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1 Human Research Protection Program

The University of Mississippi Medical Center (UMMC) fosters a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of UMMC. In support of this, UMMC has established a Human Research Protection Program (HRPP). The UMMC HRPP, in partnership with its research community, is responsible for ensuring the ethical and equitable treatment of all human research participants conducted under UMMC’s auspices.

1.1 Mission

The mission of the HRPP is to:

- Safeguard and promote the health and welfare of participants in human research by ensuring that their rights, safety and well-being are protected;
- Provide guidance and support to the research community in the conduct of human research;
- Assist the research community in ensuring compliance with relevant laws and regulations;
- To provide timely and high quality education, review and monitoring of human research projects; and
- To facilitate excellence in human research.

The HRPP includes mechanisms to:

- Monitor, evaluate and continually improve the protection of human research participants;
- Dedicate resources sufficient to do so;
- Exercise oversight of research protection;
- Educate investigators and research staff about their ethical responsibility to protect research participants;
- When appropriate, intervene in research and respond directly to concerns of research participants.

1.2 Institutional Authority

UMMC’s HRPP operates under the authority of the Organization policy “Human Research Protection Program (HRPP)”. 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 jurisdiction of the UMMC.” The HRPP Policy and these operating procedures are made available to all UMMC investigators and research staff and are posted on the Human Research Office website, http://www.umc.edu/irb/.
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 Common Rule was updated in 2018, throughout this manual references to the “pre-2018 Common Rule” (or requirements) apply to studies approved or determined exempt prior to January 21, 2019 that have not been transitioned to comply with the 2018 Common Rule. References to the “2018 Common Rule” (or requirements) or the “revised Common Rule” apply to studies approved or determined exempt on or after January 21, 2019.

**Clinical Trial.** As defined in the 2018 Common Rule and NIH Policy, clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions on biomedical or behavioral health-related outcomes. FDA regulations refer to “clinical investigations” (see definition of “research” below).

**Human Subjects Research.** 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. Note: The terms “subject” and “participant” are used interchangeably in this document.

**Research.** The Common Rule defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. Activities which meet this definition constitute research whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

For purposes of this part [the Common Rule], the following activities are deemed not to be research: (1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected. (2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters). (3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes. (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. [45 CFR 46.102(l)]
For the purposes of this policy, a “systematic investigation” is an activity that involves a prospective study plan which 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.

The FDA has defined “research” as being synonymous with the term “clinical investigation”. A clinical investigation, as defined by FDA regulations, means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under Sections 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)]

Experiments that must meet the requirements for prior submission to the Food and Drug Administration under Section 505(i) of the Federal Food, Drug, and Cosmetic Act means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]

Experiments that must meet the requirements for prior submission to the Food and Drug Administration under Section 520(g) of the Federal Food, Drug, and Cosmetic Act means any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)]

Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is considered to be FDA-regulated research. [21 CFR 50.3(c), 21 CFR 56.102(c)]

**Human Research Participant/Human Subject.** A human subject as defined by the Common Rule is a living individual about whom an investigator conducting research (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. [45 CFR 46.102(e)(1)]

- **Intervention** means both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes. [45 CFR 46.102(e)(2)]
- **Interaction** means communication or interpersonal contact between investigator and subject.
- **Private information** means 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 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).

- **Identifiable private information** means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information. [45 CFR 46.102(e)(5)].

- **Identifiable biospecimen** means a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen [45 CFR 46.102(e)(6)]

**Legally authorized representative** means 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.

**Public health authority** means an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate.

For research covered by FDA regulations, human subject means an individual who is or becomes a participant in a clinical investigation, 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 specimen an investigational device is used or tested or used as a control.

**Test Article.** The FDA defines “Test article” as any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act [42 U.S.C. 262 and 263b-263n]. [21 CFR 50.3(j)]

Test articles covered under the FDA regulations include, but are not limited to:

a) **Human drugs** – The primary intended use of the product is achieved through chemical action or by being metabolized by the body. A drug is defined as a substance recognized by an official pharmacopoeia or formulary; a substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; a substance (other than food) intended to affect the structure or any function of the body; a substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device. Biological products are included within this definition and are generally covered by the same laws and regulations, but differences exist regarding their manufacturing processes (chemical process versus biological process.) [http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm](http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm)

b) **Medical Devices** - A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or
the United States Pharmacopoeia, or any supplement to them; intended for use in the
diagnosis of disease or other conditions, in the cure, mitigation, treatment, or
prevention of disease, in man or other animals; or intended to affect the structure or
any function of the body of man or other animals, and which does not achieve any of its
primary intended purposes through chemical action within or on the body of man or
other animals and which is not dependent upon being metabolized for the achievement
of any of its primary intended
purposes." [http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overvie
w/ClassifyYourDevice/ucm051512.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overvie
w/ClassifyYourDevice/ucm051512.htm)

c) **Biological Products** - include a wide range of products such as vaccines, blood and blood
components, allergenics, somatic cells, gene therapy, tissues, and recombinant
therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or
complex combinations of these substances, or may be living entities such as cells and
tissues. Biologics are isolated from a variety of natural sources — human, animal, or
microorganism — and may be produced by biotechnology methods and other cutting-
edge technologies. Gene-based and cellular biologics, for example, often are at the
forefront of biomedical research, and may be used to treat a variety of medical
conditions for which no other treatments are
available. [http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm](http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm)

d) **Dietary Supplements** – A dietary supplement is a product taken by mouth that is
intended to supplement the diet and that contains one or more "dietary ingredients." The "dietary ingredients" in these products may include vitamins, minerals, herbs or
other botanicals, amino acids, and other substances found in the human diet, such as
enzymes. When a dietary supplement meets the definition of drug, it is regulated as
such.

e) **Medical Foods** – A medical food, as defined in section 5(b) of the Orphan Drug Act (21
U.S.C. 360ee (b) (3)), is a food which is formulated to be consumed or administered
enterally under the supervision of a physician and which is intended for the specific
dietary management of a disease or condition for which distinctive nutritional
requirements, based on recognized scientific principles, are established by medical
evaluation.

f) **Mobile Medical Apps** - Mobile apps are software programs that run on smartphones
and other mobile communication devices. They can also be accessories that attach to a
smartphone or other mobile communication devices, or a combination of accessories
and software. Mobile medical apps are medical devices that are mobile apps, meet the
definition of a medical device and are an accessory to a regulated medical device or
transform a mobile platform into a regulated medical device.

g) **Radioactive Drugs** – The term radioactive drug means any substance defined as a drug
which exhibits spontaneous disintegration of unstable nuclei with the emission of
nuclear particles or photons and includes any nonradioactive reagent kit or nuclide
generator which is intended to be used in the preparation of any such substance but
does not include drugs such as carbon-containing compounds or potassium-containing
salts which contain trace quantities of naturally occurring radionuclides. The term "radioactive drug" includes "radioactive biological product".

h) **Radiation-Emitting Electronic Products** - a radiation-emitting electronic product as any electrically-powered product that can emit any form of radiation on the electromagnetic spectrum. These include a variety of medical and non-medical products such as mammography devices, magnetic resonance imaging (MRI) devices, laser toys, laser pointers, liquid crystal displays (LCDs), and light emitting diodes (LEDs).

### 1.4 Ethical Principles

UMMC is committed to conducting research with the highest regard for the welfare of human research participants. With the exception of transnational research, where consideration of alternative ethical principles may apply (See Section 25), UMMC 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 are:

1) **Respect for Persons**, which is ensured by obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations.
2) **Beneficence**, which is ensured by assuring that possible benefits are maximized and possible risks are minimized to all human research participants.
3) **Justice**, which is ensured by the equitable selection of research participants.

UMMC’s HRPP, in partnership with its research community, is responsible for ensuring the ethical and equitable treatment of all human participants in research conducted under its jurisdiction.

### 1.5 Regulatory Compliance

The HRPP facilitates compliance with federal regulations, state and local law and organizational policies. Human subjects research at UMMC is conducted in accordance with applicable regulations and requirements including, but not limited to, the following:

Research conducted, supported, or otherwise subject to regulation by any federal department or agency which adopts the Common Rule is reviewed and conducted in accordance with the Common Rule. 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.

Research subject to FDA regulations is reviewed and conducted in accordance with applicable regulations including, but not limited to, 21 CFR 50, 21 CFR 56, 21 CFR 312 and 21 CFR 812.

Research involving the use of Protected Health Information is reviewed and conducted in accordance with the Health Insurance Portability and Accountability Act (HIPAA), 45 CFR Parts 160, 162, and 164.
Research conducted or supported by the U.S. Department of Education (ED) is subject to the Common Rule with regulations published at 34 CFR 97. In addition to the Common Rule, human subjects research involving education records conducted at institutions receiving ED funding must comply with additional requirements, including the Family Educational Rights and Privacy Act (FERPA) (34 CFR 99) and the Protection of Pupil Rights Amendment (PPRA) (34 CFR 98). Investigators should consult these regulations and resources provided by ED when developing their research protocol. The IRB will evaluate the research in accordance with these regulations when applicable. See the Special Topics section of this manual for more information.

Research supported by the Department of Defense (DoD) is reviewed and conducted in compliance with 32 CFR 219, 10 USC 980, applicable parts of title 21 CFR (50, 56, 312, 600, 812), DoD Instruction 3216.02, DoD Directive 3210.07, and applicable additional requirements from respective DoD component(s). See the Special Topics section of this manual for more information.

Research conducted or supported by the Department of Justice (DoJ) is subject to the pre-2018 Common Rule, including Subpart C, with regulations published at 28 CFR 46. The DoJ has established additional requirements for research conducted with the federal Bureau of Prisons (28 CFR 512) and research involving the National Institute of Justice (28 CFR 22). Investigators should consult these regulations and resources provided by NIJ when developing their research protocol. The IRB evaluates the research in accordance with these regulations when applicable. See the Special Topics section of this manual for more information.

1.5.1 Management of pre-existing studies subject to the Common Rule

For research subject to the Common Rule, the following outlines when the pre-2018 rule or the revised rule will apply to research conducted at UMMC.

A. Research subject to the pre-2018 Common Rule requirements. The pre-2018 requirements will apply to the following studies, unless a study is transitioned to comply with the revised rule as described in Section B below:

- All studies initially approved, waived under .101(i), or determined exempt before January 21, 2019 will be subject to the pre-2018 requirements through the close of study.
- Studies subject to Department of Justice (DOJ) regulations at 28 CFR 46.

B. Research subject to the revised Common Rule (2018 requirements). The 2018 requirements will apply to the following studies:

- All studies initially approved, waived under .101(i), or determined exempt on or after January 21, 2019 will be subject to the 2018 requirements.
- On or after January 21, 2019, Institutions have the flexibility to transition individual studies described in the first bullet of section A and agree to comply with the 2018 requirements if they so choose. The study must comply with the
revised rule on the date the determination to transition is documented. This option does not apply to research subject to DOJ regulations.

1.6 International Conference on Harmonization-Good Clinical Practice (ICH-GCP)

UMMC applies the International Conference on Harmonization (“ICH”) Good Clinical Practices (“GCP”) Guidelines (sometimes referred to as “ICH-GCP” or “E6”) to industry-sponsored clinical trials of drugs when required by a sponsor or funding agency. UMMC applies the ICH-GCP guidelines only to the extent that they are compatible with FDA, DHHS, and other applicable regulations. See the Special Topics section of this manual for more information.

1.7 Federalwide Assurance (FWA) and IRB Registration

The 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). An FWA is an institution’s assurance to the federal government that human research conducted at that site is in compliance with federal regulations pertaining to the protection of human research participants.

In its FWA, UMMC has opted to limit the application of the FWA to non-exempt human research conducted or supported by DHHS or federal agencies that have adopted the Common Rule.

When human subjects research is not subject to the Common Rule or FDA regulations, UMMC ensures that human research subjects benefit from equivalent protections by applying the Common Rule standards, with purposeful deviations that do not meaningfully diminish protections as noted within this manual.

Likewise, federal regulations require IRBs to register with DHHS if they will review human subjects research conducted or supported by DHHS or research subject to FDA regulations. UMMC’s HRPP/IRB office (Human Research Office) maintains its FWA and IRB registration(s) in accordance with applicable regulations and guidance provided by OHRP and FDA.

The HHS registration system database can be used to verify the status of UMMC’s FWA, IORG, and IRB registration.

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<th>UMMC’s Federal Registration Numbers</th>
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<tr>
<td><strong>FWA</strong></td>
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<td><strong>IRB Registration</strong></td>
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1.8 Research Under the Auspices of UMMC

Research under the auspices of UMMC includes research conducted at or using any property or facility of UMMC, conducted by or under the direction of any employee or agent of UMMC (including students) in connection with his or her UMMC position or responsibilities, or involving the use of UMMC's non-public information (e.g., medical records) to identify, contact, or study human subjects. The research may be externally funded, funded from internal sources, or conducted without direct funding.

All human subjects research under the auspices of UMMC is under the jurisdiction of the UMMC HRPP. Human subjects research in which UMMC is engaged (per OHRP or FDA guidelines) is under the jurisdiction of the UMMC IRB, unless UMMC chooses to rely upon another IRB for review and ongoing IRB oversight of the research (the IRB of record for the research).

Employee or Agent. For the purposes of this document, employee or agent refers to individuals who: (1) act on behalf of the organization; (2) exercise organizational authority or responsibility; or (3) perform organizationally designated activities. “Employees and agents” can include staff, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation.

Engagement. The Department of Health and Human Services (HHS) regulations [45 CFR 46.103(a)] require that an institution “engaged” in human subjects research conducted or supported by a Federal Department or Agency provide the Office for Human Research Protections (OHRP) with a satisfactory assurance of compliance with the HHS regulations, unless the research is exempt under 45 CFR 46.101(b) or 45 CFR 46.104 (2018 rule). “In general, an institution is considered engaged in a particular non-exempt human subjects research project 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.” In general, institutions that receive an award through a grant, contract, or cooperative agreement directly from HHS for the non-exempt human subjects research (i.e. awardee institutions) are also considered engaged in research even where all activities involving human subjects are carried out by employees or agents of another institution.

FDA regulations are oriented to the responsibilities of IRBs, investigators, and sponsors as opposed to institutions. In general, FDA-regulated research conducted in UMMC facilities or by UMMC Principal or Sub-Investigators (as defined on the FDA 1572 or delegation of responsibilities log) requires review by a UMMC-designated IRB. Exceptions to this requirement may be granted on a case-by-case basis (e.g., when UMMC’s involvement in the research is limited to the provision of a common diagnostic procedure and associated reading or analysis).

The Human Research Office Director, with the assistance of an IRB Chair or Vice Chair, Human Research Office staff and legal counsel as needed, will determine whether UMMC is engaged in
a particular research study. Investigators and other institutions may not independently determine UMMC’s engagement.

When UMMC is engaged in research, the Institutional Official may choose to enter into an agreement to cede review to an external IRB.


1.9 Written policies and procedures

UMMC’s Standard Operating Policies and Procedures for Human Research Protection detail the policies and regulations governing research with human participants and the requirements for submitting research proposals for review by UMMC IRBs. The policies and procedures are reviewed annually and revised by the Human Research Office Director as needed. Substantive changes are reviewed by the IRB members, Institutional Official and other offices, as applicable, with policies and procedures revised as the need for changes are identified.

The Human Research Office keeps UMMC’s research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website, through email and other forums. The policies and procedures are available on UMMC’s Human Research Office website and copies available upon request. Changes to the policies and procedures are communicated to investigators and research staff by email, newsletters and/or in-person venues. Changes to the policies and procedures are communicated to IRB members and staff during in person meetings.

1.10 UMMC’s HRPP Structure

The HRPP consists of the following individuals and committees: the Institutional Official, the Director of the HRPP/Director of the Human Research Office, Human Research Office staff, the IRB(s), the Institutional Biosafety Committee (e.g., for gene transfer research), Radiation Safety Committee, Compliance Committee (Conflict of Interest), Office of Research and Sponsored Programs, Legal Counsel, investigators, research staff and research pharmacy staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human research participants.

The following officials, administrative units and individuals have primary responsibilities for the protection of human research participants:

1.10.1 Institutional Official

The ultimate responsibility of the HRPP resides with the Institutional Official (IO) of the program. The IO is legally authorized to represent UMMC. He/she is the signatory of the FWA
and assumes the obligations of the FWA. At UMMC the Associate Vice Chancellor for Research is the IO. The IO is responsible for ensuring that the UMMC HRPP and IRBs have the resources and support necessary to comply with all institutional policies, laws, and regulations that govern human research. Such resources include, but are not limited to:

- Staffing commensurate with the size and complexity of the research program;
- Appropriate office space, meeting space, equipment, materials, and technology;
- Resources for the production, maintenance, and secure storage of HRPP and IRB records;
- Resources for auditing and other compliance activities and investigation of non-compliance;
- Access to legal counsel; and
- Supporting educational opportunities related to human research protections for IRB members, relevant administrative staff, and all members of the research team.

At a minimum of annually, the IO reviews HRPP and IRB functions, requirements, and resources and makes adjustments as needed.

The IO is also responsible for:

- Fostering, supporting and maintaining an institutional culture that supports the ethical conduct of all human research and the adherence to regulations and institutional policies;
- Ensuring that the IRBs function independently by, among other mechanisms, being directly accessible to the IRB Chair(s) and members if they experience undue influence or if they have concerns about the function of the IRB;
- Oversight of the Institutional Review Board (IRB);
- Oversight over the conduct of human subjects research under the auspices of UMMC;
- Supporting training and educational opportunities for IRB members and staff to support their ability to review research in accordance with ethical standards and applicable regulations;
- Supporting training and educational opportunities for investigators and research staff to support their ability to conduct research in accordance with ethical standards and applicable regulations; and
- Taking action as necessary to ensure the protection of human subjects and compliance with regulatory and other requirements.

The IO has the authority to suspend, terminate, or disapprove research or take other actions, such as sanctions or restrictions of research privileges or uses of research data, as necessary, to ensure the proper conduct of research, the protection of human subjects, the autonomy and authority of the IRB, compliance with regulatory and other requirements, or to protect the
interests of UMMC. However, the IO may not approve research that has been disapproved (or not yet approved) by the IRB.

The IO must complete appropriate training on human research protections [for example CITI]. The Human Research Office provides on-going continuing education for the IO concerning human research protections.

The IO is made known to employees of the organization and is accessible by phone, email, in person or other methods of communication. The IRB Chairmen and Human Research Office Director have direct access to the IO for any concerns or issues related to the HRPP.

In the performance of these duties, the IO has the authority to delegate such activities as may be necessary in order to effectively administer the program. However, the IO is ultimately responsible and is expected to be knowledgeable about all human research protections responsibilities at the organization.

1.10.2 Director of the HRPP

The Human Research Office Director 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 the administration of the IRB;

2. Advising the IO on key matters regarding research at UMMC;

3. Implementing UMMC’s HRPP policies and procedures;

4. Overseeing the administration of the HRPP and IRB, including the supervision of staff;

5. Overseeing the administration of IRB Reliance Agreements and Independent Investigator Agreements;

6. Submitting, implementing and maintaining an approved FWA through the IO and the U.S. Department of Health and Human Services Office for Human Research Protections (OHRP);

7. Managing the finances of UMMC’s Human Research Office and IRBs;

8. Assisting the IRB in its efforts to review research and ensure the protection of human subjects;

9. Assisting investigators in their efforts to carry out UMMC’s research mission;

10. Developing and implementing improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program;

11. Developing training requirements as required and as appropriate for investigators, IRB members and research staff, and ensuring that training is completed on a timely basis;
12. Serving as the primary contact at UMMC for the Office for Human Research Protections (OHRP) of the U.S. Department of Health and Human Services, the Food & Drug Administration (FDA) and other federal regulatory agencies;

13. Serving as an internal expert resource for questions and other matters regarding the protection of human subjects.

1.10.3 HRPP Staff

In addition to the leadership structure described above, other support staff members for the Human Research Office and IRBs include Human Research Office Associate Director, Education Specialist, IRB Coordinator and IRB Specialist. The HRPP and IRB staff for UMMC comply with all ethical standards and practices. The duties and responsibilities for all staff are found in their respective job descriptions, and their performance is evaluated on an annual basis. The UMMC HRPP and IRB Office staff reports to the Human Research Office Director, who has day-to-day responsibilities for its operations.

1.10.4 Institutional Review Board (IRB)

UMMC has two IRBs, with members recommended by the IO and appointed by the UMMC Vice Chancellor. The IRB prospectively reviews and makes decisions concerning all human research under the auspices of UMMC unless it has been determined that UMMC is not engaged in the research or UMMC has entered into agreement with an external IRB to serve as the IRB of record. The IRB is responsible for the protection of rights and welfare of human research participants at UMMC, through review and oversight of safe and ethical research. It discharges this duty by complying with the requirements of federal and state regulations, the FWA, and institutional policies.

The IRB functions independently of, but in coordination with, other institutional committees and officials. The IRB, however, makes an independent determination whether to approve, require modification to, or disapprove research based upon whether human research participants are adequately protected.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the institution. However, those officials may not approve human research that has not been approved or has been disapproved by the IRB.

UMMC has a signed Reliance Agreement with the NCI CIRBs and other external IRBs, and may also rely upon the services of those IRBs.

UMMC also uses the services of commercial external IRBs including WIRB, Advarra and others. External IRBs are primarily relied upon for the review and oversight of industry-sponsored clinical trials. UMMC may enter into other reliance agreements for other reasons, for example, when required as a term or condition of a grant.
1.10.5 Legal Counsel’s Office

The UMMC HRPP relies on UMMC’s Legal Counsel for the interpretation and application of state law and the laws of any other jurisdiction where UMMC research is conducted, as they apply to human research. Counsel is available to provide guidance on other relevant topics as needed.

1.10.6 Department Chairs and/or Institutional Leaders

Department Chairs, and institutional leaders when the Department Chair is the PI, are responsible for ensuring that the investigator is qualified by training and experience to conduct the proposed research.

Department chairs/leaders are required to review all proposals before they are submitted to the IRB for review. The signature of the Department chair or leader indicates that (1) the PI is qualified and has the necessary resources to safely conduct the study, and (2) attests to the scientific merit of a study, which means

- The research uses procedures consistent with sound research design;
- The research design is sound enough to reasonably expect the research to answer its proposed question.

1.10.7 Principal Investigator

The Principal Investigator (PI) is ultimately responsible for the protection of human research participants in research they conduct or oversee. The PI is expected to abide by the highest ethical standards and develop a research plan that incorporates the principles of the Belmont Report. He/she is expected to conduct research in accordance with the IRB approved research plan and to personally conduct or oversee all aspects of the research.

In addition to complying with all applicable regulatory policies and standards, the PI must comply with organizational and administrative requirements for conducting research. The PI is responsible for ensuring that all investigators and research staff complete all organization required trainings as well as training for their specific responsibilities in any given research study. When investigational drugs or devices are used, the PI is responsible for ensuring an appropriate plan for their storage, security, dispensing, accounting, and disposal.

The IRB reviews investigator qualifications when reviewing research and may determine that an investigator may not serve as PI or may require the addition of other investigators to supplement the expertise available on the research team or to conduct or oversee certain aspects of the research.

The PI for human subjects research under the auspices of UMMC must be a full time faculty or staff member or an affiliate faculty member with a full time faculty member identified as Co-PI.

Individuals who are debarred, disqualified, or otherwise restricted from participation in research or as a recipient of grant funds for research by a federal, state, or other agency may not serve as PI.
Individuals with a history of compliance issues related to the conduct of research (e.g., recipients of an FDA Warning Letter) will be considered on a case-by-case basis. Factors to consider include whether corrective actions have been accepted as adequate, whether information from an audit or quality review indicates that the issues have been resolved, and similar considerations.

1.10.8 Other Related Units

1.10.8.1 Sponsored Programs Administration

Sponsored Programs Administration staff review all research agreements with federal, foundation, or non-profit sponsors. This ensures that all terms of the award are in compliance with institutional policies. Only designated senior individuals within Sponsored Programs Administration have the authority to approve funding proposals and to execute research agreements on behalf of the institution.

Sponsored Programs Administration ensures that required AAHRPP language (see Section 20.2) is included in contracts. Sponsored Programs Administration has access to the IRB submission to confirm that the contract and the consent document(s) are consistent in terms of costs to research participants and the party responsible for payment in case of injury.

When the grant or contract agreement includes human research activities that will be conducted by investigators who are not employees or agents of UMMC, a subcontract is executed between UMMC and the collaborating institution. The subcontract includes the requirement for the collaborating institution to assure compliance with federal regulations for the protection of human research participants and to provide documentation of current and ongoing IRB approval. The collaborating institution must also ensure that key personnel involved in human research are in compliance with the NIH policy on education in the protection of human research participants and provide documentation of education of key personnel to UMMC when NIH is funding the study.

1.10.8.2 Pharmacy

Investigators are required to provide the Pharmacy with complete information about all IRB approved research that takes place at UMMC and under its jurisdiction. The Department of Pharmacy Services assures that information about all studies involving drugs used in research is shared with Pharmacy Staff as appropriate.

UMMC’s Pharmacy is responsible for storing, accounting for, dispensing, and compounding of most investigational drugs used in research, whether conducted inpatient or outpatient. The manufacture/compounding of drug products not commercially available is coordinated by UMMC’s Pharmacy Services. Waivers from use of the UMMC pharmacy for handling investigational drugs are considered on a case by case basis by the UMMC pharmacy and IRB, with required information regarding storage, accounting and dispensing.

The Pharmacy is available to provide guidance to investigators on the management of study drugs.
1.18.1.3 Compliance

UMMC’s Office of Integrity and Compliance has a Research Compliance division that supports the research mission of UMMC and its affiliated hospitals by providing independent oversight of research compliance programs, activities, and processes to ensure quality and integrity in research. The Director of the Office of Integrity and Compliance reports to UMMC’s Vice Chancellor. The Office of Integrity and Compliance serves as a resource for UMMC’s Human Research Office, the IRBs and individual investigators and research staff; provides education and training; facilitates the development of system-wide research policies and procedures; conducts study audits and ensures post-approval monitoring of all human research studies and coordinates and monitors research management activities for compliance with federal, state and local laws and regulations and institutional policies.

1.10.8.4 Relationship Among Components

UMMC’s Research Compliance Subcommittee, chaired by the Institutional Official/Associate Vice-Chancellor for Research, meets bi-monthly to help ensure research compliance. Representatives of the IRB, Human Research Office, Sponsored Programs (pre and post award), Legal, Radiation Safety, Institutional Biosafety, IACUC and Laboratory Animal Facilities, Pharmacy, Office of Integrity and Compliance and Investigators are members of this subcommittee, which reports determinations to the UMMC Compliance Committee.

UMMC also has a Research Advisory Committee (RAC) charged with fostering excellence in research and research training, to assist with strategic planning for research development and research facilities, and to provide recommendations to the Vice Chancellor for Health Affairs. The RAC, chaired by the Institutional Official/Associate Vice-Chancellor for Research, meets monthly. Legal, Sponsored Programs, Investigators, institutional leadership and research compliance committees are represented at its meetings.

1.10.9 Protocol-Specific Coordination

In addition to IRB approval, an Investigator must obtain and document the approval, support, or permission of other individuals and departments or entities impacted by the research and approval by other oversight committees, as applicable, including, but not limited to:

- University Hospitals
- Pharmacy
- Radiology
- Nuclear Medicine
- Nursing
- Permission to enter classrooms or hospital units
- Permission from external research locations (sites)
- Departmental approvals
- Database access permissions
- Institutional Biosafety Committee
When applicable, a letter of support, collaboration, permission, or approval from the designated authority, is included in the Initial Protocol Application to the IRB. The application is reviewed in the Human Research Office to ensure that all necessary letters are included. The IRB may request review or consultation with any of the above listed or other organizational committees or components even when such review or consultation is not required by policy.

If the research sites, or research personnel, are also under the jurisdiction of another IRB, documentation of the external IRB’s approval or agreement to cede or waive review is required.

Other committees and officials may not approve human research to commence that has not been approved by or that has been disapproved by the IRB.
2 Quality Assurance

UMMC performs Quality Assurance and Improvement activities for the purposes of monitoring the safety of ongoing studies and measuring and improving human research protection effectiveness, quality, and compliance with organizational policies and procedures and applicable federal, state, and local laws.

2.1 External Monitoring, Audit, and Inspection Reports

The HRPP, Office of Integrity and Compliance, Legal, Department Chairs and Investigational Pharmacy, if applicable, should be notified in advance, whenever possible, of upcoming audits or inspections of research whether the study is reviewed by the UMMC IRB or an external IRB on UMMC’s behalf. Representatives from each of the offices identified above may participate in entrance or exit interviews and otherwise observe or support the audit or inspection. These representatives may also assist in the development of any responses necessary to audits or inspections.

When research is under the oversight of the UMMC IRB, all reports from external monitors, auditors, or inspectors are submitted by investigators to the IRB for review. The IRB Chair or designee reviews such reports to look for issues that could impact the rights or welfare of human research participants and for issues indicative of possible serious or continuing non-compliance. If such issues are identified, the report is forwarded to the convened IRB to determine what additional actions are necessary.

When UMMC is engaged in research reviewed by an external IRB, all reports from audits or inspections must be submitted to the HRPP for review. The HRPP may require corrective actions (CAP), a follow up review, or other actions as needed to ensure the protection of human subjects and to support compliance.

Reports indicative of any negative actions by a government oversight office regarding research conducted at or by UMMC, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated (classification as “OAI” is typically made after the FDA has the opportunity to review any responses to a 483), FDA Restrictions Placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections must be reported to the HRPP/IRB office by phone or email upon notice regardless of whether the research is reviewed by the UMMC IRB or an external IRB. See Section 21 for more information.

2.2 Investigator Compliance Reviews

The Office of Integrity and Compliance is responsible for conducting post-approval directed (“for cause”) audits and periodic (not “for cause”) compliance audits of human subjects research conducted under the auspices of UMMC. Additionally, the IRB may appoint a subcommittee for the purpose of conducting a for-cause or not for-cause compliance audit of one or more research plans under its jurisdiction. The subcommittee may be composed of IRB members and staff from within, or individuals from and outside of the organization.
Compliance reviews are conducted to assess investigator compliance with federal, state, and local law, the IRB-approved protocol and UMMC policies, to identify areas for improvement, and to provide recommendations based on existing policies and procedures. The results of compliance reviews are reported to the Human Research Office Director, the UMMC IRB (when it is the IRB of record), the investigator and the Research Compliance Sub-Committee, which reports to the institutional Compliance Committee, and other UMMC leadership as appropriate. IRB reporting and evaluation of non-compliance is handled according to the procedures of the IRB of record.

If during the course of a review it is identified that research participants may have been exposed to unexpected serious harm or risk of harm, the reviewer promptly reports such findings to the Human Research Office Director and the IRB of record.

If issues are identified that indicate possible misconduct in research, the procedures in the UMMC research misconduct policy are initiated.

Compliance reviews may include:

a) Requesting progress reports from investigators
b) Examining investigator-held research records and records held by other ancillary services
c) Reviewing source documentation
d) Reviewing the recruitment process and materials
e) Reviewing consent materials and documentation of consent
f) Observing the consent process and other research activities
g) Verifying HIPAA authorization
h) Interviewing investigators and research staff
i) Interviewing research participants
j) Reviewing projects to verify from sources other than the investigator that no unapproved changes have occurred since previous review
k) Conducting other monitoring or auditing activities as deemed appropriate by the HRPP or IRB.

2.3 IRB Compliance Reviews

The UMMC Office of Integrity and Compliance periodically reviews the activities of the IRB to assess compliance with regulatory requirements and to identify areas for improvement; this includes a review of IRB records at least annually. Review activities may include:

a) Review of the IRB minutes to evaluate whether adequate documentation of the meeting discussion and any required determinations has occurred, and that quorum was met and maintained
b) Reviewing IRB files to evaluate whether adequate documentation of exemptions, expedited review and other ancillary reviews, as applicable, have occurred
c) Review consent forms to evaluation whether all required elements are included
d) Reviewing the IRB database to evaluate whether all required fields are completed accurately;

e) Verifying IRB approvals for external sites or investigators

f) Reviewing metrics (for example, time from submission to first review) to evaluate the quality, efficiency, and effectiveness of the IRB review process

g) Other review activities as appropriate

Results of IRB compliance reviews are reported to the Institutional Official, the Research Compliance Sub-Committee and the Human Research Office. The HRO Director and IRB Chairmen review the results of IRB compliance reviews with the IRB and the Institutional Official. If any deficiencies are noted in the review, a corrective action plan is developed by the Director and Chairmen and approved by the Institutional Official. The Director has responsibility for implementing and reporting progress on the corrective action plan, the results of which are evaluated by the Institutional Official.

2.4 HRPP Quality Assessment and Improvement

An annual meeting of the Institutional Official, the Human Research Office Director and Assistant Director is held to establish a written quality improvement plan to assess compliance and the quality, efficiency, and effectiveness of the HRPP at the beginning of each fiscal year. At a minimum the plan will include:

- The goals of the plan with respect to achieving and maintaining compliance (e.g., ensuring that consent forms contain all required and application elements)

- At least one objective to achieve or maintain compliance

- At least one measure of compliance

- The methods to assess compliance and make improvements (e.g., via an IRB Compliance Review (see Section 2.3)

- The goals of the plan with respect to achieving targeted levels of quality, efficiency and effectiveness (e.g. IRB review timelines)

- At least one objective of quality, efficiency, or effectiveness

- At least one measure of quality, efficiency, or effectiveness

- The methods to assess quality, efficiency, or effectiveness and make improvements. Quality, efficiency, and effectiveness are quantitatively measured by the Human Research Office’s internal data tracking and metrics, and are qualitatively measured through feedback from investigators, research staff and administrative officials.
Results of the prior fiscal year’s plan are reviewed by the Institutional Official, the Human Research Office Director and Assistant Director to identify trends and opportunities for improvement at the beginning of the fiscal year. If problems are identified and changes required, the Human Research Office Director, with consultation from the Institutional Official, the IRB Chairs and Vice-Chairs, and Director of the Office of Integrity and Compliance, as needed, collaborate in the development of a corrective action plan, its implementation, and evaluation of its effectiveness. Any corrective action plan will be approved and incorporated within the new fiscal year’s quality improvement plan.

The Human Research Office tracks internal data and metrics that are informative when considering HRPP and IRB efficiency, effectiveness, workload, and resources. Metrics are reported to the Institution through the Human Research Office’s website at least twice per year, and are discussed with the Institutional Official and Research Compliance Subcommittee annually.
3 Education & Training

3.1 Training / Ongoing Education of IRB Chairman, Members, and Staff

Recognizing that a vital component of a comprehensive human research protection program is an education program, UMMC is committed to providing training and an on-going educational process for IRB members and the staff of the IRB and Human Research Office, related to ethical concerns and regulatory and organizational requirements for the protection of human research participants.

Orientation

New IRB members, including alternate members, meet with the IRB Chairman or member of the Human Research Office staff for an orientation session. At the session, IRB processes, regulations and resources are reviewed. Each new member receives a copy of:

- The Belmont Report;
- Institutional Review Board Member Handbook (Amdur and Bankert);
- Federal regulations relevant to the IRB.

Initial Education

IRB members and Human Research Office administrators and staff complete the required modules in the CITI Course in the Protection of Human Research Subjects (biomedical and social behavioral track), including the IRB Member Module - “What Every New IRB Member Needs to Know” and the module on Conflicts of Interest. Community members are expected to review the “I Have Agreed to be an IRB Community Member. Now What?” module as well. Members are encouraged to also complete PRIM&R’s Ethical Research Oversight Course (E-ROC).

Continuing Education

To ensure that oversight of human research is ethically grounded and the decisions made by the IRB are consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB.

In addition to CITI training, UMMC also uses the following activities as a means for offering continuing education to IRB members and Human Research Office administrators and staff:

- In-service training at IRB meetings;
- Training workshops and webinars;
- Copies of appropriate publications;
- Distribution of articles, announcements, guidance, presentations and other materials relevant to human subjects research

The activities for continuing education vary on a yearly basis depending on areas of need, as determined by the HRPP Director. When possible, the HRPP provides support for staff and IRB members to attend PRIM&R, OHRP and other relevant conferences and regional meetings.
The Director determines minimum attendance requirements for continuing education. Fulfillment of training requirements is included as part of the evaluation of the performance of IRB members, alternates, and staff. Continuing failure to complete training may result in a member’s service being discontinued or not renewed.

3.2 Training / Ongoing Education of Investigators and Research Team

Another vital component of a comprehensive human research protection program is an education program for all individuals involved with human research participants. UMMC is committed to providing training and ongoing education for investigators and research staff on human subjects research protections and relevant topics.

3.2.1 Initial Education

Investigators and research staff must complete UMMC required core modules in the CITI Course in the Protection of Human Research Subjects relevant to the type of research being conducted and including the modules on Conflicts of Interest. UMMC’s CITI training requirements are outlined on the Human Research Office webpage.

Evidence of current training (date of completion within 3 years of application date) for each member of the research team must be included in every new research study application and application for continuing review. New study applications and addition of study personnel may not move forward for IRB review without evidence of current training.

Investigators are not able to create a new research plan until the initial education requirement has been completed.

Research plans and applications for continuing review and amendments are accepted and reviewed if the PI’s training requirements are current, but co-investigators and members of the research team who have not yet completed the initial requirement or whose training has expired may not participate in the study until the requirement has been met.

Waiver of Initial Education

If individuals can provide documentation verifying that they have successfully completed human subject research training equivalent to that required by UMMC they may request a waiver of the requirement for UMMC’s specific training requirements. The Human Research Office staff and Director will review the documentation and determine if it satisfies organizational standards.

3.2.2 Continuing Education and Recertification

Investigators and research staff must meet UMMC’s continuing education requirement every three (3) years after certification of Initial Education for as long as they are involved in research with human participants. There is no exception to this requirement.

Evidence of CITI education status is validated within the IRB application, (new, continuing review and amendments). New research plans and applications for continuing review and
amendments are not reviewed until the Principal Investigator’s continuing education is up to date. Co-Investigators and members of the research team whose educational requirements are not up to date may not participate in the study until the CITI requirements are current.

Periodically, UMMC will also provide additional training on topics relevant to human subject protections, regulations, policies and standards, and IRB submission processes and requirements. Training may be provided via in-service, workshops, webinars, e-Learning, or through the distribution of articles, presentations, and other materials. Investigators and staff may request training or offer training suggestions by contacting the Human Research Office.
Human Subjects and Research Determinations

The responsibility for initial determination whether an activity constitutes research rests with the individual with primary responsibility for the activity. This individual should make this determination based on the definitions of “research” and “clinical investigation” as provided by the Common Rule and FDA regulations, respectively. Consultation with the Human Research Office is encouraged. Investigators may use the UMMC Self-Certification form to assist in this determination. Because the analysis can be complex, individuals with any questions regarding the applicability of the regulations to their activities are urged to request a determination that an activity does or does not involve research. Such requests are submitted by completing the Initial Application in the IRB electronic system or by sending the request and specified materials via email to the Human Research Office for review.

The responsibility for initial determination whether an activity involves human subjects rests with the investigator. Under the Common Rule, information is considered identifiable, and thus involving human subjects, when the identity of the subject is or may readily be ascertained by the investigator or associated with the information. It should be noted that this definition differs significantly from de-identified in accordance with HIPAA standards. FDA regulations do not incorporate the concept of “identifiability” in the evaluation of whether an activity is a clinical investigation (or research) subject to FDA regulations. For example, the use of de-identified human specimens to evaluate the safety or effectiveness of a diagnostic device is considered human subjects research subject to FDA regulations. Investigators may use the UMMC Self-Certification form to assist in this determination. Investigators are urged to submit for a determination whenever they are uncertain if a research study involves “human subjects” as defined by the Common Rule or FDA. Such requests are submitted by completing the Initial Application in the IRB electronic system or by sending the request and specified materials via email to the Human Research Office for review.

Determinations whether an activity constitutes human subject research will be made by the IRB Chair or designated member reviewer according to the definitions in Section 1.3, applicable federal regulations, and federal guidance. Such requests are submitted by completing the Initial Application in the IRB electronic system and a determination letter will be issued via the IRB electronic system to document the determination.

Human subjects research determinations must be determined prospectively (i.e., before the proposed activity or research begins). Conducting human subjects research without IRB approval or exemption is noncompliance and will be managed as described in Section 17.
5 Exempt Determinations

All research using human participants must be approved by UMMC. While certain categories of human research are exempt from the requirements of 45 CFR 46, exempt research is subject to review for determination of exempt status. At UMMC, exemptions are reviewed and granted by the IRB Chair, Alternate Chair or Vice-Chair.

Individuals involved in making the determination of an IRB exempt status of a proposed research project cannot be involved in the proposed research or have any apparent conflict of interest.

While exempt studies are exempt from the requirements of the Common Rule [45 CFR 46] (i.e., IRB approval and consent are not required), they do require a determination of exempt status and are not exempt from ethical considerations, such as honoring the principles described in the Belmont Report. The individual making the determination of exemption determines whether to require additional protections for research participants in keeping with ethical principles (e.g., requiring disclosure/consent, etc.).

5.1 Limitations on Exemptions

For research subject to the pre-2018 requirements, including research subject to DOJ regulations:

Children: The exemption for research involving survey or interview procedures or observations of public behavior (#2) does NOT apply to research in children, except for research involving observations of public behavior when the investigator does not participate in the activities being observed.

Prisoners: Exemptions do NOT apply. IRB review is required.

For research subject to the revised Common Rule (2018 requirements):

Children: Exemption #2(i) and (ii) for research involving survey or interview procedures or observations of public behavior does NOT apply to research in children, except for research involving observations of public behavior when the investigator does not participate in the activities being observed. Exemption #2(iii), where identifiable information is obtained and the IRB conducts a limited IRB review, is NOT applicable to research in children. Exemption #3 does NOT apply to research involving children. [45 CFR 46.104(b)(3)]

Prisoners: Exemptions do not apply except for research aimed at involving a broader subject population that only incidentally includes prisoners. [45 CFR 46.104(b)(2)]
5.2 Categories of Exempt Research

With the above-referenced limitations, research activities not regulated by the FDA (See Section 5.3 for FDA Exemptions) in which the only involvement of human participants is determined to be in one or more of the following categories are exempt from the requirements of 45 CFR 46:

For research subject to the pre-2018 Common Rule requirements, including research subject to DOJ regulations:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as
   (i) research on regular and special education instructional strategies, or
   (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
   (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
   (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject’s financial standing, employability, or reputation.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2), if:
   (i) the human subjects are elected or appointed public officials or candidates for public office; or
   (ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information is maintained throughout the research and thereafter.

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

   **NOTE:** In order to be eligible for this exemption, all of the materials have to exist at the time the research is proposed.

5. Research and demonstration projects which are conducted by or subject to the approval of federal department or agency heads, and which are designed to study, evaluate, or otherwise examine:
(i) Public benefit or service programs;
(ii) Procedures for obtaining benefits or services under those programs;
(iii) Possible changes in or alternatives to those programs or procedures; or
(iv) Possible changes in methods or levels of payment for benefits or services under those programs.

The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).

The research demonstration project must be conducted pursuant to specific federal statutory authority, there must be no statutory requirements of IRB review, the research must not involve significant physical invasions or intrusions upon the privacy of subjects, and the exemption must be invoked only with authorization or concurrence by the federal funding agency.

6. Taste and food quality evaluation 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 FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

For research subject to the revised Common Rule (2018 requirements):

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 readily be ascertained, directly or through identifiers linked to the subjects;
   ii. Any disclosure of the human subjects’ responses outside 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 advancement, or reputation; or

iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by .111(a)(7): 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 subject prospectively agrees to the intervention and information collection and at least one of the following criteria 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 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 advancement, or reputation; or

C. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by .111(a)(7): 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 an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received 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 purposes 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 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 nonresearch 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 using authorities 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 website
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 evaluation 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.

UMMC has decided not to adopt broad consent, and Exempt categories 7 & 8 will not be recognized as categories for exemption at the Institution.

5.3 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements for prior IRB review and approval:

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. [21 CFR 56.104(c)]
   
   **Note:** See Section 15.7 for detailed discussion of this exemption.

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. [21 CFR 56.104(d)]

5.4 Procedures for Exempt Determination

In order to obtain an exempt determination, investigators submit via the IRB electronic submission system:

1. A completed Initial Application, which includes verification of current CITI training for all study personnel;
2. The study protocol
3. All recruitment materials, information sheets, consent forms, scripts, surveys, questionnaires or diaries
4. Letter(s) of permission from any non-UMMC performance site and
5. If sponsored/funded, one copy of the grant application(s) and/or contract.

When the research requires limited IRB review or a HIPAA determination (i.e., waivers or alterations of the requirement for HIPAA authorization), the review may be conducted using expedited review procedures by the IRB Chair or an experienced Chair-designated member of the IRB. As with all other research subject to IRB review requirements, when conducting limited IRB review the IRB has the authority to approve, require modifications in (to secure approval), or disapprove all research activities; and to suspend or terminate IRB approval. Actions of disapproval may only be made by the convened IRB. [45 CFR 46.109(a), 45 CFR 46.110]

Proposed modifications to the aspects of research subject to limited IRB review must be submitted to and approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the subject(s), in which case the change must be promptly reported to the IRB (i.e., within 5 business days). [45 CFR 46.108(a)(3)(iii)]

Continuing review is generally not required for research determined to be exempt, even when that research is subject to limited IRB review. However, the IRB may determine that continuing review is required for a particular study subject to limited IRB review, in which case it shall document the reasons for its determination in the IRB record and communicate the requirement to the investigator in the IRB determination letter. [45 CFR 46.109(f)(ii), 45 CFR 46.115(a)(3)]

The reviewer (IRB Chair, Alternate Chair or Vice-Chair) reviews all requests for exemptions and determines whether the request meets the definition of research involving human participants and, if it does, determines whether the proposed research is eligible for exemption. The reviewer determines whether to require additional protections for research participants, in keeping with the guidelines of the Belmont Report. The reviewer’s determinations are documented in the IRB electronic system. The application, review and determination letter are recorded and maintained in the same manner and for the same length of time as other IRB review documentation. Once exemption review is completed, IRB staff sends written notification of the results of the review to the investigator.

Exempt determinations include an expiration date, with the maximum time being 364 days. If the investigator wants the research to extend beyond the expiration date, the investigator must submit an annual progress report. This process allows the investigator and the organization the opportunity to review and update the research activity and determine if it continues to qualify for exemption. Investigators are required to report any proposed modifications to the research during the course of the study, including the addition of study personnel so that current CITI training can be verified and COI evaluated prior to their involvement in the research. The reviewer determines if the modified study continues to qualify for exemption. Investigators are also required to submit a Final Report – exempt study completion report at the end of the study, to ensure that the organization can maintain an accurate database of active research.
6 IRB Reliance

When engaged in multi-site research, research involving external collaborators, or research that is otherwise under the jurisdiction of more than one IRB, UMMC acknowledges that each organization is responsible for safeguarding the rights and welfare of human research participants and for complying with applicable federal regulations. UMMC may choose to review the research in its entirety, only those components of the research in which UMMC is engaged, rely on the review of another qualified IRB, or make other arrangements for avoiding duplication of effort. When UMMC is the prime awardee on an HHS grant, it will ensure that at least one IRB reviews the research in its entirety.

When relying upon another IRB or when serving as the reviewing IRB for an outside organization or external investigator, a formal relationship must be established between UMMC and the outside organization or investigator through an IRB Reliance Agreement, Authorization Agreement, Investigator Agreement, a Memorandum of Understanding, or other such written agreement. The written agreement must be executed before UMMC will accept any human research proposals from the outside organization or investigator or rely on the review of an external IRB.

