumes the obligations of the FWA.

The IO also holds ultimate responsibility for:

1. oversight of the Institutional Review Board (IRB);
2. oversight over the conduct of research conducted by all CMU investigators;
3. assuring that IRB members are appropriately trained to review research in accordance with ethical standards and applicable regulations;
4. assuring that all investigators are appropriately trained to conduct research in accordance with ethical standards and applicable regulations.

1.9.2 Director Office of Research Compliance

The Director of the Office of Research Compliance (DRC) is appointed by and reports to the IO and is responsible for:

1. Developing, managing and evaluating policies and procedures that ensure compliance with all state and federal regulations governing research. This includes monitoring changes in regulations and policies that relate to human research protection and overseeing all aspects of the HRPP program.
2. Advising the IO on key matters regarding research at CMU.
3. Implementing the institution's HRPP policy and standard operating procedures.
4. Submitting, implementing, and maintaining an approved FWA through the VPR/DGS and the Department of Health and Human Services Office of Human Research Protection (OHRP).
5. Submits reports to AAHRPP to maintain accreditation.
6. Managing the budget of the CMU HRPP.
7. Assisting investigators in their efforts to carry out Central Michigan University's research mission.
8. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program.
9. Developing and implementing educational plans for IRB members, staff, and investigators.
10. Developing training requirements as mandated and appropriate for investigators, subcommittee members, and research staff, and ensuring that training is completed on a timely basis.
11. Exercising day-to-day responsibility for the operation of the HRPP office, including supervision of HRPP staff.
12. Responding to questions from faculty, students, and staff.
13. Working closely with the Chair of the IRB and on the development of policy and procedures as well as organizing and documenting the review process.

1.9.3 Institutional Review Board (IRB)

IRB members are appointed by the IO. The IRB prospectively reviews and make decisions concerning all human subjects research conducted at CMU facilities by its employees or agents or under its auspices. The IRB is responsible for protecting the rights and welfare of human research subjects at the CMU. It discharges this duty by complying with the requirements of the Common Rule, state regulations, the FWA, and institutional policies [See Section 2 for a detailed discussion of the IRB].

1.9.4 Investigator

The investigator is the ultimate protector of the human subjects who participate in research. The investigator must abide by the highest ethical standards and must a protocol that incorporates the principles of the *Belmont Report*. The investigator is expected to conduct research in accordance with the approved research protocol and to oversee all aspects of the research by providing supervision of support staff, including oversight of the informed consent process. All subjects must give informed consent (unless this condition is explicitly waived by the IRB), and the investigator must establish and maintain an open line of communication with all research subjects within his/her responsibility. In addition to complying with all the policies and standards of the governing regulatory bodies, the investigator must comply with institutional and administrative requirements for conducting research. The investigator is responsible for ensuring that all research staff complete appropriate training and must obtain all required approvals prior to initiating research. When investigational drugs or devices are used, the investigator is responsible for providing and following written procedures for their storage, security, dispensing, and disposal.

1.9.5 Office of General Counsel

The CMU HRPP relies on Central Michigan University Office of General Counsel for the interpretations and applications of Michigan law and the laws of any other jurisdiction where research is conducted as they apply to human subjects research.

1.9.6 Office of Sponsored Programs

Office of Sponsored Programs staff review all research agreements with federal and state sponsors, and research agreements from foundation or non-profit sponsors that are not processed through the CMU Advancement Office. This institutional review ensures that all terms of the award are in compliance with institutional policies. Only designated senior individuals within the Office of Sponsored Programs have the authority to approve research proposals and to execute research agreements on behalf of the institution. As a further control, internal documents retained by the Office of Sponsored Programs as part of the application process for extramural funding include a copy of the proposal submitted to the external agency, the proposed budget, the financial disclosure statement, and the internal transmittal document.

When the grant or contract agreement includes activities that will be conducted by investigators who are not employees or agents of CMU, and where funding will be provided to the collaborating institution, a subcontract is executed between CMU and the collaborating institution. If human subject research is involved, the subcontract includes the requirement for the collaborating institution to assure compliance with federal regulations for the protection of human subjects in research, including any training requirements for personnel. The collaborating institution must maintain documentation of compliance fulfilment of all federal, sponsor, and institutional requirements and provide it to CMU upon request.