IRB reliance agreements establish the authorities, roles, and responsibilities of the reviewing IRB and the relying organization. The procedures for reliance, including for communication, information-sharing, and reports, may be outlined in the reliance agreement, in SOPs, or other written materials. UMMC's Office of Research and Sponsored Programs, Pre-Award Division, utilizes a checklist to ensure that reliance agreements and any accompanying materials address all requirements and are consistent with UMMC standards. To support compliance, UMMC makes every effort to ensure as much consistency as possible across reliance agreements.

Requests for UMMC to either rely upon an external IRB or to serve as the IRB of record for an external organization or investigator should be submitted as early as possible in the grant/contract process by submitting a reliance request with information about the applicable study or group of studies and external IRB, if applicable, to the Institutional Official.

6.1 Requests for UMMC to Serve as the Reviewing IRB

Upon request, UMMC will evaluate on a case-by-case basis whether it can effectively serve as the IRB of record for a proposed multi-site study. The main evaluation criteria are:

- The risk level of the study
- The number of sites
- The experience level of the U-M PI/study team
- The level of administrative resources available to the PI/study team to manage/coordinate the project
- Whether the UMMC PI holds the funding grant
If UMMC declines to serve as the IRB of record, UMMC will consider one of its approved commercial IRBs or another IRB identified by the UMMC PI.

When the UMMC IRB serves as the reviewing IRB for another organization, the requirements and procedures outlined throughout this manual apply unless an alternative procedure has been agreed to in the reliance agreement or outlined in a companion document.

For example, alternative procedures may be used for any of the following:

1. Management and documentation of scientific review, other ancillary reviews, and institutional permissions for research;
2. Training requirements and verification of qualifications and credentials for external investigators and staff;
3. For-cause and not-for-cause compliance reviews;
4. The disclosure and management of conflicts of interest. In all cases, any COIs and CMPs identified and developed by the relying organization will be communicated to the reviewing IRB. The reviewing IRB will determine the acceptability of the plan in accordance with their policies and procedures.
5. Review and management of matters such as site-specific consent language, HIPAA (e.g., authorizations, waivers, alterations), noncompliance, unanticipated problems, and federal reports;
6. Ensuring concordance between any applicable grant and the IRB application/protocol'
7. Procedures for and type of IRB review (e.g., expedited, convened) of additional sites after the research protocol is IRB-approved;
8. Procedures for submission and review of interim reports and continuing review materials; and/or
9. The communication of IRB determinations and other information to external investigators and organizations.

6.2 External IRB Review of UMMC Research

All non-exempt human subject research (or exempt research for which limited IRB review takes place pursuant to § __.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8)) in which UMMC is engaged must be reviewed and approved by the UMMC IRB or an external IRB upon which UMMC has agreed to rely prior to the initiation of the research. See Section 1.8 for information regarding engagement.

UMMC has agreements in place to engage the services of external IRBs for the review of some research. Existing agreements include those with:

- WCG
- Advarra
- Alpha IRB
- NCI’s Adult CIRB for NCI research involving adult participants
- NCI’s Pediatric CIRB for NCI research involving children
Research that falls within the above parameters must be registered with the UMMC Human Research Office prior to initiation of the study at UMMC, following the procedures outlined in Section 6.2.1. Post-approval requirements are summarized in Section 6.2.2.

UMMC may also choose to enter into an agreement to rely upon other external IRBs, most commonly when required as a condition of a grant or contract.

The UMMC IO and Human Research Office evaluate the following factors, and others as appropriate, when considering a request to rely upon an external IRB:

1. The accreditation status of the proposed IRB;
2. The compliance history of the IRB (e.g., outcomes of prior audits or inspections, corrective actions);
3. Prior experience with the IRB;
4. The federal IRB registration and organizational FWA, as applicable;
5. The expertise and experience of the proposed IRB (e.g., with reviewing the type of research, research procedures, and subject population(s));
6. The research activities that will be conducted at or by UMMC;
7. The risks and complexities of the proposed research;
8. The proposed reliance terms and procedures including the procedures for collaborative management of matters such as conflicts of interest, noncompliance, unanticipated problems, and federal reports;
9. The plan for review and allowance of the incorporation of site-specific consent language; and
10. The plan for incorporation of other relevant local requirements or context information in the review process.

When reliance on a non-accredited IRB is proposed, the evaluation may also take into consideration one or more of the following based upon the risks of the research, the research activities in which UMMC will be involved and UMMC’s familiarity with the IRB:

1. When the research is minimal risk (or the activities in which UMMC is involved are minimal risk), a statement of assurance from the proposed IRB that its review will be consistent with applicable ethical and regulatory standards, and that it will report any regulatory investigations, citations, or actions taken regarding the reviewing IRB, and, when applicable, to the organization’s FWA;
2. An attestation about, or summary of, any quality assessment of the reviewing IRB such as evaluation by an external consultant or internal evaluation of compliance using the FDA’s self-evaluation checklist or AAHRPP’s self-evaluation instrument;
3. The willingness of the external IRB to accommodate requests for relevant minutes and other records of the proposed study;
4. The willingness of the external IRB to accommodate a request for someone from the relying organization to serve as a consultant to the IRB or to observe the review of the proposed study; and/or
5. An assessment of the external IRB’s policies and procedures.
The external IRBs that serve as the IRB of record for UMMC research have the same authority as the UMMC IRB and all determinations and requirements of the external IRBs are equally binding. Investigators must be familiar with and comply with the external IRB’s policies and procedures and any additional requirements or procedures outlined in the IRB reliance agreement or companion materials (e.g., reliance SOPs). UMMC will support compliance with the terms of reliance agreements by providing investigators with information relevant to their responsibilities, such as a copy or summary of the agreement, an information sheet, or reliance SOPs.

Regardless of which IRB is designated to review a research project, UMMC is responsible for the conduct of the research in which it engages. Research reviewed by external IRBs remains subject to review, approval, and oversight by UMMC and must adhere to all applicable policies, procedures, and requirements, including those of the UMMC HRPP.

6.2.1 Registration of Studies Reviewed by External IRBs

Prior to study initiation at UMMC, UMMC investigators must register studies that are relying upon an external IRB and provide basic information about the research to the Human Research Office by completing an abbreviated Initial Application form in the IRB electronic submission system which will include a copy of the IRB approval, approved protocol, and supporting documentation, including consent document(s) and recruitment material as applicable. The Human Research Office will review the information and verify that CITI training, COI review, and any other applicable approvals or requirements, including local context information, have been completed. When applicable, the Human Research Office staff will forward requests for waiver or alteration of HIPAA authorization and any relevant materials to the UMMC IRB Chair or a designated expedited reviewer for review. The UMMC investigator will be notified via the UMMC electronic submission system when the study has been released to begin at UMMC.

6.2.2 Post-Approval Requirements

Investigators approved through external IRB review must still report local unanticipated problems, complaints, and any noncompliance to the UMMC Human Research Office via the electronic submission system in addition to reporting to the external IRB. Copies of the report submitted to the external IRB are generally acceptable, but additional information may be requested on an as-needed basis. Investigators must also submit copies of continuing review reports, modifications and updated protocols, updated consent forms, study closures, and the corresponding IRB approval or acknowledgment.

Changes in PI and the addition of other research team members must be submitted to the Human Research Office via the electronic submission system prior to the new PI or research team member assuming any study responsibilities. This allows for verification of CITI training, COI review, and any other applicable requirements prior to participation.

Notices about and reports from external monitors, auditors, or inspectors must be provided to the Human Research Office Section 2.1 of this manual.
Any of the following issues must be reported immediately (ASAP upon notice) to the UMMC Human Research Office by phone or email:

- Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated (classification as “OAI” is typically made after the FDA has the opportunity to review any responses to a 483), FDA Restrictions Placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections;
- Any litigation, arbitration, or settlements initiated related to human research protections; and/or
- Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding UMMC’s HRPP.

See Section 21 for more information. Investigators are reminded that other UMMC reporting requirements, such as to the Office of Integrity and Compliance, Office of Information Security and Risk Management, remain applicable in addition to HRPP reporting requirements.

### 6.3 NIH Single IRB (sIRB) for Multi-Site Research

In June 2016, the National Institutes of Health (NIH) released a final policy requiring domestic awardees and domestic sites of NIH-funded multi-site research to use a single IRB (sIRB) for review of non-exempt human subject research unless there is justification for an exception. This policy is intended to streamline the IRB review process and reduce inefficiencies and redundancies while maintaining and enhancing subject protections. The policy does not apply to career development, research training, or fellowship awards, nor to sites that are not conducting the same protocol as the other sites (e.g., sites providing statistical support or laboratory analysis only) or to foreign sites.

Exceptions to the policy are automatic when local IRB review is required by federal, tribal, or state law/regulation/policy and when the proposed research is the “child” of a grant that predates the requirement for sIRB review. Such exceptions and the basis (and information regarding the “parent” study, when applicable) should be cited in the proposed sIRB plan and, when the exception is based on law/regulation/policy, apply only to the site(s) to which the law/regulation/policy applies. Other exceptions will be considered when there is compelling justification. The site(s) and justification for why the site(s) cannot rely on the single IRB of record should be included in the proposed sIRB plan. The NIH will consider the exception request and inform the applicant of the outcome.

#### 6.3.1 Selection and Designation of a sIRB

Investigators submitting applications for NIH-funded multi-site research must describe the sIRB plan in the funding proposal (grant application or contract proposal), and, if applicable, may request direct cost funding to cover additional costs related to the requirements of the NIH.
policy. The sIRB can be the IRB at one of the participating sites or an independent, fee-based IRB.

When UMMC will be the prime awardee, UMMC investigators submitting applications for NIH-funded multi-site research must describe the sIRB plan in the funding proposal (grant application or contract proposal and may identify one of the commercial IRBs with which UMMC has a contract to serve as the sIRB. The Office of Research and Sponsored Programs Pre-Award Division will assist investigators with information to include in the proposal regarding direct costs. Requests for an alternative IRB option when UMMC will be the prime awardee are directed to the Human Research Office Director. The Director will consult with others within the organization as needed and make a recommendation to the IO for consideration. When UMMC will not be the prime awardee, investigators should, as early in the process as possible, submit a request for UMMC to rely upon an external IRB as the sIRB by submitting a reliance request with information about the applicable study or group of studies and external IRB, if applicable, to the Institutional Official.

6.3.2 Reliance Agreements for sIRB Studies

A Reliance Agreement (or “Authorization Agreement”) between the sIRB and the participating sites is required. The Reliance Agreement documents the respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

Reliance Agreements should describe the responsibilities of all parties and how communication between parties will occur, for example, notifications of the outcome of regulatory review and management of federally-mandated reports such as reports of unanticipated problems, serious or continuing noncompliance, and suspensions or terminations of IRB approval. When IRB certification requirements apply (e.g., for NIH Genomic Data Sharing), the agreement or written procedures should indicate who is responsible for meeting the certification requirements. The agreement or written procedures should also specify points of contact and contact information for the sIRB and relying institution(s).

The institution that is awarded the funding for the research is responsible for maintaining all agreements and for ensuring that adequate and appropriate communication channels between the sIRB and participating sites are in place. Participating sites are responsible for maintaining copies of the site agreement in accordance with the terms of their FWA.

6.3.3 Responsibilities

The sIRB will be responsible for compliance with the regulatory requirements for IRBs specified in the federal regulations (i.e., 45 CFR 46 and other applicable regulations) and for any other responsibilities outlined in the reliance agreement and/or procedures. Participating sites (Relying institutions) are responsible for providing relevant local context information to the sIRB, ensuring that the research is conducted in accordance with applicable regulations and the determinations and requirements of the sIRB, and for other responsibilities, as outlined in the reliance agreement and/or procedures.
When an external IRB serves as the sIRB for a study in which UMMC is engaged, investigators must register the study with UMMC’s Human Research Office prior to study initiation following the procedures outlined in Section 6.2.1. Post-approval requirements are summarized in Section 6.2.2.

Research reviewed by external IRBs remains subject to review, approval, and oversight by UMMC and must adhere to all applicable policies, procedures, and requirements, including those of the UMMC HRPP.
7 Research Previously Approved by Another IRB

When an investigator transfers human subjects research that was previously approved by another IRB to UMMC, the investigator must:

- Submit the research for review by the UMMC IRB or determination of exemption; or
- Submit a request for UMMC to rely upon the existing IRB of record (such requests must be approved by both organizations)

Research determined to be exempt at the previous institution will be reviewed according to the procedures in Section 5. All other research must be submitted as if it were undergoing initial review and will be reviewed under expedited review or by the convened IRB. Research activities under the auspices of UMMC cannot commence until all necessary approvals are in place, including approval by the UMMC IRB or an IRB reliance agreement is executed (and the transferred activities are approved by the IRB of record).

For research transfers where stopping research interventions or procedures might harm participants, the investigator can request permission from both organizations to continue the research under the oversight of the prior organization’s IRB until final UMMC IRB approval is obtained.
8 Institutional Review Board

UMMC has established two Institutional Review Boards (IRB) to ensure the protection of human participants in research conducted under the auspices of UMMC.

Although UMMC has authorized a number of IRBs to fulfill the review and oversight function, all on-site IRBs follow the same policies and procedures. For purposes of this manual, all on-site IRBs are referred to as the UMMC IRB.

8.1 IRB Authority

The IRB derives its authority from UMMC policy, as cited in Section 1.2. Under the federal regulations, IRBs have the authority:

1. To approve, require modifications to secure approval, or disapprove human research activities including exempt research activities under 45 CFR 46.104 of the revised Common Rule for which limited IRB review is a condition of exemption (under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7), and (8));

2. To require that informed consent be obtained and documented in accordance with regulatory and policy requirements unless the criteria for the waiver or alteration of such requirements has been satisfied and approved by the IRB. The IRB may require that information, in addition to that specifically mentioned in the regulations, be given to research participants when, in the IRB's judgment, the information would meaningfully add to the protection of the rights and welfare of participants;

3. To research subject to the revised Common Rule (2018 requirements): To conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described in Section 10.5;

   When research is subject to other regulations (e.g., pre-2018 Common Rule, FDA, DOJ) or requirements (e.g., grant or contract terms) that require continuing review, the IRB will conduct continuing review of research at intervals appropriate to the degree of risk of the research, but not less than once per year;

4. To suspend or terminate approval of research not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to participants;

5. To observe, or have a third party observe, the consent process; and

6. To observe, or have a third party observe, the conduct of the research.

The IRB functions independently. Attempts to coerce or otherwise unduly influence the actions of the IRB are forbidden by policy, and are to be reported as described in Section 8.6. Likewise, the IRB must remain free from the influence of financial and other organizational interests. No individual with responsibility for the business and financial interests of the organization may serve on the IRB.
Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of UMMC. However, those officials may NOT approve research if it has not been approved or has been disapproved by the IRB. Reviewing officials may strengthen requirements and/or conditions, or add other modifications before approval or may require approval by an additional committee, office or person. Previously approved research proposals and/or consent forms must be re-approved by the IRB before initiating any changes or modifications that result from such additional organizational reviews.

8.2 Roles and Responsibilities

8.2.1 IRB Chair

The IO, in consultation with the Director of the Human Research Office, appoints the IRB Chair. The IRB Chair, in consultation with the IO and the Director of the Human Research Office, appoints the IRB Vice Chair.

The IRB Chair should be a highly respected individual, from within UMMC, fully capable of managing the IRB, and the matters brought before it with fairness and impartiality. The task of making the IRB a respected part of the research community falls primarily on the shoulders of the Chair. The IRB must be perceived to be fair, impartial and immune to pressure by administration, the investigators whose research plans are brought before it, and other committees and departments.

The IRB Chair is responsible for conducting the meetings and conducting expedited reviews, and may designate other experienced IRB members to perform duties such as expedited reviews and other IRB functions.

The IRB Chair is authorized to take immediate action to suspend a study or studies if participants may be at risk of harm, when serious noncompliance may have occurred, or for any other reason where such action is appropriate. Such action requires subsequent notice to and review by the convened IRB.

The IRB Chair advises the IO and the Director of the Human Research Office about IRB member performance.

The performance of the IRB Chair is reviewed on an annual basis by the Director of the Human Research Office in consultation with the IO. Feedback of this review is provided to the Chair. If the Chair is not acting in accordance with the IRB’s mission, following policies and procedures, has an undue number of absences, or not fulfilling the responsibilities of the Chair, he/she may be removed.

8.2.2 IRB Vice Chair

The Vice Chair serves as the Chair of the IRB in the absence of the Chair and has the same qualifications, authority, and duties as the Chair.

The performance of the IRB Vice Chair is reviewed on an annual basis by the Director of the Human Research Office and the IRB Chair, in consultation with the IO. Feedback of the review is
provided to the Vice Chair. If the Vice Chair is not acting in accordance with the IRB’s mission, following policies and procedures, has an undue number of absences, or not fulfilling his/her responsibilities, he/she may be removed.

8.2.3 IRB Members

The role of an IRB member is to ensure that human research activities comply with federal regulations, state and local laws, and organizational policies and procedures, by:

1. Completing member education and training, both initial and on-going (See Section 3.1)
2. Maintaining the confidentiality of IRB deliberations and research reviewed by the IRB
3. Conducting and documenting reviews timely
4. Attending IRB meetings as scheduled

Members are expected to attend a minimum of 75% of all meetings. If a member is unable to attend a scheduled meeting, they are expected to inform the IRB administrative staff in advance.

If an IRB member is to be absent for an extended period of time, he/she is expected to notify the IRB administrative staff in advance. If the member has a designated alternate, the alternate can serve during the primary member’s absence. If the member does not have a designated alternate and the member’s area of expertise is needed and not represented by another member an alternate for the absent member may be obtained.

5. Recusing self from discussion, review and vote when he/she has a conflict of interest.

The member may be asked to return during deliberations to answer questions or provide additional information.

6. Participating in subcommittees of the IRB if requested and available.

7. Conduct himself/herself in a professional and collegial manner.

Experienced members may be designated by the Chair to conduct expedited reviews.

The performance of IRB members is reviewed on an annual basis by the IRB Chair and the Director of the Human Research Office. Feedback of this review is provided to the members. Members who are not acting in accordance with the IRB’s mission, not following policies and procedures, have an undue number of absences or otherwise not fulfilling the responsibilities of membership, may be removed.

8.2.4 Alternate IRB members

The appointment and function of alternate IRB members is the same as that for primary IRB members. An alternate's expertise and perspective should be comparable to those of the primary member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting, in part or in full, or when the regular member has a conflict of interest in regard to a protocol under review. When an alternate member substitutes for a primary member, the alternate member receives and reviews the same materials prior to the IRB meeting that the primary member received.
The IRB roster identifies the primary member(s) or class of members (e.g., physician scientist) for whom each alternate member may substitute. The alternate member is not counted toward meeting quorum as a voting member unless the primary member is absent. The IRB minutes document when an alternate member replaces a primary member.

Experienced alternate members may be designated by the Chair to conduct expedited reviews.

8.2.5 Subcommittees of the IRB

The IRB Chair, in consultation with the Human Research Office Director, may appoint IRB members to a subcommittee of the IRB to review issues and to make recommendations to the IRB (e.g., to supplement the IRB’s review of research proposals or to review of reports of potential unanticipated problems or noncompliance). The number and composition of the subcommittee shall depend on the scope of duties delegated by the IRB Chair. Any such subcommittee cannot approve research or issue determinations that require review by the convened IRB.

8.3 Composition of IRB Membership

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of the research that comes before it and possess the professional competence necessary to review specific research activities. The structure and composition of the UMMC IRB is based upon regulatory requirements and the characteristics of the research it reviews. A member of the IRB may fill multiple membership position requirements (e.g., nonscientist and unaffiliated).

1. The IRB will have at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the organization. The IRB shall not consist entirely of members of one profession.

2. The IRB will be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human research participants.

3. In addition to possessing the professional competence necessary to review specific research activities, the IRB includes members able to ascertain the acceptability of proposed research in terms of organizational commitments and regulations, applicable law, and standards of professional conduct and practice.

4. The IRB will include members who are knowledgeable about and experienced working with participants who are vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, or individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons), that are regularly included in the research under its review.
5. Every effort is made to ensure that the IRB does not consist entirely of men or women, including the organization's consideration of qualified persons of both sexes, so long as no appointment is made to the IRB solely on the basis of gender.

6. The IRB includes at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

7. The IRB includes at least one member who is not otherwise affiliated with the organization and who is not part of the immediate family of a person who is affiliated with the organization.

8. The IRB includes at least one member who represents the general perspective of participants.

Individuals from UMMC’s Office of Research and Sponsored Programs, Office of Development or Office of Technology Transfer may not serve as members of the IRB or carry out day-to-day operations of the review process. Individuals from these offices may provide information to the IRB and attend IRB meetings as invited guests.

The IRB Chair and the Human Research Office Director review the membership and composition of the IRB annually to determine if it continues to meet regulatory and organizational requirements.

8.3.1 Appointment of Members to the IRB

When the need for a new IRB member or alternate is identified, the IRB Chair, Vice Chair, current IRB member and/or the Human Research Office Director informs the IO and seeks out qualified candidates. Department Chairmen and others may forward nominations to the IRB Chair, IO or to the Human Research Office Director.

The final decision in selecting a new member is made by the Institutional Official, in consultation with, the IRB Chair and the Human Research Office Director.

Appointments are made by the UMMC Vice Chancellor, for a one year term, with a renewable, unlimited term of service. Any change in appointment, including reappointment or removal, requires written notification. Members may resign by written or email notification to the IRB Chair or Human Research Office Director.

The Human Research Office Director will ensure that changes in IRB membership are reported via the federal IRB registration process, in accordance with the instructions provided on OHRP’s website.

8.4 Liability Coverage for IRB Members

UMMC is a state-supported institution covered by the Mississippi Tort Claims Act. Coverage under the Tort Claims Act applies to employees and persons acting on behalf of and in service to UMMC in an official capacity, temporarily or permanently for acts or omissions within the scope of their duties or authorized activity.
8.5 Use of Consultants

When necessary, the IRB Chair, IRB members or the Human Research Office Director may solicit individuals from within the organization or outside of the organization with the expertise to assist in the review of research or issues which require expertise beyond or in addition to that available on the IRB. The IRB Office ensures that all relevant materials are provided to the consultant reviewer prior to the convened meeting or expedited review.

Consultants are subject to UMMC’s Conflict of Interest Policy and must confirm that they do not have a conflict of interest prior to review. Individuals who have a conflict of interest or whose spouse or immediate family member(s) has a conflict of interest in the research, including any relationship to the sponsor, are not invited to provide consultation.

The consultant’s findings are presented to the IRB for consideration either in person or in writing. If the findings are presented while in attendance at an IRB meeting, the consultant may assist in the IRB’s deliberations, but may not participate in the vote.

Written statements from consultants are kept in the IRB study records. Key information provided by consultants at meetings is documented in the minutes.

Ad hoc or informal consultations requested by individual members (rather than the convened board) are processed by the Human Research Office in a manner that protects the investigator’s confidentiality and is in compliance with the IRB conflict of interest policy.

8.6 Reporting and Investigation of Allegations of Undue Influence

If an IRB Chair, member, or staff person feels that the IRB has been unduly influenced by any party, he/she shall make a confidential report to the Human Research Office Director or IO.

Undue influence means attempting to interfere with the normal functioning and decision making of the IRB or to influence an IRB member, staff, or any other member of the research team outside of the established processes or normal and accepted methods in order to obtain a particular result, decision or action by the IRB or one of its members or staff.

The Human Research Office Director or IO ensure that a thorough investigation is conducted, and if the allegation is determined valid, that corrective action is taken to prevent additional occurrences. In the event that the allegation is regarding the IO, the matter is referred to the Vice Chancellor and the Office of Integrity and Compliance for investigation and any necessary action.
9 IRB Actions, Failure to Respond, Appeals

9.1 IRB Actions

In conducting its review of research, the IRB may take any of the actions listed below. With the exception of disapproval, the actions listed below may be used for either expedited or convened board review, including limited review under the 2018 requirements. Disapproval can only be decided at a convened IRB meeting. An expedited reviewer cannot disapprove a study.

Approval  The research, proposed modification to previously approved research, or another item is approved. The IRB has made all of the determinations required for approval (i.e., approval criteria and any applicable special determinations (e.g., waivers, alterations, vulnerable population determinations, etc.)). No further action is needed.

Revisions Required  The research, proposed modification to previously approved research, or other item requires revisions that must be addressed before the item may be approved. The IRB may require:

1. Confirmation of specific assumptions or understanding on the part of the IRB regarding how the research will be conducted (e.g., confirmation that research excludes children);
2. Submission of additional documentation;
3. Precise language changes to the study, consent, or other study documents; or
4. Substantive changes to the study, consent, or other study documents along with clearly stated parameters that the changes must satisfy.

When the convened IRB requires revisions, the IRB will designate who will review responsive materials from the investigator and determine that the conditions have been satisfied. If the IRB determines that, considering the scope and nature of the revisions, it is able, based on the assumption that the conditions are satisfied, to make all of the determinations required for approval the IRB staff may be designated to review responsive materials for verification. Based upon the nature and scope of the revisions the IRB may also designate the IRB Chair and/or one of more members to review responsive materials, to ensure appropriate expertise for review. If upon review the conditions have not been satisfied, or are only partially satisfied, the responsive materials must be referred to the convened IRB for review. When an expedited reviewer requires revisions the original expedited reviewer (and/or other qualified individual(s)) will receive the response materials and review for verification.

After verification, the following will be documented in IRB records and written communication to the investigator:

1. The date when verification was made that all IRB conditions have been satisfied (i.e., the “approval date”, which is also the “effective date” at UMMC), and;
2. For initial approval and continuing reviews, the date by which continuing review must occur (i.e., the “expiration date”)

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The IRB will be informed of the outcome of the review of the investigator’s response in the next available meeting agenda.

**Partial Approval or Approval with Limitations or Restrictions**
This action may be taken when the IRB approves some but not all components of the research, while other components of the research require modification or clarification and may not begin or continue until approved by the IRB. For example, the IRB could determine that a study may begin but that children cannot be enrolled until the investigator submits, and the IRB approves, a plan for assent; the IRB could stipulate that the approval for the local site only includes adult participants; the IRB could approve one phase of the research but require that a modification is submitted before future phases begin; or the IRB could limit the research responsibilities of an investigator due to a COI.

**Tabled**  This action is taken by the convened IRB when modifications are required of the nature or amount that the full IRB cannot make or specify exact changes or parameters, or additional information or clarification is needed in order to determine that one or more criteria for approval are satisfied (e.g., the risks and benefits cannot be assessed until additional information is provided.).

The action is documented in the IRB minutes and is communicated to the investigator in writing.

When review is tabled, the responsive materials from the investigator will be provided to the convened IRB for review at a subsequent meeting.

**Disapprove**  This action is taken when the convened IRB determines that the proposed research activity does not satisfy the criteria for approval and that it cannot be modified to render it approvable (or the sponsor or investigator will not make necessary modifications that would render the research approvable).

**Approve for Development Only**  Per HHS regulations at 45 CFR 46.118, there are circumstances in which a sponsoring department or agency may require certification of IRB approval as a condition of submitting for or releasing funds but before definitive plans for the involvement of human subjects have been developed (e.g., grants in which the procedures involving human subjects are dependent on preliminary activities such as the completion of animal studies or development of instruments). In these circumstances, the IRB may approved for development only without having reviewed the as yet undeveloped procedures or materials. The IRB Chair or designee will review the available information (i.e., the grant or proposal and any supplemental information provided by the investigator) and, if appropriate, will provide certification of IRB approval for development only. Approvals for development only will note that IRB approval must be obtained before any activities involving human subjects may commence.

In addition to the above actions, the IRB may **acknowledge** reports and other items that don’t involve prospective changes to already approved research. For example, the IRB may acknowledge the report of a protocol deviation but approve, require modifications in, or disapprove any associated corrective action plan. Further, the IRB may approve an item but include **comments** noting certain requirements, restrictions, or understandings. For example,
with collaborative research, the IRB may note that approval must also be obtained from another IRB with jurisdiction and that the letter documenting that approval must submitted to the UMMC IRB before human research activities involving the collaborating organization or personnel may commence.

9.2 Failure to Respond

Upon review of a research study, the IRB may require changes or request certain information from an investigator. Failure to respond to IRB required changes or requests for information within 60 days (or less if the IRB determines that the information must be submitted earlier to ensure protection of the research participants) may result in suspension or termination of IRB approval for the study. For studies that have not yet been approved, the study submission may be administratively withdrawn. At its discretion, the IRB may grant an extension beyond 60 days if the investigator contacts the IRB office prior to the deadline and presents sufficient cause for delay.

9.3 Reporting IRB Actions

All IRB actions are communicated to the investigator, and designated contact person for the research study, via information in the IRB electronic system within ten (10) working days, whenever possible, of the review. When applicable, a stamped copy of the approved consent, permission and/or assent forms will also be available. For IRB actions of revisions required or tabled, the notification will include a list of the conditions or requirements that must be satisfied or responded to. For a disapproval, suspension, or termination, the notification will include the basis for the action and will offer the investigator an opportunity to respond in person or in writing.

The IRB reports its findings and actions to the organization in the form of its minutes, which are distributed by IRB staff to the UMMC IO.

9.4 Appeal of IRB Decisions

When the IRB suspends, terminates, or disapproves research, the IRB letter communicating the decision will include the basis for the action and will offer the investigator the opportunity to respond in person or in writing. Additionally, whenever an investigator disagrees with an IRB requirement or decision, or believes that providing the IRB with additional information may result in a different outcome, the investigator may request that the IRB reconsider its decision by submitting a request in writing to the IRB Chair. The request must contain the basis for the appeal, including any substantive new information that the Board did not have the opportunity to consider previously. The request is scheduled for review at a convened IRB meeting and the Investigator invited to attend the meeting to discuss the request and provide information, but will be asked to leave prior to the IRB’s final deliberations and vote.
10 IRB Review Process

The UMMC IRB reviews and ensures that research under its oversight meets all required ethical and regulatory criteria for initial and continuing review and any modifications of approved research. The IRB may conduct its review using the following review methods:

- Expedited Review
- Review by Convened IRB

10.1 Expedited Review

For research subject to the pre-2018 Common Rule, FDA or DOJ regulations, or other requirement that requires reviewer determination of minimal risk, an IRB may use the expedited review procedure to review:

1. Some or all of the research appearing on the list of categories of research eligible for expedited review and found by the reviewer(s) to involve no more than minimal risk.

2. Minor changes in research previously approved by the convened IRB. Note: review of minor changes does not alter the end-date of study approval.

For research subject to the revised Common Rule (2018 requirements), an IRB may use the expedited review process to review:

1. When the research activities involve only procedures appearing on the federal register list of categories of research eligible for expedited review unless the reviewer determines, and documents the rationale for the determination, that the research involves more than minimal risk.

2. Research for which limited IRB review is a condition of exemption under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8).

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—used by the IRB.

10.1.1 Definitions

**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.

**Minor Change:** A minor change is one which, in the judgment of the IRB reviewer, makes no substantial alteration in:

1. The acceptability of the risk-to-benefit analysis or increases the level of risks to participants;

2. The research design or methods (for example, adding procedures that are not eligible for expedited review (See Section 10.1.2) are considered more than a minor change);
3. The number of participants to be enrolled in the research locally;

4. The qualifications of the research team (i.e., the change does not negatively impact the expertise available to conduct the research);

5. The facilities available to support safe conduct of the research; or

6. Any other factor which would warrant review of the proposed changes by the convened IRB.

Minor changes also include the addition of sites to a protocol approved by the convened IRB so long as the investigator(s)/site(s) do not have a conflict of interest, potential compliance concerns (e.g., a 483 that has not been adequately resolved), or any other investigator or site-specific concerns (e.g., qualifications, facilities, or resources to safely conduct the research).

In addition, if a study is transitioned from the pre-2018 Common Rule to comply with the 2018 requirements, the IRB may consider an investigator modification of the consent form to be consistent with the 2018 requirements to represent a minor change to the research. If such a determination is made, the IRB may use the expedited review procedure to evaluate the consent form changes, as permitted under §46.110(b)(1)(ii).

10.1.2 Categories of Research Eligible for Expedited Review

UMMC applies the categories of research eligible for expedited review, which were published in the Federal Register notice 63 FR 60364-60367, November 9, 1998.

The activities listed below should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human participants.

The categories in this list apply regardless of the age of participants, except as noted in category 2.

The expedited review procedure may not be used where identification of participants and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to a participant’s financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

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

Research Categories one (1) through seven (7) may be used for both initial and continuing IRB review:

(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, 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. (Note: Children are defined as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.)

(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 gum base 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; (k) vaginal swabs that do not go beyond the cervical os; rectal swabs that do not go beyond the rectum; and nasal swabs that do not go beyond the nares.

(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. (Note: 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 DHHS regulations
for the protection of human subjects. See Exempt Categories and 45 CFR 46 101(b)(2) and b(3).
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 DHHS
regulations for the protection of human subjects. See Exempt Categories and 45 CFR
46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

Categories 8 and 9 apply only to continuing review.

(8) Continuing review of research previously approved by the convened IRB as follows:

   (a) Where (i) the research at UMMC 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 (Note: “Long-term follow-
       up” includes research interactions that involve no more than minimal risk to subjects (e.g.,
       quality of life surveys); and collection of follow-up data from procedures or interventions
       that would have been done as part of routine clinical practice to monitor a subject for
disease progression or recurrence, regardless of whether the procedures or interventions
       are described in the research study, but not interventions that would not have been
       performed for clinical purposes, even if the research interventions involve no more than
       minimal risk.); or

   (b) Where no subjects have ever been enrolled at UMMC and no additional risks have been
       identified (Note: “no additional risks have been identified” means that neither the
       investigator nor the IRB has identified any additional risks from any institution engaged in
       the research project or from any other relevant source since the IRB’s most recent prior
       review.); or

   (c) Where the remaining research activities at UMMC are limited to data analysis. (Note:
       Simply maintaining individually identifiable private information without using, studying, or
analyzing such information is not human subject research and thus does not require continuing review.

(9) Continuing review of research previously approved by the IRB at a convened meeting that meets the following conditions:

- The research is not conducted under an investigational new drug application (IND) or an investigational device exemption (IDE);
- Expedited review categories (2) through (8) do not apply to the research;
- The IRB has determined and documented at a convened meeting that the research, or the remaining research activity involving human subjects, involves no greater than minimal risk to the subjects; and
- No additional risks of the research have been identified. (Note: “no additional risks have been identified” means that neither the investigator nor the IRB has identified any additional risks from any institution engaged in the research project or from any other relevant source since the IRB’s most recent prior review.)

10.1.3 Expedited Review Procedures

Under an expedited review procedure, IRB review is carried out by the IRB Chair, Vice Chair, Alternate Chair or by one or more reviewers designated by the Chair from among experienced members and alternate members of the IRB. Designated reviewers must be professionally competent (i.e., experienced with and having demonstrated the ability to apply IRB review requirements and with appropriate scientific or scholarly expertise) to conduct expedited reviews.

IRB members with a conflict of interest in the research (See Section 23.2) will not be selected as a reviewer, but may answer questions about the research if requested.

When reviewing research under an expedited review procedure, the IRB Chair, or designated reviewer, receives and reviews all documentation submitted (the same documentation is submitted for all studies, whether expedited and convened review). This requirement applies to all categories of submissions including initial reviews, continuing reviews, and modifications. The reviewer determines and documents the regulatory criteria allowing use of the expedited review procedure in the IRB’s electronic system. When a reviewer determines that research subject to the revised Common Rule (the 2018 requirements) falls within the expedited categories but involves more than minimal risk, the reviewer will document the rationale for that determination in the IRB’s electronic system. If the research does not meet the criteria for expedited review, the reviewer indicates that the research requires review by the convened IRB and the research study is placed on the next available IRB meeting agenda.

In reviewing the research, the expedited reviewer(s) will apply the same criteria for review and approval of research described throughout this manual and may exercise all of the authorities of the IRB except that the reviewer(s) may not disapprove the research. A research activity may only be disapproved by the convened IRB.
The Reviewer selects approve, require revisions or refer to the convened IRB for review on the Review screen in the IRB’s electronic system and returns it to the IRB Office. If additional information is requested, the investigator receives an email notification and a task in the IRB electronic system that identifies the information being requested. If the reviewer selects approve, the reviewer documents that the research meets the regulatory criteria for approval and a letter documenting approval is prepared by the IRB staff and provided to the investigator.

In the event that expedited review is carried out by more than one IRB member and the reviewers disagree, the IRB Chair may make a final determination or the study is referred to the convened IRB for review.

10.1.4 Informing the IRB

A list of all approvals by expedited review is part of the IRB meeting agenda and sent to all members of the IRB, including limited IRB reviews conducted using expedited review procedures. Any IRB member can click on a link within the agenda to review any study that appears on the agenda or may request to review a hard copy of any study by contacting the IRB Office.

10.2 Convened IRB Meetings

Except when an expedited review procedure is used, the IRB conducts initial and continuing review of all non-exempt research, and exempt research subject to limited IRB review, at convened meetings at which a quorum of the members is present.

10.2.1 IRB Meeting Schedule

Each IRB meets on a regular basis throughout the year (usually once per month). The schedule for IRB meetings is posted on the IRB website, https://www.umc.edu/Research/Research-Offices/Human-Research-Office/Institutional%20Review%20Board/Meeting-Dates-and-Deadlines.html, but may vary due to holidays or lack of quorum. Special meetings may be called as needed by the IRB Chair or HRO Director.

10.2.2 Pre-Review

The Human Research Office staff conducts a pre-review of submissions for determination of completeness and accuracy. Only complete submissions are placed on the IRB meeting agenda for review. Depending upon timing of the submission, the investigator is informed either through the IRB electronic submission system, by e-mail, phone or in person of missing materials and/or information and the necessary date of receipt for inclusion on the agenda. If an investigator is submitting for the first time or is not be well-versed in the submission procedures, consultations can be arranged with IRB staff.
10.2.3 Reviewers

After it has been determined that a submission is complete, the IRB coordinator, with the assistance of the IRB Chair as needed, assigns submissions for review, paying close attention to the subject matter of the research, the potential reviewer’s area(s) of expertise and representation for any vulnerable populations involved in the research. Two reviewers are assigned to each Initial Review, and one reviewer is assigned to each Continuing Review and Amendment. Where possible, the reviewer for each Continuing Review and Amendment is one of the original reviewers for the study. A reviewer may be assigned several submissions or other items for review. When the IRB is presented with a research study which may be outside of the knowledge base or representative capacity of the IRB members, an outside consultant will be sought (See Section 8.5). Research studies for which appropriate expertise cannot be obtained for a given meeting are deferred to another meeting when appropriate expertise is available.

The named reviewer(s) are responsible for:

1. Having a thorough knowledge of all of the details of the proposed research;
2. Performing an in-depth review of the proposed research;
3. Leading the discussion at the IRB meeting, and leading the IRB through the regulatory criteria for approval and any required determinations.

All IRB members receive and are expected to review all studies, not just those to which they are assigned as a reviewer.

When there is sufficient advance notice that a reviewer will be absent from the meeting, a new reviewer is assigned, provided that the new reviewer will have sufficient time to review the materials in advance of the meeting. An absent reviewer can submit written comments for presentation at the convened meeting, but any recommendation does not count as a vote.

10.2.4 Materials received by the IRB

For inclusion on an IRB meeting agenda, all required materials must be submitted to the IRB office within 13 days prior to the convened meeting date. When a submission is time-sensitive, the IRB office may make an exception to this rule provided that there is still sufficient time for all members to review the submission materials. The meeting agenda is prepared by the IRB coordinator, in consultation with the Human Research Office Director, IRB Chair or Vice-Chair, as needed. All IRB members receive the meeting agenda, which includes a list of research approved under expedited review procedures since the last meeting, applicable administrative items, continuing education materials and research submission materials at least 7 business days before the scheduled meeting to allow sufficient time for the review process. A time-sensitive item may be added to the agenda less than 7 business days in advance if circumstances warrant and the IRB staff have contacted the IRB members and verified that they will have sufficient time for review.
All IRB members have access in the IRB electronic system to all materials submitted for all studies on the agenda, which include the following, as applicable:

- The complete Protocol;
- The application form;
- Proposed and/or currently approved Consent / Parental Permission / Assent Form(s); Proposed recruitment materials, including advertisements intended to be seen or heard by potential study participants;
- Any other materials, such as questionnaires or diaries;
- Grant application(s);
- Investigator Brochure(s)

Additionally, for HHS-supported multicenter clinical trials, the IRB should receive and review a copy of the HHS-approved sample consent forms and the complete HHS-approved protocol, if they exist.

If an IRB member requires additional information to complete the review, he/she may contact the investigator directly or may contact the IRB Office to make the request of the investigator. Any additional information should be provided to the other IRB members.

**10.2.5 Quorum**

A quorum of the IRB consists of a majority (more than half) of the voting membership, including at least one member whose primary concern is in a non-scientific area. When research involving an investigational new drug is on the agenda for review, a physician is required for quorum. At IRB meetings, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote.

The IRB Chair, with the assistance of the IRB staff, confirms that quorum is present before calling the meeting to order. The IRB Chair, with the assistance of the IRB staff, is responsible for ensuring that the IRB meeting remains appropriately convened. The IRB Staff notifies the IRB Chair when a quorum is not present. If quorum is not maintained, either by losing a majority of the members, losing all non-scientific members or another required member, the IRB will not take votes until quorum is restored.

A sign-in sheet is maintained for each convened meeting. Attendance and vote count are documented by the IRB Staff for each individual study on the agenda within the review area of the IRB’s electronic system.

It is generally expected that more than one scientific member, at least one unaffiliated member and at least one member who represents the general perspective of participants (one individual can serve in both capacities) is present at all IRB meetings. The IRB may, on occasion, meet without this representation; however, this is the exception (i.e., no more than 20% of meetings).
If the IRB regularly reviews research that involves a vulnerable category of participants, such as children, prisoners, pregnant women, or persons with impaired decision-making capacity, one or more individuals (e.g., IRB members, alternate members, or consultants) who are knowledgeable about and experienced with that population should be present during the review of the research.

IRB members are considered present and participating at a convened IRB meeting when either physically present or participating through electronic means (e.g., teleconferencing or video conferencing) that permits them to listen to and speak during IRB deliberations and voting. Whether or not physically present, the IRB member must have received all pertinent materials prior to the meeting and must be able to participate actively and equally in all discussions.

Opinions of absent members may be considered by the attending IRB members but may not be counted as votes or to satisfy the quorum for convened meetings.

10.2.6 Meeting Procedures

Once it has been determined that a quorum is in place the IRB Chair calls the meeting to order. The Chair reminds IRB members to recuse themselves from any discussion and vote when they have a conflict (and the member leaves the room prior to the start of the discussion).

The IRB reviews all submissions for initial and continuing review, requests for revisions and final reports. The reviewers present an overview of the research and assist the Chair in leading the IRB through a discussion of the regulatory criteria for approval or other required determinations. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

The IRB coordinator and Human Research Office Director take notes of the proceedings and the IRB coordinator is responsible for preparing the meeting minutes.

10.2.7 Guests

Investigators and research staff may be invited to the IRB meeting, at the discretion of the IRB, to make a brief presentation or to answer questions about proposed or ongoing research. The investigator/research staff may not be present for the deliberations or vote on the research.

The Human Research Office Director and staff regularly attend IRB meetings and may participate in the IRB discussion and deliberations, but are not IRB members and may not vote.

Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair and the Human Research Office staff. Such guests are asked to sign a confidentiality agreement, do not participate in discussion unless requested by the IRB, and may not vote.

10.3 Criteria for IRB Approval of Research

In order for the IRB to approve human subjects research, either through expedited review or by the convened IRB, it must determine that the following requirements are, or remain, satisfied.
(1) Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) For research subject to the pre-2018 Common Rule, or FDA or DOJ regulations:
Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

For research subject to the revised Common Rule (2018 requirements): Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving subjects vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.116].

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.117].

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(8) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.
10.3.1 Risk/Benefit Assessment

The goal of the assessment is to ensure that the risks to research participants posed by participation in the research are justified by the anticipated benefits to participants or society. The IRB must:

- Judge whether the anticipated benefit, either of new knowledge or of improved health or other direct benefit for the research participant, justifies asking any person to undertake the risks; and
- Disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of proposed research involves a series of steps:

1. **Identify the risks** associated with the research, as distinguished from the risks of activities, diagnostic tests, treatments, or therapies participants would receive even if not participating in research;

2. **Determine whether the risks are minimized** to the extent possible by evaluating the necessity of procedures that impart risk and whether the data could be gained by procedures that are already being performed for other purposes or by alternative procedures that impart less risk;

3. **Identify the anticipated benefits** to be derived from the research, both direct benefits to participants and possible benefits to society, science and others;

4. **Determine whether the risks are reasonable in relation to the benefits**, if any, and assess the importance of the knowledge to be gained;

In evaluating the risks and benefits, the IRB should consider only those risks and benefits that may result from the research, as distinguished from risks and benefits participants would receive even if not participating in the research. The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks and benefits that fall within the purview of its responsibility.

The IRB should not consider any compensation that participants will receive to be a benefit of the research.

When research participants are assigned to different arms or otherwise undergo differing interventions, procedures, or exposures, the evaluation of risk and benefit should be made for each group (i.e., a “component analysis’). This is especially important when a subset of participants will have no possibility of direct benefit but will be exposed to greater than minimal risks.

10.3.1.1 Scientific or Scholarly Review

In order to assess the risks and benefits of the proposed research, the IRB must determine that:
• The research uses procedures consistent with sound research design; and
• The research design is sound enough to reasonably expect the research to answer its proposed question.

In making this determination, the IRB may draw on its own knowledge and expertise, or the IRB may draw on the knowledge and expertise of others, such as reviews by a funding agency, or departmental review. When scientific or scholarly review is conducted by an individual or entity external to the IRB, documentation of the outcome and details of the review is provided to the IRB through its electronic system with the application under review.

10.3.2 Equitable Selection of Participants

The IRB evaluates whether the selection of subjects is equitable with respect to gender, age, class, etc. by reviewing the IRB application and all supporting material. The IRB will not approve a study that does not provide adequately for the equitable selection of research participants or does not provide an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research. In making this determination, the IRB evaluates:

• The purposes of the research;
• The setting in which the research occurs;
• Scientific and ethical justification for including vulnerable populations or subjects vulnerable to coercion or undue influence such as children, prisoners, pregnant women, mentally disabled persons, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons;
• The scientific and ethical justification for excluding classes of persons who might benefit from the research; and
• The inclusion/exclusion criteria, and the procedures/materials intended for use for the identification and recruitment of potential participants.

At the time of continuing review the IRB evaluates whether subject selection has been equitable.

10.3.2.1 Recruitment of Participants

The investigator provides the IRB with a plan for recruitment of all potential participants. All recruiting materials are submitted to the IRB, including advertisements, flyers, scripts, information sheets and brochures. The IRB ensures that the recruitment plan and materials appropriately protect the rights and welfare of prospective participants (e.g., do not present undue influence). See Section 10.4.9 for a discussion of IRB review of advertisements and Section 10.4.10 for a discussion of IRB review of payments.
10.3.3 Informed Consent

The IRB ensures that informed consent will be sought from each prospective participant or the participant’s legally authorized representative (LAR), in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. In addition, the IRB ensures that informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27. The IRB ensures, as part of its review, that the information in the consent document and process is consistent with the research plan, and, when applicable, the HIPAA authorization. See Section 13 for detailed policies on informed consent.

10.3.4 Data and Safety Monitoring

For research that is more than minimal risk, the investigator should submit a data and safety monitoring (DSM) plan. The plan may be included within the protocol. The plan should describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to participants or others, descriptions of interim safety reviews and the procedures planned for providing monitoring results to the IRB. DSM may be performed by a researcher, medical monitor, safety monitoring committee, or other means, as appropriate.

The IRB reviews the safety monitoring plan and determines if it makes adequate provision for monitoring data to ensure the safety of participants and address problems that may arise over the course of the study. If a plan is not submitted, the IRB determines whether is required, and, depending on the circumstances, what the plan should include. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study.

The principles the IRB applies in evaluating the adequacy of a proposed DSM plan include:

- Monitoring is commensurate with the nature, complexity, size and risk involved;
- Monitoring is timely; frequency commensurate with risk; and conclusions reported to the IRB;
- For low risk studies, close monitoring by the study investigator or an independent individual may be adequate and appropriate, with prompt reporting of problems to the IRB, sponsor and regulatory bodies, as applicable;
- For greater than minimal risk studies that do not include a plan for monitoring by a Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), and that are blinded, multi-site, involve vulnerable populations, or involve high-risk interventions or procedures, the IRB will carefully evaluate the proposed DSM plan and may require establishment of a DSMB, DMC, or other methods to enhance the monitoring and management of participant safety.

Data and Safety Monitoring plans should specify:

- The entity or person(s) who will perform the monitoring, and the independence or affiliation that the entity or person(s) has with the sponsor or investigator;
• The safety information that will be collected and monitored, including serious adverse events and unanticipated problems;
• The frequency of review of safety data;
• The procedure for analysis and interpretation of the data;
• The procedure for review of scientific literature and data from other sources that may inform the safety or conduct of the study;
• The conditions that will trigger a suspension or termination of the research (i.e., stopping rules), if applicable;
• The procedure for reporting to the IRB, including a summary description of what information, or type of information, will be provided.

For a Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), the plan should also describe the composition of the board or committee. Generally, a DSMB should be composed of experts in all scientific disciplines needed to interpret the data and ensure participant safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease/condition and treatment under study should be part of the monitoring group or be available if warranted.

The National Institutes of Health (NIH) requires the establishment of DSMBs for multi-site clinical trials involving interventions that entail potential risk to participants.

When DSMBs or DMCs are used, during continuing review the IRB may rely on a current statement, or the most recent report, from the DSMB or DMC which indicates that it has and will continue to review study-wide adverse events, study wide interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

10.3.5 Privacy and Confidentiality

The IRB determines if adequate procedures are in place to protect the privacy of participants and to maintain the confidentiality of the data.

10.3.5.1 Definitions

Privacy: Having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. It is the state or condition of being free from unauthorized intrusion, being observed or disturbed by other people.

Confidentiality: Methods used to ensure that information obtained by investigators about participants is not improperly divulged.

Private information: Information that occurs in a context in which an individual can reasonably expect that no observation or recording is taking 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).
**Sensitive Information:** Data or information, on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, unauthorized access, misuse, alteration, or loss or destruction of the information (e.g., could reasonably place the participant at risk of criminal or civil liability or be damaging to the participant’s financial standing, employability, or reputation).

**Identifiable information:** Information where the identity of the participant is or may readily be ascertained by the investigator or associated with the information.

**10.3.5.2 Privacy**

The IRB must determine whether the activities in the research appropriately protect the privacy of potential and actual participants. In order to make that determination, the IRB must obtain information regarding how the investigators plan to access participants and/or participants’ private, identifiable information and the participants’ expectations of privacy in the situation. Investigators must have appropriate authorization to access participants or the participants’ information.

In developing strategies for the protection of participants’ privacy, consideration is given to:

1. Methods used to identify and contact potential participants;
2. Settings in which an individual will be interacting with an investigator;
3. Appropriateness of personnel and others present for research activities;
4. Methods used to verify the identity of participants prior to disclosing information;
5. Methods used to obtain information about participants, and the nature of the requested information, including whether the data is the minimum necessary to achieve the aims of the research;
6. Information that is obtained about individuals other than the “target subjects,” (e.g., a participant provides information about a family member for a survey) and whether such individuals meet the regulatory definition of “human subject”.

**10.3.5.3 Confidentiality**

The IRB must determine if appropriate protections are in place to minimize the likelihood that information about participants will be inappropriately divulged. Safeguards designed to protect confidentiality should be commensurate with the potential of harm from unauthorized, inappropriate or unintentional disclosure.

The IRB assesses whether there are adequate provisions to protect data confidentiality by evaluating the methods used to obtain, record, share, and store information about individuals who may be recruited to participate in studies and about participants. The investigator will provide the IRB with a plan regarding the procedures to be taken to protect the confidentiality of research data and sensitive information. The investigator will provide information regarding information security procedures and plans to address the protection of paper documents, other physical media (e.g., audio or videotapes), and electronic data, and information regarding the
use, maintenance, storage, and transmission of information. The IRB will review the
information received from the investigator and determine whether the confidentiality of
research data is sufficiently protected. In some cases, the IRB may also require that a Certificate
of Confidentiality is obtained to protect data from compelled disclosure (See Section 26.3).
In reviewing confidentiality protections, the IRB considers whether or not the data or other
information accessed or gathered for research purposes is sensitive and the nature, probability,
and magnitude of harms that would be likely to result from a disclosure of collected
information outside the research. The IRB considers regulations and organizational policies and
will evaluate the effectiveness of proposed de-identification techniques, coding systems,
encryption methods, methods of transmission, storage facilities, access limitations, and other
relevant factors in determining the adequacy of confidentiality protections.

Research regulated by the FDA that involves the use of electronic data collection/storage
systems must also comply with the requirements of 21 CFR Part 11.

10.3.6 Vulnerable Populations

Certain individuals, by nature of age or mental, physical, economic, educational, or other
circumstances, may be more vulnerable to coercion or undue influence than others. At the
time of initial review, and when a proposed modification includes the involvement of
vulnerable populations, the IRB considers the scientific and ethical reasons for including
vulnerable participants in the research. The IRB may determine and require that, when
appropriate, additional safeguards be put into place for vulnerable participants.

For a discussion about the IRB’s review process for specific populations of vulnerable
participants, see Section 14.

10.4 Additional Considerations

10.4.1 Determination of Risk Level

At the time of initial review, the IRB makes a determination regarding the risks associated with
the research. Risks associated with the research are classified as either “minimal” or “greater
than minimal”, with additional classifications as required by the regulatory subparts or FDA
regulations. Risk determinations may vary over the life of a research study, depending on the
procedures and risks that participants are exposed to as the research progresses. The IRB may
reevaluate risk determination with modifications to the research, at continuing review, and
when new information becomes available. The determination of risk level, whether by the
convened IRB or the expedited reviewer, are documented within the review screen(s) and
reflected on the overall protocol information in the IRB’s electronic system.

10.4.2 Period of Approval

At the time of initial review and at continuing review, the IRB makes a determination regarding
the period of approval. All studies are reviewed by the IRB at intervals appropriate to the
degree of risk, but no less than once per year. In some circumstances, a shorter review interval
(e.g., semi-annually, quarterly, or after accrual of a specific number of participants) may be required (see below). For all studies (whether convened or expedited review) the IRB’s electronic system and meeting minutes reflect the approval start and end date and the review frequency is documented in the IRB’s electronic system.

IRB approval is considered to have lapsed at the end of the day of the expiration date of the approval (i.e., the expiration date is the last day research can be conducted). For a new study reviewed by the IRB, the approval commences on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB or expedited reviewer approves the research or the date when it has been verified that the requirements of the IRB have been satisfied following an action of Revisions Required. When continuing review is required, the expiration date of the initial approval period, which is the date by which the first continuing review must occur, may be as late as one year after the effective date of initial IRB approval.

For continuing reviews of a research study, the date the convened IRB or the date that the expedited reviewer conducts continuing review and approves the study determines the latest permissible date of the next continuing review (when continuing review is required). The approval date and approval expiration date, when applicable, are clearly noted on IRB determination letters and must be strictly adhered to. Investigators should allow sufficient time for development and review of continuing review submissions. As a courtesy, the IRB electronic system sends reminders to the investigator prior to the study’s expiration date, notifying him or her that the study is due for a continuing review or when approval has expired.

IRB review of a proposed modification to research ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full research project, not simply a change to it.

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur before midnight of the date when IRB approval expires. If the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur.

### 10.4.3 Review More Often Than Annually

The following factors are considered when determining which studies require review more frequently than once per year:

1. The probability and magnitude of anticipated risks to participants;
2. The likely medical/psychological/social/legal/educational condition of the proposed participants;
3. The qualifications of the investigator and other members of the research team;
4. The specific experience of the investigator and other members of the research team in conducting similar research;
5. The nature and frequency of adverse events observed in similar research;
6. The novelty of the research, which may make unanticipated events/problems more likely;
7. The involvement of vulnerable populations likely to be subject to undue influence or coercion (e.g., terminally ill);
8. A history of serious or continuing non-compliance on the part of the investigator;
9. Any other factors that the IRB deems relevant.

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of participants enrolled. If a maximum number of participants is used to define the approval period, it is understood that the approval period in no case can exceed one year, unless the study does not require a continuing review, and that the number of participants enrolled determines the approval period only when that number of participants is enrolled in less than one year. If an approval period of less than one year is specified by the IRB for research that is subject to continuing review, the reason for more frequent review is documented in the electronic protocol record, meeting minutes or the expedited reviewer’s review comments.

10.4.4 Independent Verification That No Material Changes Have Occurred

The IRB recognizes that protecting the rights and welfare of study participants sometimes requires that the IRB use sources other than the investigator to independently verify that no material changes occurred during the IRB-designated approval period.

In support of this requirement, the UMMC IRB requires the submission of other reportable information (See Section 19) including reports from external monitors, auditors, or inspectors (See Section 2.1).

The IRB will also determine the need for verification from outside sources on a case-by-case basis. The following factors will be considered when determining which studies require independent verification:

1. The nature, probability, and magnitude of anticipated risks to participants;
2. The degree of uncertainty regarding the risks involved;
3. Whether the research involves novel therapies or procedures;
4. The vulnerability(ies) of the study population(s);
5. The rate of enrollment;
6. The experience and expertise of the investigators;
7. The IRB’s previous experience with the investigators or the sponsor (e.g., compliance history, participant complaints, etc.);
8. The probable nature and frequency of changes that may ordinarily be expected in the type of research;
9. Whether the research undergoes routine independent monitoring;

10. Whether concerns about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources; and

11. Any other factors that suggest independent verification is warranted.

In making a determination about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period, or may require such verification at the time of any other review (e.g., continuing review, amendments, interim reports) or when a complaint, concern or allegation is received.

If any material changes have occurred without IRB review and approval, the IRB decides the corrective action to be taken (See Section 17 on Non-compliance).

10.4.5 Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may determine that monitoring of the consent process by an impartial observer (e.g., consent monitor) is required in order to reduce the possibility of coercion and undue influence, ensure that the approved consent process is being followed, and/or ensure that participants are truly giving informed consent.

Such monitoring may be particularly warranted for:

1. High risk studies;

2. Studies that involve particularly complicated procedures or interventions;

3. Studies where recruitment will occur in situations or circumstances that may negatively impact the consent process (e.g., the Emergency Room);

4. Studies involving highly vulnerable populations (e.g., ICU patients, children who are wards);

5. Studies involving study staff with minimal experience in obtaining consent; or

6. Other situations when the IRB has concerns that the consent process may not be/is not being conducted appropriately (e.g., prior investigator non-compliance, etc.).

Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project.

If the IRB determines that consent monitoring is required, the IRB may consult with the Human Research Office Director, the Office of Integrity and Compliance, and others to develop an appropriate plan. The consent monitoring may be conducted by HRPP or IRB staff, IRB members or another appropriate party. The investigator is notified of the IRB’s determination and the reasons for the determination. Arrangements are made with the investigator for the monitoring of the consent process, typically for a specified number of participants. When observing the consent process, the monitor will evaluate whether:
- The informed consent process was appropriately conducted and documented;
- The participant had sufficient time to consider study participation, and to ask questions and have them answered;
- The consent process involved coercion or undue influence;
- The information was accurate and conveyed in understandable language; and
- The participant appeared to understand the information and gave voluntary consent.

Following the monitoring, a report of the findings is submitted to the IRB, which determines the appropriate action to be taken, if any.

10.4.6 Investigator Qualifications

The IRB reviews credentials, curriculum vitae, resumes, or other relevant materials to determine whether investigators and members of the research team are appropriately qualified to conduct the research. The IRB may rely upon other UMMC processes (e.g., credentialing) to inform this determination.

10.4.7 Significant New Findings

During the course of research, significant new knowledge or findings about the research, the test article, and/or the condition under study may develop. The investigator must report any significant new findings to the IRB and the IRB reviews them with regard to the impact on the participants’ rights and welfare. Because the new knowledge or findings may affect the risks or benefits to participants or participants’ willingness to continue in the research, the IRB may require, during the ongoing review process, that the investigator contact participants to inform them of the new information. The IRB communicates this requirement to the investigator. If the study is still enrolling participants, the consent document should be updated. The IRB may require that the currently enrolled participants give consent to continue participation or otherwise provided with the new information. The IRB may also require that participants who are no longer in the study be provided with the new information, (e.g., late emerging safety information).

10.4.8 Conflicts of Interest (COI)

The IRB research application solicits information about investigator and research staff COI disclosure and any COI management plan in place. As part of its review process, the IRB makes a final determination as to whether any COI is adequately addressed and protects the human participants in the research. When there is an institutional COI, the IRB has final authority to determine whether the conflict and management plan, if any, allow the study to be approved. (See Section 23 for a more detailed discussion of COI.)
10.4.9 Advertisements and Recruitment Materials

The IRB must review and approve any and all advertisements prior to posting, use or distribution. The IRB will review:

1. The information contained in the materials;
2. The mode/method of its communication;
3. The final copy of printed materials; and
4. The proposed script and final version of any audio/video taped advertisements/recruitment materials.

This information is submitted to the IRB with the initial application or, if proposed after study approval, as an amendment.

The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence on potential participants to participate. This includes, but is not limited to:

1. Statements implying a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the research plan;
2. Claims, either explicit or implicit, that the test article (drug, biologic or device) or intervention is safe or effective for the purpose(s) under investigation;
3. Claims, either explicit or implicit, that the test article is equivalent or superior to any other drug, biologic, device or intervention.
4. Using terms like “new treatment,” “new medication,” or “new drug” without explaining that the test article or intervention is experimental/investigational;
5. Promising “free medical treatment” when the intent is only to say participants will not be charged for taking part in the investigation;
6. Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media;
7. Offers for a coupon good for a discount on the purchase price of an investigational product once it has been approved for marketing; and
8. The inclusion of exculpatory language.

The UMMC IRB does not allow the following phrases/language in the material:

1. Where an experimental drug, device or treatment is part of the study, terms like “new treatment”, “new medication” or “new drug” are not allowed and the test article must be referred to as experimental.
2. Specific payment amounts may not be identified.
3. Exculpatory language.
4. Promise of free medical treatment
Recruitment materials should be limited to the information prospective participants need to determine possible eligibility and interest. The following items must be included:

1. The name and address of the investigator and/or research facility;
2. The condition being studied and/or the purpose of the research;
3. The location of the research and the person or office to contact for further information.
4. A clear statement that that study involves research and not treatment.

When appropriately worded the material may also include:

1. In summary form, the criteria used to determine eligibility for the study;
2. The time or other commitment required;
3. A brief list of potential benefits.

Once approved by the IRB, an advertisement may not be altered or manipulated in any way without prior IRB approval.

Directory listings of research such as ClinicalTrials.Gov are not considered advertisements and do not require IRB review and approval if the listing is limited to the following basic information: title, purpose of the study, research plan summary, basic eligibility criteria, study site location(s), and how to contact the study site for further information.

The first contact prospective study participants make is often with a person who follows a script to determine basic eligibility for the specific study. The IRB reviews the script and procedures to ensure that the screening procedures adequately protect the rights and welfare of prospective participants.

10.4.10 Payments and Reimbursement

Payments to research participants are commonly proposed as an incentive for participation in recognition of the time, effort, inconveniences, and discomforts that participation in the proposed research may entail. In contrast to payments, reimbursement is provided to cover actual costs incurred by participants as a result of participation (e.g., travel, parking, lodging, etc.). Payment arrangements should be managed separately from reimbursement whenever possible because the ethical considerations differ (as well as the potential tax implications). Reimbursement offsets costs and may decrease financial risks associated with participation and in doing so may facilitate equitable selection of participants. In contrast, the amount, timing, and nature of payments may unduly influence potential participants’ decision-making, influencing them to accept discomforts or risks that they otherwise would find unacceptable and interfering with truly voluntary informed consent. Payment arrangements may also create issues with equitable selection of participants, including the societal distribution of research risks and benefits and the generalizability of the research results.

The IRB must consider the proposed amount of payment, the method and timing of disbursement, the study population, the recruitment methods and materials, and the information provided within the proposed consent form in order to evaluate the acceptability
of a proposed payment plan. The IRB does not consider payment as a benefit when weighing the risks and benefits of the research, as payment is an incentive not a benefit of the research.

The proposed amount and schedule of payments and the justification or basis for payment are included in the IRB application. Such justification should substantiate that proposed payments are reasonable and commensurate with the time and inconveniences associated with study participation and do not constitute (or appear to constitute) undue pressure on the potential participant to volunteer for the study.

When research involves multiple visits or interactions, payment must be prorated and not be contingent upon the participant completing the entire study. Any amount paid as a bonus for completion of the entire study may not be so great that it could unduly induce a participant to remain in the study when he/she otherwise would have withdrawn.

The consent form must describe the terms of payment including the amount and schedule of payments and any conditions under which participants will receive partial payment (e.g., if they withdraw from the study before participation is complete) or no payment. Plans to reimburse participants for incurred expenses must also be outlined in the IRB application and described in the consent document.

UMMC has policies in place to address how and what information is collected and reported for participants who receive the amount of compensation required to be reported to the Internal Revenue Service (IRS). When applicable the consent form must disclose the information that will be collected (e.g., Social Security Number), who will be provided or have access to the information and the circumstances that necessitate IRS reporting.

10.4.11 Non-Monetary Gifts and Incentives

Similar to financial incentives, non-monetary gifts or incentives can also present problems of undue influence or coercion that impact a potential participant’s ability to fully and freely consider participation in research.

If participants are provided with non-monetary gifts or tokens of appreciation, such as course credit, tote bags, books, toys, or other such materials, the approximate retail value must be described to the IRB, along with a description, photo, or sample product to review.

The IRB reviews all gifts and incentives, being particularly sensitive to the influence of power or authority, whether perceived or actual, over free decision-making. Overt coercion (e.g., threatening loss of credit, or access to services or programs, to which potential participants are otherwise entitled) is never appropriate. Moreover, it must be clear that choosing not to participate will not adversely affect an individual’s relationship with the organization, its staff or the provision of services in any way (e.g., access to medical care).

Investigators should carefully structure incentives and methods of disbursement so that the incentive may serve as a factor in the decision to participate, but not serve to unduly influence or coerce participation.
10.4.12 State and Local Laws

The IRB considers and adheres to all applicable state and local laws in the jurisdictions where the research is taking place. The HRPP and IRB rely on UMMC Counsel for the interpretation and application of Mississippi law and the laws of any other jurisdiction where the research is being conducted as they apply to participants in human research. The IRB ensures that consent forms are consistent with applicable state and local laws.

10.5 Continuing Review

For research subject to the pre-2018 Common Rule, FDA or DOJ regulations, and any research where continuing review is required by applicable regulations, policy, or other requirements:
The IRB conducts a continuing review of ongoing research at intervals that are appropriate to the level of risk for each research plan, but not less than once per year. The date by which continuing review must occur is recorded in the IRB electronic system, the applicable IRB minutes or other IRB records and on initial and continuing review approval letters. Continuing review must occur as long as the research remains active including when the remaining research activities are limited to the analysis of private identifiable information.

For research subject to the revised Common Rule (2018 requirements): The IRB will conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described below. When applicable, the date by which continuing review must occur will be recorded in the IRB electronic system and on initial and continuing review approval letters.

Unless an IRB determines otherwise, continuing review of research subject to the 2018 Common Rule (the revised Common Rule) is not required in the following circumstances:

- Research eligible for expedited review in accordance with 45 CFR 46.110;
- Research reviewed by the IRB in accordance with the limited IRB review described in Section 5.4;
- 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.

The IRB may determine that continuing review is required for any research protocol that falls within the above criteria. For example, the IRB may determine that continuing review is required when:

1. Required by other applicable regulations (e.g., FDA);
2. Required by the terms of a grant, contract, or other agreement;
3. Recommended by Federal guidance (e.g., OHRP recommends that IRB’s require continuing review of research that falls within expedited categories 8(b) and 9);
4. The research involves topics, procedures, or data that may be considered sensitive or controversial;
5. The research involves particularly vulnerable subjects or circumstances that increase subjects’ vulnerability;
6. An investigator has minimal experience in research or the research type, topic, or procedures; and/or
7. An investigator has a history of noncompliance.

When the IRB determines that continuing review is required for such research, it will document the rationale in the IRB record and communicate the requirement to the investigator in the IRB determination letter.

10.5.1 Continuing Review Process

As a courtesy to investigators, the IRB electronic system sends 3 renewal reminders, 90, 60 and 30 days prior to expiration; however, it is the investigator’s responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted. No changes may be made with the continuing review submission.

Investigators must submit the following for continuing review:

1. The most recent report from the DSMB or DMC (if applicable);
2. The most recent multi-center progress report (if applicable); and
3. The continuing review application form (progress report).

The current approved protocol and, as applicable, recruitment material and consent document(s) automatically pull into and are part of the application, as is study personnel CITI training information. All information is submitted electronically and IRB members have access to the complete study file at all times.

10.5.2 IRB Considerations for Continuing Review

In order to re-approve research at the time of continuing review, the IRB must determine that the regulatory criteria for approval continue to be satisfied. Because the research was previously found to satisfy the criteria for approval, the IRB focuses its considerations at the time of continuing review on whether any new information is available that would affect the IRB’s prior determination that the criteria for approval are satisfied. The IRB pays particular attention to four aspects of the research:

1. Risk assessment and monitoring;
2. Adequacy of the informed consent process;
3. Local investigator and organizational issues; and
4. Research progress.
10.5.3 Convened Board Review

In conducting continuing review of research not eligible for expedited review, all IRB members are provided with access to all of the materials listed in Section 10.2.4 and are responsible for reviewing the Continuing Review Application, the project summary, the current consent document(s), when applicable, the progress report, and, if applicable, the data and safety monitoring report, and multi-center study progress reports. The Reviewer is responsible for reviewing the complete materials submitted for continuing review including the complete research plan and is given access to the complete IRB file. At the meeting, the Reviewer assists the Chair in leading the IRB through the discussion of the submission, their evaluation and recommendation.

Review of currently approved consent documents occurs during the continuing review of research by the IRB. If the Continuing Review contains information that might alter the protocol, study procedures or consent document, for example the identification of new risks, the IRB considers whether changes are needed to the consent document, protocol or study procedures. If a change is needed, the submission of an amendment is required.

10.5.4 Expedited Review

In conducting continuing review under expedited procedures, the reviewer receives all of the previously noted materials. The reviewer determines whether the research meets the criteria for continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval.

For research subject to the pre-2018 Common Rule, or FDA or DOJ regulations:

If research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) (see Expedited Review Categories in Section 10.2.1). It is also possible that research activities that previously qualified for expedited review, have changed or will change, such that expedited IRB review is no longer permitted for continuing review.

For research subject to the revised Common Rule (2018 requirements):

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, unless it has progressed to the point that it involves only one or both of the following:

- 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;

and in limited circumstances described by expedited review categories (8) and (9) (see Expedited Review Categories in Section 10.1.2).
When continuing review is not required (See Section 10.5) for research subject to the 2018 Common Rule and the IRB reviewer determines that continuing review is required, the reviewer shall document the rationale in the checklist.

10.5.5 Possible IRB Actions after Continuing Review

At the time of Continuing Review, the Convened IRB or IRB Member(s) conducting expedited review may take any of the following actions described in Section 9.

If an IRB member conducting expedited review believes that continuation of the study should be disapproved, the review is referred to the convened IRB. If the IRB has significant concerns, the IRB may vote to suspend or terminate the research (See Section 11 for a detailed discussion of suspensions and terminations).

If the Continuing Review determination is Revisions Required, the IRB specifies any conditions that must be satisfied before an investigator can continue particular research activities related to those conditions or requirements that must be adhered to until the conditions of approval have been satisfied. For example, if at the time of continuing review, the IRB requires the investigator to change the research protocol to include a specific new procedure for screening prospective participants, the IRB could approve the research with the following condition: “Research activities involving currently enrolled participants may continue, but no new participants may be enrolled until a designated IRB member reviews a revised protocol and verifies that the protocol includes the new screening procedure.” Additionally, the IRB may specify a time period for the condition(s) to be satisfied, as long as the activity with conditions is not begun/restarted until approval is granted.

10.5.6 Lapse in Approval

The regulations permit no grace period or approval extension after approval expires. Research that continues after the approval period has expired is research conducted without IRB approval. If re-approval does not occur before the stated expiration date, all research activities must stop, including recruitment (media advertisements must be withdrawn), enrollment, consent, interventions, interactions, and data collection. This occurs even if the investigator has provided the continuing information before the expiration date. Expiration Notices are sent to Investigators the day following approval expiration. This occurs even if the investigator has submitted a Continuing Review application. The notice reminds investigators that all research activities must stop.

The lapse of IRB approval due to a failure to complete continuing review and obtain re-approval prior to expiration of the prior approval does not ordinarily constitute a suspension or termination of IRB approval, for federal reporting purposes; however, the failure to meet continuing review obligations may be grounds for suspension or termination of the research. If the IRB notes a pattern of non-compliance with the requirements for continuing review (e.g., an investigator repeatedly or deliberately neglects to submit materials for continuing review in a timely fashion or the IRB itself is not meeting the continuing review dates), the IRB should determine the reasons for the non-compliance and take appropriate corrective actions. The IRB
must report to FDA/OHRP any instance of serious or continuing non-compliance with FDA regulations or IRB requirements or determinations.

### 10.5.6.1 Management of Enrolled Participants During Lapse

While enrollment of new participants cannot occur after the expiration of IRB approval, the IRB recognizes that temporarily continuing participation of participants already enrolled may be necessary or appropriate, for example, when the research interventions hold out the prospect of direct benefit to the participants, or when withholding those interventions or safety monitoring procedures would place participants at increased risk. In these instances, the investigator must, at the earliest opportunity, contact the IRB office and submit a request to continue those research activities that are in the best interests of participants. Such a request should specifically list the research activities that should continue, provide justification, and indicate whether the request applies to all or only some participants. The IRB Chair or designee will review the request and provide a determination regarding what activities, if any, may continue during the lapse. Such a determination may include a time limit or other conditions or restrictions. If the IRB decides that participants already enrolled should continue to receive the interventions that were being administered to participants under the research project, data collection (especially safety information) should also continue for such participants. When there is insufficient time to obtain an IRB determination (e.g., the study regimen includes daily administration of an experimental agent), the investigator may make an initial determination, in consultation with the participants' treating physician, if appropriate. In such cases, the investigator must, as soon as possible, notify the IRB and submit a request for confirmation that the IRB agrees with the determination. The IRB Chair or designee reviews the request and provides a determination. In the event that the IRB does not agree with the investigator's determination, or only agrees in part (e.g., agrees that some but not all of the activities are in the best interests of participants), the IRB notifies the investigator who must then comply with the IRB's requirements or request a re-review of the determination by providing additional justification or information that the IRB may not have considered.

### 10.6 Amendment of an Approved Protocol

Investigators may wish to modify or amend their approved applications. Investigators must seek IRB approval before making any changes, no matter how minor, in approved research - even though the changes are planned for the period for which IRB approval has already been given - unless the change is necessary to eliminate an immediate hazard to the participant (in which case the IRB must then be notified at once).

Investigators should consider whether the proposed changes to the research alter the original scope, purpose, or intent of the research. When the research itself is fundamentally changed, the IRB usually requires a new study application rather than allow such changes to be made through an amendment to the existing research plan.
10.6.1 Procedures

Investigators proposing to modify a study must submit an Amendment form and all supporting documents identified in the form via the IRB electronic system for review. The modifications may not be implemented until the IRB has reviewed and approved the proposed changes. When the modification involves the addition of investigators or study personnel, the investigators/personnel may not assume any study responsibilities involving human participants or their identifiable data until the IRB has approved their participation.

The Amendment form is a version of the initial application, with additional questions specific to the amendment. All changes made to the form are documented and called out within the form. IRB staff reviews the submission and makes an initial determination whether the proposed change(s) may be approved through an expedited review process, if the changes are minor, or whether the modification warrants convened board review. The reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed change(s) may be approved through the expedited review procedure and, if not, must refer the research study for convened board review.

10.6.2 Convened IRB Review of Amendments

When a proposed change in a research study is not minor, or when a proposed change to an expedited study renders it no longer eligible for expedited review, the convened IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research participants. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the participants’ continued welfare.

All IRB members are provided and review all documents provided by the investigator. The complete IRB file is available to all members at all times in the IRB electronic submission system.

At the meeting, the Reviewer presents an overview of the proposed changes and assists the IRB Chair in leading the IRB through the criteria for approval and evaluating whether the Modification alters any previous determinations or necessitates additional determinations. The IRB considers whether information about the changes might relate to participants’ willingness to continue to take part in the research and if so, whether to provide that information to past/current/future participants.

10.6.3 Expedited Review of Amendments

An IRB may use expedited review procedures to review changes to expedited research (as long as the proposed changes would not make the research no longer eligible for expedited review) and for minor changes to studies normally subject to convened IRB review.

An expedited review may be carried out by the IRB Chair and/or experienced designee(s) among the IRB members.
The reviewer(s) determines whether the amendment meets the criteria allowing review using the expedited procedure, and if so, whether the research with the proposed modifications continues to meet the regulatory criteria for approval. The reviewer(s) will also evaluate whether the modification alters any previous determinations (e.g., a Subpart determination), or necessitates any additional determinations (e.g., for vulnerable populations); and consider whether information about the changes might relate to participants’ willingness to continue to take part in the research and if so, whether to provide that information to past/current/future participants.

10.6.4 Possible IRB Actions after Amendment Review

As with initial review, the convened IRB or IRB Member(s) conducting expedited review may take any of the actions described in Section 9. (See Section 9 for a detailed description of these actions).

If an IRB member conducting expedited review believes that the proposed amendment should be disapproved, he/she will refer the proposed amendment to the convened board for review. If the proposed changes raise significant concerns on the part of the IRB, the IRB may vote to suspend or terminate the research (See Section 11 for a detailed discussion of suspensions and terminations).

10.6.5 Protocol Exceptions

Protocol exceptions are circumstances in which the investigator wishes to deviate from eligibility criteria or one or more of the specific procedures called for in a protocol. Unlike changes that apply to all subsequent participants in the research, an exception only applies to a specific participant or group of participants.

Exceptions are planned, and the investigator gets approval from the sponsor, if applicable, and the IRB ahead of time. Depending on the nature of the exception, an expedited review may be possible. For an exception to be approved under expedited review, the research as a whole must be eligible for expedited review, or, for convened board research, the proposed exceptions must not increase risk or decrease benefit, negatively impact the risk/benefit analysis, negatively affect the participant’s rights, safety, or welfare, or negatively affect the integrity of the resultant data.

Procedures for exceptions are the same as for a Protocol Amendment. The investigator must submit an Amendment application, along with any revised documentation to be presented to the participant(s) and documentation of sponsor approval, if applicable.

The only time a protocol/Research Plan exception does not require prior sponsor and IRB approval is when the exception is necessary to avoid an immediate hazard to the participant. In such cases, the exception must be submitted to the IRB as soon as possible.
10.7 Closing a Research Study

The completion or early termination of the study is a change in activity and must be reported to the IRB. Although participants are no longer "at risk" under the study, a Final Report to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

Studies may be closed when the involvement of human participants ceases (interventions, interactions, observations, and the gathering, use, study, and analysis of identifiable private information, including specimens, are all complete).

For multi-center research, the study may be closed once all research activities (as above) are complete at UMMC or any site for which the UMMC IRB is the “IRB of record”. If the investigator is serving as the lead investigator or UMMC is the coordinating center the study must remain open as long as the coordinating center is still receiving, studying, using, or analyzing identifiable private information from other sites (even if local interventions, interactions, observations, and data gathering are complete).

Investigators submit a Final Report to the IRB, providing a summary of the research activity and any findings available at that time.

Investigators may maintain the data that they collected, including identifiable private data, if this is consistent with the IRB-approved research plan. However, investigators may not conduct any additional analysis of identified data without re-applying for IRB approval. Investigators must continue to protect the confidentiality of the data as described to the IRB and honor any other commitments that were agreed to as part of the approved research including, for example, future use of data or specimens, provision of research results to participants, and provision of any outstanding payments or compensation.

The IRB reviews Final Reports by expedited review for minimal risk studies and by convened review for greater than minimal risk studies, and either approves the closure of the study or requests additional information or confirmation of facts from the investigator.
11 Suspensions, Terminations and Investigator Holds

11.1 Suspension/Termination

IRB approval may be suspended or terminated if research is not being conducted in accordance with IRB or regulatory requirements or has been associated with unexpected problems or serious harm to subjects. See Section 16 for a discussion of unanticipated problems and Section 17 for a discussion of non-compliance. The IRB’s authority to suspend or terminate research applies to all research subject to IRB approval, including exempt research with limited IRB review and research for which continuing review is no longer required.

The IO, applicable School Dean and Vice Chancellor have the authority to suspend or terminate the organization’s approval for research. Such actions will be promptly reported to the IRB so that the IRB can review the circumstances and take any necessary actions relevant to IRB review and oversight.

Suspension of IRB approval is a directive of the convened IRB or IRB Chair or Vice Chair to temporarily stop some or all previously approved research activities. The IRB Chair or Vice Chair may temporarily suspend IRB approval, in part or in full, when the available information suggests that actions must be taken to protect human research participants or the integrity of the research, prior to the next convened meeting of the IRB. Suspensions made by the IRB Chair or Vice Chair will be reported to the next scheduled meeting of the convened IRB. The convened IRB will determine if the suspension should continue or be modified. Suspended research studies remain open and require continuing review. Investigators must continue to provide reports to the IRB and sponsors just as if there had never been a suspension (i.e., all events that need to be reported during a study need to continue to be reported during the suspension period).

When approval of some or all research activities is suspended by the IRB, the IRB considers whether notification of study participants is required and any actions necessary to ensure that the rights, safety, and welfare of participants are appropriately protected.

The IRB shall notify the investigator in writing of a suspension; a call or email may precede the written notice when appropriate. The written notice of suspension will include a statement of the reason(s) for the IRB’s actions and any requirements or conditions associated with the suspension (e.g., notification of participants). The investigator shall be provided with an opportunity to respond in person or in writing.

Suspensions of IRB approval are reported promptly to the UMMC IO, Department Chair, Office of Integrity and Compliance and Office of Research and Sponsored Programs, study sponsor(s), including federal department or agency heads, as applicable and federal oversight agencies as applicable. See Section 20 for a detailed discussion of reporting requirements.

Termination of IRB approval is a directive of the convened IRB to permanently stop all activities in a previously approved research study. Terminated research studies are closed and no longer require continuing review.
When study approval is terminated by the IRB, in addition to stopping all research activities, the IRB considers whether notification of participants is required and any actions necessary to ensure that the rights, safety, and welfare of research participants are appropriately protected.

The IRB will notify the investigator in writing of a study termination; a call or email may precede the written notice when appropriate. The written notice shall include a statement of the reasons for the IRB's actions and any requirements associated with the termination (e.g., notification of participants). The investigator shall be provided with an opportunity to respond in person or in writing.

Terminations of IRB approval are reported promptly to the UMMC IO, Department Chair, Office of Integrity and Compliance and Office of Research and Sponsored Programs, study sponsor(s), including federal department or agency heads, as applicable, and federal oversight agencies as applicable. See Section 20 for a detailed discussion of reporting requirements.

11.2 Investigator Hold

An investigator may request an investigator hold when the investigator wishes to temporarily or permanently stop some or all approved research activities. Such a hold is initiated by an investigator, but must be immediately reported to the IRB so that the IRB can consider whether any additional actions are necessary to protect research participants. Investigator holds are not equivalent to IRB suspensions or terminations.

11.2.1 Procedures

1. Investigators submit an amendment to the IRB via the IRB electronic system that includes:
   a. A description of the research activities to be stopped;
   b. The reason(s) for the hold;
   c. Proposed action(s) to be taken to protect current participants;
   d. Any action(s) to be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate risk of harm.

2. Upon receipt, the amendment is either placed on the agenda of the next available IRB meeting for review (greater than minimal risk studies) or referred to the IRB Chair or Vice Chair for review (minimal risk studies).

3. For greater than minimal risk studies, the IRB determines whether any additional procedures need to be followed to protect the rights and welfare of current and/or former participants. For minimal risk studies, the IRB Chair or Vice Chair, in consultation with the Human Research Office Director and/or staff and investigator, determines whether any additional procedures need to be followed to protect the rights and welfare of current and/or former participants. (See Section 11.3).

4. For greater than minimal risk studies, the IRB determines if currently enrolled participants and/or former participants should be notified of the hold, and if notified,
how and when. For minimal risk studies, the IRB Chair or Vice Chair, in consultation with the Human Research Office Director and/or staff and investigator, determine if currently enrolled participants and/or former participants should be notified of the hold, and if notified, how and when.

To lift the hold the investigator must submit an amendment to the IRB via the IRB electronic system to request the hold be lifted. The IRB will consider whether participants are appropriately protected, if the research remains approvable and if any changes need to be made before the hold may be lifted.

11.3 Protection of Currently Enrolled and Former Participants

Before a study hold, termination, or suspension is put into effect the IRB Chair, Vice Chair or convened IRB considers whether any additional procedures need to be followed to protect the rights and welfare of current and/or former participants. Such procedures might include:

- Transferring participants to another investigator/site
- Making arrangements for clinical care outside the research
- Allowing continuation of some research activities under the supervision of an independent monitor
- Requiring or permitting follow-up of participants for safety reasons
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor
- Notification of current participants
- Notification of former participants
12  Documentation and Records

UMMC’s Human Research Office maintains adequate documentation of the IRB’s activities. All records are accessible for inspection and copying by authorized representatives of the FDA, OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

12.1  IRB Records

IRB records include, but are not limited to:

1. Written operating procedures
2. IRB membership rosters
3. IRB member files, including documentation of appointments, experience, education/training and expertise
4. IRB correspondence including reports to regulatory agencies
5. IRB Protocol Files (See Section 12.2)
6. Documentation of exemptions including exemption related to emergency use, uses and when limited IRB review is a condition of exemption
7. Convened IRB meeting minutes
8. Documentation of review by an external IRB, when appropriate
9. Documentation of IRB reliance and cooperative review agreements
   a. For nonexempt research involving human subjects covered by the 2018 revised Common Rule (or exempt research for which limited IRB review takes place as described in Section 5.4) that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall document the institution’s reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy [the Common Rule] (e.g., in a written agreement between the institution and the IRB, by implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol)
10. UMMC’s Federalwide Assurance
11. Federal IRB Registrations
12. Documentation of complaints and any related findings and/or resolution
12.2 IRB Study Files

The IRB maintains a separate file for each application (including expanded access), HUD, emergency use or report it receives for review. Applications are submitted through the IRB electronic system and assigned a unique identification number by the system.

As applicable, protocol files include, but are not limited to:

1. The initial application and all associated documents and materials;
2. Requests for revisions and all associated documents and materials;
3. Continuing review/progress reports and all associated documents and material, including the rationale for conducting continuing review of research that otherwise would not require continuing review under the revised Common Rule as described in Section 10.5;
4. Final reports and all associated documents and materials;
5. Reports submitted after study or HUD approval including reports of significant new findings, data and safety monitoring reports, protocol violation reports, complaints, noncompliance, and reports of injuries to participants, including reports of potential unanticipated adverse device events and unanticipated problems involving risks to participants or others;
6. IRB-approved consent, parental permission, and assent forms;
7. DHHS-approved sample consent form and protocol;
8. DHHS grant application
9. Documentation of scientific or scholarly review (if available);
10. Documentation of the type of IRB review. For exempt determinations and expedited review, this will include the category under which the review is allowed;
11. For expedited review, documentation of any findings and determinations required by the regulations and study-specific findings supporting those determinations, including, but not limited to, waiver or alteration of consent, waiver of documentation of consent, research involving pregnant women, fetuses, and neonates, research involving prisoners, and research involving children are recorded in the IRB electronic system. For research reviewed by the convened board these findings and determinations are recorded in the minutes;
12. For expedited review, documentation of the risk determination and period of approval are recorded in the IRB electronic system. For research reviewed by the convened board these determinations are recorded in the minutes;
13. For research subject to the pre-2018 Common Rule, or FDA or DOJ regulations: Documentation of all IRB review actions;
14. For research subject to the revised Common Rule (2018 requirements): For expedited review, the rationale for an expedited reviewer’s determination under 45 CFR
46.110(b)(1)(i) that research appearing on the expedited review list described in 45 CFR 46.110(a) is more than minimal risk. For research reviewed by the convened board the risk determination and period of approval, when applicable, are recorded in the minutes.

15. Notification of expiration of IRB approval to the investigator;
16. Notification of suspension or termination of research;
17. Letters to investigator informing them of IRB review outcomes;
18. IRB correspondence to and from investigators related to the protocol;
19. All other IRB correspondence related to the research;
20. For studies evaluating the safety or effectiveness of medical devices, documentation of the device determination (exempt, non-significant risk, significant risk);
21. Reports of unanticipated problems involving risk to subjects or others; and
22. Any statements of significant new findings provided to study participants.

12.3 The IRB Minutes

While IRB reviewers may enter notes into the IRB electronic system in advance of IRB meetings to help them prepare for discussion, the IRB minutes serve as the official record of the convened IRB’s deliberations, determinations, and actions. There is no expectation that reviewer notes and meeting minutes match as notes reflect the informal thoughts of a single individual before hearing the commentary and viewpoints of other members. However, if there is a substantive disconnect between a reviewer’s notes and the discussion recorded in the IRB minutes, a notation may be added either to the reviewer’s notes or the IRB minutes explaining the reason and resolution (for example, when a reviewer becomes aware of information that resolves their concern prior to the meeting but after they had submitted their comments). Draft minutes of IRB meetings are compiled and reviewed by the Human Research Office Director, IRB Chair and Vice Chair. Once accepted the minutes are distributed to the members and may not be altered by anyone including a higher organizational authority.

A copy of IRB minutes for each IRB meeting are made available to the IO.

Minutes of IRB meetings and accompanying documentation contain sufficient detail to show the following, as applicable:

1. Attendance
   a. Names of members and alternates present
   b. Names of members and alternate members who are participating through videoconference or teleconference.
   c. Names of alternate(s) attending in lieu of absent members.

   **Note:** The attendance list identifies members present. The vote on each action, documented electronically, reflects the number of members present for the vote on
each item. The name of each member present for the vote of each item is also
documented electronically, as well as the name of each member who recuses
himself or herself because of a conflict of interest.

d. Names of consultants present, a brief explanation of their expertise, and
documentation to support that the consultant(s) did not vote

e. Names of investigators present
f. Names of guests present

2. The presence of a quorum throughout the meeting, including the presence of one
member whose primary concern is in a non-scientific area.

3. Administrative items reviewed or discussed

4. Continuing Education

5. Actions taken, including separate deliberations, actions, and votes for each research
study undergoing review by the convened IRB.

6. Vote counts on each action (Total Number voting; Number voting for; Number voting
against; Number abstaining; Number recused). When a member is recused due to
conflict of interest, the name of the member and reason for the recusal will be noted;

7. Basis or justification for actions disapproving or requiring changes in research

8. Summary of controverted issues and their resolution. For example, when there is a “No”
vote, the minutes should provide insight into the reason, bringing the matter to a vote
may be the resolution. Likewise, when the IRB debates or engages in significant
deliberation regarding an issue, the minutes should document the discussion and the
resolution even when all members are in agreement at the end.

9. Approval period for initial and continuing reviews, when applicable, including
identification of research that warrants review more often than annually and the basis
for that determination;

10. For research subject to the revised Common Rule (2018 requirements): The rationale
for requiring continuing review of research that otherwise would not require continuing
review as described in Section 10.5;

11. Risk determination for initial and continuing reviews, and modifications when the
modification alters the prior risk determination

12. Justification for deletion or substantive modification of information concerning risks or
alternative procedures contained in the DHHS-approved sample consent document.

13. Study-specific findings supporting that the research meets each of the required criteria
when approving a consent procedure that does not include or that alters some or all of
the required elements of informed consent, or when waiving the requirement to obtain
informed consent altogether.
14. Study-specific findings supporting that the research meets each of the required criteria when the requirements for documentation of consent are waived

15. Study-specific findings supporting that the research meets each of the criteria for approval for vulnerable populations under any applicable Subparts

16. Exempt/Significant risk/non-significant risk device determinations and the basis for those determinations

17. Determinations of conflict of interest and acceptance or modification of conflict management plans

18. Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research.

19. Review and determinations related to interim reports (e.g., unanticipated problems or safety reports; serious or continuing non-compliance; suspensions or terminations)

20. A list of research approved under expedited review procedures, including limited IRB reviews conducted using expedited procedures, since the last report

21. When an IRB member or alternate has a conflict of interest (see Section 23.2) with the research under review, an indication that the IRB member or alternate was not present during the final deliberation or vote

22. Key information provided by consultants

12.4 IRB Membership Roster

A membership list of IRB members is maintained and submitted to OHRP as required. The list contains the following information about members:

1. Name

2. Earned degree(s)

3. Employment or other relationship between each member and the organization (i.e., affiliated or non-affiliated). To be categorized as non-affiliated, neither the member nor an immediate family member of the member may be affiliated with UMMC

4. Status as scientist or non-scientist. Absent extenuating circumstances, members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline are considered a scientist for the purposes of the roster. Members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline are considered a nonscientist. Physicians, nurses and pharmacists are considered scientists.

5. Indications of experience, such as board certifications, licenses, and areas of practice sufficient to describe each member’s chief anticipated contributions to IRB deliberations.
6. Representative capacities of each IRB member; including which IRB member(s) is a prisoner representative, and which IRB members are knowledgeable about or experienced in working with children, pregnant women, individuals with impaired decision-making capacity, and other vulnerable populations, or other subjects vulnerable to coercion or undue influence commonly involved in UMMC research.

7. Role on the IRB (Chair, Vice-Chair, Member, Alternate Member)

8. Voting status

9. For alternate members, the primary member or class of members for whom the member could substitute

The IRB office must keep the IRB membership list current. Changes in IRB membership are reported to OHRO and FDA on the federal IRB registration site within 90 days of the change.

12.5 Documentation of Exemptions

Documentation of verified exemptions consists of the reviewer’s citation of a specific exemption category and written determination that the activity described in the investigator’s proposed study meets the conditions of the cited exemption category, as detailed in Section 5. When an exemption includes limited IRB review under the revised Common Rule (2018 requirements), the documentation will include this fact and the IRB action taken on those aspects of the research subject to limited IRB review in accordance with the procedures described for the review procedures used (expedited or convened board) elsewhere in this manual.