1.9.7 Office of Information Technology

The HRPP has established a very close working relationship with the Office of Information Technology. OIT Directors from various academic units: sit on the IRB and actively participate in

protocol review; offer technical assitance to investigators developing applications to conduct research involving human subjects; and offer educational presentations for the board.

1.9.8 Office of Risk Management

The IRB consults the Office of Risk Management when questions arise about liability insurance coverage for investigators conducting research in other states or countries.

1.9.9 Relationship Among Components

The IRB functions independently of, but in coordination with, other institutional regulatory committees. The IRB, however, makes its independent determination whether to approve, require modifications in order to secure approval, or disapprove a protocol based upon whether human subjects are adequately protected.

1.10 HRPP Operations

1.10.1 HRPP Office

Operation of the office is the responsibility of the DRC assisted by clerical and other support staff in the Office of Research Compliance.

1.10.2 Director of the Office of Research Compliance

The Director of the Office of Research Compliance (DRC) is responsible for all aspects of the IRB throughout the review process of a research proposal involving human subjects. This responsibility includes the initial review of documents and screening of research proposals prior to their review by the IRB as well as serving as the liaison, if needed, between the investigators and the IRB. The DRC reviews the IRB minutes for accuracy and ensures proper documentation of discussions, including controverted issues discussed and actions taken by the IRB during its convened meetings.

1.10.3 Selection, Supervision, and Evaluation of HRPP Supporting Staff

All HRPP staff who support the IRB and HRPP are selected by the DRC according to CMU Human Resources policies and procedures.

1.11 HRPP Resources

The HRPP Office is located in Foust Hall and has the necessary office, meeting, and storage space and equipment to perform the functions required by the HRPP. The adequacy of personnel and non-personnel resources of the HRPP program is assessed annually by the DRC in consultation with the HRPP staff.

The CMU IO provides resources to the IRB and HRPP Office, including adequate meeting and office space, and staff for conducting IRB business. Office equipment and supplies, including technical support, file cabinets, computers, internet access, and copy machines, are made available to the IRB and staff. Resources provided for the IRB and HRPP Office are reviewed by the DRC and IO during the annual budget review process.

1.12 Conduct of Quality Assurance/Quality Improvement Activities

The objective of Central Michigan University's HRPP Quality Assurance / Quality Improvement Plan is to measure and improve human research protection effectiveness, efficacy, and compliance with organizational policies and procedures and applicable federal, state, and local laws. The Quality Assurance / Quality Improvement Plan will be managed and implemented by the DRC.

1.12.1 Investigator Audits and Compliance Reviews

Directed ("for cause") audits and periodic (not "for cause") compliance reviews will be conducted to assess investigator compliance with federal, state, and local laws as well as Central Michigan University policies; identify areas for improvement; and suggest process improvements. Directed audits of IRB-approved research studies are authorized by the IRB Chair in response to identified concerns. Periodic compliance reviews are conducted using a systematic method to review IRB-approved research on a regular basis. The results are reported to the IO and the IRB Chair.

Activities of auditors during directed audits and periodic compliance reviews may include, but are not limited to:

1. Requesting progress reports from researchers;
2. Evaluating the integrity of data security;
3. Examining investigator-held research records;
4. Contacting research subjects;
5. Observing research sites where research involving human research subjects and/or the informed consent process is being conducted;
6. Evaluating advertisements and other recruiting materials as deemed appropriate by the IRB;
7. Reviewing projects to verify from sources other than the researcher that no unapproved changes have occurred since previous review;
8. Monitoring conflict of interest concerns to assure the consent documents include the appropriate information and disclosures;
9. Monitoring HIPAA or FERPA authorizations;
10. Conducting other monitoring or auditing activities as deemed appropriate by the IRB.

1.12.2 External Site Audits and Compliance Reviews

External directed audits and periodic compliance reviews will be conducted, as needed, at non-Central Michigan University sites, where the CMU IRB serves as the "IRB of Record," to assess compliance with federal, state, and local law; research subject safety; and IRB policies and procedures. These reviews may include items listed in section 1.12.1 above. Operational deficiencies are discussed with the IRB Chair and remediation plans are developed.