12.6 Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure include: the specific permissible category(ies) or status as exempt but requiring limited IRB review; that the activity described by the investigator satisfies all of the criteria for approval; the approval period (when applicable) and any determinations required by the regulations including study-specific findings justifying the following determinations:

1. Approving a procedure which waives or alters the informed consent process;
2. Approving a request for waiver or alteration of the requirement for documentation of consent;
3. Approving research involving pregnant women, human fetuses, or neonates;
4. Approving research involving children

12.7 Access to IRB Records

IRB protocol files are secured in the IRB electronic system and in an abbreviated paper file with access controlled by the IRB office. Likewise, investigators control access to investigator records in the electronic system. All other IRB records (e.g., membership rosters) are kept secure in a limited access file on UMMC’s servers, locked filing cabinets and/or locked rooms.
Absent extenuating circumstances, access to IRB records is limited to the IO, HRPP Director, HRPP and IRB staff, IRB members, authorized organizational officials, and officials of federal and state regulatory agencies (e.g., OHRP and FDA). Research investigators are provided reasonable access to files related to their research. Appropriate accreditation bodies are provided access. Records are accessible for inspection and copying by authorized representatives of federal regulatory agencies during regular business hours.

IRB member rosters are only provided to regulatory agencies, accreditation bodies, and persons or offices within UMMC with a legitimate need (e.g., Compliance, Legal). A memorandum documenting compliance with pertinent federal rules and regulations, IRB membership requirements, and with UMMC’s Federalwide Assurance is available and provided to sponsors and others upon request.

All other access to IRB records is limited to those who have legitimate need for them, as determined by the IO or Human Research Office Director or Associate Director.

12.8 Record Retention

In order to comply with the requirements of OHRP, FDA, HIPAA and the UMMC record retention policy IRB paper files are maintained for at least six (6) years after completion of the research. IRB electronic records are maintained indefinitely.
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Obtaining Informed Consent from Research Participants

No investigator conducting research under the jurisdiction of UMMC may involve a human being as a research participant without obtaining the legally effective informed consent of the participant or the participant’s legally authorized representative unless a waiver of consent has been approved by the IRB of record. Except as provided in Sections 13.10, 13.11 and 13.12, informed consent must be documented by the use of a written consent form approved by the IRB.

The IRB evaluates both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants.

The following procedures describe the requirements for obtaining consent from participants in research conducted under the auspices of UMMC. When the UMMC IRB is serving as the IRB of record for external sites or personnel, the below requirements may be adapted as appropriate based upon the local context where the research will occur (e.g., who may serve as a LAR).

13.1  Basic Requirements

The requirement to obtain the legally effective informed consent of an individual before involving him/her in research is one of the central protections provided for by the Federal regulations and UMMC’s HRPP. Investigators are required to obtain legally effective informed consent from a participant or the participant’s LAR unless the requirement has been waived by the IRB. When informed consent is required, it must be sought prospectively, and properly documented.

The informed consent process involves three key features: (1) disclosing to the prospective research participant information needed to make an informed decision; (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether or not to participate in the research.

Informed consent is more than just a signature on a form. It is a process of information exchange that includes discussion, questions and answers and signing the consent document. The informed consent process is the critical communication link between the prospective research participant and an investigator, beginning with the initial approach by an investigator and continuing through the completion of the research study. Investigators must have received the appropriate training and be knowledgeable about the study procedures, potential risks, anticipated benefits, and alternatives in order that they may appropriately describe the research and answer questions. The exchange of information between the investigator and study participant can occur via one or more of the following modes of communication, among others; face to face dialogue; mail; electronic interface, telephone, or fax; however, obtaining informed consent must allow for a dialogue so that the potential participant has the opportunity to ask questions and receive responses. Investigators must obtain consent prior to entering a participant into a study, gathering data about a participant, and/or conducting any procedures required by the research plan, including screening procedures, unless consent is waived by the IRB.
If someone other than the investigator conducts the consent discussion and obtains consent, the investigator needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. The person so delegated must be knowledgeable about the research to be conducted and the consent process, and must have the expertise to be able to answer questions about the study including those regarding risks, procedures, and alternatives. When the UMMC IRB is the IRB of record the application solicits information regarding who will obtain consent and proposed changes to the personnel authorized to obtain consent must be submitted to the UMMC IRB for approval.

Sample or draft consent documents may be developed by a sponsor or network. However, the IRB of record is the final authority on the content of the consent documents that are presented to potential study participants.

**For research subject to the revised Common Rule (2018 requirements):**

1. **Before involving a human subject in research, an investigator shall obtain** the legally effective informed consent of the subject or the subject’s LAR
2. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the LAR sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence
3. The information that is given to the subject or the LAR shall be in language understandable to the subject or the LAR
4. The prospective subject or the LAR 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
5. Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR 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
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 LAR’s understanding of the reasons why one might or might not want to participate
7. No informed consent may include any exculpatory language through which the subject or the LAR 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.

These informed consent requirements are not intended to preempt any applicable federal, state, or local laws that require additional information to be disclosed for informed consent to be legally effective.
13.2 Informed Consent Process

1. The potential participant must have the legal and mental capacity to give consent. For a participant without that capacity, permission must be obtained from a legally authorized representative/legal guardian.

2. The potential participant or the participant’s LAR/legal guardian must have sufficient opportunity to read the consent document, when applicable.

3. The potential participant or the participant’s LAR/legal guardian must be given the opportunity to ask questions and have them answered.

4. The potential participant or the participant’s LAR/legal guardian must be given sufficient opportunity to consider whether to participate.

5. The consent process shall be under circumstances that minimize the possibility of coercion or undue influence.

6. The consent information must be presented in language that is understandable to the potential participant or the participant’s LAR/legal guardian. To the extent possible, the language should be understandable by a person who is educated to 8th grade level and layman’s terms should be used in the description of the research. The IRB may require or allow different readability standards based upon the characteristics of the target study population.

7. For participants with Limited English Proficiency (LEP), informed consent must be obtained in a language that is understandable to the participant (or LAR/legal guardian). In accordance with this policy, the UMMC IRB requires that informed consent discussions include a reliable interpreter when the prospective participant does not understand the language of the person who is obtaining consent, and, in most circumstances, that consent materials are translated by a certified translator.

8. The informed consent process may not include any exculpatory language through which the participant is made to waive, or appears to waive any of his/her legal rights or through which any entity (including the investigator, the sponsor, UMMC or UMMC employees or agents) are released from liability for negligence, or appear to be so released.

9. The investigator is responsible for ensuring that each prospective study participant is adequately informed about all aspects of the research and understands the information provided.

13.3 Legally Authorized Representative (LAR)

A Legally Authorized Representative (LAR) is defined by 45 CFR 46.102(c) and 21 CFR 50.3 as “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.”
Who may serve as LAR is determined by state law. Under Mississippi law, the order of authority to provide consent on behalf of another is as follows:

- Heath care agent
- Court-appointed guardian
- The spouse, unless legally separated
- An adult child
- A parent
- An adult brother or sister

A Legal Guardian is a person appointed by a court of appropriate jurisdiction.

When the UMMC IRB serves as the IRB of record for external sites and the use of LARs is proposed, information regarding relevant state law and local policy will be sought (local context information) and applied.

LARs should be well informed regarding their roles and responsibilities when asked to provide surrogate consent. In addition to the consent information, LARs should be informed that their obligation is to try to determine what the potential participant would do if able to provide consent, or if the potential participant's wishes cannot be determined, what they think is in the person's best interest.

Investigators must describe the intended use of LARs in their submission to the IRB. The IRB determines whether the use of LARs is appropriate for a given research study.

Further discussion and procedures for assessment of capacity and inclusion of adults with impaired decision-making capacity in research are described in Section 14.7.

### 13.4 Basic Elements of Informed Consent

To be valid, the consent process must provide the following basic elements of information to potential study participants:

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;
2. A description of any reasonably foreseeable risks or discomforts to the subject;
3. A description of any benefits to the subject or to others which may reasonably be expected from the research;
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained;

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;

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;

8. Contact information for the research team for questions, concerns, or complaints;

9. Contact information for someone independent of the research team for problems, concerns, questions, or input

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

11. For research subject to the revised Common Rule (2018 requirements): One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

   a. A statement that identifiers might be removed from the identifiable private information or identifiable 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

   b. 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.

12. For FDA-regulated studies, a statement that notes the possibility that the Food and Drug Administration may inspect the records;

13. For “applicable” FDA-regulated clinical trials, the following statement must be included verbatim:

   “A description of this clinical trial will be available on [http://www.ClinicalTrials.gov](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.”
13.5 Additional elements of informed consent to be applied, as appropriate:

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;
2. Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent;
3. Any additional costs to the subject that may result from participation in the research;
4. The amount and schedule of all payments;
5. The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject;
6. 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;
7. The approximate number of subjects involved in the study;
8. For research subject to the revised Common Rule (2018 requirements):
   a. 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;
   b. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;
   c. 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 sequence of that specimen)

13.6 UMMC Requirements

In addition to the federal elements of consent described above, UMMC has defined specific additional information that must be included in consent documents when applicable to the research (e.g., 1099 language). These requirements are included in the UMMC consent form template available on the IRB’s website (https://www.umc.edu/Research/files/irb-consent-template-1-171.docx) for investigator and reviewer reference.

13.7 Participant Withdrawal or Termination

A participant enrolled in a research study may decide to withdraw from the research, or an investigator may decide to terminate a participant’s participation in research regardless of whether the participant wishes to continue participating. Investigators must plan for the possibility that participants will withdraw from research and include a discussion of what withdrawal will mean and how it will be handled in their research plans and consent documents.
When seeking informed consent, the following information regarding data retention and use must be included:

1. For FDA-regulated clinical trials: When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remain part of the study database and may not be removed. This should be disclosed in the consent document;

2. For research not subject to FDA regulations: The investigator should inform participants whether the investigator or study sponsor intends to either: (1) retain and analyze already collected data relating to the participant up to the time of withdrawal; or (2) that the investigator or study sponsor will destroy the data relating to the participant if so requested and exclude the data from any analysis.

When a participant’s withdrawal request is limited to discontinuation of the primary interventional component of a research study, research activities involving other types of participation for which the participant previously gave consent may continue. Investigators should ask a participant who is withdrawing whether the participant wishes to participate in continued follow-up and further data collection subsequent to withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant would distinguish between study-related interventions and procedures and continued follow-up in person, by phone, or via records review.

If a participant withdraws from the interventional portion of the study, but agrees to continued follow-up as described in the previous paragraph, the investigator must obtain the participant’s informed consent for this limited participation in the study (assuming such a situation was not described in the original consent document). IRB approval of consent documents for these purposes would be required.

If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up, the investigator may not access or gather additional private information about the participant for purposes related to the study. However, an investigator may review study data related to the participant collected prior to the participant’s withdrawal from the study, and may consult public records, such as those establishing survival status.

13.8 Documentation of Informed Consent

Except as provided in Sections 13.10, 13.11 and 13.12, informed consent must be documented by the use of a written consent form approved by the IRB. The consent form must be a written consent document that embodies the basic and required additional elements of informed consent. The consent form may be read to the potential participant or the potential participant’s LAR, but the potential participant or LAR must be given adequate opportunity to read it before it is signed. Although the regulations allow for the use of a “short form” consent document, UMMC does not utilize this option.
1. Informed consent is documented by the use of a written consent form approved by the IRB and signed (including in an electronic format) and dated by the participant or the participant’s legally authorized representative at the time of consent.

2. The name of the person obtaining consent and the date consent is obtained is documented on the consent form.

3. A written copy of the signed and dated consent form is given to the person signing the form. The investigator retains the signed original in the research records. When the research involves a participant’s care, diagnosis or treatment, a copy of the consent form is uploaded into the electronic health record.

For research subject to the pre-2018 Common Rule, or FDA or DOJ regulations: A written consent document that embodies the basic and required additional elements of informed consent. The consent form may be read to the subject or the subject's LAR, but the subject or LAR must be given adequate opportunity to read it before it is signed;

For research subject to the revised Common Rule (2018 requirements): A written consent document that embodies the basic and required additional elements of informed consent. The investigator shall give either the subject or the subject’s LAR adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject’s LAR

13.9 Special Consent Circumstances

13.9.1 Enrollment of persons with limited English-language proficiency

1. Expected enrollment: In some studies, the investigator may be able to anticipate enrollment of persons who do not speak or read, or have limited proficiency in, oral or written English. When the target population includes such persons or the investigator and/or the IRB otherwise anticipates that the consent process will be conducted in a language other than English, the IRB requires a translated consent document and other participant materials, as applicable. Generally, translated consent forms should not be prepared until the final approved version of the English-language version is available. In order to ensure that translated documents are accurate, the investigator may choose to provide a certified translation, or to provide a translated document with an independent back-translation.

2. Unexpected enrollment: If a person who does not speak or read, or has limited proficiency in, English unexpectedly presents for possible enrollment, an IRB-approved translated version of the written consent document may not be available for use. Investigators should carefully consider the ethical and legal ramifications of enrolling a participant when a language barrier exists. If the participant does not clearly understand the information presented during the consent process or in subsequent discussions, his/her consent may not be informed, and therefore, not effective.
3. **Use of interpreters in the consent process**: Unless the person obtaining consent is fluent in the prospective participant’s language, an interpreter is necessary to facilitate the consent discussion. Preferably someone who is independent of the participant (i.e., not a family member) should assist in presenting information and obtaining consent. Whenever possible, interpreters should be provided copies of the translated consent document before (24 to 48 hours if possible) the consent discussion with the participant.

13.9.2 **Braille consent document**

For blind participants who read Braille, the IRB may approve a consent document prepared in Braille. In order to assure that a Braille consent document is accurate, the IRB may require a transcription into print text or review of the document by someone who reads Braille. If possible, the participant signs the Braille consent document; otherwise oral consent is obtained, witnessed and documented as described under “Oral Consent” (see Section 13.9.4).

13.9.3 **Obtaining consent using American Sign Language (ASL)**

For deaf participants who are fluent in ASL, the IRB may approve a consent process using ASL and the IRB-approved written consent form. When this process is approved, the individual authorized to obtain consent from the prospective participant must use a certified interpreter fluent in ASL to conduct the consent process and the documentation of the consent process must conform to the requirements set forth in Section 13.8.

13.9.4 **Oral Consent**

When a potential participant is unable to read a written consent form (for example, is blind or illiterate), the IRB may approve an oral consent process, provided the potential participant (1) has the ability to understand the concepts of the study and evaluate the risks and benefits of being in the study when it is explained orally and (2) is able to indicate approval or disapproval to study entry.

For research that is no more than minimal risk, documentation of consent may be waived according to the criteria in Section 13.11.

For greater than minimal risk research, the consent form must be read to the potential participant and the participant must be given an opportunity to ask questions. An audiotape approved by the IRB may also be used. If capable of doing so, the participant signs, or marks an X to signify consent. If that is not possible, the participant provides oral consent. The person obtaining consent and a witness sign the written study consent form with a statement that documents that an oral process was used and, if necessary, that the participant gave oral consent. The consent process is also documented in the participant’s research record. A signed copy of the consent form is given to the participant and, whenever possible, the document(s) should be provided to the participant on audio or video-tape.
13.9.5 Physically-Challenged Participants

A person who is physically challenged (e.g., physically unable to talk or write) can enroll in research if competent and able to indicate voluntary consent to participate. Whenever possible, the participants should sign the consent form or make his/her mark by initialing or making an X. As with oral consent, a witness to the consent process is recommended and the circumstances and consent process should be carefully documented in the research records.

13.10 Waiver or Alteration of Informed Consent

General Waiver or Alteration:

For research subject to the pre-2018 Common Rule, or FDA or DOJ regulations: An IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

(a) The research or clinical investigation involves no more than minimal risk to the subjects;
(b) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
(c) The research could not practicably be carried out without the waiver or alteration; and
(d) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

This option applies to both FDA-regulated and DHHS-conducted or supported research.

For research subject to the revised Common Rule (2018 requirements): An IRB may waive the requirement to obtain informed consent, provided the IRB finds and documents that the below criteria are satisfied. An IRB may not waive or alter broad consent (See Section 13.13), nor may it waive consent for the storage, maintenance, or secondary research use of identifiable biospecimens if an individual was asked to provide broad consent in accordance with Section 13.13 and refused.

Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an “alteration”), provided that the IRB finds and documents that the below criteria are satisfied. An IRB may not omit or alter any of the general requirements for informed consent (See Section 13.1).

1. The research or clinical investigation involves no more than minimal risk to the subjects;
2. The research or clinical investigation could not practicably be carried out without requested waiver or alteration;
3. 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;
4. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
5. Whenever appropriate, the subjects or LARs will be provided with additional pertinent information after participation.

Public Benefit or Service Programs Waiver or Alterations

For research subject to the pre-2018 Common Rule or DOJ regulations:

In addition, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

(a) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
   1. Public benefit or service programs;
   2. Procedures for obtaining benefits or services under those programs;
   3. Possible changes in or alternatives to those programs or procedures; or
   4. Possible changes in methods or levels of payment for benefits or services under those programs; and,

(b) The research could not practicably be carried out without the waiver or alteration.

For research subject to the revised Common Rule (2018 requirements):

An IRB may waive the requirement to obtain informed consent, provided the IRB finds and documents that the below criteria are satisfied. An IRB may not waive or alter broad consent (See Section 13.13), nor may it waive consent for the storage, maintenance, or secondary research use of identifiable biospecimens if an individual was asked to provide broad consent in accordance with Section 13.13 and refused.

Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an “alteration”) (See Sections 13.4 and 13.5), provided that the IRB finds and documents that the below criteria are satisfied. An IRB may not omit or alter any of the general requirements for informed consent (See Section 13.1).

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
   a. Public benefit or service programs;
   b. Procedures for obtaining benefits or services under those programs;
   c. Possible changes in or alternatives to those programs or procedures; or
d. Possible changes in methods or levels of payment for benefits or services under those programs; and

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

The Public Benefit or Service Programs Waiver or Alterations option does not apply to FDA-regulated research. Waivers of consent are not permissible under either option for federally-funded research using Newborn Dried Blood Spots.

13.10.1 Screening, recruiting, or determining eligibility

For research subject to the revised Common Rule: 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 authorized representative, if either of the following conditions are met:

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

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

13.11 Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all participants if it finds either that:

1. 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 (e.g., domestic violence research where the primary risk is discovery by the abuser).

Subjects must be asked whether they want documentation linking them with the research, and their wishes must govern

This option does not apply to FDA-regulated research

OR

2. 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. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-investigators (e.g., marketing surveys, telemarketing).

This option does apply to FDA-regulated research, most commonly in the context of minimal risk screening activities that are necessary to determine eligibility for enrollment in a clinical trial.

OR
3. If the subjects or LARs 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 alternative mechanism for documenting that informed consent was obtained.

This option does not apply to research subject to the pre-2018 Common Rule or to FDA or DOJ regulations.

Unless the IRB has granted a full waiver of the requirement to obtain informed consent, investigators who seek and receive approval for a waiver of documentation of consent still must perform an adequate consent process.

In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to participants, and the IRB considers whether to require the investigator to provide participants with a written statement regarding the research.

**13.12 Waiver of Informed Consent for Planned Emergency Research**

The conduct of planned research in life-threatening emergencies where the requirement to obtain prospective informed consent has been waived by the IRB is covered by 21 CFR 50.24 for FDA-regulated research and by the waiver articulated by DHHS at 61 FR 51531-33 for non-FDA-regulated research.

The FDA exception from informed consent requirements for emergency research, 21 CFR 50.24, permits planned research in an emergency setting when human participants who are in need of emergency medical intervention cannot provide legally effective informed consent themselves and there is generally insufficient time and opportunity to locate and obtain consent from their LAR.

The Secretary of Health and Human Services (DHHS) has implemented an Emergency Research Consent Waiver under 45 CFR 46.101(i), with provisions equivalent to those of the FDA with the exception of the requirements specified in Sections 13.12.2.1 and 13.12.2.2. The DHHS waiver is not applicable to research involving prisoners, pregnant women, fetuses, or in vitro fertilization.

**13.12.1 Definitions**

**Planned Emergency Research:** Research that involves participants who are in a life-threatening situation for which available therapies or diagnostics are unproven or unsatisfactory and because of the participants’ medical condition and the unavailability of LARs it is generally not possible to obtain legally effective informed consent.

**Family Member:** For this section means a legally competent adult with one of the following relationships to the participant: spouse; parent; child (including adopted children); siblings and
spouses of siblings; and any individual related by blood or affinity whose close association with
the participant is the equivalent of a family relationship.

13.12.2 Procedures

The IRB may approve the planned emergency research without requiring informed consent of
all research participants prior to initiating the research intervention if the IRB finds and
documents that the following conditions have been met:

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

(2) Obtaining informed consent is not feasible because:

(i) Participants will not be able to give informed consent as a result of their medical
condition;

(ii) The intervention under investigation must be administered before consent from the
participant’s LAR is feasible; and

(iii) There is no reasonable way to prospectively identify the individuals likely to become
eligible for participation in the research.

(3) Participation in the research holds out the prospect of direct benefit to participants
because:

(i) Participants are facing a life-threatening situation that necessitates intervention;

(ii) Appropriate animal and other preclinical studies have been conducted, and the
information derived from those studies and related evidence support the potential for
the intervention to provide a direct benefit to the individual participant; and

(iii) Risks associated with the research are reasonable in relation to what is known about
the medical condition of the potential class of participants, the risks and benefits of
standard therapy, if any, and what is known about the risks and benefits of the
proposed intervention or activity.

(4) The research could not practicably be carried out without the waiver.

(5) The proposed research plan defines the length of the potential therapeutic window based
on scientific evidence, and the investigator has committed to attempting to contact a LAR for
each participant within that window of time and, if feasible, to ask the LAR contacted for
consent within that window rather than proceeding without consent. The investigator will
summarize efforts made to contact LARs and make this information available to the IRB at the
time of continuing review.

(6) The IRB has reviewed and approved informed consent procedures and an informed consent
document consistent with Sections 46.116 and 46.117 of 45 CFR 46 and Sections 50.20, 50.25
and 50.27 of 21 CFR 50. These procedures and the informed consent document are to be used
with participants or their LAR in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a participant’s participation in the research consistent with paragraph (7)(v) of this section.

(7) Additional protections of the rights and welfare of the participants will be provided, including, at least:

(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the community(ies) in which the research will be conducted and from which participants will be drawn;

(ii) Public disclosure to the community(ies) in which the research will be conducted and from which participants will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

(iii) Public disclosure of sufficient information following completion of the research to apprise the community and other researchers of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent data monitoring committee to exercise oversight of the research; and

(v) If obtaining informed consent is not feasible and a LAR is not reasonably available, the investigator has committed, if feasible, to attempt to contact a non-LAR family member of the potential participant within the potential therapeutic window and ask whether he or she objects to the participant’s participation in the research. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The IRB will ensure that procedures are in place to inform, at the earliest feasible opportunity, each participant, or, if the participant remains incapacitated, the participant’s LAR, or if such a representative is not reasonably available, a family member, of the participant’s inclusion in the research, the details of the research and other information contained in the informed consent document, including that participation may be discontinued at any time without penalty or loss of benefits to which the participant is otherwise entitled. If a LAR or family member is told about the research and the participant’s condition improves, the participant is informed as soon as feasible. If a participant is entered into research with waived consent and the participant dies before a LAR or family member can be contacted, information about the research is provided to the LAR or family member, if feasible.

13.12.2.1 FDA-regulated Planned Emergency Research

1) A licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation must concur that the conditions described in Section 13.11.2 are satisfied.

2) Studies involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational
device exemption (IDE) that clearly identifies that such studies may include participants who are not able to give consent. The submission of those studies in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under 312.30 or 812.35.

3) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided in the regulations or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to the FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

4) The IRB determinations and documentation required in Section 13.11.2 and paragraph 3 are retained by the IRB indefinitely in an electronic format indefinitely, and available for inspection and copying by FDA in accordance with 56.115(b).

13.12.2 Documentation and Reporting of Planned Emergency Research Not Subject to FDA Regulations

The IRB responsible for the review, approval, and continuing review of the research must approve both the research and a waiver of informed consent and have (i) found and documented that the research is not subject to regulations codified by the FDA at 21 CFR Part 50, and (ii) found and documented and reported to the OHRP that the conditions required in Section 13.11.2 have been met.

13.13 Broad Consent

Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes) is permitted, although optional, under the 2018 Common Rule. However, UMMC elects not to recognize the practice of broad consent for research at this time.

When UMMC investigators propose research involving the use of identifiable private information and/or identifiable biospecimens research obtained elsewhere by broad consent, the investigators must include documentation of the IRB approval for the storage or maintenance of the information or specimens and a copy of the consent form and/or other materials. The UMMC IRB will review the information provided with the aid of a checklist to ensure that all requirements are satisfied. The outcome of the IRB’s review will be communicated to the investigator in writing following the procedures described elsewhere in this manual.
13.14 Posting of Clinical Trial Consent Forms

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 Web site that will be established as a repository for such informed consent forms.

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 Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.

The informed consent form must be posted on the Federal Web site 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.

At this time, two publicly available federal websites that will satisfy the consent form posting requirement have been identified: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021). Additional federal websites that would satisfy the revised Common Rule’s clinical trial consent form posting requirement might be identified in the future.
14   Vulnerable Research Participants

When participants in research conducted under the auspices of UMMC are likely to be vulnerable to coercion or undue influence or have diminished decision-making capacity, the research must include additional safeguards to protect the rights and welfare of these participants. The IRB must ensure that all of the regulatory requirements for the protection of participants are met and that appropriate additional protections for vulnerable participants are in place.

14.1   Definitions

**Children.** Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research is conducted.

According to Mississippi law, a person may consent to his or her own medical care at the age of eighteen. Mississippi law also allows an emancipated minor to consent for his or her own medical care. An emancipated minor is defined as an individual under the age of 18 who (i) is or has been married; (ii) has been adjudicated emancipated by a court of competent jurisdiction; or (iii) has been adjudicated emancipated for the purpose of making health care decisions by a court of competent jurisdiction. Mississippi law allows any adult or emancipated minor to consent to participate in research. Unemancipated minors may participate in research conducted in accordance with federal law. [MS Code Ann. 41-41-17]

**NOTE:** For research conducted in jurisdictions other than Mississippi, the research must comply with the laws regarding the legal age of consent in the relevant jurisdiction(s). Legal counsel will be consulted with regard to the laws in other jurisdictions or such “local context” information will be sought through other means (e.g., according to the terms of a reliance agreement).

**Guardian.** A guardian is an individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care. [45 CFR 46.402(e)]

In Mississippi “Guardian” is defined as a judicially appointed guardian or conservator having authority to make a health-care decision for an individual. [MS Code Ann 41-41-203]

**NOTE:** For research conducted in jurisdictions other than Mississippi, the research must comply with the laws regarding guardianship in the relevant jurisdiction(s). Legal counsel will be consulted with regard to the laws in other jurisdictions or such “local context” information will be sought through other means (e.g., according to the terms of a reliance agreement).

**Fetus.** A fetus means the product of conception from implantation until delivery [45 CFR 46.202(c)].

**Dead fetus.** A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord [45 CFR 46.202(a)].
**Delivery.** A delivery is a complete separation of the fetus from the woman by expulsion or extraction or any other means [45 CFR 46.202(b)].

**Neonate.** A neonate is a newborn [45 CFR 46.202(d)].

**Viable.** As it pertains to the neonate, viable means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration [45 CFR 46.202(h)]. If a neonate is viable, then, for the purposes of participation in research, the neonate is considered a child and the rules regarding participation of children in research apply.

**Nonviable neonate.** A nonviable neonate means a neonate after delivery that, although living, is not viable [45 CFR 46.202(e)].

**Pregnancy.** A pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery [45 CFR 46.202(f)].

**Prisoner.** A prisoner is 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 that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing [45 CFR 303(c)].

### 14.2 Involvement of Vulnerable Populations in Research

When the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, the review process should include one or more individuals who are knowledgeable about or experienced in working with these participants. When the IRB does not have the relevant expertise among its membership it may seek such expertise through the use of consultants.

45 CFR 46 has additional subparts designed to provide extra protections for certain defined vulnerable populations which also have additional requirements for IRBs.

- **Subpart B** - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
- **Subpart C** - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
- **Subpart D** - Additional Protections for Children Involved as Subjects in Research

DHHS-conducted or supported research that involves any of these populations must comply with the requirements of the relevant subparts. Research regulated by the FDA includes equivalent protections and obligations when research involves children (Subpart D). Research conducted, supported or otherwise regulated by other federal agencies may or may not be covered by the subparts.
In its FWA, UMMC limits its commitment to apply Subparts B, C, and D to non-exempt human subjects research conducted or supported by DHHS or any other federal agency that requires compliance with the Subpart(s) (B, C, or D) applicable to the research.

14.3 Procedures

The following policies and procedures apply to all research involving vulnerable populations under the oversight of the UMMC IRB regardless of funding. Subsequent sections address additional procedures and requirements that apply to specific populations.

**Initial Review of Research Proposal**

1. The investigator identifies the potential to enroll vulnerable participants in the proposed research at initial review and provides the justification for their inclusion in the study.

2. The investigator describes safeguards to protect the participant’s rights and welfare in the research proposal;

3. IRB staff, in collaboration with the IRB Chair as needed, ensure that the IRB has the relevant expertise with the vulnerable population, and, if necessary, arrange for consultation. When the research involves no more that minimal risk and is eligible for expedited review, the designated reviewer may determine the need for additional expertise to ensure the protection of the vulnerable population(s);

4. The IRB evaluates the proposed inclusion of vulnerable population(s) in the research and the safeguards proposed by the investigator, taking into consideration the following factors, as applicable to the research:
   a. Whether inclusion of vulnerable populations is ethically and scientifically appropriate;
   b. Whether the proposed plans, including the settings and circumstances, for the identification and recruitment of participants, and for obtaining consent or parental permission, ensure equitable selection of participants and promote voluntariness;
   c. Whether the proposed research confers any direct benefit, whether the benefit is available outside of the research, and whether access to the benefit may unduly influence participation by vulnerable populations;
   d. Whether any costs or plans for participant compensation may exclude or unduly influence participation by vulnerable populations;
   e. Whether the provisions for privacy and confidentiality adequately protect vulnerable populations; and
   f. Other relevant considerations as appropriate for the population(s) and the circumstances of the research

5. The IRB will determine whether the inclusion of the vulnerable population(s) is appropriate and whether the proposed plan adequately safeguards the rights and welfare of these participants. When appropriate, the IRB may restrict or disallow the inclusion of vulnerable populations or may require modifications to the research plan to enhance protections or to monitor the effectiveness of protections. For example, the
IRB could require review more than annually, periodic HRPP QA/QI reviews, independent routine monitoring, or the use of a research participant advocate or consent monitor.

**Modifications to Research**

1. When an investigator proposes to add the inclusion of a vulnerable population after research has already been approved by the IRB, the investigator must submit a modification request to the IRB identifying the population they would like to add, justification for inclusion of the population, and any modifications to the research plan to ensure protection of the participants’ rights and welfare.

   The IRB staff and IRB will follow the procedures outlined for initial review above.

**Continuing Review**

1. At continuing review, the investigator should identify the number and categories of vulnerable participants enrolled and any problems that arose relevant to their rights and welfare. When research does not include any interaction or intervention with participants, and such information is not gathered, this should be noted on the continuing review report.

2. IRB staff, in collaboration with the IRB Chair as needed, ensure that the IRB has the relevant expertise with the vulnerable population, and, if necessary, arrange for consultation. When the research involves no more that minimal risk and is eligible for expedited review, the designated reviewer may determine the need for additional expertise to ensure the protection of the vulnerable population(s).

3. The IRB reviews the continuing review information, and any relevant information reported to the IRB during the period of approval, and determines whether the inclusion of vulnerable populations and the plans to protect the rights and welfare of vulnerable participants remains appropriate.

**14.4 Research Involving Pregnant Women, Human Fetuses and Neonates**

The following applies to all research involving pregnant women, human fetuses, and neonates reviewed by the UMMC IRB. DHHS-specific requirements are noted in the appropriate sections.

If a woman becomes pregnant while participating in a study that has not been approved for inclusion of pregnant women, the IRB must be notified immediately so that the IRB can determine whether the participant may continue in the research, whether additional safeguards are needed, and to make the determinations required by the regulations and these policies.
14.4.1 Research Involving Pregnant Women or Fetuses

14.4.1.1 Research Not Conducted or Supported by DHHS

For research not conducted or supported by DHHS where the risk to pregnant women and fetus is no more than minimal, no additional safeguards are required by policy and there are no restrictions on the involvement of pregnant women in research. However, the IRB may determine that additional safeguards or restrictions are warranted for a specific study.

Pregnant women or fetuses may be involved in research not funded by DHHS involving more than minimal risk to pregnant women and/or fetuses if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent;
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children (as defined in Section 14.1) who are pregnant, assent and permission are obtained in accord with the requirements of state law and the IRB;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. The IRB may allow individuals whose normal responsibilities include determining the viability of fetuses to be engaged in the research, if their involvement in the determination of viability for an individual fetus cannot be avoided. Confirmation of the determination regarding viability will be sought from a qualified individual who is not otherwise engaged in the research whenever possible prior to involving the participant(s) in the research. The opinion of the independent qualified individual will be documented and made available upon request to the IRB or HRPP representative.
When advance confirmation is not possible, the investigator will obtain it as soon as she/he can after enrollment, but in all cases within 5 business days. The circumstances that prohibited prospective confirmation of viability and the outcome of the subsequent consultation are reported to the IRB within 10 business days.

14.4.1.2 Research Conducted or Supported by DHHS

For DHHS-conducted or supported research 45 CFR Subpart B applies to all non-exempt human subject research involving pregnant women, fetuses, and neonates.

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.

2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

3. Any risk is the least possible for achieving the objectives of the research;

4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent.

5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

7. For children (as defined in Section 14.1) who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent in Section 14.6.2;

8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

14.4.2 Research involving Neonates of Uncertain Viability or Nonviable Neonates

14.4.2.1 Research Not Conducted or Supported by DHHS

Neonates of uncertain viability and nonviable neonates may be involved in research involving more than minimal risk if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

3. The IRB may allow individuals whose normal responsibilities include determining the viability of neonates to be engaged in the research, if their involvement in the determination of viability for an individual neonate cannot be avoided. In such cases, confirmation of the determination regarding viability must be made by a qualified individual who is not otherwise engaged in the research whenever possible prior to beginning the research. The opinion of the independent qualified individual will be documented and made available upon request to the IRB or HRPP representative. When advance confirmation is not possible, the investigator will obtain it as soon as she/he can after enrollment, but in all cases within 5 business days. The circumstances that prohibited prospective confirmation of viability and the outcome of the subsequent consultation will be reported to the IRB within 10 business days.

4. The requirements for Neonates of Uncertain Viability or Nonviable Neonates (see below in this section) have been met, as applicable.

Neonates of Uncertain Viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

The IRB determines that:

1. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or

2. The purpose of the research is the development of important knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

3. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with the provisions of permission and assent,
except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

**Nonviable Neonates.** After delivery, nonviable neonates may not be involved in research unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained in accord with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply.

However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a LAR of either or both of the parents of a nonviable neonate will not suffice.

14.4.2.2 Research Conducted or Supported by DHHS

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
3. Individuals engaged in the research will have no part in determining the viability of a neonate.
4. The requirements for Neonates of Uncertain Viability or Nonviable Neonates (see below in this section) have been met, as applicable.

**Neonates of Uncertain Viability.** Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

1. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
2. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

3. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's LAR is obtained in accord with the provisions of permission and assent, except that the consent of the father or his LAR need not be obtained if the pregnancy resulted from rape or incest.

**Nonviable Neonates.** After delivery, nonviable neonates may not be involved in research unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained in accord with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply.

However, if either parent is unable to consent because of unavailability or incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a LAR of either or both of the parents of a nonviable neonate will not suffice.

**14.4.3 Viable Neonates**

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements for research involving children (i.e., a viable neonate is a child for purposes of applying federal regulations and UMMC policies).

**14.4.4 Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material**

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

If information associated with material described above in this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research participants and all pertinent sections of these policies and procedures are applicable.
14.4.5 Research Not Otherwise Approvable

14.4.5.1 Research Not Conducted or Supported by DHHS

If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research if:

1. The research in fact satisfies the conditions detailed above, as applicable; or
2. All of the following:
   a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
   b. The research will be conducted in accord with sound ethical principles; and
   c. Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.

14.4.5.2 Research Conducted or Supported by DHHS

DHHS conducted or supported research that falls in this category must be approved by the Secretary of Health and Human Services. If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the research will be sent to OHRP for DHHS review.

14.5 Research Involving Prisoners

The following applies to all research involving prisoners, regardless of funding source. The requirements in this section are consistent with Subpart C of 45 CFR 46, which applies to DHHS-funded or supported research.

14.5.1 Applicability

UMMC does not plan to engage in research involving prisoners. If UMMC were selected as a site for a multi-center study involving prisoners it would rely upon a properly constituted IRB from an institution participating in the research for the review. §46.304(b).
14.5.2 Incarceration of Enrolled Participants

If a participant becomes a prisoner while enrolled in a research study that was not reviewed according to Subpart C, the investigator must promptly notify the IRB and the IRB will:

1. Confirm that the participant meets the definition of a prisoner.
2. Consult with the investigator to determine if it is in the best interests of the participant to continue participation in the study, in part or in full.
3. If the participant should continue, one of two options are available:
   a. Identify an appropriately constituted IRB to review the research, have it reviewed under Subpart C and keep the participant enrolled in the study. If some of the requirements of Subpart C cannot be met or are not applicable (e.g., procedures for the selection of participants within the prison), but it is in the best interests of the participant to remain in the study, keep the participant enrolled and inform OHRP of the decision along with the justification.
   b. Remove the participant from the study and keep the participant on the study intervention under an alternate mechanism such as compassionate use or off label use.
4. If a participant is incarcerated temporarily while enrolled in a study:
   a. If the temporary incarceration has no effect on the study (i.e., there is no need for study activities to take place during the temporary incarceration), keep the participant enrolled.
   b. If the temporary incarceration has an effect on the study, follow the above guidance.

14.6 Research Involving Children

The following applies to all research involving children, regardless of funding source. The requirements in this section are consistent with Subpart D of 45 CFR 46, which applies to DHHS-funded research and Subpart D of 21 CFR 50, which applies to FDA-regulated research involving children.

14.6.1 Allowable Categories

In addition to the IRB’s normal duties, research involving children must be reviewed by the IRB to determine if it fits within and is permissible under one or more federally-defined categories (OHRP/FDA). Each procedure or intervention that the child will undergo for the research must be taken into consideration, and, if the research includes more than one study group assignment (e.g., placebo vs. active, investigational agent vs. comparator) a component analysis must be conducted by the IRB and the category determination must be made for each group assignment. The categories are as follows:
1. **[45 CFR 46.404/21 CFR 50.51]** Research/Clinical Investigations not involving greater than minimal risk  
   Research determined not to involve greater than minimal risk to child participants may be approved by the IRB only if the IRB finds and documents that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians as set forth in Section 14.6.2.

2. **[45 CFR 46.405/21 CFR 50.52]** Research/Clinical Investigations involving greater than minimal risk but presenting the prospect of direct benefit to the individual participant  
   Research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual participant, or by a monitoring procedure that is likely to contribute to the participant’s well-being, may be approved by the IRB only if the IRB finds and documents that:
   - The risk is justified by the anticipated benefit to the participants;
   - The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative options; and
   - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 14.6.2.

3. **[45 CFR 46.406/21 CFR 50.53]** Research/Clinical Investigations involving greater than minimal risk and no prospect of direct benefit to the individual participant, but likely to yield generalizable knowledge about the participant’s disorder or condition.  
   Research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual participant, or by a monitoring procedure which is not likely to contribute to the well-being of the participant, may be approved by the IRB only if the IRB finds and documents that:
   - The risk represents a minor increase over minimal risk;
   - The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
   - The intervention or procedure is likely to yield generalizable knowledge about the participants’ disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; and
   - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 14.6.2.

4. **[45 CFR 46.407/21 CFR 50.54]** Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children.  
   When the IRB does not believe that the research meets the requirements of any of the above categories, and the IRB finds and documents that the research presents a reasonable opportunity to further the understanding, prevention, or
alleviation of a serious problem affecting the health or welfare of children, the IRB shall refer the research for further review as follows:

- HHS conducted or supported research in this category will be referred for review by the Secretary of Health and Human Services. However, before doing so the IRB must determine that the proposed research also meets all of the requirements of the Common Rule.

- FDA-regulated research in this category will be referred for review by the Commissioner of Food and Drugs.

- For research that is not DHHS conducted or supported and not FDA-regulated, the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research if:
  - The research in fact satisfies the conditions of the previous categories, as applicable; or
  - All of the following:
    - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
    - The research will be conducted in accord with sound ethical principles; and
    - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 14.6.2.

### 14.6.2 Parental Permission and Assent

#### 14.6.2.1 Parental Permission

The IRB must determine that adequate provisions have been made for soliciting the permission of each child’s parent or guardian.

Parents or guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described in Section 13.

The IRB may find that the permission of one parent is sufficient for research to be conducted under Categories 1 [45 CFR 46.404/21 CFR 50.51] & 2 [45 CFR 46.405/21 CFR 50.52] above. The IRB’s determination of whether permission must be obtained from one or both parents will be documented in the reviewer’s notes when a study receives expedited review, and in meeting minutes when reviewed by the convened committee.

Permission from both parents is required for research to be conducted under Categories 3 [45 CFR 46.406/21 CFR 50.53] and 4 [45 CFR 46.407/21 CFR 50.54] above unless:
1. One parent is deceased, unknown, incompetent, or not reasonably available; or
2. When only one parent has legal responsibility for the care and custody of the child.

The IRB may waive the requirement for obtaining permission from a parent or legal guardian if:

- The research meets the provisions for waiver in Section 13.10 or
- For research that is not FDA-regulated, if the IRB determines that the research is designed to study conditions in children for which parental or guardian permission is not a reasonable requirement to protect participants (for example, neglected or abused children), provided that an appropriate mechanism for protecting the children who will participate in the research is substituted, and that the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism will depend upon the nature and purpose of the activities described in the protocol/research plan, the risks and anticipated benefits to the research participants, and the child’s age, maturity, status, and condition.

Permission from parents or legal guardians must be documented in accordance with and to the extent required by Section 13.8.

14.6.2.2 Assent from Children

The IRB is responsible for determining that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. This judgment may be made for all children to be involved in the study, or for each child, as the IRB deems appropriate.

If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the participants are capable of giving assent, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accordance with the applicable regulations. It is important to note that the FDA regulations do permit the IRB to waive the assent requirement if it finds and documents that:

1. The clinical investigation involves no more than minimal risk to the participants;
2. The waiver will not adversely affect the rights and welfare of the participants;
3. The clinical investigation could not practicably be carried out without the waiver; and
4. Whenever appropriate, the participants will be provided with additional pertinent information after participation.

Because “assent” means a child’s affirmative agreement to participate in research, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way.
The IRB should take into account the nature of the proposed research activity and the age, maturity, and psychological state of the children involved when reviewing the proposed assent procedure and the form and content of the information conveyed to prospective participants. For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission. For children whose age and maturity level limits their ability to fully comprehend the nature of the research activity, but who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (for example, what the experience will be, how long it will take, whether it might involve any pain or discomfort). The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree he or she is capable, what his or her participation in research will involve.

Parents and children will not always agree on whether a child should participate in research. Where the IRB has indicated that the assent of the child is required in order for him or her to be enrolled in the study, dissent from the child overrides permission from a parent. Similarly, a child typically cannot decide to be in research over the objections of a parent. There are individual exceptions to these guidelines but in general, children should not be forced to be research participants, even when permission has been given by their parents.

**Documentation of Assent**

When the IRB determines that assent is required, it also is also responsible for determining whether and how assent must be documented. When the research targets the very young child or children unable or with limited capacity to read or write, an oral presentation accompanied perhaps by some pictures with documentation of assent by the person obtaining assent in a research note is likely more appropriate than providing the child a form to sign. In this case, the investigator should provide the IRB with a proposed script and any materials that they intend to use in explaining the research.

When the research targets children who are likely able to read and write, investigators should propose a process and form that is age appropriate and study specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study. The assent form should:

1. Tell why the research is being conducted;
2. Describe what will happen and for how long or how often;
3. Say it's up to the child to participate and that it's okay to say no;
4. Explain if it will hurt and if so for how long and how often;
5. Say what the child's other choices are;
6. Describe any good things that might happen;
7. Say whether there is any compensation for participating; and
8. Ask for questions.

Illustrations might be helpful, and larger type and other age appropriate improvements are encouraged when they have the potential to enhance comprehension. Studies involving older children or adolescents should include more information and may use more complex language.

14.6.2.3 Children Who are Wards

Children who are wards of the State or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406/21 CFR 50.53 or 45 CFR 46.407/21 CFR 50.54 (Categories 3 and 4 in Section 14.6.1), only if such research is:

1. Related to their status as wards; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.

If the research meets the condition(s) above, an advocate must be appointed for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in loco parentis.

The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

14.7 Adults with Impaired Decision-Making Capacity

When vulnerable populations are included in research, regulations require that additional safeguards are put in place to protect the rights and welfare of these participants. [45 CFR 46.111(b)/21 CFR 56.111(b)] Adults who lack or who have impaired, fluctuating, or diminishing decision-making capacity (collectively referred to as “adults with impaired decision-making capacity” in this section) are particularly vulnerable. Investigators and IRBs must carefully consider whether inclusion of such participants in a research study is appropriate; and when it is, must consider how best to ensure that these participants are adequately protected. The principals and procedures outlined in this section are intended to assist UMMC investigators and the IRB with the development and review of research involving adults with impaired decision-making capacity.

14.7.1 Informed Consent

Obtaining legally effective informed consent before involving human participants in research is one of the central ethical principles described in the Belmont Report and provided for by federal regulations governing research.
The informed consent process involves three key features: (1) providing the prospective participant the information needed to make an informed decision (in language understandable to him or her); (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether to participate in the research.

Among other requirements, for consent to be legally effective, the potential participant or his/her LAR must have the necessary decision-making capacity to make a rational and meaningful choice about whether to participate (or continue participating) in a study.

14.7.2 Decision-Making Capacity

“Decision-making capacity” refers to a potential participant’s ability to make a rationale and meaningful decision about whether or not to participate in a research study. This ability is generally thought to include at least the following four elements:

1. Understanding, i.e., the ability to comprehend the disclosed information about the nature and purpose of the study, the procedures involved, the risks and benefits of participating versus not participating, and the voluntary nature of participating;
2. Appreciation, i.e., the ability to appreciate the significance of the disclosed information and the potential risks and benefits for one’s own situation and condition;
3. Reasoning, i.e., the ability to engage in a reasoning process about the risks and benefits of participating versus alternatives, and;
4. Choice, i.e., the ability to express a choice about whether or not to participate.

“Decision-making capacity” should not be confused with the legal concept of “competence.” While the court may consider information about a person’s decision-making capacity in making a competency determination, the terms are not synonymous. Incompetence is a legal determination made by a court of law. For example, someone who is judged legally incompetent to manage their financial affairs may retain sufficient decision-making capacity to make meaningful decisions about participating in a research protocol. Likewise, people who have normal cognitive functioning and are considered legally competent may be put into circumstances where their decision-making capacity is temporarily impaired by a physical or mental condition or by alcohol or drugs.

Decision-making capacity is protocol and situation-specific. A person may have capacity to consent to participate in low risk research in usual circumstances, but not have the capacity to consent to a higher risk protocol when she/he is under significant stress or faced with unfamiliar circumstances.

14.7.3 Inclusion of Adults with Impaired Decision-Making Capacity in Research

Research involving adult participants who do not have the ability to provide consent or with impaired decision-making capacity should only be conducted when the aims of the research cannot reasonably be achieved without their participation. Investigators must disclose to the IRB both plans and justification for including adults with impaired decision-making capacity in a
given research proposal. If adults with questionable or fluctuating capacity will be included, investigators must specify procedures for assessing capacity prior to obtaining informed consent and, if appropriate, for re-evaluating capacity during study participation. If a prospective participant’s capacity to consent is expected to diminish, the investigator should consider requesting that the prospective participant designate a future LAR, including the future LAR in the initial consent process, and obtaining written documentation of the participant’s wishes regarding participation in the research. When the study includes participants likely to regain capacity to consent while the research is ongoing, the investigator should include provisions to inform him/her of participation and seek consent for continued participation.

Plans for evaluation of capacity should be tailored to the participant population and the risks and nature of the research. In some instances, assessment by a qualified investigator may be appropriate. However, an independent, qualified assessor should evaluate participants’ capacity when the risks of the research are more than a minor increase over minimal or the investigator is in a position of authority over a prospective participant. In all cases, the person(s) evaluating capacity must be qualified to do so and use appropriate, validated tools and methods (e.g., University of California, San Diego Brief Assessment of Capacity to Consent [UBACC], MacArthur Competence Assessment Tool for Clinical Research [MacCAT-CR]). Assessments of capacity should be documented in the research record, and when appropriate, in the medical record.

Under some circumstances, it may be possible for investigators to enable adults with a degree of decisional impairment to make voluntary and informed decisions to consent, assent, or refuse participation in research. Potential measures include repetitive teaching, audiovisual presentations, and oral or written recall tests. Other measures might include follow-up questions to assess understanding, videotaping or audio-taping of consent discussions, use of waiting periods to allow more time for the potential participant to consider the information that has been presented, or involvement of a trusted family member or friend in the disclosure and decision-making process. Audio or videotapes, electronic presentations, or written materials used to promote understanding must be provided to the IRB for review and approval prior to use.

When a prospective participant is deemed to lack capacity to consent to participate in research, investigators may obtain informed consent from the individuals’ surrogate or LAR (See Section 13.3). Under these circumstances, the prospective participant should still be informed about the research in a manner compatible with the participant’s likely understanding and, if possible, be asked to assent to participate. Potential participants who express resistance or dissent (by word, gesture, or action) to either participation or use of surrogate consent, should be excluded from the study. Some participants may initially assent but later resist participation. Under no circumstances may an investigator or caregiver override a participant’s dissent or resistance. When assent is possible for some or all participants, the investigator should provide the IRB with an assent plan that describes when and how assent will be obtained, provisions that will be taken to promote understanding and voluntariness, how assent will be documented, and a
copy of the assent form. If the investigator intends to use audio or video recordings to document assent, provisions to ensure the security of the recordings should be described to the IRB.

When inclusion of adults with impaired decision-making capacity is not anticipated and a plan for inclusion of such participants has not been reviewed and approved by the IRB, and an enrolled participant becomes unable to provide consent or impaired in decision-making capacity, the investigator is responsible for promptly notifying the IRB (as soon as possible but within 5 business days). The investigator should consider whether continuing participation is appropriate and, if so, present a plan to the IRB for surrogate consent from a LAR and, if appropriate, a plan to periodically evaluate capacity and re-obtain consent if possible.

14.7.4 IRB Review

The IRB review process will include at least one member, or a consultant, who is experienced with or otherwise knowledgeable about the population when the research involves greater than minimal risk, or the research is minimal risk but includes interactions with participants, and the proposed participant population includes adults with impaired decision-making capacity.

In evaluating research, the IRB must be able to determine that the risks to participants are reasonable not only in relation to any benefits, but also in relation to the importance of the knowledge that may reasonably be expected to result. In considering the risks of research involving adults with impaired decision-making capacity, the IRB should consider whether any components of the research involve risks that are greater for participants with diminished capacity. For example, whether participants might experience increased sensitivity or discomfort to certain stimuli or may not be able to verbalize or otherwise demonstrate when they are experiencing discomfort or pain.

As appropriate to the research, the IRB will consider the following in evaluating research involving adults with impaired decision-making capacity:

1. Whether the aims of the research cannot reasonably be achieved without inclusion of the population;
2. Whether the research is likely to improve the understanding of the condition, disease, or issue affecting the participant population;
3. Whether any experimental procedure or interventions have undergone pre-clinical testing or human testing on other populations and whether the data from that testing supports its use in the proposed research;
4. Whether the procedures or interventions that the participant will undergo in the research place him/her at increased risk and whether appropriate mechanisms are in place to minimize risks, when possible;
5. Whether the data and safety monitoring plan, including any stopping rules, is appropriate given the risks of the research and the vulnerability of the population;

6. Whether the procedures for withdrawing individual participants from the research are appropriate;

7. Whether the recruitment procedures, consent process, and any plans for financial compensation support voluntariness and minimize the likelihood of undue influence or coercion;

8. Whether participants will be exposed to financial or other risks that they might not consider acceptable if they had the capacity to provide consent, and whether appropriate mechanisms have been put into place to minimize these risks;

9. Whether the procedures for determining capacity to provide consent, and for evaluating capacity on an ongoing basis, if applicable, are appropriate;

10. Whether the procedures for informing participants who regain capacity about their involvement in the research, and for obtaining consent for on-going participation, if applicable, are appropriate;

11. Whether assent should be required when possible, and, if so, if the proposed procedures to obtain and document assent are appropriate;

12. Whether periodic re-evaluation of capacity and/or periodic re-consent should be required; and

13. Whether a research participant advocate or consent monitor should be required, for some or all participants.

In general, the IRB will only approve research involving participants unable to provide consent or with impaired decision-making capacity when the aims of the research cannot reasonably be achieved without inclusion of the population, and there are appropriate provisions to: (1) evaluate capacity, (2) obtain consent (and assent if possible), and (3) otherwise protect participants.

14.8 RESERVED
15 FDA-Regulated Research

FDA regulations apply to research that involves an FDA-regulated test article in a clinical investigation involving human subjects as defined by the FDA regulations. For FDA-regulated research, the IRB must apply the FDA regulations at 21 CFR 50 and 21 CFR 56. If required by organizational policy or a FWA, 45 CFR 46 must also be applied.

Clinical trials with investigational drugs must be conducted according to FDA’s IND regulations, 21 CFR Part 312, and other applicable FDA regulations. Evaluations of the safety or effectiveness of a medical device must be conducted according to FDA’s IDE regulations, 21 CFR Part 812, and other applicable FDA regulations.

The following procedures describe the review of FDA-regulated research by the UMMC IRB.

15.1 Definitions

Biologic. Biological products include a wide range of products such as vaccines, blood and blood components, allergens, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other technologies. In general, the term "drugs" includes therapeutic biological products.

Clinical Investigation. Clinical investigation means any experiment that involves a test article and one or more human participants and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies. [21 CFR 50.3(c)]

Dietary Supplement. A dietary supplement is a product taken by mouth that is intended to supplement the diet and that contains a dietary ingredient. The dietary ingredients in these products can include vitamins, minerals, herbs and other botanicals, amino acids, other dietary substances intended to supplement the diet, and concentrates, metabolites, constituents, extracts, or combinations of the preceding types of ingredients. [21 U.S.C. 321(ff)].

Emergency Use. Emergency use is defined as the use of a test article on a human participant in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. [21 CFR 56.102(d)]

Humanitarian Use Device (HUD). A Humanitarian Use Device is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year.
Investigational Drug. Investigational or experimental drugs are new drugs that have not yet been approved by the FDA or approved drugs that are being studied in a clinical investigation.

Investigational Device. Investigational device means a device (including a transitional device) that is the object of an investigation. Investigation, as it pertains to devices, means a clinical investigation or research involving one or more participants to determine the safety or effectiveness of a device.

IND. IND means an investigational new drug application in accordance with 21 CFR Part 312.

IDE. IDE means an investigational device exemption in accordance with 21 CFR 812.

In Vitro Diagnostic Product (IVD). In vitro diagnostic products are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. [21 CFR 809.3(a)]

Non-Significant Risk (NSR) Device. A non-significant risk device is an investigational device that does not meet the definition of a significant risk device.

Significant Risk (SR) Device. Significant risk device means an investigational device that:

(1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or

(2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or

(3) 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; or

(4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. [21 CFR 812.3(m)]

15.2 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of FDA regulations for IRB review:

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 at the institution is subject to IRB review. [21 CFR §56.104(c)]

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. [21 CFR §56.104(d)]
15.3 Investigator Responsibilities

The investigator holds additional responsibilities when conducting a clinical investigation subject to FDA regulations. These responsibilities include, but are not limited to, the following:

1. The investigator is responsible for indicating on the IRB application that the proposed research is FDA-regulated and for providing relevant information regarding the test article.

2. The investigator is responsible for ensuring that a clinical investigation is conducted according to the signed investigator statement for clinical investigations of drugs (including biological products) or agreement for clinical investigations of medical devices, the investigational plan and other applicable regulations, and any requirements imposed by the FDA or IRB.

3. The investigator is responsible for personally conducting or supervising the investigation. When certain study-related tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

4. The investigator must maintain a list of the appropriately qualified persons to whom significant trial-related duties have been delegated. This list should also describe the delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks (e.g., it can refer to an individual’s CV on file and/or training conducted by the investigator/sponsor), and identify the dates of involvement in the study. An investigator should maintain separate lists for each study conducted by the investigator.

5. The investigator is responsible for protecting the rights, safety, and welfare of study participants under their care during a clinical trial. This responsibility includes:

   • Informing participants that the test article is being used for investigational purposes and ensuring that the requirements relating to obtaining informed consent are met

   • Providing or arranging for reasonable medical care for study participants for medical problems arising during participation in the trial that are, or could be, related to the study intervention

   • Providing reasonable access to needed medical care, either by the investigator or by another identified, qualified individual (e.g., when the investigator is unavailable, or when specialized care is needed)

   • Adhering to the protocol/research plan so that study participants are not exposed to unreasonable risks

   • Informing the participant’s primary physician about the participant’s participation in the study if the participant has a primary physician and the participant agrees to the primary physician being informed
6. The investigator is responsible for reading and understanding the information in the investigator brochure or device risk information, including the potential risks and side effects of the drug or device.

7. The investigator is responsible for maintaining adequate and accurate records in accordance with FDA regulations and for making those records available for inspection by the FDA. These records include: correspondence with other investigators, the IRB, the sponsor, monitors, or the FDA; drug and device accountability records; case histories; consent forms; and documentation that consent was obtained prior to any participation in the study. Records submitted to the IRB are retained indefinitely in an electronic format. UMMC record retention policy requires records be maintained for 6 years following completion of the study. Other regulations, such as HIPAA, organizational policies, or contractual agreements with sponsors may necessitate retention for a longer period of time.

8. The investigator is responsible for controlling drugs, biological products, and devices according to FDA regulations and the Controlled Substances Act, if applicable.

9. For research reviewed by the UMMC IRB, the investigator proposing the clinical investigation is required to provide a plan – to be evaluated by the IRB - that includes storage, security, and dispensing of the test article.
   a. The investigator is responsible for investigational drug accountability that includes storage, security, dispensing, administration, return, disposition, and records of accountability. Such details are provided in the IRB submission and reviewed by the IRB for acceptability
   b. The investigator may delegate in writing, as part of the IRB submission, the responsibility detailed above to Investigational Drug Services.
   c. Investigational drugs and devices must be labeled in accordance with federal and state standards.
   d. All devices received for a study must be stored in a locked environment under secure control with limited access. When applicable, proper instructions on the use of the device must be provided to study participants. A log must be kept regarding the receipt, use, and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

10. The investigator shall furnish all reports required by the sponsor of the research including adverse events, progress reports, safety reports, final reports, and financial disclosure reports.

11. The investigator will permit inspection of research records by the sponsor, sponsor representatives, the FDA, OHRP, accrediting bodies, UMMC HRPP, IRB and Office of Integrity and Compliance representatives and any other agencies or individuals entitled to inspect such records under regulation, organizational policy, or contractual agreement.
15.4 Dietary Supplements

Research involving dietary supplements may or may not fall under FDA regulations. Under the Dietary Supplement Health and Education Act (DSHEA) of 1994, a dietary supplement is not considered a drug and is not subject to the premarket approval requirements for drugs if the intended use for which it is marketed is only to affect the structure or any function of the body (i.e., not intended to be used for a therapeutic purpose). Whether a study falls under FDA oversight is determined by the intent of the clinical investigation. If the clinical investigation is intended only to evaluate the dietary supplement’s effect on the structure or function of the body, FDA regulations do not apply. If the study is intended to evaluate the dietary supplement’s ability to diagnose, cure, mitigate, treat, or prevent a disease, then FDA regulations apply. Studies involving the ingestion of dietary supplements that are not subject to FDA oversight are still research, and must be reviewed by the IRB.

Whether an IND is needed for a study evaluating a dietary supplement is determined by the intent of the study. If the study is intended only to evaluate the dietary supplement’s effect on the structure or function of the body, an IND is not required. If the study is intended to evaluate the dietary supplement’s ability to diagnose, cure, mitigate, treat, or prevent a disease, an IND is required under part 312.

The investigator must supply the IRB with sufficient information to determine that the criteria for approval are satisfied and to determine or verify whether or not the research requires an IND. Applications should provide detail consistent with that expected on a drug protocol/research plan and consistent with the level of risk associated or anticipated with the research. At a minimum, the research plan should provide the following information regarding the supplement: Name, Manufacturer, Formulation, Dosage, Method/Route of Administration, Mechanism of Action, Known Drug Interactions, Risk Profile, IND number (or justification for why an IND is unnecessary), documentation of approval for use in humans, documentation or certification of Quality or Purity and an accountability plan for the product describing where it will be stored and how it will be dispensed, usage tracked and final disposition, disposal or return. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included.

15.5 Clinical Investigations of Articles Regulated as Drugs and Devices

15.5.1 IND/IDE Requirements

For studies evaluating the safety or effectiveness of medical devices or experiments using drugs, biologics, dietary supplements, and other compounds that may be considered a drug under FDA regulations, the investigator must indicate on the IRB application whether or not an IDE or IND is in place, and, if not, the basis for why an IDE or IND is not needed. Documentation of the IND/IDE must be provided by the sponsor or the sponsor-investigator. Documentation of the IND/IDE could be a:

1. Industry sponsored study with IND/IDE number indicated on the protocol/research plan.
2. Letter/communication from FDA.
3. Letter/communication from industry sponsor.

4. Other document and/or communication verifying the IND/IDE.

For investigational devices, the study may be exempt from IDE requirements or, in the case of Non-significant Risk (NSR) device studies, follow abbreviated IDE requirements which do not require formal approval by the FDA. If the sponsor has identified a device study as exempt or NSR, then the investigator should include documentation with the submission providing the basis for exempt or NSR categorization. If the FDA has determined that the study is exempt or NSR, documentation of that determination must be provided.

The IRB will review the application and, based upon the documentation provided and determine:

1. That there is an approved IND/IDE in place;
2. That the FDA has determined that an IND is not required or that a device study is IDE-exempt or NSR.

If neither of the above determinations apply, the IRB will determine whether an IND is necessary, or a device study is exempt, NSR, or must be submitted to the FDA for an IDE or for a determination, using the criteria below.

The IRB cannot grant approval to the research until the IND/IDE status is determined, and, if necessary, an approved IND or IDE is in place.

15.5.2 IND Exemptions

For drugs, an IND is not necessary if the research falls in one of the following seven (7) categories:

1. 21 CFR 312.2(b)(1): The drug being used in the research is lawfully marketed in the United States and all of the following requirements are met:
   a. The research 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
   b. In the case of a prescription drug, the research is not intended to support a significant change in the advertising for the product;
   c. The research does not involve a route of administration, dose, subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
   d. The research is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];
   e. The research is conducted in compliance with the requirements of 21 CFR 312.7 (i.e., the research is not intended to promote or commercialize the drug product); and
   f. The research does not intend to invoke FDA regulations for planned emergency research [21 CFR 50.24].
Please Note: FDA has provided specific guidance for evaluating whether this exemption applies to studies of marketed drugs/biologics for the treatment of cancer.

2. **21 CFR 312.2(b)(2):** For clinical investigations involving defined in vitro diagnostic biological products (blood grouping serum, reagent red blood cells and anti-human globulin), an IND is not necessary if a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and b) it is shipped in compliance with 21 CFR 312.160

3. **21 CFR 312.2(b)(5):** A clinical investigation involving use of a placebo is exempt from the requirements of part 312 if the investigation does not otherwise require submission of an IND.

4. **21 CFR 320.31(b) and (d):** Bioavailability or Bioequivalence (BA/BE) studies if all of the following conditions are met:
   a. The drug product does not contain a new chemical entity [21 CFR 314.108], is not radioactively labeled, and is not cytotoxic;
   b. 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;
   c. The investigation is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]; and
   d. The sponsor meets the requirements for retention of test article samples [21 CFR 320.31(d)(1)] and safety reporting [21 CFR 320.31(d)(3)].

5. **21 CFR 361.1:** Research using a radioactive drug or biological product if all of the following conditions are met:
   a. It involves basic research not intended for immediate therapeutic, diagnostic, or similar purposes, or otherwise to determine the safety and efficacy of the product;
   b. The use in humans is approved by a Radioactive Drug Research Committee (RDRC) that is composed and approved by FDA;
   c. The dose to be administered is known not to cause any clinically detectable pharmacological effect in humans; and
   d. The total amount of radiation to be administered as part of the study is the smallest radiation dose practical to perform the study without jeopardizing the benefits of the study and is within specified limits.

6. FDA practices enforcement discretion for research using cold isotopes of unapproved drugs if all of the following conditions are met:
   a. The research is intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a drug labeled with a cold isotope or regarding human physiology, pathophysiology, or biochemistry;
   b. The research is not intended for immediate therapeutic, diagnostic, or preventive benefit to the study subject;
   c. The dose to be administered is known not to cause any clinically detectable pharmacologic effect in humans based on clinical data from published literature or other valid human studies;
d. The quality of the cold isotope meets relevant quality standards; and

e. The investigation is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively].

15.5.3 IDE Exemptions

For clinical investigations of medical devices, an IDE is not necessary if:

1. The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;

2. The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence (a “501k” device);

3. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
   a. Is noninvasive,
   b. Does not require an invasive sampling procedure that presents significant risk,
   c. Does not by design or intention introduce energy into a subject, and
   d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;

4. The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;

5. The research involves a device intended solely for veterinary use;

6. The research involves a device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c);

7. The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

15.5.4 Significant and Non-Significant Risk Device Studies

A device study is a Non-Significant Risk (NSR) Device study if it is not IDE exempt and does not meet the definition of a Significant Risk (SR) Device study.

Under 21 CFR 812.3(m), a SR device means an 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; or
• Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

If the FDA has already determined a study to be SR or NSR, documentation evidencing such should be provided to the IRB as described in Section 15.5.1. The FDA’s determination is final and the IRB does not have to make the device risk determination.

Unless the FDA has already made a device risk determination for the study, the IRB will review studies that the sponsor or investigator have put forth as NSR at a convened meeting to determine if the device represents SR or NSR.

The sponsor or sponsor-investigator is responsible for providing the IRB with an explanation describing the basis for the initial determination of NSR and any other information that may help the IRB in evaluating the risk of the study (e.g., reports of prior investigations of the device). The IRB will review the information provided, including, but not limited to: a description of the device, reports of prior investigations of the device (if applicable), the proposed investigational plan, and participant selection criteria.

The NSR/SR determination made by the IRB is based on the proposed use of the device in the investigation, not on the device alone. The IRB considers the nature of any harms that may result from use of the device, including potential harms from additional procedures participants undergo as part of the investigation (e.g., procedures for inserting, implanting, or deploying the device). The IRB may consult with the FDA or require the sponsor or investigator to obtain a determination from the FDA. The IRB documents the SR or NSR determination in the electronic protocol records and the basis for it in the meeting minutes and provides the investigator, and sponsor when applicable, with the determination in writing.

Non-significant risk device studies do not require submission of an IDE application to the FDA but must be conducted in accordance with the abbreviated requirements of IDE regulations (21 CFR 812.2(b)). Under the abbreviated requirements, the following categories of investigations are considered to have approved applications for IDE’s, unless FDA has notified a sponsor under 812.20(a) that approval of an application is required:

(1) An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor (or sponsor-investigator):

   (i) Labels the device in accordance with 812.5;
(ii) Obtains IRB approval of the investigation after presenting the reviewing IRB with an explanation of why the device is not a significant risk device, and maintains such approval;

(iii) Ensures that each investigator participating in an investigation of the device obtains from each participant under the investigator’s care, informed consent under 21 CFR Part 50 and documents it, unless documentation is waived by an IRB under 56.109(c).

(iv) Complies with the requirements of 812.46 with respect to monitoring investigations;

(v) Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through (10);

(vi) Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and

(vii) Complies with the prohibitions in 812.7 against promotion and other practices.

When the FDA or IRB determines that a study is SR the IRB does not approve the study until an IDE is obtained.

15.6 Humanitarian Use Devices

A Humanitarian Use Device (HUD) is an approved (marketed) medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year [21 CFR 814.3(n)]. Federal law requires that IRBs approve the use of an HUD at a facility. Once approved, the clinical use of the HUD may be considered as any other approved device, with the caution that effectiveness has not been shown in clinical trials.

15.6.1 Definitions

Humanitarian Device Exemption: A Humanitarian Device Exemption (HDE) is a “premarket approval application” submitted to FDA pursuant to Subpart A, 21 CFR Part 814 “seeking a humanitarian device exemption from the effectiveness requirements of sections 514 and 515 of the [FD&C Act] as authorized by section 520(m)(2) of the [FD&C Act].” HDE approval is based upon, among other criteria, a determination by FDA that the HUD does not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use while taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

HDE Holder: The HDE Holder is a person who, or entity that, obtains approval of an HDE from the FDA.
15.6.2 IRB Review Requirements

A Humanitarian Use Device (HUD) may only be used after the IRB has approved its use, except in certain emergencies. The HDE holder is responsible for ensuring that a HUD is provided only to facilities having an IRB constituted and acting in accordance with the FDA’s regulations governing IRBs (21 CFR Part 56), including continuing review of use of the device.

When a HUD is used in a clinical investigation (i.e., research involving one or more participants to determine the safety or effectiveness of the HUD), the full requirements for IRB review and informed consent apply (21 CFR 50 and 56), as well as other applicable regulations. It is essential to differentiate whether the HUD is being studied for the indication(s) in its approved labeling or for different indication(s). When the HUD is being studied for the indication(s) in its approved labeling, the IDE regulations at 21 CFR 812 do not apply. However, when the HUD is being studied for a different indication(s), 21 CFR 812 applies, including the requirement for a FDA-approved IDE before starting the clinical investigation of a Significant Risk device.

15.6.3 Procedures

The relevant requirements and procedures for investigators and for IRB review described elsewhere in this manual apply to clinical investigations of HUDs. The material within this section applies to diagnostic or treatment uses of HUDs.

The health care provider seeking approval for diagnostic or treatment use of a HUD at UMMC is responsible for obtaining IRB approval prior to use of the HUD at UMMC and for complying with the applicable regulations, including those for medical device reporting, institutional policies, and the requirements of the IRB.

Health care providers seeking initial IRB approval for diagnostic or treatment use of a HUD for the indication(s) in the HUDs approved labeling should submit the following materials to the IRB:

1. IRB application
2. A copy of the HDE approval letter from the FDA
3. A description of the device, such as a device brochure
4. The patient information packet for the HUD
5. The proposed clinical consent process and document.
6. Other relevant materials as identified in the IRB application

The IRB reviews the proposal at a convened meeting ensuring that appropriate expertise is available either within the membership in attendance or via the use of consultants. The IRB reviews the risks to patients that are described in the product labeling and other materials, the proposed procedures to ensure that risks are minimized, and evaluates whether the risks are reasonable in relation to the potential benefits to patients at the facility. The IRB evaluates the patient information packet and proposed consent process and document and determines if the materials are adequate and appropriate for the patient population.
The IRB may specify limitations on the use of the device, require additional screening and follow up procedures, require interim reports to the IRB, require continuing review more often than annually, or set other conditions or requirements as appropriate to minimize risks to patients and ensure the safe use of the device in the facility.

Once use of the HUD is approved, the health care provider is responsible for submitting any proposed changes to the IRB-approved plan or patient materials and obtaining approval for those changes prior to implementation, unless the change is necessary to avoid or mediate an apparent immediate risk to a patient. Proposed changes are submitted with an Amendment form and accompanied by any revised materials or supporting documentation. The IRB may review these changes using expedited review procedures or refer the changes for review by the convened IRB.

The health care provider is responsible for submitting reports to the FDA, the IRB, and the manufacturer/HDE Holder whenever a HUD may have caused or contributed to a death, and must submit reports to the manufacturer (or to FDA and the IRB if the manufacturer is unknown) whenever a HUD may have caused or contributed to a serious injury (21 CFR 803.30 and 814.126(a)). Serious injury means an injury or illness that (1) is life-threatening, (2) results in permanent impairment of a bodily function or permanent damage to a body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a bodily function or permanent damage to a body structure (21 CFR 803.3). The specific requirements for this reporting are in the Medical Device Reporting (MDR) Regulation, at 21 CFR Part 803. The IRB reviews these reports via either expedited or convened review, as appropriate, and considers whether any changes are needed to the IRB-approved plan or patient materials.

The health care provider is responsible for submitting continuing review materials to the IRB sufficiently in advance of the expiration date to ensure IRB review and re-approval prior to expiration. Materials to be submitted include:

1. The Continuing Review application
2. Any safety reports or summaries provided by the HDE holder that had not previously been submitted
3. Other materials as identified on the Continuing Review Report
4. Any other new relevant information or materials

The IRB may conduct continuing review using expedited review procedures or review by the convened IRB.

15.6.4 Emergency Uses of HUDs

If an appropriately trained and licensed health care provider in an emergency situation determines that IRB approval for the use of the HUD at the facility cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval. The health care provider must provide written notification of the use to the IRB within 5 working days after the emergency use of the device, including the identification of the patient involved, the date of the use, and the reason for the use. [21 CFR 812.124]
If a HUD is approved for use in a facility, but an appropriately trained and licensed health care provider wants to use the HUD outside its approved indication(s) in an emergency or determines that there is no alternative device for a patient’s condition, the physician should consult with the HDE holder and IRB in advance if possible, obtain informed consent if possible, and ensure that reasonable measures are taken to protect the well-being of the patient such as a schedule and plan for follow up examinations and procedures to monitor the patient, taking into consideration the patient’s specific needs and what is known about the risks and benefits of the device. The provider should submit a follow up report to the HDE holder and the IRB and must comply with medical device reporting requirements.

The IRB may require additional reports, patient protection measures, or other requirements, as appropriate given the specifics of the situation.

15.7 Expanded Access to Investigational Drugs, Biologics, and Devices

Expanded access pathways, also referred to as “compassionate use”, are designed to make investigational medical products available as early in the drug and device evaluation process as possible to patients without therapeutic options, because they have exhausted or are not a good candidate for approved therapies and cannot enter a clinical trial. Expanded access refers to the use of investigational or unapproved/uncleared medical products (all referred to as “investigational” throughout this section) outside of a clinical trial, where the primary intent is treatment, rather than research. Because the products have not yet been approved by FDA as safe and effective, it is important to remember that the product may not be effective and there may be unexpected serious adverse effects and to take appropriate measures to ensure that this is understood by the patient or their LAR and to monitor for safety.

Charging for expanded access use of investigational products is discussed in Section 15.8.

15.7.1 Expanded Access to Investigational Drugs and Biologics

The FDA’s expanded access rule for investigational drugs, including biologics classified as drugs, is intended to improve access to investigational drugs for patients with serious or immediately life-threatening diseases or conditions who lack other therapeutic options and may benefit from the investigational agent. Expanded access is sometimes referred to as compassionate use or treatment use.

For the purposes of expanded access to investigational drugs, **immediately life-threatening disease or condition** means 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. **Serious disease or condition** means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. [21 CFR 312.300(b)]
Expanded access may also apply to (1) situations when a drug has been withdrawn for safety reasons, but there exists a patient population for whom the benefits of the withdrawn drug continue to outweigh the risks; (2) use of a similar, but unapproved drug (e.g., foreign-approved drug product) to provide treatment during a drug shortage; (3) use of an approved drug where availability is limited by a risk evaluation and mitigation strategy (REMS); and (4) use for other reasons. All are referred to as “investigational” for the purposes of these SOPs.

Under the FDA’s expanded access rule, access to investigational drugs for treatment purposes is available to:

- Individual patients, including in emergencies [21 CFR 312.310]
- Intermediate-size patient populations [21 CFR 312.315]

Widespread use under a treatment protocol or treatment IND [21 CFR 312.320]

The following section addresses expanded access for individual patients. Investigators seeking expanded access for intermediate-size populations or widespread use should consult with the Human Research Office. Convened IRB review is generally required for intermediate or widespread expanded access unless the FDA has issued a waiver.

Physicians seeking access to investigational drugs under expanded access should work closely with the sponsor or manufacturer, the FDA, and the UMMC Human Research Office, to determine the appropriate access mechanism and ensure that proper regulatory procedures are followed. The FDA provides information about the procedures and requirements for expanded access on a [website](#), including a link to FDA’s contact information.

### 15.7.1.1 Expanded Access to Investigational Drugs for Individual Patients

Expanded access to investigational drugs may be sought under an “Access Protocol” or an “Access IND”. FDA generally encourages Access Protocols, which are managed and submitted by the sponsor of an existing IND, because it facilitates the review of safety and other information. However, Access INDs for the treatment of individual patients are also available and commonly used when: (1) a sponsor holding an existing IND declines to be the sponsor for the individual patient use (e.g., because they prefer that the physician take on the role of sponsor-investigator); or (2) there is no existing IND.

**Sponsor or Manufacturer Approval:**

Prior to submitting to the FDA or IRB, physicians seeking expanded access to an investigational drug should contact the sponsor (e.g., for investigational drugs under a commercial IND) or manufacturer (e.g., for approved drugs under a REMS) to: (1) ensure that the investigational drug can be obtained; (2) determine whether the patient may be treated under an existing IND study, sponsor-held Access Protocol, or if the physician should seek an Access IND; and (3) determine if the drug will be provided free or if there will be a charge. A Letter of Authorization (LOA) from the sponsor or manufacturer should be obtained.

**FDA Approval:**

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When a commercial sponsor agrees to provide access under an Access Protocol, the sponsor is responsible for managing and obtaining FDA approval and all other sponsor responsibilities. A licensed physician under whose immediate direction an investigational drug is administered or dispensed for expanded access is considered an “investigator” under FDA regulations and is responsible for all investigator responsibilities under 21 CFR 312, to the extent they are applicable to expanded access.

If the sponsor or manufacturer declines treatment of the patient under an existing IND study or Access Protocol but agrees to make the investigational drug available for the patient, physicians may apply to the FDA for an individual patient Access IND using Form FDA 3926, a streamlined IND application specifically designed for such requests. Form FDA 3926, and related guidance, is available on a FDA website. Form FDA 3926 includes a section where an investigator can request approval from the FDA for alternative IRB review procedures; these alternative procedures enable review by the IRB Chair (or a Chair-designated IRB member) in lieu of review by the convened IRB. This alternative review procedure is referred to as a “concurrence review” in FDA guidance; however, the IRB Chair must review the same materials and make the same determinations as the convened board would. IRB Chair review can also be used for any post-approval reviews (e.g., unanticipated problems, continuing review, closure, etc.).

When there is an emergency situation and insufficient time to submit a written application to the FDA prior to treatment, a request to FDA for emergency use may be made by telephone (or other rapid means). A written expanded access application must be submitted within 15 days of the FDA’s authorization. For more information on emergency use, see Section 15.7.3.

A physician who obtains an Access IND is considered a “sponsor-investigator” and is responsible for the responsibilities of both sponsors and investigators under 21 CFR 312, as applicable, including IND safety reports, annual reports, and maintenance of adequate drug accountability records.

**IRB Review:**

Unless the conditions that permit an emergency use exemption (see Section 15.7.3.1) are satisfied, IRB approval must be obtained prior to initiating treatment with the investigational drug. When the FDA has authorized the use of alternative IRB review procedures (which can be presumed when the request is made on Form FDA 3926 unless the FDA specifically states that the request is denied), the review may be conducted by the IRB Chair (or designee). Otherwise, the review must be conducted by the convened IRB.

Physicians using investigational drugs under compassionate use should develop and submit an appropriate plan and schedule for treating and monitoring the patient, taking into consideration the nature of the drug and the needs of the patient. The plan should include monitoring to detect any possible problems arising from the use of the drug.

To request IRB approval for single patient expanded access, investigators should contact the IRB office and submit the following via the IRB electronic system:

1. A completed Initial Application, which includes CITI training information and COI declarations, and any additional documentation noted within it;
2. A copy of the LOA from the Commercial Sponsor or Manufacturer or other documentation supporting sponsor/manufacturer approval;

3. A copy of the information submitted to the FDA (and FDA approval, if available);

4. A copy of the Investigator’s Brochure or similar documentation that provides information regarding the potential risks and benefits of the investigational drug;

5. A copy of the plan for treating and monitoring the patient; and

6. A copy of the draft informed consent document.

The IRB may review the expanded access application prior to FDA approval being received but will not finalize approval until documentation of FDA approval is provided. The IRB will provide the investigator with written documentation of its review.

UMMC will consider reliance upon an external IRB for expanded access when the IND is held by a commercial sponsor and an external IRB has approved the protocol and is willing to accept review and oversight of additional investigators/sites. Investigators should contact the Human Research Office to discuss IRB reliance for expanded access protocols.

**Post-Approval Requirements**
Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this manual apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the participant (in which case it must be promptly reported), reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. Additionally, copies of any follow-up submissions to the FDA related to the expanded access use must be submitted to the IRB within 7 business days of the date of submission to the FDA.

**15.7.1.2 Emergency Use of Investigational Drugs**

FDA regulations permit the use of an investigational drug without IRB approval when an appropriately trained and licensed health care provider determines that IRB approval for the use of the drug cannot be obtained in time to prevent serious harm or death to a patient. The provider is expected to assess the potential for benefit from the use of the drug and to have substantial reason to believe that benefits will exist. The criteria and requirements for this Emergency Use Exemption are explained in Section 15.7.1.3.

Approval from the FDA and the Sponsor/Manufacturer must be obtained prior to initiating treatment with the drug.

Providers invoking the emergency use exemption must comply with any applicable FDA follow-up requirements including submission of safety reports, amendments, a summary following completion of treatment, and annual reports.
A copy of reports or amendments submitted to the FDA and any related correspondence must be submitted to the IRB office.

Note: DHHS regulations do not permit research activities to begin, even in an emergency, without prior IRB approval. When emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research participant under 45 CFR Part 46. However, nothing in the DHHS regulations at 45 CFR Part 46 is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state or local law.

15.7.1.3 Emergency Use Exemption from Prospective IRB Approval

Under FDA regulations at 21 CFR 56.104(c), FDA exempts the emergency use of an investigational drug (or biologic classified as a drug) from the requirement for prospective IRB approval, provided that the conditions described below are satisfied and that the emergency use is reported to the IRB within 5 working days. Any subsequent use of the investigational drug in the facility requires IRB approval. However, FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. If it appears likely that the investigational drug may need to be used again, the IRB may request that a study application is submitted which would cover future uses.

FDA defines emergency use as the use of a test article in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval [21 CFR 56.102(d)]. If all conditions described in 21 CFR 56.102(d) exist, then the emergency exemption from prospective IRB approval found at 21 CFR 56.104(c) may be used.

Life-threatening, for the purposes of 21 CFR 56.102(d), includes both life-threatening and severely debilitating.

- **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the patient must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

- **Severely debilitating** means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Unless the provisions for an emergency exception from the informed consent requirement are satisfied (see Section 15.7.1.4), informed consent must be obtained in accordance with 21 CFR 50 and documented in writing in accordance with 21 CFR 50.27.

The IRB must be notified within 5 working days after an emergency exemption is used via the submission of an Emergency Use Report in the IRB’s electronic submission system. The IRB
Chair or designated IRB member will review the report to verify that circumstances of the emergency use conformed to FDA regulations. This must not be construed as IRB approval, as an exemption from the requirement for prospective IRB approval has been invoked. When appropriate, in the event a manufacturer requires documentation from the IRB prior to the emergency use, the IRB Chair or designee will review the proposed use, and, if appropriate, provide a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c). Reports of emergency uses will be brought to the convened IRB for their information.

Investigators are reminded that they must comply with all other organizational policies and requirements applicable to the use of the investigational or unapproved drugs.

15.7.1.4 Emergency Exception from the Informed Consent Requirement

An exception under FDA regulations at 21 CFR 50.23(a-c) permits the emergency use of an investigational drug without informed consent when the investigator and an independent physician who is not otherwise participating in the clinical investigation (the emergency use) certify in writing all four of the following conditions:

1. The patient is confronted by a life-threatening situation necessitating the use of the test article;
2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the patient;
3. Time is not sufficient to obtain consent from the patient’s LAR; and
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient’s life.

If immediate use of the test article is, in the investigator’s opinion, required to preserve the life of the patient, and time is not sufficient to obtain the independent physician determination in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

The IRB must be notified within 5 working days when an emergency consent exception is invoked via the submission of an Emergency Use Report in the IRB’s electronic submission system. The IRB Chair or designated IRB member will review the report to verify that circumstances of the emergency exception conformed to FDA regulations.

15.7.2 Expanded Access to Investigational and Unapproved/Uncleared Medical Devices

As with investigational drugs, unapproved medical devices may normally only be used in humans in an approved clinical trial under the supervision of a participating clinical investigator. However, there may be circumstances under which a health care provider may wish to use an unapproved device when a patient is facing life-threatening circumstances or suffering from a
serious disease or condition for which no other alternative therapy or diagnostic exists or is a satisfactory option for the patient.

FDA has made the following mechanisms available for these circumstances:

- Emergency Use
- Compassionate Use (or Single Patient/Small Group Access)
- Treatment Use

Investigators seeking access to investigational or unapproved devices under one of the above provisions, should work closely with the sponsor or manufacturer, the FDA, and the UMMC Human Research Office to ensure that proper regulatory procedures are followed.

FDA has made information about expanded access to medical devices available on its website, [https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYo urDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm#emergency](https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm#emergency).

### 15.7.2.1 Compassionate Use of Investigational/Unapproved Medical Devices

The compassionate use provision under expanded access provides a mechanism for accessing investigational devices for an individual patient or small groups of patients when the treating physician believes the device may provide a diagnostic or treatment benefit. Compassionate use can be used for devices being studied in a clinical trial under an IDE for patients who do not qualify for inclusion in the trial, and for devices for which an IDE does not exist. The following criteria must be satisfied:

1. The patient has a life-threatening or serious disease or condition; and
2. No generally acceptable alternative treatment for the condition exists.

The medical device company must agree to make the medical device available for the proposed compassionate use. FDA and IRB approval are required before the device may be used under the compassionate use provision.

**FDA Approval:**
When there is an IDE for the device, the IDE sponsor submits an IDE supplement requesting approval for the compassionate use under [21 CFR 812.35(a)](https://www.fda.gov/medical-devices/ide-sponsor-submits-an-ide-supplement-requesting-approval-for-the-compassionate-use-under-21-cfr-812-35a).

When there is not an IDE for the device, the physician or manufacturer submits the following information to the FDA:

1. A description of the device (provided by the manufacturer);
2. Authorization from the device manufacturer for the use;
3. A description of the patient’s condition and the circumstances necessitating treatment or diagnostics (when seeking small group access, the number of patients to be treated;
4. A discussion of why alternative therapies/diagnostics are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition; and

5. The patient protection measures that will be followed, including:
   a. A draft of the informed consent document that will be used;
   b. Clearance from the institution as specified by their policies (see below);
   c. Concurrence of the IRB Chair or Chair-designated IRB member (prior to FDA request when possible); and
   d. An independent assessment from an uninvolved physician.

When concurrence of the IRB Chair cannot be obtained in advance of the submission to the FDA, the request should indicate that concurrence from the IRB Chair will be obtained prior to use of the device. Proof of IRB Chair concurrence must be submitted with the follow-up report to the FDA after the patient is treated (or the diagnostic is used).

When the compassionate use is conducted under an IDE, a licensed provider who receives an investigational device is an “investigator” under FDA regulations and is responsible and accountable for all applicable investigator responsibilities under 21 CFR 812 (IDE regulations), 21 CFR 50 (Informed Consent), and 21 CFR 56 (IRB).

When the provider obtains an IDE for compassionate use, the provider is considered a “sponsor-investigator” and is responsible for the responsibilities of both sponsors and investigators under 21 CFR 812, as applicable, including medical device reports and progress reports.

IRB Review:

Unless the conditions that permit an emergency use exemption are satisfied (see Section 15.7.2.3), IRB approval must be obtained prior to initiating treatment with the investigational device. When the request is for single-patient compassionate use, the review may be conducted by the IRB Chair (or designee). Otherwise, the review must be conducted by the convened IRB.

Physicians using medical devices under compassionate use should develop and submit an appropriate plan and schedule for treating and monitoring the patient, taking into consideration the nature of the device and the needs of the patient. The plan should include monitoring to detect any possible problems arising from the use of the device.

To request IRB approval for compassionate use, investigators should contact the IRB office and submit the following via the IRB electronic system:

1. A completed Initial Application, which includes current IRB training status and COI information, and any additional documentation noted within it;
2. A copy of the information submitted to the FDA (and FDA approval, if available);
3. A copy of the device brochure, Instructions for Use, or other similar documentation that provides information regarding the potential risks and benefits of the device;
4. A copy of the plan for treating and monitoring the patient; and
5. A copy of the draft informed consent document.

The IRB may review the expanded access application prior to FDA approval being received but will not approve until receipt of FDA approval has been received. The IRB will provide the investigator with written documentation of its review.

UMMC may consider reliance upon an external IRB for Compassionate Use protocols on a case-by-case basis when the IDE is held by a commercial sponsor and an external IRB has already approved the protocol and is willing to accept review and oversight of additional investigators/sites. Investigators should contact the Human Research Office to discuss IRB reliance for Compassionate Use protocols.

**Post-Approval Requirements**

Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this manual apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the patient (in which case it must be promptly reported), reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. Additionally, a follow-up report to the FDA is required following a compassionate use by whomever submitted the original request to the FDA. The report should include summary information regarding patient outcome and any problems that occurred as a result of the device. A copy of the follow-up report to the FDA and any other post-approval submissions or reports to the FDA must be submitted to the IRB within 7 business days of the date of submission to the FDA.

**15.7.2.2 Treatment Use of Investigational/Unapproved Medical Devices**

During the course of a clinical trial under an IDE, if the data suggest that the device under study is effective, the trial may be expanded to include additional patients with life-threatening or serious diseases under the Treatment Use provision for expanded access. “Treatment Use” also applies to the use of a device for diagnostic purposes under these same conditions. [21 CFR 812.36](#)

The following criteria must be satisfied for Treatment Use to apply:

1. The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
2. There is no comparable or satisfactory alternative device available to treat or diagnose the disease or condition in the intended patient population;
3. The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or all clinical trials have been completed; and

4. The sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence.

The IDE sponsor is responsible for applying for a Treatment Use IDE.

A licensed provider who receives an investigational device for treatment use under a Treatment Use IDE is an “investigator” under FDA regulations and is responsible and accountable for all applicable investigator responsibilities under 21 CFR 812 (IDE regulations), 21 CFR 50 (Informed Consent), and 21 CFR 56 (IRB).

IRB Review:
IRB approval is required before the investigational device/diagnostic is used, following the standard procedures for IRB submissions.

UMMC may consider reliance upon an external IRB for Treatment Use IDE protocols on a case-by-case basis when an external IRB has already approved the protocol and is willing to accept review and oversight of additional investigators/sites. Investigators should contact the Human Research Office to discuss IRB reliance for Treatment Use IDEs.

Post-Approval Requirements
Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this manual apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the patient (in which case it must be promptly reported), for reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. Additionally, the semi-annual (applicable until the marketing application is filed) or annual (applicable after the marketing application is filed) progress report from the sponsor must be submitted to the IRB within 7 business days of receipt.

15.7.2.3 Emergency Use of Investigational Devices

FDA regulations permit the emergency use of an investigational or unapproved device without prior approval by the FDA or IRB when an appropriately trained and licensed health care provider determines that:

- The patient has a life-threatening or serious disease or condition that needs immediate treatment;
- No generally acceptable alternative treatment for the condition exists; and
- Because of the immediate need to use the device, there is no time to use existing procedures to obtain FDA approval for the use.
FDA expects the provider to make the determination that the above criteria are satisfied, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist. Because prior FDA approval is not required, FDA expects providers planning the emergency use of an investigational device to obtain as many of the following as possible:

- An independent assessment from an uninvolved physician;
- Authorization from the device manufacturer;
- Concurrence of the IRB Chair or designee;
- Institutional clearance; and
- Informed consent from the patient or legally authorized representative.

At UMMC providers planning the emergency use of an investigational or unapproved device must contact the Human Research Office as early in the process as possible and submit the Emergency Use Report and the supporting documentation called for in the form for review by the IRB Chair or designee. The IRB Chair or designee will review the information provided and determine whether the use conforms with FDA’s requirements and expectations and whether the provisions for the protection of the patient appear adequate using the applicable criteria at 21 CFR 50 and 56 as guidelines (e.g., minimization of risks, risk/benefit, safety monitoring, informed consent, etc.).

The emergency use must be reported to the FDA by the IDE Sponsor, when one exists, or by the provider if no IDE exists. Information regarding what to include in the report and where to submit it is available on FDA’s website. When the provider is responsible for the FDA report, a copy of the report and any related correspondence must be submitted to the IRB office.

Reports of emergency uses will be brought to the convened IRB for their information.

Providers are reminded that they must comply with all other organizational policies and requirements applicable to the use of the investigational or unapproved devices.

### 15.8 Charging Participants for Investigational Products

FDA regulations do not prohibit charging participants or their insurers for investigational products so long as those charges comply with specified criteria. FDA approval of such charges does not obviate the investigator’s and IRB’s responsibility to minimize risks to participants (Beneficence), to ensure that the risks and burdens associated with research are equitably distributed (Justice), and to ensure that participants are properly informed and not unduly influenced to accept an otherwise unacceptable risk or cost in order to access a benefit (Respect for Persons). Any costs to participants or insurers must be described in the IRB application and informed consent document.
15.8.1 Charging for Investigational Medical Devices and Radiological Health Products

IDE regulations allow sponsors to charge for an investigational device, however, the charge may not exceed the amount necessary to recover the costs of manufacture, research, development, and handling of the investigational device [21 CFR 812.7(b)]. Sponsors must justify the proposed charges for the device in the IDE application, state the amount to be charged, and explain why the charge does not constitute commercialization [21 CFR 812.20(b)(8)].

15.8.2 Charging for Investigational Drugs and Biologics

FDA rules regarding charging for Investigational Drugs Under an IDE:

- Provide general criteria for authorizing charging for an investigational drug [21 CFR 312.8(a)]
- Provide criteria for charging for an investigational drug in a clinical trial [21 CFR 312.8(b)]
- Set forth criteria for charging for an investigational drug for an expanded access for treatment use [21 CFR 312.8(c)]
- Establish criteria for determining what costs can be recovered when charging for an investigational drug [21 CFR 312.8(d)]

Additional information is available in FDA guidance: Charging for Investigational Drugs Under an IND — Questions and Answers.
16 Unanticipated Problems Involving Risks to Participants or Others

UMMC complies with DHHS and FDA regulations which require organizations to have written policies on reporting unanticipated problems involving risks to subjects or others (UP).

This section provides definitions and procedures for the reporting of UPs to the UMMC IRB. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 6.