1.12.3 Disposition of Quality Assurance Reports

The results of all quality assurance activities are reported to the DRC and the IRB Chair. Any noncompliance will be handled according to the procedures in Section 10. If an audit or review finds that subjects in a research project have been exposed to unexpected serious risk, the reviewer will promptly report such findings to the DRC and the IRB Chair for immediate action.

1.12.4 HRPP Internal Compliance Reviews

Internal directed audits and random internal compliance reviews will be conducted. The results may impact current practices, may require additional educational activities, and will be reported to the VPR/DGS. The DRC or designee will:

1. Review the IRB minutes to determine that adequate documentation of the meeting discussion has occurred. This review will include assessing the documentation surrounding the discussion for protections of vulnerable populations as well as other risk/benefit ratio and consent issues that are included in the criteria for approval;
2. Assess the IRB minutes to assure that a quorum was met and maintained;
3. Assess the current adverse-event reporting process;
4. Assess privacy provisions, according to HIPAA, have been adequately reviewed, discussed, and documented in the IRB minutes;
5. Evaluate the continuing review discussions to assure they are substantive and meaningful and that no lapse has occurred since the previous IRB review;
6. Observe IRB meetings or other related activities;
7. Review IRB files to assure retention of appropriate documentation and consistent organization of the IRB file according to current policies and procedures;
8. Review the IRB database to assure tasks are completed accurately;
9. Verify that reviews are completed;;
10. Verify IRB approvals for collaborating institutions or external performance sites;
11. Review the appropriate metrics (e.g., time from submission to first review) to evaluate the quality, efficiency, and effectiveness of the IRB review process;
12. Review the workload of IRB staff to evaluate appropriate staffing level;
13. Perform other monitoring or auditing activities deemed appropriate by the IRB.

The IO will review the results of internal compliance reviews with the DRC. If any deficiencies are noted in the review, a corrective action plan will be developed by the DRC and approved by the IO. The DRC will be responsible for implementing the corrective action plan, the results of which will be evaluated by the IO.

1.12.5 Quality Improvement

All quality assurance reports, both research-related and HRPP-related, will be reviewed by the DRC and the IO to determine if systemic changes are required in the HRPP to prevent re-occurrence of noncompliance. If so, a corrective action plan will be developed, implemented, and evaluated by the DRC and IO.

1.12.6 Examples of Quality Improvement and Quality Assessment Activities

An example of an objective to achieve or maintain compliance would be determining whether IRB minutes meet standards listed at Sec 4.3 of these SOPs. The measure of compliance is the percentage of required elements that are consistently present in the minutes. The method to assess compliance is to use a checklist based on the required elements (at Sec 4.3 of these SOPs) and evaluate minutes for 6-month blocks of time.

An example of efficiency of IRB operations is timely review of protocols using exemption determinations, expedited review procedures and review at convened meeting. Efficiency is measured by time to complete a review of a protocol. The efficiency is assessed by comparing our data to data published by AAHRPP.

1.13 Collaborative Research Projects

In the conduct of collaborative research projects, CMU acknowledges that each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. When CMU is engaged in only part of a cooperative research project, the CMU IRB only needs to approve the part(s) of the research in which the CMU investigator is engaged. For example, if CMU is operating the statistical center for a multicenter trial that receives identifiable private information from multiple other institutions, the CMU IRB reviews and approves the research activities related to the receipt and processing of the identifiable private information by the statistical center.

When a cooperative agreement exists, CMU may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. A formal relationship must be established between Central Michigan University and the other institution through either a Cooperative Agreement or a Memorandum of Understanding. This relationship must be formalized before Central Michigan University will accept any human research proposals from the other institution or rely on the review of the other institution.

It is the policy of CMU to assure that all facilities participating in a human subjects study receive adequate documentation about the study to protect the interests of study participants. Before a study can begin, it must be approved by the IRBs of record for each participating facility and, where appropriate, the IRB of record for the coordinating facility.

For collaborative research, the PI must identify all institutions participating in the research, the responsible IRB(s), and the procedures for dissemination of protocol information (e.g., IRB initial and continuing approvals, relevant reports of unanticipated problems, protocol modifications, and interim reports) among all participating institutions.

When CMU relies on another IRB, the DRC will review the policies and procedures of the IRB to ensure that they meet CMU standards. If the other IRB is part of an accredited HRPP, then it will be assumed that adequate protections are in place to protect human subjects.