16.1 Definitions

Unanticipated problems involving risk to participants or others (UPs) refer to any incident, experience, outcome, or new information that:

1. Is unexpected; and
2. Is at least possibly related to participation in the research; and
3. Indicates that participants or others are at a greater risk of harm (including physical, psychological, economic, legal or social harm) than was previously known or recognized

UPs also encompass Unanticipated Adverse Device Effects, as defined below.

Unexpected The incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the research procedures that are described in the study-related documents, such as the IRB-approved research protocol/research plan and informed consent documents; and the characteristics of the population being studied.

Related There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

Adverse Event For the purposes of these policies and procedures, an adverse event (AE) is any untoward or unfavorable occurrence in a human participant, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with participation in the research, whether or not considered related to participation in the research. Adverse events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research.

Unanticipated Adverse Device Effect An Unanticipated Adverse Device Effect (UADE) means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that related to the rights, safety, or welfare of participants [21 CFR 812.3(s)].
16.2 Procedures

16.2.1 Reporting

Adverse events in clinical trials must be reported to the sponsor in compliance with FDA regulations and sponsor requirements. Unless specifically required by the IRB for a given protocol, the UMMC IRB does not accept reports of adverse events that are not UPs.

With one exception, noted below, Investigators must report the following events or issues to the IRB as soon as possible but within 10 business days after the investigator first learns of the event using the Unanticipated Problem form in the IRB electronic system. Note: The study-related death of a UMMC research participant must be reported within 48 hours of notice. If investigators are uncertain but believe that the event might represent an UP, a report should be submitted.

Examples of UPs include:

1. A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angioedema, agranulocytosis, hepatic injury, or Stevens-Johnson syndrome);

2. A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study population (e.g., tendon rupture, progressive multifocal leukoencephalopathy);

3. Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveals higher rate in the drug treatment arm versus a control). A summary and analyses supporting the determination should accompany the report;

4. An AE that is described or addressed in the investigator’s brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations. For example, if transaminase elevation is listed in the investigator’s brochure and hepatic necrosis is observed in study subjects, hepatic necrosis would be considered an unanticipated problem involving risk to human subjects. A discussion of the divergence from the expected specificity or severity should accompany the report;

5. A serious AE that is described or addressed in the investigator’s brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison). A discussion of the divergence from the expected rate should accompany the report;
6. AEs involving direct harm to participants enrolled by the local investigator which in the opinion of the investigator or sponsor, may represent an UP;

7. IND Safety Reports from sponsors that meet the criteria for an UP. Such reports must be accompanied by an analysis from the sponsor explaining why the report represents an UP and whether it has been reported to the FDA as such;

8. Unanticipated adverse device effects (UADEs);

9. Any other AE or safety finding (e.g. based on animal or epidemiologic data) that indicates participants or others might be at risk of serious, unanticipated harms that are reasonably related to the research. These would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of participants. An explanation of the conclusion should accompany the report.

10. Reports (including reports from DSMBs/DMCs) that indicate that risks are greater than previously known or that indicate that the research should be modified, suspended, or halted.

11. Sponsor or lead investigator/coordinating center imposed suspension or termination of some or all research activities;

12. An unanticipated event related to the research that exposes participants to potential risk but that does not involve direct harm to participants;

13. A breach of confidentiality or loss of research data (e.g., a laptop or thumb drive is lost or stolen);

14. An unanticipated event related to the research that results in actual harm or exposes individuals other than the research participants (e.g., investigators, research assistants, students, the public, etc.) to potential risk;

15. New information that indicates increased risk, new risk(s), or decrease to potential benefit from what was previously understood. Examples include:
   a. An interim analysis or safety monitoring report indicates that the frequency or magnitude of harms or benefits may be different than initially presented to the IRB;
   b. A report or publication that indicates the risks, benefits, or merit of the research are different from what was previously understood.

16.2.2 IRB Review

1. Upon receipt of the UP Report, the IRB staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information.

2. The IRB Chair or designated reviewer receives and reviews the report and makes an initial determination as to whether the event represents an UP. If needed, the Chair or designee may request additional information from the investigator, sponsor, or others.
(including study committees, such as data monitoring committees, data safety monitoring boards, or steering committees).

3. If the reviewer determines that the problem does not meet the definition of an UP, he/she will determine whether any additional actions are necessary to ensure the protection of participants. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be recorded in review notes in the electronic system and communicated to the investigator.

4. If the reviewer determines that the event may be an UP, the report will be referred for review by the convened IRB. The convened IRB will determine whether the event is a UP and whether any additional actions, such as those outlined below, are necessary to ensure the protection of participants. If needed, the IRB may request additional information from the investigator, sponsor, or others (including study committees, such as data monitoring committees, data safety monitoring boards, or steering committees). The results of the review will be recorded in the IRB minutes and communicated to the investigator.

5. Based upon the circumstances, the IRB may take any of the following actions, or others, to ensure the protection of participants:
   a. Requiring modifications to the protocol or plan or procedures for implantation of the research as described in the application and other materials submitted to the IRB;
   b. Revise the continuing review timetable;
   c. Modify the consent process;
   d. Modify the consent, permission and/or assent document(s), as applicable;
   e. Require additional information be provided to current participants (e.g., whenever the information may relate to the participant’s rights, welfare, or willingness to continue participation);
   f. Provide additional information to participants who have completed the study;
   g. Require additional training of the investigator and/or study staff;
   h. Require that current participants consent to continue participation;
   i. Monitor the research;
   j. Monitor the consent process;
   k. Report or refer to appropriate parties (e.g., the IO, Office of Integrity and Compliance, Risk Management, Office of Information Security);
   l. Suspend IRB approval;
   m. Terminate IRB approval;
   n. Other actions as appropriate given the specific circumstances.
When the IRB determines that an event is an UP, the IRB staff will follow the procedures for reporting to regulatory agencies, sponsors, and organizational officials in Section 20. When appropriate, a preliminary report may be submitted while more information is obtained to inform the determination or actions.
17 Noncompliance

This section provides definitions and procedures for the reporting and review of known or suspected noncompliance for research under the oversight of the UMMC IRB. Research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 6.2.

In conducting its review of protocol deviations, unanticipated problems, subject complaints, and other reportable events, the IRB will also consider whether the event or issue was caused by, contributed to, or otherwise related to noncompliance.

17.1 Definitions

Noncompliance is defined as failure to follow federal, state, or local regulations governing human subject research or institutional policies related to human subject research, or the requirements or determinations of the IRB. Noncompliance may be minor, serious or continuing.

Serious noncompliance is defined as noncompliance that, in the judgment of the convened IRB, creates an increase in risks to participants, adversely affects the rights, welfare or safety of participants or others, may affect participants’ willingness to participate in the research or adversely affects the scientific integrity of the study. Willful violation of regulations and/or policies may also constitute serious noncompliance.

Continuing noncompliance is defined as a pattern of noncompliance that, in the judgment of the convened IRB, suggests a likelihood that instances of noncompliance will continue unless the IRB or institution intervenes.

Allegation of Noncompliance is defined as an unproven assertion of noncompliance.

17.2 Reporting

Investigators and their study staff are required to report instances of possible non-compliance to the IRB. The investigator is responsible for reporting possible non-compliance by study personnel. Any individual or employee may report observed or apparent instances of non-compliance. The reporting party is responsible for making the report in good faith, maintaining confidentiality and cooperating with any IRB and/or organizational review of the report.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report non-compliance, he or she may contact the Human Research Office Director, IRB Chair or the Office of Integrity and Compliance directly to discuss the situation informally.

Reports of alleged serious or continuing non-compliance must be submitted to the IRB Office within 10 working days of discovery. The report must include a complete description of the alleged non-compliance, including any personnel involved.

Reports of alleged minor non-compliance are reported at the time of Continuing Review. If the IRB, or IRB Chair if review is by expedited review, finds that the non-compliance may be serious
or continuing, the review and reporting requirements for serious or continuing non-compliance are followed.

Reports may be made anonymously.

### 17.3 Review Procedures

1. Upon receipt of a report the Human Research Office staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information. If the report came from someone other than the investigator, verbally, by email, or by other means, the Human Research Office staff will develop a written report summarizing the available information. If the information provided suggests that participants or others may be at risk of harm without immediate intervention or that research misconduct may have occurred, the Human Research Office Director, IRB Chair or Vice Chair, and, when appropriate, the IO, will be notified so that they can take any necessary steps to ensure the safety of participants or others or investigate the matter.

2. The IRB Chair or designated reviewer receives and reviews the report and makes an initial determination as to whether the event represents noncompliance, and, if so, if the noncompliance may be serious or continuing. If needed, the reviewer may request additional information from the investigator or others. When circumstances warrant, the Human Research Office Director may bypass this step and assign the report for convened board review.

3. If the reviewer determines that the event or issue is not noncompliance, or is noncompliance but not serious or continuing, he/she will review any proposed corrective and preventative action plans and determine if the plan is acceptable as proposed or if modifications to the plan or additional actions are required. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be recorded in the electronic system and communicated to the investigator.

4. If the reviewer determines that the event or issue may be serious or continuing noncompliance, the report will be referred for review by the convened IRB. The convened IRB will determine whether the event is serious or continuing noncompliance. The IRB will review any proposed corrective and preventative action plans and determine if the plan is acceptable as proposed or if modifications to the plan or additional actions, such as those outline below, are necessary to ensure the protection of human participants. If needed, the IRB may request additional information from the investigator or others. The results of the review will be recorded in the IRB minutes and communicated to the investigator.

5. When the IRB determines that an event is serious or continuing noncompliance, the IRB may take any of the following actions, or others, to ensure the protection of human participants:

   a. Require modifications to the protocol or research plan
b. Revise the continuing review timetable  
c. Modify the consent process  
d. Modify the consent, permission and/or assent document(s), as applicable  
e. Provide additional information to current participants (e.g., whenever the information may relate to the participant’s willingness to continue participation)  
f. Provide additional information to participants who have completed participation in the study  
g. Require additional training of the investigator and/or study staff  
h. Require that current participants consent to continue participation  
i. Monitor the research  
j. Monitor the consent process  
k. Report or refer to appropriate parties (e.g., IO, Office of Integrity and Compliance, Risk Management, Office of Information Security)  
l. Suspend IRB approval  
m. Terminate IRB approval  
n. Other actions as appropriate given the specific circumstances  

6. When the IRB determines that an event is serious or continuing noncompliance, the IRB staff will follow the procedures for reporting to regulatory agencies, sponsors, and organizational officials in Section 20. When appropriate, a preliminary report may be submitted while more information is obtained to inform the determination or actions.  

7. Investigators may request that the IRB reconsider its determination by following the procedures in Section 9.4.
18 Complaints

The HRPP and IRB will be responsive and sensitive to the complaints or concerns expressed by participants or others and will respond to all complaints or concerns in a confidential and timely manner. The PI and all other research team members are responsible for the safety and welfare of all participants enrolled in their studies. When investigators or team members hear complaints or concerns from participants, he/she will try to resolve them.

Investigators conducting research under the auspices of UMMC must report complaints to the UMMC Human Research Office, regardless of who serves as the IRB of record. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 6.2. Investigators conducting research under the oversight of the UMMC IRB report complaints via email, in-person or phone call. Investigators are encouraged to contact the Human Research Office Director or IO when they are having difficulty resolving a complaint or concern, and whenever circumstances warrant (e.g., immediate attention is needed).

When the HRPP or IRB office is the direct recipient of complaints or concerns, the staff will do the following:

1. Document the complaint or allegation. When appropriate, the staff may request that the complainant submit the complaint in writing.
2. Reassure the complainant that the HRPP/IRB will take all necessary measures to inquire into the circumstances and to address the issue.
3. Provide written confirmation of receipt of the complaint to the complainant, if the complainant is willing to provide contact information.
4. Convey the information to the IRB of record in a timely manner.
5. When appropriate, contact the investigator for additional information or to assist with resolution.
6. When appropriate, contact other resources (e.g., Office of Integrity and Compliance, Risk Management, Patient Relations, Legal) to assist with information-gathering or resolution.

For research under the oversight of the UMMC IRB, the IRB Chair or designee will consider the complaint or concern and take any reasonable steps necessary to investigate and/or resolve the issue, if appropriate, prior to review and consideration by the IRB. A report will be provided to the IRB at the next available meeting if the research is subject to convened IRB review, or provided to the designated expedited reviewer if the research is eligible for expedited review. When reviewing complaints, the IRB will consider whether the complaint was the result of, or related to, an UP or noncompliance, and, if so, will follow the relevant procedures. The IRB Chair or designated expedited reviewer may refer any complaint for review by the convened IRB. The IRB minutes, or reviewer comments for expedited reviews, will reflect the action(s) taken and, if necessary, notice to the appropriate officials and/or agencies.
The Human Research Office will maintain written copies of complaints and concerns and will document the investigation and resolution. The complainant will be notified promptly following resolution of the complaint or concern, when appropriate, and if contact information has been provided. If the Human Research Office or IRB receives a complaint, or identifies information while investigating a complaint, that is indicative of possible misconduct in research, UMMC’s Office of Integrity and Compliance and the IO will be notified immediately.
19 Other Reportable Information

When research is under the oversight of the UMMC IRB, in addition to UPs, noncompliance, and complaints, any change to the research implemented without IRB approval and any information that may impact the rights, safety, or welfare of participants or inform the IRB’s oversight of the research must be reported to the IRB within 10 business days of discovery using the Unanticipated Problem or Amendment form, as applicable. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 6.2.

Other reportable information includes, but is not limited to, the following:

1. Changes made to the research without prior IRB approval to eliminate apparent immediate hazards to the participant(s);
2. Protocol Deviations - any variation from the IRB approved research plan that happens without prior review and approval of the IRB and isn’t necessary to eliminate apparent immediate hazards to the participant(s);
3. Monitoring, audit, and inspection reports in accordance with Section 2.1 of this manual;
4. Notice of:
   a. Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated (classification as “OAI” is typically made after FDA has had the opportunity to review the responses to a 483), FDA Restrictions Placed on IRBs or Investigators, and any corresponding compliance actions taken under non-US authorities related to human research protections.
   b. Any final resolution of litigation, arbitration, or settlements related to human research protections at UMMC.
   c. Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding human subjects research conducted at or by UMMC or UMMC’s program for the protection of human research participants.

   NOTE: The above events (4.a, b, and/or c) must be reported to the HRPP/IRB office by phone or email as soon as anyone becomes aware, with the formal submission within the 10-day timeline as noted above. See Section 21 for more information.
5. Sponsor or coordinating center reports;
6. Data Safety Monitoring reports, including reports from DSMBs, DMCs, and others;
7. Enrollment or inclusion of vulnerable populations not previously approved by the IRB for the study (e.g., prisoner, pregnant woman, neonate, child, adult with impaired decision-making capacity);
8. When an existing participant becomes a member of a vulnerable population not previously approved by the IRB for inclusion in the study (e.g., incarceration, pregnancy, or change in decision-making capacity of an already enrolled participant);

9. Holds, suspensions, or terminations of a study, in part or in full, by an investigator, sponsor, or others;

10. Changes that impact the ability of the PI to conduct or supervise the study, temporarily or permanently;

11. Changes that impact the qualifications of investigators or research staff members such as actions taken by regulatory authorities, licensing boards, or credentialing committees;

12. New information that may impact the rights, welfare, or willingness of participants to continue in the research.

### 19.1 Review Procedures

1. Upon receipt of the report, the IRB staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information. If the information provided suggests that participants may be at risk of harm without immediate intervention or that research misconduct may have occurred, the HRPP Director, IRB Chair, and, when appropriate, the IO will be notified so that they can take any necessary steps to ensure the safety of participants or investigate the matter.

2. The IRB Chair or designated reviewer receives and reviews the report and if the report may represent an UP or noncompliance, reviews the report as described in Section 16 or 17. When circumstances warrant, the Human Research Office Director may bypass this step and assign the report for convened board review.

3. If the reviewer determines that the event or issue is not noncompliance or an UP, he/she will review the event or issue, any proposed corrective and preventative action plans, and determine if any additional actions are needed to ensure the protection of participants. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be recorded in the electronic IRB system and communicated to the investigator.
20 Reporting to Federal Agencies, Departments and Organizational Officials

Federal regulations require prompt reporting to appropriate institutional officials and, as applicable, the federal department or agency of (i) any unanticipated problems involving risk to participants or others; (ii) any serious or continuing non-compliance with the applicable federal regulations or the requirements or determinations of the IRB; and (iii) any suspension or termination of IRB approval. UMMC IRB complies with this requirement as outlined below. When research is under the oversight of an external IRB, the terms of the agreement with that IRB will guide reporting.

20.1 Procedures

IRB staff will initiate these procedures as soon as the IRB takes any of the following actions:

a. Determines that an event is considered an unanticipated problem involving risk to participants or others;

b. Determines serious or continuing non-compliance; or

c. Suspends or terminates approval of research

1) The Human Research Office Director or designee prepares reports or letters that include the following information:

a. Reason for the report (Unanticipated problem involving risks to participants or others, serious or continuing non-compliance, suspension or termination of IRB approval of research);

b. Name of the institution involved;

c. Title of the research project and/or grant proposal in which the problem occurred;

d. Name of the investigator on the project;

e. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (e.g., grant, contract, or cooperative agreement);

f. A detailed description of the problem including the findings of the organization and the reasons for the IRB’s decision;

g. Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol/research plan, suspend enrollment, terminate the research, revise the informed consent document, inform participants, increase monitoring of participants, etc.);

h. Plans, if any, to send a follow-up or final report by a specific date, upon completion of an investigation or when a corrective action plan has been implemented;

2) The IRB Chair and the IO review the letter and recommend modifications as needed.

3) The IO is the signatory for the report or letter.
4) A copy of the report is added to the next available IRB meeting agenda, as an administrative item and sent to:

a. The Institutional Official

b. Federal departments or agencies, as follows:
   • OHRP, if the study is subject to DHHS regulations or subject to a DHHS FWA.
   • FDA, if the study is subject to FDA regulations.
   • If the study is conducted or funded by a Common Rule agency other than DHHS, the report is sent to OHRP or the head of the federal agency, as required by the agency.
   • If the study is conducted or supported by a federal agency that has not adopted the Common Rule, and reporting is required, the report is sent to the party identified by the agency.

Reporting to a regulatory agency is not required if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by another party (e.g., sponsor). Reports are not submitted to federal departments or agencies such as OHRP or FDA unless the research is subject to federal regulations or another mandate that necessitates such reporting.

c. Investigator
d. Sponsor, if applicable
e. Investigator’s Department Chair
f. Dean of the applicable UMMC school (School of Medicine, School of Nursing, School of Dentistry, School of Health Related Professions, School of Pharmacy)
g. The Privacy Officer, if the event involved unauthorized use, loss, or disclosure of individually-identifiable patient information from a covered entity

h. The Information Security Officer, if the event involved violation of information security requirements

i. Office of Integrity and Compliance

j. Office of Research and Sponsored Programs, if applicable

k. Office of Risk Management, if appropriate
l. Others as deemed appropriate by the IO

The Human Research Office Director ensures that all steps of this policy are completed within 30 working days of the determination. For more serious actions, the Director expedites reporting. If additional time is needed to gather facts, or determine corrective actions, a preliminary report will be submitted within 30 days, to be followed by a final report as described above.
21 Reporting to AAHRPP

UMMC’s HRPP is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). In addition to the information that UMMC routinely provides to AAHRPP in annual reports and the re-accreditation application, AAHRPP requires that any of the following are reported to AAHRPP asap but generally within 48 hours after the organization or any researcher (if the researcher is notified rather than the organization) becomes aware:

- Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions Placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections;
- Any final resolution of litigation, arbitration, or settlements related to human research protections under the auspices of UMMC; and/or
- Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding UMMC’s HRPP.

The Human Research Office Director (or designee) is responsible for ensuring that such reports are made to AAHRPP and for informing appropriate organizational officials. Investigators, research staff, HRPP/IRB staff, IRB members, and other organizational officials or offices (e.g., the IO, Office of Integrity and Compliance, Legal, Public Affairs) are responsible for informing the HRPP/IRB office as soon as they become aware of any of the above so that these reporting obligations may be fulfilled.
22 Investigator Responsibilities

The Principal Investigator (PI) is ultimately responsible for the conduct of research. If tasks are delegated to appropriately trained and qualified members of the research team, the PI must maintain oversight and retain ultimate responsibility for the proper conduct of the research.

Within the regulations, the term ‘investigator’ refers to individuals involved in the design, conduct, or reporting of the research. Such involvement could include one or more of the following:

- Designing the research
- Obtaining information about living individuals by intervening or interacting with them for research purposes
- Obtaining identifiable private information about living individuals for research purposes
- Obtaining the voluntary informed consent of individuals to be participants in research
- Studying, interpreting, or analyzing identifiable private information or data for research purposes.

22.1 Responsibilities

Investigators who conduct research involving human participants must:

1. Develop and conduct research in accordance with the ethical principles in the Belmont Report;
2. Have a research plan that is scientifically sound and minimizes risk to participants;
3. Ensure that the study includes a plan for the just, fair, and equitable recruitment and selection of participants;
4. When some or all of the participants are likely to be vulnerable to coercion or undue influence include additional safeguards in the study to protect the rights and welfare of these participants;
5. Ensure that the study includes adequate provisions for the monitoring of participants and data to ensure participant safety;
6. Ensure that there are adequate provisions to protect the privacy interests of participants;
7. Ensure that there are adequate provisions to protect the confidentiality of data;
8. Have sufficient resources necessary to protect human participants, including:
   a. Access to a population that would allow recruitment of the required number of participants;
   b. Sufficient time to conduct and complete the research;
   c. Adequate number of qualified staff;
d. Adequate facilities;
e. Necessary equipment;
f. A plan to ensure proper supervision of the research, including a plan for periods of absence or decreased availability;
g. When appropriate, a plan to ensure the availability of medical, psychological, or other support services that participants might require during or as a result of their participation;

9. Ensure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to perform such under the laws of Mississippi and UMMC policies;

10. Ensure that all study personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based;

11. Ensure that all study personnel are adequately trained and informed about the research and their specific duties and functions.

12. Promptly report any changes in study personnel, including investigators, to the IRB for review and approval (investigators and staff may not begin work on the research until IRB-approved);

13. Protect the rights, safety, and welfare of research participants;

14. Ensure that when PHI is accessed, used or disclosed, legally effective HIPAA authorization is obtained for each research participant, unless the IRB has approved a waiver of the requirement;

15. Ensure that the information in the consent/permission/assent form(s) is consistent with that in the protocol, and associated grant or contract, and HIPAA authorization, as applicable;

16. Obtain and document informed consent and ensure that no human research participant is involved in the research prior to obtaining consent or permission from the legally authorized representative, unless a waiver of the requirement has been approved by the IRB;

17. Have a procedure to receive questions, complaints, or requests for additional information from participants and respond appropriately;

18. Ensure that all information provided to the IRB is accurate and complete so that the IRB may fulfill its responsibilities to review the research and make the required determinations;

19. Ensure that all research involving human participants receives IRB review and approval or a determination of exemption in writing before research begins;

20. Ensure that all additional required reviews and approvals (e.g., COI, IBC, Radiation Safety, Investigational Pharmacy, as applicable) are in place before the research begins;
21. Comply with all IRB decisions, conditions, and requirements;

22. Ensure that studies receive timely continuing IRB review and approval;

23. Report unanticipated problems, deviations, complaints, noncompliance, suspensions, terminations, and any other reportable events to the IRB and the organization, as required by regulations and policy;

24. Notify the IRB if information becomes available that suggests a change to the potential risks, benefits, merit or feasibility of the research;

25. Obtain IRB review and approval before changes are made to the research unless a change is necessary to eliminate apparent immediate hazards to the participant(s);

26. Seek HRPP or IRB assistance when in doubt about whether proposed research requires IRB review;

27. Retain records for the time period and in the manner described to and approved by the IRB and as required by applicable regulations, agreements and policies.

Additional investigator responsibilities, including specific responsibilities for investigators engaged in FDA-regulated research are described throughout this document.

22.1.1 Record Retention

Investigator research records, including, but not limited to, signed consent forms and HIPAA authorizations, participant records and data, test article records, IRB records (submission materials, IRB determinations and associated documentation, correspondence to and from the IRB, etc.), and sponsor/grant records must be retained in accordance with regulatory, organizational, IRB, sponsor or grantor, and journal or publication standards. Records must be maintained securely with limited access. Disposal of investigator records must be done in such a manner that no identifying information can be linked to research data. When research is sponsored or grant-supported, consult the contract, grant terms, or other relevant agreements prior to destroying or transferring any records. If there are questions or allegations about the validity of the data or the appropriate conduct of the research, all records must be retained until such questions or allegations have been completely resolved.

UMMC’s Record Retention policy, which includes provisions for ownership of data, requires the retention of study records in accordance with regulatory, organizational and sponsor or grantor requirements, but no less than six (6) years following completion of the research. The following summarizes a few of the more common regulatory requirements:

1. OHRP – research records must be retained for at least 3 years after the completion of the research

2. HIPAA – Research authorizations, or documentation of waivers or alterations of authorization, must be held for a minimum of 6 years after the authorization or waiver/alterations was last obtained or in effect, whichever is later

3. FDA – Drugs (& biologics classified as drugs) - For a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being
investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

4. **FDA – Devices** (& biologics classified as devices) - 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.

### 22.2 Investigator Concerns

Investigators who have concerns regarding UMMC’s HRPP or IRB(s) or regarding the conduct of research at UMMC or the external IRBs UMMC relies upon should convey them to the Human Research Office Director, the IO, or other responsible party (e.g., supervisor, college dean, Department Chair), as appropriate. The recipient of the concern will consider the issue, and, if deemed necessary, seek additional information. The recipient of the concern may convene the parties involved, including the investigator, or a subcommittee to investigate and form a response or decide if procedural or policy modifications are warranted. In addition, the IRB Chair and/or the Human Research Office Director are available to address investigators’ questions, concerns and suggestions.

Anyone with concerns may also report via the Compliance hotline.

In addition to these SOPs, which are made available on UMMC’s Human Research Office website, there is information on the website about concerns or complaints.

Consistent with UMMC policies, there will be no retaliation against anyone who reports concerns in good faith.
23 Sponsored Research

It is UMMC policy that any sponsored research conducted under the auspices of UMMC is conducted in accordance with federal guidelines and ethical standards. The following describe the procedures to ensure that all sponsored research meets this requirement.

23.1 Definitions

Sponsor: Sponsor means the company, institution, individual donor, or organization responsible for the initiation, management or financing of a research study.

Sponsored research: Sponsored research means research funded through a grant or contract that involves a specified statement of work (e.g., the research proposal), including clinical trials involving investigational drugs, devices or biologics.

23.2 Responsibility

Sponsor grants, contracts, and other written agreements are reviewed for the following by the Office of Research and Sponsored Programs, in consultation with the Human Research Office, as necessary:

1. All contracts with a sponsor include a clause that addresses medical care for research participants with a research-related injury, when appropriate.
2. If the sponsor conducts research site monitoring visits or monitoring activities remotely, the contract includes a clause that the Sponsor promptly report findings that could affect the safety of participants or influence the conduct of the study to the investigator or UMMC.
3. If the sponsor has the responsibility to conduct data and safety monitoring, the contract includes a clause that addresses provisions for data monitoring to ensure the safety of participants and for providing data and safety monitoring reports to the investigator or UMMC.
4. All contracts with a sponsor include a plan for disseminating findings from the research and the roles that investigators and Sponsors play in the publication or disclosure of results.
5. When participant safety could be directly affected by study results after the study has ended, the contract has a clause that the investigator or UMMC will be notified of the results in order to consider informing participants.
6. Payment in exchange for referral of prospective participants from investigators (physicians) (“finder’s fees”) is not permitted. Payment designed to accelerate recruitment that are tied to the rate or timing of enrollment (“bonus payments”) is also not permitted.
Conflict of Interest in Research

Openness and honesty in research are indicators of integrity and responsibility, characteristics that promote quality research and strengthen the research process. It is UMMC policy to preserve public trust in the integrity and quality of research by reducing actual or perceived conflict of interest (“COI”) in the conduct of research. COI in research is any interest that competes with an organization’s or individual’s obligation to protect the rights and welfare of research participants, the integrity of a research study, or the credibility of the research program. A conflict of interest can be financial or non-financial. A conflict of interest should be eliminated when possible and disclosed and effectively managed when it cannot be eliminated.

Researcher Conflicts of Interest

Pursuant to the UMMC Policy on Conflicts of Interest, the UMMC Compliance Committee maintains a Conflict of Interest Working Group. UMMC’s Human Research Office and IRBs collaborate with the COI Working Group to ensure that COI of investigators and research staff are identified and managed before the IRB completes its review of any research application.

24.1 Procedures

24.1.1 Disclosure of Researcher COI

For IRB purposes, researcher conflict review occurs at the time of new study submission, continuing review, with the addition of a new investigator or research staff, and whenever an investigator or research staff updates his/her UMMC COI disclosure indicating a new or changed interest. When a submission identifies the need for conflict review, the researcher/study personnel with the conflict is responsible for reporting the potential conflict to the Office of Integrity and Compliance, which forwards the report to the COI Working Group. In the event a conflict that requires disclosure or management is identified, the COI Working Group provides the IRB with a written summary of the conflict and the conflict management plan (‘CMP’) approved by the Working Group. If the COI Working Group has not completed its review, the IRB defers the research study review or prohibits participation by the researcher with a potential COI until the COI Committee review process is completed and the results are made available to the IRB. When the research is under the purview of an external IRB, any conflicts identified as the result of COI review and any CMP are provided to the external IRB in accordance with the applicable Reliance Agreement.

24.1.1.2 Evaluation of COI

The IRB reviews COIs and CMPs to determine:

- Whether the COI affects the rights or welfare of research participants;
- Whether the COI might adversely affect the integrity or credibility of the research or the research program; and
• Whether the CMP effectively protects research participants and the integrity and credibility of the research and the research program.

During its review the IRB considers:
• How the research is supported or financed;
• The nature and extent of the conflict;
• The role and responsibilities of the conflicted individual in the design, conduct, and reporting of the research; and
• The ability of the conflicted individual to influence the outcome of the research.

24.1.1.3 Management of COI

The IRB has final authority to determine whether the research, the COI, and the CMP, if any, allow the research to be approved. For studies where the COI Working Group has issued a CMP, the IRB shall either affirm the CMP before approving the research or request changes to strengthen it. The IRB can require additional measures to manage a COI, but may not weaken a CMP issued by the COI Working Group.

For example, in addition to the CMP, the IRB may require:

1. Disclosure of the COI to research participants during the consent process and/or in the consent document;
2. Modification of the research plan or safety monitoring plan;
3. Monitoring of research by a third party;
4. Disqualification of the conflicted party from participation in all or a portion of the research;
5. Appointment of a non-conflicted PI;
6. Divestiture of significant financial interests;
7. Severance of relationships that create actual or potential conflicts.

In the event the conflict cannot be effectively managed, the IRB may disapprove the research.

24.2 IRB Member Conflict of Interest

No IRB member or alternate may participate in the review of any research project (in which the member has a COI, except to provide information as requested. It is the responsibility of each IRB member to disclose any COI related to a study submitted for review and recuse him/herself from the deliberations and vote by leaving the room.

The IRB staff ensures that IRB members and alternates are not assigned to conduct reviews of studies for which the member has a conflict and reminds members of conflicts at convened meetings as needed to ensure recusal.
IRB members, alternates, or consultants may be considered to have a conflicting interest requiring recusal when they, or an immediate member of their family, have any of the following:

1. Involvement in the design, conduct, and reporting of the research;
2. Significant financial interests related to the research being reviewed, as described in the UMMC Conflict of Interest Policy; or
3. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a study.

At the beginning of each IRB meeting the IRB Chair reminds members that they must recuse themselves from the discussion and vote of a specific research study in which they have a conflict. If a conflicted member is participating by conference call, videoconference or web meeting, the member’s participation (connection) is terminated for discussion and voting.

IRB members with a conflicting interest are not counted towards quorum for the particular review and are not present for the discussion. Recusals of members with COIs are recorded in the minutes.

### 24.3 Institutional Conflict of Interest

Pursuant to the UMMC Policy on Institutional Conflicts of Interest, the UMMC Compliance Committee COI Working Group serves as the Conflict of Interest Committee (“COI Committee”). As a matter of policy, UMMC will not participate in a human subjects’ research project when it has an institutional financial interest. An exception to this policy may be made only when the COI Committee determines that circumstances exist to merit an exception and a conflict management plan is adopted to maintain research integrity and serve the best interests of participants enrolled in the research. UMMC’s Human Research Office and IRBs collaborate with the COI Committee to ensure that institutional COI is identified and managed before the IRB completes its review of any research application.

### 24.4 Recruitment Incentives

Payment arrangements among sponsors, organizations, investigators, and those referring research participants present a conflict of interest and may place participants at risk of undue influence or cause inequitable selection. Payment in exchange for referrals of prospective participants (“finder’s fees”) is not permitted. Similarly, payments designed to accelerate recruitment that is tied to the rate or timing of enrollment (“bonus payments”) are also not permitted. Bonus payments do not include payments for items or services.
25 Participant Outreach

UMMC is committed to ensuring that educational opportunities are offered to research participants, prospective research participants, and members of the community which will enhance understanding of research involving human participants at UMMC and provide the opportunity for input, to seek information and to express concerns.

The following procedures describe how UMMC fulfils that commitment.

25.1 Responsibility

The Human Research Office Director and IO ensure the following:

25.2 Outreach Resources and Educational Materials

1. The Human Research Office website includes information on how to contact UMMC with any questions or concerns about specific research projects or research in general and a listing of relevant research-related links, including a link to the UMMC Research Partnerships site which has information about specific studies and opportunities for participation.

2. UMMC hospitals, clinics, schools and the Human Research Office display flyers on research at UMMC and brochures on becoming a research volunteer and Volunteering for a Clinical Trial. Additional copies of the brochures are available upon request.

3. The Human Research Office website includes a “Contact Us” link that allows members of the community to ask questions, express concerns, or provide feedback. Provision of contact information by the person is optional.

4. UMMC periodically provides presentations related to research to community organizations.

5. UMMC holds at least one “Research Day” annually, to which members of the public are invited.

25.3 Evaluation

Each year UMMC evaluates its outreach activities and makes changes when appropriate. The Human Research Office Director or Associate Director, in consultation with the IO and/or IRB Chair(s), as appropriate, reviews:

1. The specific community outreach activities being used;

2. Whether or not these community outreach activities have an evaluative component (e.g., evaluation instrument distributed to participants), and if so whether the feedback was positive, negative, or neutral and if any suggestions were made that could be used to enhance future activities;

3. The number of times the participants’ webpage is visited;
4. Feedback provided via the “Contact Us” mechanism on the Human Research Office website;

5. Feedback provided from other sources (unaffiliated IRB members, investigators, research staff, students, etc.).

The results of the review are used to evaluate the outreach activities and to identify additional resources that may be needed to meet the participant outreach needs of the research community.
Health Insurance Portability and Accountability Act (HIPAA)

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) required the creation of a Privacy Rule for identifiable health information. While the primary impact of the Privacy Rule is on the routine provision of and billing for health care, the Rule also affects the conduct and oversight of research.

The Privacy Rule defines individually identifiable health information transmitted or maintained by a covered entity in any form (electronic, written or oral) as “protected health information” (PHI) and establishes the conditions under which investigators may access and use this information in the conduct of research.

26.1 Definitions

Access: Access is the mechanism of obtaining or using information electronically, on paper, or other medium for the purpose of performing an official function.

Accounting of Disclosures: Information that describes a covered entity’s disclosures of PHI other than for treatment, payment, and health care operations; disclosures made with Authorization; and certain other limited disclosures. For those categories of disclosures that need to be in the accounting, the accounting must include disclosures that have occurred during the 6 years (or a shorter time period at the request of the individual) prior to the date of the request for an accounting.

Authorization: An individual’s written permission to allow a covered entity to use or disclose specified PHI for a particular purpose. Except as otherwise permitted by the Privacy Rule, a covered entity may not use or disclose PHI for research purposes without a valid Authorization.

Covered entity: A health plan, a health care clearinghouse, or a health care provider who or that transmits health information in electronic form in connection with a transaction for which DHHS has adopted a standard.

Data Use Agreement: An agreement into which the covered entity enters with the intended recipient of a limited data set that establishes the ways in which the information in the limited data set may be used and how it is protected.

De-identified. Data is considered de-identified under HIPAA when they do not identify an individual, and there is no reasonable basis to believe that the data can be used to identify an individual. The Privacy Rule defines two methods for de-identifying PHI: (1) when the PHI is stripped of all 18 HIPAA-defined identifying elements and the covered entity does not have actual knowledge that the information could be used alone or in combination with other information to identify an individual who is a subject of the information (Safe Harbor method); or (2) when an appropriate expert determines that the risk is very small that the information could be used, alone or in combination with other reasonably available information, by an
anticipated recipient to identify an individual who is a subject of the information (Expert Determination method).

**Designated Record Set:** A group of records maintained by or for a covered entity that includes (1) medical and billing records about individuals maintained by or for a covered health care provider; (2) enrollment, payment, claims adjudication, and case or medical management record systems maintained by or for a health plan; or (3) used, in whole or in part, by or for the covered entity to make decisions about individuals. A record is any item, collection, or grouping of information that includes PHI and is maintained, collected, used, or disseminated by or for a covered entity.

**Disclosure:** The release, transfer, access to, or divulging of information in any other manner outside the entity holding the information.

**Genetic Information.** Genetic information means, with respect to an individual, information about: (i) The individual's genetic tests; (ii) The genetic tests of family members of the individual; (iii) The manifestation of a disease or disorder in family members of such individual; or (iv) Any request for, or receipt of, genetic services, or participation in clinical research which includes genetic services, by the individual or any family member of the individual.

Genetic information concerning an individual or family member of an individual includes the genetic information of: (i) A fetus carried by the individual or family member who is a pregnant woman; and (ii) Any embryo legally held by an individual or family member utilizing an assisted reproductive technology. Genetic information excludes information about the sex or age of any individual.

**Genetic services.** A genetic test; genetic counseling (including obtaining, interpreting, or assessing genetic information); or genetic education.

**Genetic test** means an analysis of human DNA, RNA, chromosomes, proteins, or metabolites, if the analysis detects genotypes, mutations, or chromosomal changes. Genetic test does not include an analysis of proteins or metabolites that is directly related to a manifested disease, disorder, or pathological condition.

**Health Information:** Health Information means any information, whether oral or recorded in any form or medium, that (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.

**Individually Identifiable Health Information:** Information that is a subset of health information, including demographic information collected from an individual, and (1) is created or received by a health care provider, health plan, employer, or health care clearinghouse; and
(2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; and (a) that identifies the individual; or (b) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

**Limited Data Set:** Refers to data sets that exclude 16 categories of direct identifiers that are specified in the Privacy Rule. Limited Data Sets may be used or disclosed, for purposes of research, public health, or health care operations, without obtaining either an individual’s Authorization or a waiver or alteration of Authorization for its use and disclosure, only if the covered entity obtains satisfactory assurances in the form of a Data Use Agreement. Limited Data Sets are not de-identified information under the Privacy Rule.

**Minimum Necessary:** The least PHI necessary to accomplish the intended purpose of the use, disclosure, or request. Unless an exception applies, this standard applies to a covered entity when using or disclosing PHI or when requesting PHI from another covered entity. A covered entity that is using or disclosing PHI for research without Authorization must make reasonable efforts to limit PHI to the minimum necessary. A covered entity may rely, if reasonable under the circumstances, on documentation of IRB or Privacy Board approval or other appropriate representations and documentation under section 164.512(i) as establishing that the request for PHI for the research meets the minimum necessary requirements.

**Privacy Board:** A board that is established to review and approve requests for waiver or alteration of Authorization in connection with the use or disclosure of PHI as an alternative to obtaining waiver or alteration from an IRB. A Privacy Board consists of members with varying backgrounds and appropriate professional competencies as necessary to review the effect of the research plan on an individual’s privacy rights and related interests. The board must include at least one member who is not affiliated with the covered entity, is not affiliated with any entity conducting or sponsoring the research, and is not related to any person who is affiliated with any such entities. A Privacy Board cannot have any member participating in a review of any project in which the member has a conflict of interest.

**Protected Health Information:** PHI means individually identifiable health information transmitted by electronic media, maintained in electronic media, or transmitted or maintained in any other form or medium. PHI excludes individually identifiable health information in education records covered by the Family Educational Rights and Privacy Act, as amended, 20 U.S.C. 1232g; records described at 20 U.S.C. 1232g(a)(4)(B)(iv); in employment records held by a covered entity in its role as employer; and regarding a person who has been deceased for more than 50 years.

**Psychotherapy Notes.** Psychotherapy notes means notes recorded (in any medium) by a health care provider who is a mental health professional documenting or analyzing the contents of conversation during a private counseling session or a group, joint, or family counseling session and that are separated from the rest of the individual's medical record. Psychotherapy notes excludes medication prescription and monitoring, counseling session start and stop times, the modalities and frequencies of treatment furnished, results of clinical tests, and any
summary of the following items: Diagnosis, functional status, the treatment plan, symptoms, prognosis, and progress to date.

**Research:** A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. This includes the development of research repositories and databases for research.

**Use:** The sharing, employment, application, utilization, examination, or analysis of individually identifiable health information within the covered entity or health care component (for hybrid entities) that maintains such information.

**Waiver or Alteration of Authorization:** The documentation that the covered entity obtains from an investigator, IRB or Privacy Board that documents that the IRB or Privacy Board has waived or altered the Privacy Rule’s requirement that an individual must authorize a covered entity to use or disclose the individual’s PHI for research purposes.

**Workforce:** Employees, volunteers, trainees, and other persons whose conduct, in the performance of work for a covered entity, is under the direct control of the covered entity, whether or not they are paid by the covered entity.

### 26.2 The IRB’s Role under the Privacy Rule

Under the Privacy Rule, IRBs have the authority to consider, and act upon, requests for a partial or complete waiver or alteration of the Privacy Rule's Authorization requirement for uses and disclosures of PHI for research. Although the Common Rule and FDA regulations include protections to help ensure the privacy of research participants and the confidentiality of information, the Privacy Rule supplements these protections where HIPAA is applicable, by requiring covered entities to implement specific measures to safeguard the privacy of PHI. If certain conditions are met, an IRB may grant a waiver or an alteration of the Authorization requirement for research uses or disclosures of PHI.

At UMMC the UMMC IRB fulfills the functions of a Privacy Board for human research.

The Privacy Rule does not change the composition of an IRB. When acting upon a request to waive or alter the Authorization requirement, the IRB must follow the procedural requirements of the Common Rule and, if applicable, FDA regulations, including the review procedure (convened or expedited).

When a request for waiver or alteration of the Authorization requirement is considered by the convened IRB, a majority of the IRB members must be present at the meeting, including at least one member whose primary concerns are in nonscientific areas. Approval of a request to waive or alter the Privacy Rule's Authorization requirement must be approved by a majority of the IRB members present at the convened meeting. If a member of the IRB has a conflict of interest with respect to the use and disclosure for which a waiver or alteration is being sought, that member may not participate in the review.
When a request for review falls within the DHHS established categories of research that may be reviewed by an IRB through an expedited review procedure, or is a minor change in previously approved research the request for a waiver or alteration of the Authorization requirement may also be done by expedited review. The review may be carried out by the IRB Chair or by one or more experienced reviewers designated by the Chair from among the IRB members. An IRB member with a conflict of interest may not conduct the review. The IRB must have a method for keeping all its members advised of requests granted by expedited review.

IRB documentation of approval of a waiver or alteration of the authorization requirement includes:

- The identity of the approving IRB
- The date on which the waiver or alteration was approved
- A statement that the IRB has determined that all the specified criteria for a waiver or an alteration were met
- A brief description of the PHI for which use or access has been determined by the IRB to be necessary
- A statement that the waiver or alteration was reviewed and approved under either convened or expedited review procedures; and
- The signature of the IRB Chair or the Chair's designee.

UMMC will not release PHI to investigators or other third parties without individual authorization or proper documentation of IRB or Privacy Board approval of a waiver or alteration of the requirement.

### 26.3 Authorization

Except as otherwise permitted, the Privacy Rule requires that a research participant authorize the use or disclosure of his/her PHI in research. This authorization is distinct from the participant’s consent to participate in research, which is required under the Common Rule and FDA regulations. A valid authorization must be written in plain language and contain required statements and core elements [45 CFR 164.508(c)]. Under the Privacy Rule, a HIPAA Authorization may be combined with the consent document for research. At UMMC authorization language is incorporated into the research consent document. When the consent document is combined with an Authorization, as it is at UMMC, 45 CFR part 46 and 21 CFR part 56 require IRB review of the combined document.

Template consent documents, which include the required HIPAA authorization elements, are available on the Human Research Office website.

Once executed, a signed copy is provided to the individual providing authorization. Signed authorizations are retained by UMMC for at least 6 years from the date of creation or the date it was last in effect, whichever is later.
A research participant has the right to revoke his/her authorization at any time. Investigators are not required to retrieve information that was disclosed under the authorization before learning of the revocation. Additionally, investigators may continue to use and disclose PHI already obtained for the research under an authorization to the extent necessary to protect the integrity of the research.

When an Authorization permits disclosure of PHI to a person or organization that is not a covered entity (such as a sponsor or funding source), the Privacy Rule does not continue to protect the PHI disclosed to such entity. However, other federal and state laws and agreements between the covered entity and recipient, such as a Business Associate Agreement (BAA) or Confidentiality Agreement, may establish continuing protections for the disclosed information. Under the Common Rule or FDA regulations, an IRB may impose further restrictions on the use or disclosure of research information to protect research participants.

Authorization Core Elements:

1. A description of the PHI to be used or disclosed, identifying the information in a specific and meaningful manner.
2. The names or other specific identification of the person or persons (or class of persons) authorized to make the requested use or disclosure.
3. The names or other specific identification of the person or persons (or class of persons) to whom the covered entity may make the requested use or disclosure.
4. A description of each purpose of the requested use or disclosure.
5. Authorization expiration date or expiration event that relates to the individual or to the purpose of the use or disclosure (“end of the research study” or “none” are permissible for research, including for the creation and maintenance of a research database or repository).
6. Signature of the individual and date. If the individual’s legally authorized representative signs the Authorization, a description of the representative’s authority to act for the individual must also be provided.

Authorization Required Statements:

1. A statement of the individual’s right to revoke his/her Authorization and how to do so, and, if applicable, the exceptions to the right to revoke his/her Authorization or reference to the corresponding section of the covered entity’s notice of privacy practices.
2. Whether treatment, payment, enrollment, or eligibility of benefits can be conditioned on Authorization, including research-related treatment and consequences of refusing to sign the Authorization, if applicable.
3. A statement of the potential risk that PHI will be re-disclosed by the recipient. This may be a general statement that the Privacy Rule may no longer protect health information disclosed to the recipient.

26.4 Waiver or Alteration of the Authorization Requirement

Obtaining signed authorization to access and use of PHI for research is not always feasible. The Privacy Rule contains criteria for waiver or alteration of authorization. If a covered entity has used or disclosed PHI for research pursuant to a waiver or alteration of authorization, documentation of the approval of the waiver or authorization must be retained for 6 years from the date of its creation or the date it was last in effect, whichever is later. This is in addition to any other documentation requirements that might apply.

For research uses and disclosures of PHI, the IRB may approve a waiver or alteration of the authorization requirement in whole or in part. A complete waiver of authorization occurs when the IRB determines that no authorization is required for a covered entity to use and disclose PHI for a particular research project. A partial waiver of authorization occurs when the IRB determines that a covered entity does not need authorization for all PHI uses and disclosures for defined research purposes, such as accessing PHI for research recruitment purposes. The IRB may also approve a request that removes some, but not all, required elements or statements of an authorization (an alteration).

In order for the IRB to waive or alter authorization, the Privacy Rule (45 CFR 164.512(i)(2)(ii)) requires the IRB to determine the following:

1. The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
   a. An adequate plan to protect health information identifiers from improper use and disclosure.
   b. An adequate plan to destroy identifiers at the earliest opportunity consistent with conduct of the research (absent a healthcare or research justification for retaining them or a legal requirement to do so).
   c. Adequate written assurances that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

2. The research could not practicably be conducted without the waiver or alteration.

3. The research could not practicably be conducted without access to and use of the PHI.
The Privacy Rule allows institutions to rely on a waiver or an alteration of Authorization obtained from a single IRB or Privacy Board to be used to obtain or release PHI in connection with a multi-site project.

26.5 Activities Preparatory to Research

Under the preparatory to research provision of the Privacy Rule, a covered entity may permit an investigator to use PHI for purposes preparatory to research such as assessing the feasibility of conducting a research project, developing a grant application, or identifying potential participants.

The covered entity must obtain from the investigator representations that (1) the use or disclosure is requested solely to review PHI as necessary to prepare a research plan or for similar purposes preparatory to research, (2) the PHI will not be removed (physically taken out of a facility, or downloaded and retained on the investigator’s device) from the covered entity in the course of review, and (3) the PHI for which access is requested is necessary for the research. \[45\text{ CFR 164.512(i)(1)(ii)}\]

Federal guidance has drawn a distinction between activities that may be undertaken by a researcher who is a member of the covered entity’s workforce, e.g., an employee of the covered entity, and a researcher who is not part of the covered entity’s workforce. This guidance indicates that researchers may use PHI under the preparatory to research provision to identify potential study participants, so long as no PHI is removed from the covered entity and the remaining two representations set forth above can be made. However, the guidance also indicates that researchers may not use PHI obtained pursuant to the “preparatory to research” provision to contact potential study subjects unless (i) the researcher is a member of the covered entity’s workforce, or (ii) the researcher enters into a BAA with the covered entity. Therefore, if the researcher is not a workforce member or business associate of the covered entity, then the researcher may contact potential study participants only pursuant to a partial waiver of authorization from the reviewing IRB or privacy board, or pursuant to the Authorization of the participant.

At UMMC, this is accomplished by the investigator submitting either a request to the Center for Informatics and Analytics Honest Broker (for projects in development) or a request to the IRB for partial waiver of consent and authorization for screening purposes, either in the Initial Application or a Request for Change to an existing IRB-approved study.

26.6 Research Using Decedent’s Information

The HIPAA Privacy Rule protects the individually identifiable health information about a decedent for 50 years following the date of death of the individual. When a researcher seeks to use PHI from decedents for a research protocol, the researcher must (1) obtain authorization from the personal representative of the decedent (i.e., the person under applicable law with authority to act on behalf of the decedent or the decedent’s estate), (2) obtain a waiver of the requirement to obtain authorization from the IRB, or (3) attest to the covered entity holding...
the PHI that the use or disclosure is solely for research on the PHI of decedents, that the PHI being sought is necessary for the research, and, if requested by the covered entity, provide documentation of the death of the individuals about whom information is being sought.

At UMMC, the attestation option identified above is accomplished by submitting a request to the Center for Informatics and Analytics Honest Broker.

26.7 Storage and Use of PHI for Future Research

The Privacy Rule recognizes the creation of a research database or a specimen repository to be a research activity if the data/specimens to be stored contain PHI. When researchers establish a database or repository containing PHI for the purposes of future research, or intend to maintain the PHI following completion of a primary study for potential future research use, individual authorization for the storage of PHI for such future research must be sought unless the IRB has determined that the criteria for a waiver of the authorization requirement are satisfied. An authorization for use and/or disclosure of the stored PHI for future research must describe the future research uses and/or disclosures in sufficient detail to allow the potential subject to make an informed decision. The Privacy Rule does not require that an authorization describe each specific future study if the particular studies to be conducted are not yet determined. Instead, the authorization must adequately describe future purposes such that it would be reasonable for the participant to expect that his/her PHI could be used or disclosed for such research. When developing the description of potential future research uses, the investigator should be cognizant of uses of information/specimens that the community may consider particularly sensitive, such as genetics, mental health, studies of origin, and use of tissues that may have cultural significance, including whether any state laws may impose additional consent requirements with respect to any of these sensitive categories of information.

The authorization for future research can be a stand-alone document or may be incorporated into the authorization for the establishment of the database or repository or for the primary study, unless the research involves the use or disclosure of psychotherapy notes. Authorizations for the use or disclosure of psychotherapy notes can only be combined with another authorization for a use or disclosure of psychotherapy notes.

If the authorization for future research is combined with the authorization for the primary study, the authorization must clearly differentiate between the authorization for the primary study and the authorization for the unspecified future research activities, and allow the participant to opt-in to the future research. Opt-outs for future research are not permitted under the Privacy Rule because an opt-out process does not provide individuals with a clear ability to authorize the use of their information/specimens for future research, and may be viewed as coercive.

It is important to note that securing a HIPAA authorization for unspecified future research activities may not, by itself, satisfy all applicable legal consent requirements. The Common
Rule, FDA regulations, and state laws also must be considered, as applicable, in evaluating whether the information (including PHI) or identifiable biospecimens may be used for future research projects.

### 26.8 Ancillary Studies

Participation in ancillary studies not essential to the primary aims of the research should be on a voluntary basis. This is particularly important when the primary research offers a potential benefit, such as treatment, that might compel the potential participant to agree to something that he/she otherwise would not.

HIPAA reinforces this ethical principle by explicitly stating that authorization for “unconditioned” activities, for which there is no associated treatment, benefit or other effect on the individual participant cannot be required. Authorization for unconditioned activities must involve a clear opt-in mechanism.

It is acceptable to combine the authorization for a conditioned activity, such as a clinical trial, with authorization for an unconditioned activity, such as a corollary or sub-study that does not directly benefit or effect the individual participant, provided that:

1. The authorization clearly differentiates between the conditioned and unconditioned research activities;
2. The authorization clearly allows the individual the option to opt in to the unconditioned research activities; and
3. Sufficient information is provided for the individual to be able to make an informed choice about both the conditioned and unconditioned activities.

Separate authorization must be obtained for each research activity that involves the use and disclosure of psychotherapy notes. For example, authorization for the use and disclosure of psychotherapy notes for a clinical trial cannot be combined with an authorization for the use and disclosure of those psychotherapy notes for a corollary research activity.

### 26.9 De-identification of PHI under the Privacy Rule

Covered entities may use or disclose health information that is de-identified without restriction under the Privacy Rule. The “Safe Harbor” method permits a covered entity to de-identify data by removing all 18 data elements that could be used to identify the individual or the individual’s relatives, employers, or household members. The covered entity also must have no actual knowledge that the remaining information could be used alone or in combination with other information to identify individuals. Under this method, the identifiers that must be removed are the following:

1) Names;
2) All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:
a. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people.

b. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.

3) All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.

4) Telephone numbers;
5) Facsimile numbers;
6) Electronic mail addresses;
7) Social security numbers;
8) Medical record numbers;
9) Health plan beneficiary numbers;
10) Account numbers;
11) Certificate/license numbers;
12) Vehicle identifiers and serial numbers, including license plate numbers;
13) Device identifiers and serial numbers;
14) Web universal resource locators (URLs);
15) Internet Protocol (IP) address numbers;
16) Biometric identifiers, including fingerprints and voiceprints;
17) Full-face photographic images and any comparable images;
18) Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification.

Alternatively, a qualified statistician may certify that the risk is very small that health information could be used, alone or in combination with other available information, to identify individuals. The qualified statistician must document the methods and results of the analysis that justify such a determination. This analysis must be retained by the covered entity for 6 years from the date of its creation or when it was last acted on, whichever is later.

The Privacy Rule permits a covered entity to assign to, and retain with, the de-identified health information, a code or other means of record re-identification if that code is not derived from or related to the information about the individual and is not otherwise capable of being translated to identify the individual. The covered entity may not use or disclose the code or other means of record identification for any other purpose and may not disclose its method of re-identifying the information.
NOTE: Data that are considered de-identified under HIPAA may still be considered human subject data under the Common Rule and may require IRB review and approval. Removal of HIPAA-identifying elements does not necessarily mean that the identity of the participant is not or may not readily be ascertained by the investigator or associated with the information and thus be considered identifiable private information under the Common Rule. The reverse can also be true (and, in practice, is more likely to occur): information may not be “identifiable” under the Common Rule but, because it contains certain HIPAA identifiers, it is considered identifiable under HIPAA.

26.10 Limited Data Sets and Data Use Agreements

Limited data sets are data sets stripped of certain direct identifiers. Limited data sets may be used or disclosed only for public health, research, or health care operations purposes. Because limited data sets may contain identifiable information, they are still PHI and as such are not considered de-identified under the Privacy Rule. Unlike de-identified data, PHI in limited data sets may include: addresses other than street name or street address or post office boxes, all elements of dates (such as admission and discharge dates) and unique codes or identifiers not listed as direct identifiers. The following direct identifiers must be removed for PHI to qualify as a limited data set:

1) Names;
2) Postal address information, other than town or city, state, and ZIP code;
3) Telephone numbers;
4) Fax numbers;
5) Email addresses;
6) Social security numbers;
7) Medical record numbers;
8) Health plan beneficiary numbers;
9) Account numbers;
10) Certificate or license numbers;
11) Vehicle identifiers and license plate numbers;
12) Device identifiers and serial numbers;
13) URLs;
14) IP addresses;
15) Biometric identifiers; and
16) Full-face photographs and any comparable images.
Before disclosing a limited data set, a covered entity must enter into a Data Use Agreement (DUA) with the recipient, even when the recipient is a member of its workforce. The DUA establishes the parameters around the proposed uses and disclosures of the data, who is permitted to have access to the data, and stipulates that no other use or disclosure will be made other than as permitted by the DUA or as otherwise required by law, no attempt will be made to identify or contact individuals whose data are included in the limited data set, that appropriate safeguards are in place to protect the data from unauthorized use or disclosure, that any agents, including subcontractors, to whom the recipient provides the limited data set will agree to the same restrictions and conditions that apply to the recipient and that the recipient will report any uses or disclosures of the information that they become aware of that are not in keeping with the terms of the DUA. Data Use Agreements for the purposes of research are available through the UMMC Office of Integrity and Compliance and are submitted to the IRB along with the other project materials so that the IRB has a record of the agreement.

26.11 Research Participant Access to PHI

With few exceptions, the Privacy Rule guarantees individuals access to their medical records and other types of health information. One exception is during a clinical trial, when the participant’s right of access may be suspended while the research is in progress. The participant must be notified of and agree to the temporary denial of access when providing consent and authorization. Any such notice must also inform the individual that the right to access will be restored upon conclusion of the clinical trial. Language accommodating this exclusion is included in the applicable UMMC research consent/authorization templates.

26.12 Revoking Authorization

The Privacy Rule establishes the right for an individual to revoke his/her authorization for uses and disclosures of PHI for research, in writing, at any time, except to the extent that the covered entity has taken action in reliance on the authorization. [45 CFR 164.508(b)(5)] However, individuals providing authorization should be made aware that revoking authorization does not mean that the individual’s PHI may no longer be used in the research or be used or disclosed for other purposes.

At UMMC individuals may revoke authorization as described in the UMMC Notice of Privacy Practices and the research informed consent document, as applicable.

A covered entity may continue to use and disclose PHI that was obtained before the individual revoked authorization to the extent that the entity has taken action in reliance on the authorization. When the research is being conducted by the covered entity, the covered entity is permitted to continue using or disclosing the already obtained PHI to the extent necessary to maintain the integrity of the research (e.g., to account for a participant’s withdrawal from a study, to report adverse events, or to conduct an investigation of misconduct). A covered entity may also continue to use the PHI for other activities that are permitted under the Rule without authorization (e.g., health care operations such as QA/QI). Additionally, revoking an
authorization does not prevent the continued use or disclosure of PHI by a non-covered entity that had already received it pursuant to the authorization.

26.13 Accounting of Disclosures

The Privacy Rule grants individuals the right to a written “Accounting of Disclosures” of their Protected Health Information made by a covered entity without the individual’s authorization in the six years prior to their request for an Accounting. A covered entity must therefore keep records of such PHI disclosures for 6 years.

It is important to understand the difference between a use and a disclosure of PHI. In general, the use of PHI means use of that information within the covered entity. A disclosure of PHI means “the release, transfer, provision of access to, or divulging in any manner of information outside of the entity holding the information.” The Privacy Rule restricts both uses and disclosures of PHI, but it requires an accounting only for certain PHI disclosures.

An Accounting of Disclosures is required for:

1) Routinely Permitted Disclosures (e.g., under public health authority, to regulatory agencies, to persons with FDA-related responsibilities) with limited exceptions (e.g., law enforcement, national security, etc.);

2) Disclosures made pursuant to:
   a. Waiver of Authorization;
   b. Research on Decedents’ Information;
   c. Reviews Preparatory to Research.

An accounting is not needed when the PHI disclosure is made:

1) For treatment, payment, or health care operations;
2) Under an Authorization for the disclosure;
3) To an individual about himself or herself;
4) As part of a limited data set under a data use agreement.

The Privacy Rule allows three methods for accounting for research-related disclosures that are made without the individual’s Authorization or other than a limited data set: (1) A standard approach, (2) a multiple-disclosures approach, and (3) an alternative for disclosures involving 50 or more individuals. Whatever approach is selected, the accounting is made in writing and provided to the requesting individual. Accounting reports to individuals may include results from more than one accounting method.

27 Special Considerations

27.1 State Mandated Reporting

Mississippi law mandates that certain persons who suspect child or elder abuse or neglect report this to the Mississippi State Department of Health.

UMMC policy requires the solicitation of informed consent from all adult research participants and, where appropriate, parental permission and assent from children involved as research participants. In situations where conditions of abuse or neglect might be revealed, mandated reporters should make themselves known as such to parents of children under age 18, to minor participants and to participants who are potential victims of abuse or neglect.

Miss. Code Ann. § 43-47-7; §43-47-37; and § 97-5-51

Investigators should consult these sources to determine if potential participants should be advised of mandatory reporting requirements during the informed consent process.

27.2 Lead Investigator/Coordinating Center

When the UMMC IRB is serving as the IRB of record for a PI or site who is serving as the lead investigator or lead/coordinating center of a multi-site or collaborative research project, the PI must describe within the protocol and IRB application how the research will be overseen and how issues relevant to the protection of human research participants (e.g., IRB initial and continuing approvals, study modifications, reports of unanticipated problems, interim results, data-safety monitoring, etc.) will be coordinated and communicated among participating sites and investigators. For FDA-regulated clinical trials, the plan should address the plan for study monitoring and for the reporting and evaluation of adverse events, significant new risk information, and any other reports mandated by regulation or policy.

The lead PI or lead/coordinating center is responsible for serving as the liaison with other participating sites and investigators and for ensuring that all participating investigators obtain IRB review and approval prior to initiating the research, maintain approval, and obtain IRB approval for modifications to the research. The UMMC IRB will evaluate whether the plan for research oversight and management of information that is relevant to the protection of human research participants is adequate.

27.3 Certificates of Confidentiality

Certificates of Confidentiality (CoC) protect research information by prohibiting certain disclosures and conditioning others upon consent from the participant. The protections and requirements of CoCs are outlined in 42 U.S.C. 241(d) and in written policies and requirements of certain Federal agencies such as NIH and CDC and are summarized below.

CoC’s are obtained as follows:
• CoCs are issued automatically when research is conducted or supported by NIH and falls within the scope of the NIH policy.

• CoCs are issued automatically when research is conducted or supported by the CDC and involves the collection of identifiable, sensitive information.

• Research that is not supported by NIH or CDC may still have the protections afforded by CoCs through successful application to the NIH, FDA, HRSA, SAMHSA, or other authorized Federal agencies or departments.

Additional information about CoCs and the application process for research not covered by the NIH policy is available on the NIH CoC Website.

27.3.1 Definitions

Identifiable, sensitive information means information that is about an individual and that is gathered or used during the course of biomedical, behavioral, clinical, or other research and

1. Through which an individual is identified; or

2. For which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

27.3.2 Protections and Requirements

When a CoC is issued, whether automatically or under an approved application, the person(s) engaged in the research must not disclose or provide the name of a participant or any information, document, or biospecimen that contains identifiable, sensitive information about the participant and that was compiled for the purposes of the research:

1. In any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, unless the disclosure is made with the consent of the individual to whom the information, document, or biospecimen pertains; or

2. To any other person not connected with the research, unless:

   a. Required by Federal, State, or local laws (e.g., adverse event reporting to the FDA, transmissible disease reporting required under State law), but excluding proceedings as described in “1” above;

   b. Necessary for the medical treatment of the participant to whom the information, document, or biospecimen pertains and made with the consent of the participant;

   c. Made with the consent of the individual to whom the information, document, or biospecimens pertains; or
d. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human research participants.

Additional Protections

Identifiable, sensitive information protected under a CoC, and all copies thereof, are immune from the legal process, and shall not, without the consent of the individual to whom the information pertains, be admissible as evidence or used in any action, suit, or other judicial, legislative, or administrative proceeding.

Identifiable, sensitive information that has been collected under a CoC, and all copies thereof, are protected for perpetuity. If identifiable, sensitive information covered by a CoC is shared with other researchers or organizations, the researchers or organizations must be informed that the information is covered by a CoC and of their responsibility to protect the information accordingly.

Nothing in the rule (42 U.S.C. 241(d)) may be construed to limit the access of a participant to information about himself or herself collected during the research.

When consent is obtained, the consent document, when applicable, and process should inform participants that a CoC is in place and describe the protections and limitations.

27.3.3 NIH and CDC

The NIH Policy on CoCs applies to “all biomedical, behavioral, clinical, or other research funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts, other transaction awards, or conducted by the NIH Intramural Research Program, that collects or uses identifiable, sensitive information” that was commenced or ongoing on or after December 13, 2016.

The CDC requirements for CoCs apply to “CDC supported research commenced or ongoing after December 13, 2016 and in which identifiable, sensitive information is collected, as defined by Section 301(d).”

CoCs are automatically granted, and the requirements of such must be complied with, whenever a NIH or CDC funded activity falls within the scope of the NIH policy or CDC’s requirements. Investigators and institutions are responsible for determining when research with NIH or CDC support are covered by a CoC.

NIH and CDC expand upon 42 U.S.C. 241(d) by explaining that NIH and CDC consider research in which identifiable, sensitive information is collected or used, to include:

- Human subjects research as defined in 45 CFR 46, including research determined to be exempt (except for exempt research when the information obtained is recorded in such
a manner that human participants cannot be identified or the identity of the human participants cannot readily be ascertained, directly or through identifiers linked to the participants);

- Research involving the collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual;

- Research that involves the generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human participants can be identified or identity can readily be ascertained; or

- Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual, as defined in subsection 301(d) of the Public Health Service Act.

27.3.4 NIH and CDC CoC Determination

At UMMC, Office of Research and Sponsored Programs (ORSP) staff will, in consultation with the investigator(s) (or Program or Project Director, if applicable), determine if the NIH policy or CDC requirements applies to research with NIH or CDC involvement or support. The questions outlined in the NIH policy and CDC requirements will be used to guide the analysis. When it has been determined that the NIH policy or CDC requirements do not apply, investigators (or Program or Project Directors, if applicable) are responsible for consulting with ORSP whenever they are proposing changes to the NIH or CDC supported activity that may impact or change the analysis.

The NIH policy and CDC requirements include additional responsibilities and requirements for internal controls and for ensuring that recipients of identifiable, sensitive information protected by a CoC understand that they are also subject to the requirements of subsection 301(d) of the Public Health Service Act.

27.3.5 Application Procedures for non-NIH, non-CDC Research

Any person engaged in human subjects research that collects or uses identifiable, sensitive information may apply for a CoC. For most research, CoCs are obtained from NIH and an investigator may apply for a CoC through the NIH Institute or Center funding research in a scientific area similar to the project.

When an investigator is conducting a research project that is covered by the Agency for Healthcare Research and Quality (AHRQ) confidentiality statute (42 U.S.C. section 299c-3(c)), a CoC is not needed (AHRQ notice NOT-HS-18-012). While the AHRQ statute does not define
“identifiable”, AHRQ applies the PHS Act definition of “identifiable, sensitive information”. Investigators should consult with AHRQ when they believe that data might be considered “non-identifiable” or when otherwise uncertain whether a research project falls within the scope of the statute.

When an investigator is conducting a research project that is covered by the Department of Justice (DoJ) confidentiality statute, 28 CFR 22, and/or a NIJ Privacy Certificate, a CoC may not be needed. Investigators should consult with DoJ/NIJ to determine whether a CoC should be obtained.

If there is an Investigational New Drug Application (IND) or an Investigational Device Exemption (IDE), the sponsor can request a CoC from the FDA. When the FDA funds or conducts research, a CoC is automatically issued.

CoCs may also be issued by other Federal agencies and departments, such as SAMSHA and HRSA.

For more information, see the NIH CoC Website.

## 27.3.6 IRB Review

Investigators are responsible for informing the IRB that a CoC is in place, or that an application for CoC has been submitted. When the CoC application is in process the IRB may condition approval upon its receipt.

For studies that are already underway, investigators must submit an Amendment request to the IRB, along with updated consent language (if applicable), when a CoC is applied for, or when automatically issued under the NIH policy or CDC requirements.

When reviewing research under a CoC, the UMMC IRB will evaluate whether the research plan is consistent with the obligations to protect information and specimens under a CoC and, when consent will be obtained, whether the proposed consent language or other form of notification properly discloses the CoC and appropriately describes the associated protections and limitations. Sample consent language is available on the NIH CoC Website and in the template consent forms available on UMMC’s Human Research Office/IRB website.

When research is not under a CoC, the IRB may require an investigator to apply for a CoC if the research includes identifiable, sensitive information and the IRB determines that a CoC is necessary to minimize risks and adequately protect participants’ privacy and the confidentiality of their information or specimens.
27.4 Case Reports Requiring IRB Review

Federal regulations at 45 CFR 46.102(d) and 45 CFR 164.501 define research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. The UMMC IRB does not consider the retrospective review and analysis of medical records for publication of a single case report or a case series involving data from up to three patients to be research, and therefore a report of 1-3 medical cases does not need to be submitted to the IRB. This is because reporting on such a small number of patients does not involve a systematic investigation, including defining a hypothesis that is then investigated prospectively and systematically, to develop or contribute to generalizable knowledge. UMMC regards such limited case report preparation as an educational activity, not research, and thus it is permissible under the Privacy Rule (HIPAA) as a part of health care operations (45 CFR 164.501) when the case report will be used internally, or in other learning environments, for educational purposes. When a larger series of patients is being evaluated for presentation or publication, the commonalities of those patients are typically explored, and conclusions are drawn (i.e., a systematic investigation). Such a systematic investigation more closely resembles prospectively designed clinical research and as such requires IRB review and approval. While drawing such a “bright line” to distinguish non-research from research may seem arbitrary, it serves as a guide to those who would prepare case reports. If an investigator intends a report of 1-3 medical cases to develop or contribute to generalizable knowledge, or to otherwise constitute research, the report should be submitted to the IRB with a request for a determination whether the case report constitutes research using the procedures outlined in Section 4. As always, anyone who is unsure whether a project requires IRB review should contact the UMMC Human Research Office for assistance.

Regardless of the number of cases, providers must comply with all applicable laws and UMMC policies related to the use and release of health information. Providers should consult with the Privacy Officer for guidance on patient privacy and HIPAA.

A guidance document confirming this policy is available on the IRB website and may be provided to journal editors or others who request confirmation of the policy.

27.5 Databases, Registries, and Biospecimen Repositories

Databases, registries, and biospecimen repositories (all referred to as repositories throughout this section) are used to store data and/or biospecimens for future use.

There are two types of repositories:

- Non-research repositories created and maintained for purposes that are unrelated to research. Such purposes may include diagnosis, treatment, billing, marketing, quality control, and public health surveillance.

- Research repositories created and maintained specifically for research purposes. Such purposes may include databases to identify prospective study participants, patient outcome information to evaluate treatment effectiveness, and tissues samples for future research. Non-research repositories that are altered to facilitate research (e.g.,
through the addition of data fields not necessary for the core purpose of the repository) are considered research repositories.

27.5.1 Non-research Repositories

Even though repositories were not created for research purposes, they may contain information that is of great interest to researchers. The creation (or operation) of non-research repositories does not involve human subjects research and does not require IRB oversight. However, IRB approval is required for the research use of identifiable private information or identifiable human specimens from non-research repositories, and, regardless of identifiability, when specimens will be used to evaluate the safety or effectiveness of a medical device. Research under the auspices of UMMC that includes the use of coded private information or specimens, must be submitted for IRB review.

Researchers submitting an application for research using data or specimens from non-research repositories must describe the source of the data/specimens and any terms, conditions, or restrictions on use. Data/specimens cannot be used for research if the person from whom the data/specimens originated objected to its use for research. Informed consent and HIPAA authorization (when applicable) must be obtained unless the IRB determines that the criteria for a waiver are satisfied.

27.5.2 Research Repositories

Research repositories involve three distinct activities:

1. Collection of data/specimens;
2. Storage and management of data/specimens; and
3. Distribution of data/specimens.

Collection

Informed consent and HIPAA authorization (when applicable) must be obtained unless the IRB determines that the criteria for a waiver are satisfied.

Informed Consent information should include:

- A clear description of
  - What data/specimens will be collected;
  - Where the data/specimens will be stored, who will have access, and how the data/specimens will be secured;
  - Whether the data/specimens will be identifiable, coded, or de-identified;
  - The types of research to be conducted and any limitations or restrictions on such; and
The conditions under which data/specimens will be released to recipient-investigators

- A statement regarding future withdrawal of the data from the study (i.e., whether participants may, in the future, request that their data be destroyed or that all personal identifiers be removed from data and how to make such a request)
- When appropriate, the plan for management of incidental findings and sharing of results

**Storage and Management**

Repositories should have written policies describing:

- The conditions under which data/specimens will be accepted (e.g., inclusion criteria)
- Informed consent
- IRB review
- The sources of data/specimens
- Whether data/specimens will be identifiable, coded, or de-identified, and, if coded, management of the linkage key; and
- Physical and procedural mechanisms for the secure receipt, storage, and distribution of data/specimens

**Distribution**

Repositories should have written policies describing:

- How data/specimens may be requested and by whom
- Any requirements associated with a request for data/specimens (e.g., verification of IRB approval or that approval is not required)
- Any limitations or restrictions on how data/specimens may be used
- Whether released data/specimens will be identifiable, coded, or de-identified, and, if coded, any circumstances under which recipient investigators will have access to or be provided with the key or other means to re-identify; and
- Agreements with recipient investigators specifying the terms of use.

**27.5.3 IRB Oversight**

IRB approval is required for the establishment and operation of a research repository when the data/specimens that are accessed, received, stored, or distributed are identifiable. In general, private information or specimens are considered individually identifiable when the identities of
participants are known to investigators/repository operators or when the data/specimens can be linked to specific individuals either directly or indirectly through coding systems.

Separate IRB approval is required for the use of data/specimens from a repository when the recipient investigator(s) know or may readily ascertain the identity of individual participants, and, regardless of identifiability, when specimens will be used to evaluate the safety or effectiveness of a medical device.

27.6 Research Involving or Generating Genetic Information

Research that generates or uses genetic information may create special risks to human participants and their relatives. These involve medical, psychosocial, legal and economic risks, such as the possible loss of privacy, insurability, and employability, and may result in stigmatization and discrimination. Information about one's own genetic make-up may also provide information about family members.

In studies involving genetic testing or analysis of genetic information, several questions should be addressed to ensure that potential risks are well understood and that the rights and interests of participants and their family members are carefully considered and planned for.

For example:
1. Is the testing intrinsic to the study? If not, has participation in the genetic testing component been provided as an opt-in?
2. Will test results be given? Is there an appropriate plan for return of results?
3. Will the participant or family member be provided the option to receive or not receive results? How will this decision be recorded?
4. Could the results provide information about individual disease risk or disease risk for family members?
5. Could other clinically relevant information or incidental findings be uncovered by the study? Is there a plan for the management of such findings?
6. Will testing that could produce clinically relevant information occur in a CLIA-certified lab? If not, are there tests available that could validate or support findings?
7. Could a change in a family relationship be disclosed, such as mistaken paternity?
8. Could/will the research provide information about the origins, ancestry, or natural history of families, indigenous peoples, tribal populations, or other populations? What are the possible risks?
9. Could/will the research generate information that could place participants or family members at risk or be stigmatizing?
10. Could/will the research generate information of other value or importance to participants or family members?
11. Are there any practical limitations on the participant’s right to withdraw from the research, withdraw data, and/or withdraw biological materials (e.g., specimens, cell lines, extracted genomic DNA)? If so, what are they?

12. How will the information and/or biological materials be protected and who will have access?

13. What is the potential for re-identification of individual participants (e.g., through the combination of their genetic information and/or materials with other sources of information (e.g., public records))? What measures can be taken to mitigate these risks?

14. Is a Certificate of Confidentiality (CoC) in place or should one be considered? (See Section 26.3)

15. Will the specimens, cell lines, or genetic information be stored and/or made available for future research? Is this provided as an opt-in when not intrinsic to the study? (See Section 26.7)

Investigators should carefully consider the above and other factors relevant to their specific study when developing the protocol, consent process, and consent form(s). The President’s Bioethics Commission, the National Academies of Sciences, Engineering, and Medicine, and others have produced reports, recommendations, and materials that investigators and the IRB may find helpful in protocol development and review, including:

- Returning Individual Research Results to Participants: Guidance for a New Research Paradigm
- Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts
- Privacy and Progress in Whole Genome Sequencing
- Genetics Research and American Indian and Alaska Native Communities
- National Human Genome Research Institute:
  - Human Subjects Research in Genomics
  - Return of Research Results
  - Data Sharing and Privacy
  - Informed Consent for Genomics Research

In addition to the ethical considerations, investigators must ensure that research involving genetic testing or use of genetic information is consistent with applicable law (e.g., GINA, HIPAA, EU GDPR, state law) and policy (e.g., NIH).

27.6.1 Genetic Information Nondiscrimination Act (GINA)

**GINA** generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against individuals based on their genetic information. This law protects individuals, including research participants, in the following ways:
• Health insurance companies and health plans are generally prohibited from requesting or requiring genetic information of an individual or their family members, including genetic information generated from research;
• If health insurance companies and health plans do receive such genetic information, they may not use it to make decisions regarding coverage, rates, or preexisting conditions; and
• Employers with 15 or more employees generally may not use genetic information for hiring, firing, promotion, or other decisions regarding terms of employment.

GINA’s protections do not extend to life insurance, disability insurance, or long-term care insurance.

GINA defines genetic information as information about:
• An individual’s genetic tests;
• Genetic tests of an individual’s family members;
• Genetic tests of any fetus of an individual or family member who is a pregnant woman, and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology;
• The manifestation of a disease or disorder in an individual's family members (family history); or
• Any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or an individual's family members.

GINA includes a “research exception” that allows health insurers and health plans who are engaged in research to request, but not require, that an individual undergo a genetic test so long as certain requirements are satisfied. Additional information on GINA and this exception are available on this OHRP website.

The UMMC IRB will consider the protections and limitations of GINA when it assesses the risks of research generating or using genetic information and the adequacy of the measures to protect privacy and maintain confidentiality. Generally, the IRB will also require that the protections and limitations of GINA are disclosed in the consent document and during the consent process when applicable. Sample language for GINA is provided in the UMMC template consent form.

27.6.2 Reserved

27.7 Genomic Data Sharing (GDS)

UMMC complies with the NIH GDS Policy, which allows for “broad and responsible sharing of genomic research data”, via submission of said data into an NIH-designated data repository. The intent of NIH’s policy is to speed discoveries to diagnose, treat, and prevent disease. To ensure consistency in the protection of human research participants, UMMC applies the NIH
principles for informed consent and for a genomic data sharing plan to all research that involves or contemplates genomic data sharing.

The NIH policy applies to grant activities requesting support from NIH for research involving the generation of large-scale human (and/or non-human) genomic data, regardless of funding level, such as:

- Research project grants (Rs);
- Program projects (Ps) and SCORs (Ss);
- Cooperative agreements for research (Us);
- Individual career development awards (Ks) that include a research component;
- S activities that include a research component; and
- All other activities that include a research component.

Also covered under this policy is research involving data derived from these activities for subsequent research. All basic and clinical research, including clinical trials, supported by NIH that involves the generation or use of large-scale genomic data fall within the scope of the policy.

The policy does not apply to:

- Institutional training grants (T32s, T34s, T35s, and TL2s);
- K12 career development awards (KL2s);
- Individual fellowships (Fs);
- Resource grants and contracts (Ss);
- Linked awards derived from previously reviewed applications (KL1, KL2, RL1, RL2, RL5, RL9, TL1, UL1);
- Facilities or coordinating centers funded through related initiatives to provide genotyping, sequencing, or other core services in support of GDS.

Because of the potential for re-identification of genomic data, Certificates of Confidentiality (CoCs) are automatically issued by the NIH for any research it supports, in part or in whole, that involves “the generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained as defined in the Federal Policy for the Protection of Human Subjects (45 CFR 46).” Research covered by the NIH policy and/or the underlying PHS Act is protected by the CoC in perpetuity; as such any downstream recipients of such information must comply with the requirements of the PHS Act. Investigators without NIH support who intend to submit genomic data to a NIH repository are encouraged to obtain a CoC.

For more information on CoCs, see Section 26.3.
27.7.1 Definitions

**Genomic data:** information derived from study of an organism’s genome, i.e., the set of DNA (including all the genes within) in every cell that provides all of the information needed to build and maintain that organism.

**Genomic Summary Results (GSR):** GSR (also referred to as “aggregate genomic data” or “genomic summary statistics”) are results from primary analyses of genomic research that convey information relevant to genomic associations with traits or diseases across datasets rather than associations specific to any one individual research participant (e.g., genotype counts and frequencies; allele counts and frequencies; effect size estimates and standard errors; likelihood; and p-values). **Sensitive GSR** refers to GSR where the privacy risks may be heightened for study populations (e.g., populations from isolated geographic regions or with rare traits) or the study populations may be more vulnerable to group harm (e.g., because the data includes potentially stigmatizing traits). Information regarding NIH’s updated policy on the access, use, and management of GSR may be found here: [https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-023.html](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-023.html)

**Large-scale data** include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, epigenomic, and gene expression data. Examples of genomic research projects that are subject to the Policy and the timeline for submission and sharing of data from such projects may be found here: [https://osp.od.nih.gov/wp-content/uploads/Supplemental_Info_GDS_Policy.pdf](https://osp.od.nih.gov/wp-content/uploads/Supplemental_Info_GDS_Policy.pdf)

**NIH-Designated Data Repository:** any data repository maintained or supported by NIH either directly or through collaboration. Examples of such repositories is available here: [https://osp.od.nih.gov/scientific-sharing/data-repositories-and-trusted-partners/](https://osp.od.nih.gov/scientific-sharing/data-repositories-and-trusted-partners/).

Data may be unrestricted or controlled access:

- **Unrestricted-Access ("Open Access"):** data are publicly available to anyone (e.g., The 1000 Genomes Project). Non-sensitive GSR are made available through unrestricted access.

- **Controlled-Access:** the data are available to an investigator for a specific project only after the investigators and institution certify to abide by specified terms and conditions and NIH has approved the use. Sensitive GSR are made available through controlled access.

27.7.2 Procedures

**IRB Submissions and GDS**

For any cell lines created or specimens to be collected, analyzed, and shared subject to the GDS Policy, the IRB expects that informed consent will be obtained from the research participant for future research uses and broad sharing of data required under the policy, including GSR. This is the case even if the specimens or cell lines are de-identified. If there are compelling scientific or legal reasons that necessitate the use of genomic data from cell lines or clinical specimens
that lack consent for research use and data sharing, investigators will need to provide a justification in the funding request to NIH for their use. The funding NIH institute/center will review the justification and decide whether to make an exception to the consent expectation. Exceptions from the NIH are not required if only some participants decline to consent to broad sharing, rather an exception request must be granted by NIH for research when consent for broad sharing has not or will not be sought.

Participants asked to allow for future research uses and broad sharing of their genomic data have the ability to decline, and still remain in the research (however their data cannot be placed into a repository or otherwise broadly shared). The only exception to this is when sharing of the data is intrinsic to the study (e.g., the purpose of the study is to establish a repository for sharing biological specimens and/or data for future research).

Sample consent language for studies subject to GDS is available from the Human Research Office. NIH and NHGRI also provides guidance and resources to assist in the development of appropriate consent forms for research involving or generating genetic or genomic data.

Applications to the UMMC IRB should include information about the proposed generation or use of genomic data including, as applicable:

- Whether the research will generate or use data subject to the NIH GDS policy;
- The name of the NIH data repository/database, or other repository or database, that data will be submitted to or acquired from;
- Whether the data is or should be classified as restricted access or unrestricted access;
- Whether the data is or should be classified as sensitive (e.g., studies involving populations from isolated geographic regions or with rare traits, studies that include data on potentially stigmatizing traits, etc.)
- Whether there are any data use limitations or modifiers (e.g., use limited to a specific disease, restricted to not-for-profit organizations, IRB approval requirement, etc.);
- The plan for informed consent and the proposed consent language; and
- A copy of the genomic data sharing plan.

The IRB will review the proposal for genomic data sharing or subsequent use of such genomic data in accordance with the criteria for approval of research and the guidelines for IRBs provided by NIH.

When UMMC is responsible for NIH Institutional Certification (see below), the IRB review will specifically address the required assurances outlined on the Extramural Institutional Certification. When appropriate, if the IRB is unable to confirm that a certification element is satisfied (e.g., because the IRB has not yet granted final approval), Provisional Institutional Certification will be provided.

Grant Applications and GDS
Investigators planning to apply to NIH for research that will generate large-scale human genomic data as defined above should contact the appropriate NIH Program/Project officials to discuss expectations and timelines for complying with this policy. Along with the grant, the following will need to be submitted:

- **Notification in a cover letter** of the intent to generate large-scale human genomic data
- **Institutional Certification** from the Office of Sponsored Programs (templates available here: [https://osp.od.nih.gov/scientific-sharing/institutional-certifications/](https://osp.od.nih.gov/scientific-sharing/institutional-certifications/)). Certification must be provided for all sites contributing samples. If more than one site is contributing samples, the primary site may submit one certification on behalf of all collaborating sites (or each site may provide their own certification if this is the site’s preference). This certification assures that:
  - The data submission is consistent, as appropriate, with applicable national, tribal, and state laws and regulations, as well as relevant institutional policies;
  - Any limitations on the research use of the data, as expressed in the informed consent documents, are delineated within the certification;
  - The identities of research participants will not be disclosed to the repositories;
  - An IRB and/or Privacy Board has reviewed the investigator’s proposal for data submission and assures that:
    - the protocol for the collection of genomic and phenotypic data is consistent with 45 CFR 46;
    - data submission and subsequent data sharing for research purposes are consistent with the informed consent of study participants from whom the data were obtained;
    - consideration was given to the risks to individual participants and their families, associated with data submitted to the repositories and subsequent sharing, including unrestricted access to GSR ; and
- that the investigator’s plan for de-identifying datasets is consistent with the standards outlined in the [NIH Genomic Data Sharing (GDS) Policy](https://osp.od.nih.gov/scientific-sharing/institutional-certifications/). In situations where the sharing of human data is not possible (i.e., the Institutional Certification criteria cannot be met), a justification is required to explain why these data cannot be shared, and an alternative data sharing plan will need to be provided. Exceptions to NIH expectations for data submission to an NIH-designated data repository will be considered on a case-by-case basis by the NIH funding Institute or Center (IC).

Investigators who wish to use controlled-access human genomic data from NIH-designated data repositories should briefly address their plans for requesting access to the data and state their intention to abide by the NIH Genomic Data User Code of Conduct in the Research Plan of the

Access to controlled-access data is dependent on an approval process that involves the relevant NIH Data Access Committee(s). Applicants may wish to secure access to the data prior to submitting their application for NIH support. Secondary users of controlled-access data are not expected to deposit their findings into NIH-designated data repositories, unless appropriate. Investigators who wish to use/download data NIH unrestricted-access repositories, including non-sensitive GSR, should use the data to promote scientific research or health; and should not use the data to re-identify individuals or generate information that could allow participant’s identities to be readily ascertained, and, in all oral and written presentations, disclosures, or publications, acknowledge the specific dataset or accession numbers and the repository through which the data were accessed.

Procedures for submitting data into, or requesting access for data from an NIH-designated repository, are available here: https://osp.od.nih.gov/scientific-sharing/researchers-institutional-certifications/.

27.8 Community Based Research

Community based research (CBR) is research that is conducted as an equal partnership between academic investigators and members of a community. In CBR projects, the community participates fully in all aspects of the research process. Community is often self-defined, but general categories of community include geographic community, a community of individuals with a common problem or issue, or a community of individuals with a common interest or goal.

Where research is being conducted in communities, investigators are encouraged to involve members of the community in the research process, including the design and implementation of research and the dissemination of results when appropriate.

The most significant community involvement is in a subset of CBR called Community Based Participatory Research (CBPR) where there is an equal partnership between academic investigators and members of a community, with the community members actively participating in all phases of the research process, including the design and implementation of research and the dissemination of results when appropriate.

Questions to be considered as CBR studies are developed, and issues that the IRB considers when reviewing CBR include, but are not limited to:

- How is the community involved or consulted in defining the need for the proposed research (i.e., getting the community’s agreement to conduct the research)?
- How is the community involved or consulted in generating the study research plan?
- How are research procedures, including recruitment strategies and consent processes assessed to ensure sensitivity and appropriateness to various communities (e.g., literacy issues, language barriers, cultural sensitivities, etc.)?
• How is the community involved in the conduct of the proposed research?
• How are community members who participate in the implementation of the research trained and supervised?
• How have “power” relationships between investigators and community members on the research team, and in recruitment strategies been considered to minimize coercion and undue influence?
• What are the risks and benefits of the research for the community as a whole?
• How are boundaries between multiple roles (e.g., investigator, counselor, peer) be maintained, i.e., what happens when the investigator/research staff is the friend, peer, service provider, doctor, nurse, social worker, educator, funder, etc.)?
• How are research outcomes disseminated to the community?
• Is there a partnership agreement or memorandum of understanding signed by UMMC or the UMMC investigator and the community partner(s) that describes how they work together?

27.9 Department of Defense

Research conducted or supported by the Department of Defense (DoD Research) is reviewed and conducted in compliance with part 219 of title 32 CFR, part 980 of title 10 USC, applicable parts of title 21 CFR (50, 56, 312, 600, 812), DoD Instruction 3216.02, DoD Directive 3210.07, and applicable additional requirements from respective DoD component(s). Support of a study generally means the provision of funding, personnel (both military and civilian DoD employees), facilities, and any other resources.

DoD components (e.g., Army, Navy) may have additional requirements. The investigator should contact the Human Research Protection Official (HRPO) for the DoD Component conducting or supporting the research to confirm. In most cases, protocols will also require review, approval and oversight by the DoD component HRPP. DoD review must be conducted before research involving human research participants can begin. The HRPO provides administrative review and approval to confirm the research is compliant with federal and DoD requirements.

UMMC assures that DoD supported research complies with all relevant DoD human subjects protection requirements, including but not limited to:

• The Belmont Report
• Title 32 Code of Federal Regulations Part 219 (32 CFR 219), Department of Defense Regulations, “Protection of Human Subjects” (DoD adoption of the “Common Rule”)
It is the responsibility of the PI to ensure compliance with DoD requirements for human subject protection. IRB staff, chairs and members will use these SOPs, DoDD 3216.02, the DoD Reviewer Checklist, and any relevant DoD component-specific instructions or materials to guide the IRB review and oversight of DoD research.

27.9.1 Key DoD Standards and Requirements

27.9.1.1 Minimal Risk

The definition of minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests” may not be interpreted to include the inherent risks certain categories of human research participants face in their everyday life. For example, the risks imposed in research involving human participants focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

27.9.1.2 Education and Training

All personnel involved in the conduct of DoD research must complete initial and continuing education in the protection of human research participants as described in this manual. Personnel must also familiarize themselves with DoD’s specific requirements by reviewing these SOPs, DoDD 3216.02, and any relevant materials specific to the DoD component. The DoD component may require additional education and/or certification to ensure that personnel are qualified to perform the research. The DoD component may evaluate the training policies of UMMC to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research.

27.9.1.3 Appointment of a Research Monitor

When DoD research involves more than minimal risk, the IRB will require and approve an independent research monitor by name. When research involves no more than minimal risk, an investigator may identify a research monitor, or the IRB or IO may appoint a monitor. There may be more than one research monitor (e.g. if different skills or experience are needed). The monitor may be an ombudsman or a member of the data safety monitoring board.
The IRB must approve a written summary of the monitors’ duties, authorities, and responsibilities and the IRB or a HRPP official shall communicate with research monitors to confirm their duties, authorities, and responsibilities.

The duties of the research monitor are determined on the basis of specific risks or concerns about the research. The monitor:

- May perform oversight functions (e.g. observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and reports of unanticipated problems involving risks to participants or others, oversee data matching, data collection and analysis).
- May discuss the research protocol with researchers, interview human participants, and consult with others outside of the study.
- Research monitors are obligated to promptly report observations and findings to the IRB or other designated official.
- The research monitor has the authority to stop a research study in progress, remove individual participants from the study, and to take whatever steps are necessary to protect the safety and well-being of participants until the IRB can assess the monitor’s report.

27.9.1.4 Additional protections for vulnerable populations

Non-exempt research involving pregnant women, fetuses, or neonates as participants must meet the requirements of Subpart B of the Common Rule, with the following modifications:

- The applicability of Subpart B is limited to non-exempt research involving:
  - Pregnant women as human participants involved in research that is more than minimal risk and that includes interventions or invasive procedures to the woman or the fetus; or
  - Involving fetuses or neonates as participants.
- For purposes of applying Subpart B, the phrase “biomedical knowledge” will be replaced with “generalizable knowledge.”
- Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

Research involving prisoners as participants must meet the requirements of Subpart C of the Common Rule, with the following modifications:

- Research involving prisoners cannot be reviewed by the expedited procedure.
• When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum. The prisoner representative may be a prisoner, an employee of the prison, or an individual not affiliated with the prison.

• In addition to the four allowable categories of research involving prisoners in Subpart C, two additional categories are allowable:
  o Epidemiological research that meets the following criteria:
    ▪ The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.
    ▪ The research presents no more than minimal risk
    ▪ The research presents no more than an inconvenience to the participant.
    ▪ Prisoners are not a particular focus of the research
  o Research that would meet the criteria for exemption described at 32 CFR 219.101(b), can be conducted but must be approved by a convened IRB and meet the requirements of subpart C, DoDD 3216.02, and other applicable requirements.

• When a previously enrolled human research participant becomes a prisoner and the research was not previously approved for the inclusion of prisoners:
  o The PI must promptly notify the IRB.
  o If the PI asserts to the IRB that it is in the best interest of the prisoner to continue to participate in the research while a prisoner, the IRB Chair may determine that the prisoner may continue to participate until the convened IRB can review the request to approve a change in the research protocol and until the IO and DoD Component office review the IRB’s approval to change the research protocol. Otherwise, the IRB Chair will require that all research interactions and interventions with the prisoner (including obtaining identifiable private information) cease until the convened IRB can review the request to approve a change in the research protocol.
  o The convened IRB, upon receipt of notification that a previously enrolled human research participant has become a prisoner, will promptly re-review the research protocol to ensure that the rights and wellbeing of the human participants, now a prisoner, are not in jeopardy. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative. If the prisoner can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner’s confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research from continuing as approved, the convened IRB may approve a change in the study to allow the prisoner to continue to participate in
the research. This approval is limited to the individual prisoner-participant and does not allow recruitment of prisoners as participants.

- This type of request for change in the research protocol cannot be reviewed and approved by expedited review. The research does not have to meet one of the six allowable DoD categories for research involving prisoners.
- UMMC will promptly report all decisions in this matter to the component HRPO. The HRPO must concur with the IRB decisions before the human research participant can continue to participate while a prisoner.

Research involving **Children** as research participants must meet the requirements of Subpart D of the Common Rule, including that:

- The exemption for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

Research involving **Military Personnel** as participants must meet the following requirements:

- Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human participants while on-duty and for approving off-duty employment or activities.
- Superiors (e.g., military and civilian supervisors, unit officers, and noncommissioned officers (NCOs)) are prohibited from influencing the decisions of their subordinates (e.g., junior enlisted personnel and equivalent civilians) regarding participation as participants in research.
- Superiors of Service members (e.g., unit officers, senior NCOs, and equivalent civilians) in the chain of command must not be present at any human participant recruitment sessions or during the consent process in which members of units under their command are afforded the opportunity to participate as research participants. When applicable, the superiors so excluded shall be afforded the opportunity to participate as research participants in a separate recruitment session.
- When research involving Service members is greater than minimal risk and recruitment occurs in a group setting, the IRB will appoint an ombudsman. The ombudsman must not be associated in any way to the research and must be present during the recruitment to monitor that the voluntary involvement or recruitment of the Service members is clearly and adequately stressed and that the information provided about the research is clear, adequate, and accurate. The ombudsman may also be the research monitor.

Research involving **DoD Civilians** as participants must meet the following requirements:
• DoD Civilians must follow their organization’s policies regarding the requirement to obtain permission to participate in research

• Supervisors (e.g., military and civilian supervisors or anyone in the supervisory structure) are prohibited from influencing the decisions of their subordinates regarding participation in research

• Supervisors (e.g., military and civilian supervisors or anyone in the supervisory structure) must not be present at any human research participant recruitment sessions or during the consent process in which DoD civilians under their supervision are afforded the opportunity to participate in the research. When applicable, supervisors so excluded shall be afforded the opportunity to participate in human subjects research in a separate recruitment session

• For research involving civilians as human participants when recruitment occurs in a group setting, the IRB will discuss appointing an ombudsman. The decision to require the appointment of an ombudsman should be based in part on the study population, the consent process, and the recruitment strategy.

Research involving other vulnerable populations must meet the following requirements:

• Investigators, IRBs, and IOs will consider the need for appropriate similar safeguards for other vulnerable populations, such as: research involving human participants and investigators in supervisor-subordinate relationships, human participants with decisional or mental impairments, human participants with a physical disability, or any other kind of human participants in circumstances that may warrant provision of additional protections. As appropriate, qualified individuals (e.g., research monitors, ombudsmen, advocates) may be appointed to perform oversight functions or assist the human participants.

27.9.1.5 Additional Consent Elements

When consent is to be obtained, the following additional elements of consent should be provided to potential participants, when applicable, unless the requirement is waived by the DoD:

1. A statement that the DoD or DoD component is funding the research; and
2. A statement that representatives of the DoD are authorized to review research records.

27.9.1.6 Limitation of Waivers and Exceptions from Informed Consent

For DoD-funded research, if the research meets the definition of “research involving a human being as an experimental subject,” informed consent must be obtained in advance from the research participant or their LAR if the participant is not capable of giving consent. If consent is to be obtained from a LAR, the IRB must determine that the research intends to benefit the individual participant.
The Assistant Secretary of Defense for Research and Engineering may waive the requirements for consent when all of the following are met:

1. The research is necessarily to advance the development of a medical product for the Military Services;
2. The research may directly benefit the individual experimental participant; and
3. The research is conducted in compliance with all other applicable laws and regulations.

Research involving a human being as an experimental subject is an activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. If the research participant does not meet the definition of “experimental subject,” policies and procedure allow the IRB to waive the consent process.

For classified research, waivers of consent are prohibited.

An exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of Defense.

27.9.1.7 Limitations on Compensation for Human Research Participants

DoDD 3216.02 describes allowable and prohibited compensation for human research participants in DoD research and for Federal personnel such as civil servants and Service members. These provisions are intended to ensure compliance with the Dual Compensation Act and 24 U.S.C. 30.

- Federal personnel while on duty and non-Federal personnel may be compensated for blood collections for research up to $50 for each blood collection
- Federal personnel are prohibited from receiving pay or compensation for research during duty hours (except for blood collection as noted above)
- Non-Federal personnel may be compensated for research participation other than blood collections in a reasonable amount, as approved by the IRB according to local prevailing rates and the nature of the research
- Federal personnel may be compensated for research if the participant is involved in the research when not on duty in the same way as human participants who are not Federal personnel (i.e., compensated for participation in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research). However, payment to off-duty Federal personnel for research participation other than blood draws must not be directly from a Federal source (payment from a Federal contractor or other non-Federal source is permissible)

Additional detail is available in DoDD 3216.02 or by consulting the component HRPO.
27.9.1.8 Reporting Requirements

The Institution must promptly (no longer than within 30 days) notify the HRPO of the following: when significant changes to the research protocol are approved by the IRB, the results of the IRB continuing review, if the IRB used to review and approve the research changes to a different IRB, when the institution is notified by any Federal department or agency or national organization that any part of its HRPP is under investigation for cause involving a DoD-supported research protocol, and all unanticipated problems involving risks to participants or others, suspensions, terminations, and serious or continuing noncompliance regarding DoD-supported research involving human research participants.

27.9.1.9 Recordkeeping Requirements

Recordkeeping requirements for DOD-supported human subjects research extend beyond the Common Rule’s requirement. DOD may require submitting records to DOD for archiving. Investigators should consult with the HRPO regarding record-keeping requirements for their research.

Records must be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component. The fact that DoD may inspect records should be disclosed in the consent process.

27.9.1.10 Addressing and Reporting Allegations of Non-Compliance with Human Research Protections

UMMC must report the initiation of all investigations of allegations of non-compliance and report the results of all such investigations (regardless of the findings) to the HRPO.

27.9.1.11 Addressing and Reporting Allegations of Research Misconduct

UMMC will adhere to the requirements of DODD 3210.7 and the terms of any DoD award when allegations or findings of research misconduct arise.

27.9.1.12 Prohibition of Research with Detainees

UMMC does not engage in research involving DoD detainees.

27.9.1.13 Classified research

UMMC does not engage in classified research.

27.9.1.14 Additional Requirements for DoD Research

IRB review must consider the scientific merit of the research. The IRB may rely on outside experts to provide an evaluation of scientific merit.
When conducting research with international populations, additional safeguards for research conducted with international populations the organization or researcher must have permission to conduct research in that country by certification or local ethics review. Researchers must follow all local laws, regulations, customs, and practices.

Disclosure regarding the provisions for research-related injury must follow the requirements of the DoD component.

Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD component HRPO after the research protocol is reviewed by the IRB. When a survey crosses DoD components, additional review may be required by DoD.

When any institution relies upon another institution’s IRB for DoD research, there must be a written agreement defining the responsibilities and authorities of each organization in complying with the terms of each institution’s Federal assurance and DoDD 3216.02.

When conducting multi-site or collaborative research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.

Civilian researchers attempting to access military participants should seek collaboration with a military researcher familiar with service-specific requirements.

27.10 Department of Education

The U.S. Department of Education (ED) is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 34 CFR 97. Research conducted or supported by ED is reviewed by the UMMC IRB in accordance with the Common Rule as described throughout this manual with the following variations and additional requirements.

ED has not adopted Subpart B (Pregnant Women, Fetuses, or Neonates) or Subpart C (Prisoners) of the Common Rule.

ED requires reporting of alleged (1) unanticipated problems involving risks to subjects or others; and, (2) serious or continuing noncompliance with the Common Rule or Subpart D (protection of children in research). Other mandated reports, as described in Section 20, are submitted to ED instead of OHRP when the research is funded or sponsored by ED. When applicable, UMMC will follow the directions for incident reporting provided on ED’s Protection of Human Subjects in Research website.

27.10.1 Family Educational Rights and Privacy Act (FERPA)

The Family Educational Rights and Privacy Act (FERPA) is a Federal law that protects the privacy of student education records at educational entities that receive funds from the ED. In general, schools must have written permission from the parent or eligible student to release any information from a student’s education record. However, FERPA allows schools to 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:

1. Develop, validate, or administer predictive tests;
2. Administer student aid programs; or
3. Improve instruction. [34 CFR 99.31(a)(6)]

A written agreement with the receiving organization is required, including:

1. The purpose, scope, and duration of the study(ies);
2. The information to be disclosed;
3. A requirement that the receiving organization uses the personally identifiable information from the educational records only for the purpose(s) of the study as stated in the agreement;
4. A requirement that the receiving organization conducts the study in a manner that does not permit personal identification of students and parents by anyone other than representatives of the organization with legitimate interests; and
5. A requirement that the receiving organization destroys or returns all personally identifiable information when the information is no longer needed for the purposes for which the study was conducted and that specified the time period in which the information must be returned or destroyed.

Education records may be released without consent under FERPA if all personally identifiable information has been removed including:

1. Students’ names and other direct identifiers, such as students’ Social Security Numbers or student numbers;
2. Indirect identifiers, such as the name of students’ parents or other family members, the students’ or families addresses, and personal characteristics or other information that would make the students’ identities easily traceable, and dates and places of birth and mothers’ maiden names;
3. Biometric records, including 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; and
4. Other information that, alone, or in combination, is linked or linkable to a student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify to student with reasonable certainty.

At UMMC, when FERPA applies, investigators must provide the IRB with information describing how they will ensure compliance with the rule. A letter of support or other documentation from the school supporting the conduct of the research should be provided. The IRB will review
the information provided to verify compliance, including verification that permission for the use of the records will be obtained or that it is not required under an allowed use or exception.

27.10.2 Protection of Pupil Rights Amendment (PPRA)

The Protection of Pupil Rights Amendment (PPRA) affords parents of elementary and secondary students certain rights regarding the conduct of survey, collection and use of information for marketing purposes, and certain physical exams. PPRA applies to the programs and activities of a state educational agency (SEA), local educational agency (LEA), and any other recipient of ED funds. These rights transfer from parents to students when students reach the age of 18 or are an emancipated minor. This section is not intended to comprehensively address PPRA, rather it addresses PPRA requirements as they most commonly relate to research.

27.10.2.1 Definitions:

Instructional Material means instructional content that is provided to a student, regardless of its format, including printed or representational materials, audio-visual materials, and materials in electronic or digital formats (such as materials accessible through the Internet). The term does not include academic tests or academic assessments.

Invasive Physical Examination means any medical examination that involves the exposure of private body parts, or any act during such examination that includes incision, insertion, or injection into the body, but does not include a hearing, vision, or scoliosis screening.

Personal Information means individually identifiable information including: (1) a student’s or parent’s first and last name; (2) a home or other physical address (including a street name and the name of a city or town); (3) a telephone number; or, (4) a Social Security Number.

Research or Experimentation Program or Project means any program or project in any program that is designed to explore or develop new or unproven teaching methods or techniques.

27.10.2.2 Rights under PPRA

When research is funded by ED, no student can be required to submit without prior consent to a survey that concerns one or more of the following protected areas:

1. Political affiliations or beliefs of the student or the student’s parent;
2. Mental and psychological problems of the student or his or her family;
3. Sex behavior and attitudes;
4. Illegal, anti-social, self-incriminating, and demeaning behavior;
5. Critical appraisals of other individuals with whom the student has close family relationships;
6. Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers;
7. Religious practices, affiliations, or beliefs of the student or student’s parent; or
8. Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.

Parents have the right to receive notice and an opportunity to opt a student out of:

1. Any other survey that concerns any of the above protected areas, regardless of funding;
2. Any non-emergency, invasive physical exam or screening required as a condition of attendance, administered by the school or its agent, that is not necessary to protect the health and safety of a student, except for hearing, vision, or scoliosis screenings, or any physical exam or screening permitted or required under state law; and
3. Activities involving collection, disclosure, or use of personal information collected from students for marketing or to sell or otherwise distribute the information to others. (This does not apply to the collection, disclosure, or use of personal information collected from students for the exclusive purpose of developing, evaluating, or providing educational products or services for, or to, students or educational institutions.)

Parents also have the right to inspect upon request and before administration or use:

1. Surveys that concern any of the protected areas and surveys created by third parties;
2. Instruments used to collect personal information from students for any of the above marketing, sales, or other distribution purposes;
3. Any instructional material used as part of the educational curriculum for the student; and
4. Instructional material, including teachers’ manuals, films, tapes, or other supplementary instructional material, which will be used in conjunction with any research or experimentation program or project.

27.10.2.3 Procedures

At UMMC, when PPRA applies, investigators should review the school’s PPRA policies and must provide the IRB with information describing how they will ensure compliance with the rule and the school’s policies. A letter of support or other documentation from the school supporting the conduct of the research and its compliance with PPRA should be provided. The IRB will review the information provided to verify compliance.

27.11 Department of Energy

The U.S. Department of Energy (DOE) is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 10 CFR 795. Research conducted or supported by
DOE, or performed in DOE facilities, is subject to additional requirements for investigators and for reviewing IRBs. These requirements are outlined in this section.

DOE Order 443.1B Chg 1 establishes DOE-specific policy and principles for the protection of human research participants. DOE Notice 443.1 outlines requirements that must be met for classified research. DOE provides additional resources on its website that investigators and IRBs may also find helpful.

UMMC’s IRB will review DOE research in accordance with the Common Rule and applicable DOE-specific requirements.

### 27.11.1 Definitions

DOE expands upon the definitions provided in the Common Rule with the following additional or modified definitions:

**Adverse Event.** Any unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subjects participation in the research, whether or not considered related to the subject’s participation in the research. A significant adverse event is an adverse event that is unexpected and substantively impacts the human subjects.

**De-identified Data.** A data set that has no, or limited, identifiers and for which a person with current knowledge of generally accepted scientific principles determines that the risk that the information could be used, alone or in combination with other reasonably available information, by an anticipated recipient, to identify an individual who is a subject of the information, has been reduced to the extent practicable. A graded approach must be used in balancing de-identification of the datasets and the usability of the dataset to accomplish the needed research.

**Generalizable.** Information/research findings that can be applied to populations or situations beyond that studied.

**Personally Identifiable Information (PII).** Any information collected or maintained about an individual, including but not limited to, education, financial transactions, medical history and criminal or employment history, and information that can be used to distinguish or trace an individual’s identity, such as his/her name, Social Security number, date and place of birth, mother’s maiden name, biometric data, and any other personal information that is linked or linkable to a specific individual.

**Research.** A systematic investigation, including research development, testing and evaluation, designed to contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported
under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

**Unanticipated Problem.** In general, to be classified as an unanticipated problem, any incident, experience, or outcome should meet all three of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied
2. Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research)
3. Likely to place subjects or others at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

### 27.11.2 Human Subjects Research

DOE requires that the following activities are managed as Human Subjects Research and require IRB review:

1. Generalizable studies in human environments (e.g., occupied homes and offices, classrooms, and transit centers like subway systems and airports) that use tracer chemicals, particles, and/or other materials, such as perfluorocarbons, to characterize airflow;
2. Generalizable studies in occupied homes and/or offices that:
   a. Manipulate the environment to achieve research aims (e.g., increasing humidity and/or reducing influx of outside air through new energy-saving ventilation systems);
   b. Test new materials (e.g., sequentially changing the filter materials in the HVAC system while monitoring the effects on air quality and energy use); or
   c. Collect information on occupants’ views of appliances, materials, or devices installed in their homes or their energy saving behaviors through surveys and focus groups. Some surveys may be online surveys administered through providers such as Amazon Mechanical Turk and Survey Monkey;
3. Human Terrain Mapping (HTM) – HTM is defined by DOE as research and data gathering activities primarily conducted for military or intelligence purposes to understand the “human terrain,”—the social, ethnographic, cultural, and political elements of the people among whom the U.S. Armed Forces are operating and/or in countries prone to political instability. This work includes observations, questionnaires, and interviews of groups of individuals, as well as modeling and analysis of collected data, and may
become the basis for U.S. military actions in such locations. In addition to HTM, such activities are often referred to as human social culture behavior (HSCB) studies.

27.11.3 Protection of Data

Research involving human participants must also comply with Federal and DOE-specific requirements for protecting Personally Identifiable Information (PII) as defined above.

Requirements include:

1. Keeping PII confidential;
2. Releasing PII only under a procedure approved by the responsible IRB and DOE;
3. Using PII only for purposes of the IRB-approved project; handling and marking documents containing PII as “containing PII or containing Protected Health Information (PHI)”;
4. Establishing and documenting safeguards to prevent unauthorized use or disclosure of PII and PHI;
5. Protecting PII stored on removable media using encryption procedures that are compliant with Federal standards (FIPS-140-2 certified);
6. Sending removable media containing PII by express overnight service with signature and tracking capability;
7. Sending passwords to encrypted files separately from the files; and
8. Using 2-factor authentication for log-on access for remote systems.

UMMC has established standards and safeguards to protect patient information and to ensure compliance with federal and state information security regulations. It is the responsibility of investigators to familiarize themselves with and comply with these standards. The use of personal laptops, desktops, portable/USB drives, and other non-UMMC devices for storage of research data is discouraged. When a non-UMMC computer or device must be used for the purposes of storing, even temporarily, or transmitting PHI or PII (Personally Identifiable Information) for research, a Policy Exception Agreement form should be completed. Additionally, any potential or known breach of a device or of research data must be reported immediately upon discovery to the IRB, the Office of Information Security and the Office of Integrity and Compliance so that appropriate steps can be taken to assess the situation, protect the information, and comply with regulations. Lost or stolen UMMC devices must also be reported to Campus Police.

Provisions for Data Security must be described in applications to the IRB and updated as necessary. When information containing direct identifiers such as Social Security numbers or PHI including data considered sensitive is to be transferred outside of the institution, the
provisions for data security may be subject to further review and approval by the Information Security Director.

See the UMMC policies on Patient Privacy and Information Security for further information.

Loss or suspected loss of PII/PHI must be reported immediately upon discovery, (as soon as aware of incident), to the: (1) DOE Program Manager or the DOE funding office HSP Program Manager, or the DOE-CIRC (866-941-2472, www.doeirc.energy.gov) if the DOE Program Manager is unreachable.

27.11.4 Classified Research

UMMC does not conduct classified DoE research.

27.11.5 DOE Employees, Contractors, and Students

DOE considers DOE personnel (employees, contractors, and students) to be vulnerable to pressures to cooperate with research conducted by their managers and/or coworkers. When the UMMC IRB reviews such research, it will consider whether the proposed plan for the recruitment, consent, and ongoing participation adequately protects vulnerable populations as described in Section 14.3. Additionally, it will consult with the DOE HSP to determine whether there are any DOE site-specific requirements that should be taken into consideration.

27.11.6 Reporting Requirements

In addition to the reporting requirements outlined throughout this manual, investigators must report the following within 48 hours to the IRB and the DOE (or NNSA) HSP Program Manager when conducting DOE research:

1. Any significant adverse events, unanticipated problems, and complaints about the research;
2. Any non-compliance with applicable regulations, IRB requirements, DOE HSP (or NNSA) program procedures or other requirements; and
3. Any suspension or termination of IRB approval.

Investigators must immediately (as soon as aware) report any finding of a suspected or a confirmed data breach involving PII as outlined in Section 26.10.3. Reports should include a description of any corrective actions to be taken. The HSP (or NNSA) Program Manager and IRB will review the report and may accept or modify the corrective action plan and take any other actions necessary to ensure the protection of human research participants and the integrity of the research.
DOJ IS NOT A SIGNATORY TO THE REVISED COMMON RULE. PER NOTICE ON NIJ’S WEBSITE, DOJ IS CONSIDERING NEXT STEPS. APPLICANTS ARE ADVISED TO MONITOR AND FOLLOW THE INSTRUCTIONS ON THIS WEBSITE.

The U.S. Department of Justice (DoJ) is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 28 CFR 46; however, DOJ has chosen not to adopt Subparts B, C and D. The National Institute of Justice (NIJ) serves as DoJ’s research arm. Confidentiality regulations for DoJ/NIJ research are described at 28 CFR 22. Research conducted within the Federal Bureau of Prisons is subject to the requirements described at 28 CFR Part 512.

This section summarizes additional requirements for the conduct and IRB review of human subjects research conducted or supported by DoJ/NIJ (including funding through grants, subgrants, contracts, subcontracts, cooperative agreements, and interagency agreements) and human subjects research conducted in the Federal Bureau of Prisons.

27.12.1 Principal Investigator Responsibilities

In addition to complying with the Common Rule requirements outlined by DoJ at 28 CFR 46, investigators conducting research supported by DoJ/NIJ have the following responsibilities:

1. Submit a Privacy Certificate to NIJ to document understanding of investigator’s obligations under the confidentiality regulations found in 28 CFR 22. NIJ provides guidelines for the certificate on its website;

2. Comply with the requirements of the Privacy Certificate, including the requirement to obtain separate written consent for the reporting of domestic, child, or elder abuse;

3. Inform participants (in the confidentiality section of the consent form) that private, identifiable information will be kept confidential and will only be used for research and statistical purposes. If, due to sample size or some unique feature, the identity of the individual cannot be maintained, the participant need to be explicitly notified. If the investigator intends to disclose any information, the participant needs to be explicitly informed what information would be disclosed, under what circumstances, and to whom. The participant must be informed of any potential risks which may result from this disclosure and must explicitly provide prior written consent;

4. When applicable, disclose in the consent form that the research is funded by DoJ/NIJ;

5. Submit a copy of the IRB approval as well as supporting documentation of the IRB’s institutional affiliation, assurance, etc. to the NIJ prior to initiation of any research activities that are not exempt from the requirements of 28 CFR 46; or Submit supporting documentation of the IRB’s determination that the research qualifies for exemption under 28 CFR 46.101(b);
6. Comply with NIJ’s policy for the protection of the privacy and well-being of participants in NIJ research studies through the statutory protection provided to private information under the authority of 42 U.S.C. § 3789g and the other DOJ regulations on the Confidentiality of Identifiable Research and Statistical Information found in 28 CFR 22;  

7. Sign and maintain an Employee Confidentiality Statement for themselves and their research staff. A model employee confidentiality statement can be found at https://www.nij.gov/funding/humansubjects/employee-confidentiality.htm; and  

8. Send a copy of all de-identified data, including copies of the informed consent document, data collection instruments, surveys and other relevant research materials to the National Archive of Criminal Justice Data.

27.12.2 Bureau of Prisons  
UMMC does not conduct research within the Federal BOP.

27.13 Environmental Protection Agency  
The Environmental Protection Agency (EPA) is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 40 CFR 26 (Subpart A). EPA has outlined additional regulations that apply to EPA research in the following subparts:

- **Subpart B** – Prohibition of Research Conducted or Supported By EPA Involving Intentional Exposure of Human Subjects who are Children or Pregnant or Nursing Women  

- **Subpart C** – Observational Research: Additional Protections for Pregnant Women and Fetuses Involved as Subjects in Observational Research Conducted or Supported by EPA  

- **Subpart D** – Observational Research: Additional Protections for Children Involved as Subjects in Observational Research Conducted or Supported by EPA  

- **Subpart K** – Basic Ethical Requirements for Third Party Human Research for Pesticides Involving Intentional Exposure of Non-Pregnant, Non-Nursing Adults  

- **Subpart L** – Prohibition of Third Party Research Involving Intentional Exposure to a Pesticide of Human Subjects who are Children or Pregnant or Nursing Women  

- **Subpart M** – Requirements for Submission of Information on the Ethical Conduct of Completed Human Research  

- **Subpart O** – Administrative Actions for Noncompliance  

- **Subpart P** – Review of Proposed and Completed Human Research
Subpart Q – Standards for Assessing Whether to Rely on the Results of Human Research in EPA Actions

Additional EPA requirements for human research are outlined in EPA Order 1000.17A “Policies and Procedures on Protection of Human Subjects in EPA Conducted or Supported Research”. EPA regulations and requirements for the protection of human research participants apply to research supported or conducted by the EPA and to research in which the intent is submission of data to the EPA.

UMMC investigators must comply with all applicable EPA requirements in addition to other applicable regulations, policies, and the requirements of the IRB of record. Investigators are responsible for clearly indicating within their IRB application materials that proposed research is subject to EPA regulations and for providing information regarding compliance with EPA requirements. The UMMC IRB will evaluate compliance by consulting this manual, regulations and guidance.

The information provided in this section summarizes key EPA standards and requirements.

27.13.1 EPA Definitions:

**Intentional Exposure** - Research involving intentional exposure of a human participant means the study of a substance in which the exposure to the substance experienced by a human research participant would not have occurred but for participation in the study.

**Observational Research** - Observational research means any human research that does not meet the definition of research involving intentional exposure of a human participant.

**Observational Human Exposure Studies** - As defined in Scientific and Ethical Approaches for Observational Exposure Studies (SEAOES), observational human exposure studies are studies that involve the collection of environmental samples, data, and information from study participants in their everyday environments as they go about their normal activities. They involve neither the deliberate exposure of participants nor the control of environmental conditions in a way that impacts the participants’ naturally occurring exposures.

**Pesticide** - Pesticide means any substance or mixture of substances meeting the definition in 7 U.S.C. 136(u) (Federal Insecticide, Fungicide, and Rodenticide Act, section 2(u)).

**Substance** – A substance includes any chemical, biological organism, or physical property tracked or regulated by the EPA or identified in an environmental statute. The Substance Registry Services (SRS) is the EPA’s central system for information about substances tracked or regulated by EPA.

**Assent** - Assent means a minor participant’s affirmative agreement to participate in research. Absent affirmative agreement, mere failure to object should not be construed as assent.
Child – A child is a person who has not attained the age of 18.

Guardian - Guardian means an individual who is authorized under applicable State, Tribal, or local law to give permission on behalf of a child to general medical care.

Parent - Parent means a child's biological or adoptive parent.

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

### 27.13.2 EPA Human Subjects Research Review Official (HSRRO) Approval

All human subjects research conducted or supported by EPA must either be approved or be acknowledged as exempt research by the EPA Human Subjects Research Review Official (HSRRO) before any work involving human participants can begin. Preliminary review by the HSRRO can be requested for any research project, contract, grant application, cooperative agreement, cooperative research and development agreement (CRADA), interagency agreement or any formal agreement involving EPA support of such studies. However, preliminary review is not required for any project, and if provided does not substitute for approval following IRB review.

To obtain approval or a concurrence of exemption by the HSRRO, researchers must submit the IRB-approved research package or documentation of exemption, including evidence of IRB approval and any correspondence between the IRB and the researchers. Researchers must also provide evidence of a Federalwide Assurance (FWA) on file with the U.S. Department of Health and Human Services (HHS) or other agency that their institution or organization will comply with regulatory provisions in the Common Rule. Upon approval or concurrence the investigator must submit documentation to the UMMC IRB with an amendment in the IRB’s electronic submission system.

### 27.13.3 PI Reporting Requirements

After research is approved, PIs are responsible for notifying EPA and the HSRRO (and HSO where applicable) of IRB suspension or termination of the research, of Unanticipated Problems Involving Risk to Subjects or Others that the IRB deems reportable, and any event that is significant enough to result in the removal of a subject from the study. In addition, for grantees of EPA, the PI must notify his/her Project Officer promptly, according to the terms specified by the IRB of record for the project.

### 27.13.4 Intentional Exposure

EPA outlines requirements and restrictions applicable to research involving intentional exposure to substances or pesticides in the following subparts:
Subpart B prohibits research involving intentional exposure (see definition above) of pregnant women, nursing women, or children.

Subpart L explicitly extends the prohibition to include intentional exposure of pregnant women, nursing women, or children to a pesticide.

Subpart K describes the requirements for third-party research involving intentional exposure of non-nursing, non-pregnant adults to substances and pesticides.

Among other provisions, Subpart K requires that:

1. Informed consent is obtained from participants (there is no provision for LARs or for waiver or alteration of consent);
2. Informed consent must be documented using a written consent form or short form method (there is no provision for waiver of documentation of consent);
3. If the research involves intentional exposure to a pesticide, the prospective participant must be informed of the identity of the pesticide and the nature of its pesticidal function (as an element of consent); and
4. The proposed research must be submitted to the EPA for approval after approval by the IRB(s). The submission requirements are outlined in §26.1125.

27.13.5 Observational Research

EPA outlines requirements and restrictions applicable to observational research involving in the following subparts:

Subpart C describes the rules that apply to observational research conducted or supported by EPA that involves pregnant women (and thus their fetuses). In summary, such research is subject to the Common Rule Subpart B requirements stipulated at 45 CFR 46.203 (Duties of IRBs), 45 CFR 46.204 (Research Involving Pregnant Women or Fetuses), and 45 CFR 46.206 (Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material).

Subpart D describes the rules that apply to observational research conducted or supported by EPA that involves children. In summary, the subpart stipulates that IRBs may only approve (and that EPA will only fund or conduct) research that satisfies all applicable conditions outlined in the subpart, including that:

1. EPA will conduct or fund observational research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §26.406.
2. EPA will not conduct or fund observational research that involves an intervention or procedure that involves greater than minimal risk to children unless the IRB finds and documents that:
   a. The intervention or procedure holds out the prospect of direct benefit to the individual participant or is likely to contribute to the participant's well-being;
   b. The risk is justified by the anticipated benefit to participants;
   c. The relation of the anticipated benefits to the risks is at least as favorable to the participants as that presented by available alternative approaches; and
   d. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §26.406.

3. §26.406 describes the requirements for permission from parents (or guardians) and for assent from children. The EPA requirements are consistent with the requirements outlined in §46.408 of 45 CFR 46. For each of the allowable categories (above) of observational research involving children, the IRB may determine that the permission of one parent is sufficient.

27.13.6 Observational Human Exposure Studies

All human observational exposure studies conducted or supported by EPA will adhere to the principles set forth in SEAOES. SEAOES addresses six major topic areas:

1. Identifying elements to be considered in study conceptualization;
2. Ensuring protection of vulnerable groups;
3. Addressing privacy and other concerns related to observational human exposure studies;
4. Creating an appropriate relationship between the participant and investigator;
5. Building and maintaining appropriate community and stakeholder relationships; and
6. Designing and implementing strategies for effective communication.

27.13.7 Other EPA Regulations

Subpart M describes the requirement for submission of information about the ethical review and conduct of research whenever a report containing the results of the research is submitted to the EPA for consideration in connection with actions that may be performed by EPA.

Subpart O describes the actions that EPA may take when they find that an IRB, institution, or investigator are not compliant with EPA’s requirements.
Subpart P describes the requirements and procedures for EPA’s and EPA’s Human Studies Review Board review of proposed and completed human research under §26.1125 and §26.1701.

Subpart Q describes the standards EPA applies in deciding whether to rely upon the results of research involving intentional exposure to substances or pesticides in EPA actions.

27.14 ICH-GCP E6

When UMMC commits to comply with ICH-GCP E6 as a term of a grant or contract, investigators and the IRB take on additional responsibilities. Investigators are responsible for clearly indicating within their IRB application materials that proposed research is subject to ICH-GCP E6 and for attesting to compliance with ICH-GCP E6 requirements. The UMMC IRB will evaluate compliance by consulting the current ICH-GCP E6 guidance posted by the FDA on its website. UMMC does not require or evaluate compliance with ICH-GCP E6 requirements that are not consistent with FDA regulations (for example, requiring the reporting to the IRB of all adverse drug reactions that are both serious and unexpected instead of requiring the reporting of unanticipated problems involving risks to subjects or others).

27.14.1 IRB Responsibilities

1. An IRB should safeguard the rights, safety, and well-being of all trial participants. Special attention should be paid to trials that may include vulnerable participants;

2. The IRB should obtain the following documents:
   a. Trial protocol(s)/amendment(s);
   b. Written informed consent form(s) and consent form updates that the investigator proposes for use in the trial;
   c. Participants recruitment procedures and materials (e.g., advertisements);
   d. Written information to be provided to participants;
   e. Investigator’s Brochure (IB) and available safety information;
   f. Information about payments and compensation available to participants;
   g. Any other documents that the IRB may need to fulfil its responsibilities.

3. The IRB should review a proposed clinical trial within a reasonable time and document its views in writing, clearly identifying the trial, the documents reviewed and the dates that actions were taken;

4. The IRB should consider the qualifications of the investigator for the proposed trial;

5. The IRB should conduct continuing review of each ongoing trial at intervals appropriate to the degree of risk to human participants, but at least once per year;

6. The IRB may request more information than is required by regulation or the ICH-GCP E6 guidance be given to participants when, in the judgment of the IRB, the additional
information would add meaningfully to the protection of the rights, safety, and/or well-being of the participants;

7. When a nontherapeutic trial is to be carried out with the consent of the participant’s LAR, the IRB should determine that the proposed protocol and/or other document(s) adequately addresses relevant ethical concerns and meets applicable regulatory requirements for such trials;

8. Where the protocol indicates that prior consent of the trial participant or the participant’s LAR is not possible, the IRB should determine that the proposed protocol and/or other document(s) adequately addresses relevant ethical concerns and meets applicable regulatory requirements for such trials (i.e., in emergency situations);

9. The IRB should review both the amount and method of payment to participants to assure that neither presents problems of coercion or undue influence on the trial participants. Payments should be prorated and not wholly contingent on completion of the trial by the participant; and

10. The IRB should ensure that information regarding payment to participants, including the methods, amounts, and schedule of payment, including the specific way payment will be prorated, is set forth in the written informed consent form.

27.14.2 Investigator Responsibilities

1. The investigator(s) should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirement(s), and should provide relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities;

2. The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator’s Brochure, in the product information, and in other information sources provided by the sponsor;

3. The investigator should be aware of, and should comply with GCP and applicable regulatory requirements;

4. The investigator should permit monitoring and auditing by the sponsor, and inspection by appropriate regulatory authorities;

5. The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties;

6. The investigator must have adequate resources to conduct the trial, including:
   a. Being able to demonstrate (e.g., based on retrospective data) the potential for recruiting the required number of participants within the agreed upon recruitment period;
   b. Sufficient time to properly conduct and complete the trial within the agreed trial period;
c. Adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely; and

d. Ensuring that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions;

7. The investigator is responsible for supervising any individual or party to whom the investigator delegates trial-related duties and functions conducted at the trial site;

8. If the investigator retains the services of any individual or party to perform trial-related duties and functions, the investigator should ensure this individual or party is qualified to perform those trial-related duties and functions and should implement procedures to ensure the integrity of the trial-related duties and functions performed and any data generated;

9. A qualified physician (or dentist, when appropriate), who is an investigator or sub-investigator on the trial, should be responsible for all trial-related medical (or dental) decisions;

10. During and following a participant’s participation in a trial, the investigator should ensure that adequate medical care is provided for any adverse events, including clinically significant laboratory values, related to the trial. The investigator should inform a participant when medical care is needed for intercurrent illness(es) of which the investigator becomes aware;

11. The investigator should inform the participant’s primary physician about the participant’s participation in the trial if the participant has a primary physician and agrees to the primary physician being informed;

12. Although a participant is not obliged to give his/her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject’s rights;

13. Before initiating a trial, the investigator must have written and dated approval/favorable opinion from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects;

14. As part of the investigator’s application to the IRB, the investigator should provide the IRB with a current copy of the Investigator’s Brochure (IB). If the IB is updated during the trial, the investigator should supply a copy of the updated IB to the IRB;

15. During the trial the investigator should provide to the IRB all documents subject to review;

16. The investigator should sign the protocol, or an alternative contract, to confirm his/her agreement to comply with the approved protocol;
17. The investigator may not implement any deviation from, or changes of, the protocol without agreement by the sponsor and prior review and documented approval from the IRB, except where necessary to eliminate an immediate hazard(s) to trial participants;

18. In addition to reporting to the IRB, when the investigator implements a deviation from or change in the protocol to eliminate an immediate hazard(s) to subject(s) without prior approval, this must be reported as soon as possible to the sponsor;

19. The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol;

20. The investigator is ultimately responsible for investigational product accountability and for all of the responsibilities for investigational product outlined in section 4.6 of ICH-GCP E6;

21. The investigator should follow the trial’s randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor (and IRB) any premature unblinding;

22. Additional requirements for Informed Consent
   a. The written informed consent form and any other written information to be provided to participants should be revised whenever important new information becomes available that may be relevant to the participant’s consent. Any revised written informed consent form, and written information should receive the IRB’s approval in advance of use. The participant or the participant’s LAR should be informed in a timely manner if new information becomes available that may be relevant to the participant’s willingness to continue participation in the trial. The communication of this information should be documented;
   b. The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the participant or the participant’s LAR;
   c. Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the participant or the participant’s LAR ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the participant or the participant’s LAR;
   d. Neither the investigator, nor the trial staff, may coerce or unduly influence a participant to participate or to continue to participate in a trial;
   e. Prior to a participant’s participation in the trial, the written informed consent form should be signed and personally dated by the participant or by the participant’s LAR, and by the person who conducted the informed consent discussion;
f. Prior to participation in the trial, the participant or the participant's LAR should receive a copy of the signed and dated written informed consent form and any other written information provided to the participants. During a participant's participation in the trial, the participant or the participant's LAR should receive a copy of the signed and dated consent form updates, if applicable, and a copy of any amendments to the written information provided to participants;

g. If a participant, or participant’s LAR if applicable, is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to participants is read and explained to the participant or the participant’s LAR, and after the participant or the participant’s LAR has orally given consent to the participant’s participation in the trial, and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant or the participant’s LAR and that informed consent was freely given by the participant or the participant’s LAR.

h. Consent for non-therapeutic trials (i.e., a trial in which there is no anticipated direct clinical benefit to the participant) must be obtained from participants who personally give consent and who sign and date the written informed consent form unless the IRB has expressly approved, in writing, that consent from a LAR is permitted;

i. The consent discussion and written informed consent form should include the following additional elements:

   i. An explanation of the trial treatment(s) and the probability for random assignment to each treatment;

   ii. An explanation of the participant’s responsibilities (avoiding any language that appears to restrict participant’s rights);

   iii. An explanation that the monitor(s), auditor(s), the IRB, and the regulatory authorities will be granted direct access to the participant’s original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or LAR is authorizing such access;

   iv. An explanation of the anticipated prorated payment, if any, to the participant for participating in the trial;
v. An explanation of the reasonably foreseeable risks or inconveniences to the participant and, when applicable, to an embryo, fetus, or nursing infant;

vi. When there is no intended clinical benefit to the participant, the participant should be made aware of this;

vii. An explanation that, to the extent permitted by applicable laws or regulations, records identifying the participant will not be made publicly available, and, if the results of the trial are published, the participant’s identity will remain confidential; and

eight. A statement that the trial has been reviewed by the IRB.

23. Investigators must comply with the requirements for records and reports outlined in section 4.9 and 8 of ICH-GCP E6;

24. Investigators must comply with the requirements for safety reporting outlined in Section 4.11 of ICH-GCP E6 including the redaction of personally identifying information; and

25. Investigators must comply with the requirements for premature termination or suspension of a trial outlined in section 4.12, including the requirements for sponsor and IRB reporting.

27.15 Transnational Research

The UMMC IRB reviews transnational research involving human participants to ensure adequate provisions are in place to protect the rights and welfare of the research participants. All policies and procedures that are applied to research conducted domestically are applied to international settings, as appropriate. Approval of research is permitted if “the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in 45 CFR 46.”

For Federally funded or supported research, approval of research for foreign institutions or sites “engaged” in research is only permitted if the foreign institution or site holds a FWA with OHRP and local IRB review and approval is obtained.

Approval of research for foreign institutions or sites “not engaged” in research is only permitted if one or more of the following circumstances exist:

- When the foreign institution or site has an established IRB/IEC, the investigator must obtain approval to conduct the research at the "not engaged" site from the site’s IRB/IEC or provide documentation that the site’s IRB/IEC has determined that approval is not necessary for the investigator to conduct the proposed research at the site.
- When the foreign institution or site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials permit the research to be conducted at the performance site.
• IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the performance site’s IRB/IEC determination, or letter of cooperation, as applicable.

The UMMC IRB seeks sufficient knowledge of the local research context by requesting approval for the project from local IRBs or ethics committees (which may or may not be OHRP-registered) and/or local letters of support. The source of this information depends on the nature of the study, the country and the resources available to the investigator. Where there is a local IRB/IEC, UMMC’s IRB must receive and review the foreign institution or site’s IRB/IEC review and approval of each study prior to beginning the research at the foreign institution or site. When appropriate, the IRB communicates and coordinates with the local institutions or ethics committees.

In settings where there are no IRBs/IECs, UMMC’s IRB may require additional verification and information from people outside the particular research project who are familiar with the customs, practices, or standards of care where the research takes place, including other IRBs or committees with experience reviewing research in the region, other UMMC investigators with knowledge of the region, or a consultant who is an expert on the region, prior to approval. These individuals may either provide a written review of a particular research plan or attend an IRB meeting to provide the UMMC IRB with recommendations based on his or her expertise.

27.15.1.1 IRB Responsibilities

In addition to the IRB review considerations discussed elsewhere in this manual, the IRB considers the following when reviewing transnational research:

1. Qualifications of the investigator and research staff to conduct research in that country, including knowledge of relevant laws, regulations, guidance and customs

2. Whether the consent process and consent documents are appropriate for the language(s) of participants and communication with the participant population and that arrangements are made to be able to communicate with participants throughout the study (e.g., to ask and answer questions)

3. How modifications to the research are handled

4. How complaints, non-compliance, protocol/research plan deviations and unanticipated problems involving risks to participants or others are handled

5. How post-approval monitoring will be managed

6. Whether the investigator has obtained the appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local or tribal).

7. When applicable, whether the investigator has provided an appropriate plan, and any necessary supporting documentation, to comply with the requirements of country law for investigational articles; and

8. Mechanisms for communicating with the investigator and research staff when they are conducting the research in other countries.
27.15.1.2 Investigator Responsibilities

The investigator conducting transnational research is responsible for:

1. Ensuring that the resources and facilities are appropriate for the nature of the research.
2. Verifying the qualifications of the investigators and research staff for conducting research in that country(ies).
3. Obtaining all appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local or tribal).
4. Complying with the requirements of country law; including, when applicable, requirements for research involving investigational articles and requirements for data management and privacy such as **EU GDPR**;
5. Ensuring that the consent process and consent document are appropriate for the language(s) of participants and communication with the participant population and arrangements are made to be able to communicate with participants throughout the study (e.g., to ask and answer questions)
6. Ensuring that the following activities occur:
   a. Initial review, continuing review and amendments
   b. Post-approval monitoring
   c. Handling of complaints, non-compliance and unanticipated problems involving risk to participants or others.
7. Not relying upon an IRB or IEC that does not have policies and procedures for the activities listed above.
8. Ensuring that reportable information such as complaints, non-compliance, protocol deviations and unanticipated problems involving risks to participants or others are communicated to the IRB.
9. Notifying the IRB promptly if a change in research activities alters the performance site’s engagement in the research (e.g., performance site “not engaged” begins to obtain consent of research participants, etc.).
10. Ensuring that there are has mechanisms in place for communicating with the IRB.

27.15.1.3 Consent Documents

The informed consent documents must be appropriate for and in a language understandable to the proposed participants. The IRB will review the proposed document(s) and either a certification of translation or a back translation of the exact content contained in the foreign language informed consent document(s) with the credentials of the translator detailed in the IRB submission. All documents, including verification of the back translation, are part of the IRB file.

27.15.1.4 Monitoring of Approved Transnational Research

The IRB is responsible for the ongoing review of transnational research conducted under its jurisdiction through the continuing review process in accordance with all applicable federal
regulations. When the IRB and a local ethics committee are both involved in the review of research, there is a plan for coordination and communication with the local IRB/IECs.

The IRB requires documentation of regular correspondence between the UMMC investigator and the foreign institution or site and may require verification from sources other than the UMMC investigator that there have been no substantial changes in the research since its last review.

27.16 UMMC Students and Employees as Research Participants

When UMMC students and/or employees are being recruited as potential research participants, investigators must ensure that there are additional safeguards for these participants. The voluntary nature of their participation must be primary and without undue influence on their decision. Investigators must emphasize to participants that neither their academic status, grades nor employment will be affected by their participation decision.

To minimize coercion, investigators should avoid, whenever possible, the use of their students and employees in procedures which are neither therapeutic nor diagnostic. Investigators should solicit student and employee participants through means such as bulletin board notices, flyers, advertisements in newspapers, and announcements in classes or laboratories other than their own. When entering a classroom to recruit students and conduct research, e.g., administer a survey, investigators should do so at the end of the class period to allow non-participating students the option of leaving the classroom (unless other arrangements have been made), thereby alleviating pressure to participate.

27.17 Student Research

27.17.1 Human Subject Research and Course Projects

Learning how to conduct ethical human subject research is an important part of a student’s educational experience. Research activities that are designed as part of a course requirement for purposes of a learning experience only and not “designed to develop or contribute to generalizable knowledge” may not require IRB review and approval if all of the following conditions are true:

- Results of the project are viewed only by the course instructor and discussed within the classroom for teaching and learning purposes.
- Results of the project are not made public through presentation (outside of the classroom) and are not published in paper or electronic format (e.g., cannot be made available on the internet, cannot be published in a journal, etc.).
- Procedures involve no more than minimal risk.
- Permissions are obtained from any facilities or organizations where research activities, including recruitment, will take place.
- Vulnerable populations are not targeted (e.g., children under age 18, prisoners, persons who are cognitively impaired, etc.).
• Data collected are recorded in such a manner that participants are not identifiable (images in videotapes and photographs and voices on audiotape are not identifiable).
• When appropriate, informed consent is obtained.

27.17.1.1 Responsibility of the Course Instructor:

The course instructor is responsible for ensuring the protection of human subjects (including a process is in place for obtaining voluntary consent from participants when appropriate), and for monitoring the students’ progress.

When designing a project, students should be instructed on the ethical conduct of research and on the preparation of the IRB application, when such is required. Instructors and students should:
• Understand the principles of the Belmont Report and their application;
• Develop appropriate consent documents and an appropriate consent process;
• Plan appropriate strategies for recruitment;
• Identify and minimize potential risks to participants or others;
• Assess the risk-benefit ratio for the project;
• Establish and maintain strict guidelines for protecting privacy and confidentiality; and
• Allow sufficient time for IRB review, if applicable, and completion of the project.

In making a determination of whether or not a class research project requires IRB review, the instructor is encouraged to use the Self-Determination form on the Human Research Office website and/or to contact the Human Research Office for assistance.

27.17.1.2 Individual Research Projects Conducted by Students

When students conduct, or participate as a research team member, in human subjects research other than class work as described above, they must follow the standard procedures for research described throughout this manual, as applicable to the research. As described in Section 1.10.7, students may not serve as PI on human subjects research conducted under the auspices of UMMC but may serve as a sub-investigator or member of the research team. When students of UMMC conduct, or participate as a research team member, in research at or with another organization, they must contact the UMMC Human Research Office to determine if review by the UMMC IRB is required, or if a reliance agreement is needed, prior to engaging in the activity. It is important to keep in mind that any human subject research activity that will ultimately contribute to part or all of a thesis, dissertation, or other type of publication or presentation must go through the IRB review process prior to enrolling participants and collecting data. IRB review/approval cannot occur after a study has begun.

Students and Advisors should contact the Human Research Office with any questions.