Office of Research and Sponsored Programs
West Virginia School of Osteopathic Medicine

Human Research Protections Program
Standard Operating Procedures

January 2019

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1. Human Research Protections Program (HRPP)

West Virginia School of Osteopathic Medicine (WVSOM) is committed to conducting research with the highest regard for the welfare of human subjects. The Institution's Human Research Protection Program (HRPP) is based on the principles of justice, beneficence, and respect for persons as set forth in Ethical Principles and Guidelines for the Protection of Human Subjects of Research (Belmont Report). Through institutional leadership and oversight, the Institution ensures that all research involving human participants is conducted in a manner that safeguards and promotes health and welfare, protects human rights, and ensures the safety and wellbeing of participants. The actions of all faculty, students and staff will conform to all applicable federal, state, and local laws and regulations. The program is committed to providing timely and high quality review and monitoring of human research projects and facilitating excellence in human subjects research. Administrative and regulatory management of the HRPP and the Institutional Review Board (IRB) are handled primarily by the Office of Research and Sponsored Programs (ORSP).

1.1 Purpose and Mission of the Human Research Protections Program

- Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and wellbeing are protected;
- Provide timely review and monitoring of human research projects;
- Facilitate excellence in human subjects research;
- Educate investigators and research staff about their ethical responsibility to protect research participants; and
- Intervene to respond directly to the concerns of research participants when appropriate.

1.2 Applicability and Institutional Authority

The HRPP operates under the authority of the policy R-05 “Human Subjects Research” adopted in August 2010. These research policies are guided by U. S. Federal regulations for the protection of human research subjects (45 CFR Part 46 also known as the “Common Rule”) and other federal, state and local regulations as applicable. This version of the IRB procedures applies to all studies initially approved on or after Jan. 21, 2019. The previous version of these procedures apply to studies approved prior to that date with the exception of section 14.1 which applies to all studies.

1.3 Definitions

Agent, as defined by the Office of Human Research Protections (OHRP), means an individual who: (1) acts on behalf of the institution; (2) exercises institutional authority/responsibility; or (3) performs institutional activities.

Clinical Trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions, which may include placebo or other control to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Common Rule means 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 Department of Health and Human Services (DHHS) regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule cite the DHHS regulations.

Department of Health and Human Services (DHHS), sometimes referred to as Health and Human Services (HHS), means the U.S. government’s principal agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves.

Engagement, as defined by the Office of Human Research Protections, includes intervention or interaction with human subjects for research purposes, obtaining informed consent from human subjects for research, or obtaining identifiable private information or identifiable biological specimens for research that includes observing or recording private behavior; using, studying, or analyzing identifiable private information or identifiable specimens provided by another institution for research purposes; and using, studying, or analyzing identifiable private information or identifiable specimens already in the possession of the investigator(s) for research purposes.

Human Subject, as defined by the Common Rule, means 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).
    - Interaction means communication or interpersonal contact between investigator and subject.
    - Intervention includes both physical procedures by which information or biospecimens are gathered (e.g. venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
    - 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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record).
    - Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
    - Identifiable specimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Human Subjects Research means any activity that meets the definition of "research" and involves "human subjects" as defined by the Common Rule. The terms "subject" and "participant" are used interchangeably in this document and have the same definition.

Institution, as defined in 45 CFR 46.102(b), means any public or private entity or agency.

Institutional Official (IO) means the individual responsible for ensuring that the HRPP/IRB at WVSOM has the resources and support to comply with all Federal regulations that govern human subjects research. The IO represents the institution as the signatory official and assumes the obligations of the institution's assurances.

Institutional Review Board (IRB) means the board designated by WVSOM to oversee and approve or disapprove research involving human subjects to protect their rights and welfare.

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.

Principal Investigator (PI) / Project Director (PD) means the individual who bears responsibility for the proper conduct of projects/research as agents of WVSOM. PIs must have the appropriate training in scientific and administrative oversight to conduct and manage a research project.

Public Health Authority means an agency or authority that is responsible for public health matters as part of its mandate.

Research, as defined by the Common Rule, means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. The following activities are NOT considered to be research for purposes of adherence to the Common Rule:

1. Scholarly and journalistic activities such as oral history, journalism, and biography 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 or assess conditions of public health importance.
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 investigative purposes.
4. Authorized operational activities in support of intelligence, homeland security, defense or other national security missions.

Written or In Writing means writing on a tangible medium or in an electronic format.

1.4 Responsibilities of the Human Research Protections Program

1.4.1 Overview of the Institutional Review Board

WVSOM has one IRB that is responsible for ensuring that the rights and welfare of human subjects are protected. The IRB has the authority to approve, require modification, or disapprove research activities covered by DHHS regulations, including exempt research activities under 45 CFR 46.104 for which limited IRB review is a condition of exemption and any proposed changes to ongoing human subjects research. The IRB has the authority to suspend or terminate approval of ongoing, approved research that is not being conducted in accordance with regulatory requirements or that has been associated with unexpected, serious harm to subjects. The research community and the IRB share responsibility for knowing the requirements of the Federal regulations, applicable state law, and institutional policies and procedures for the protection of human research participants. WVSOM's IRB members bring expertise in a variety of disciplines to ensure effective and adequate knowledge of subject populations and other factors in order to assess any risks and benefits to subjects and ensure that informed consent is obtained as required. The IRB roster includes members who are knowledgeable about the community for which the IRB regularly conducts reviews.

1.4.2 Communication & Education Responsibilities

Communication between administrators, investigators, human subjects, and institutional officials ensures dissemination of information about the ethical conduct of research and safeguards the rights and welfare of human subjects. This includes providing WVSOM's Federalwide Assurance (FWA), requiring training about Federal regulations, policies related to human research protections, and disseminating institutional policies and procedures. The HRPP education program is designed to ensure that members of the research community receive training about Federal regulations and institutional policies for the protection of human subjects. The HRPP provides resources to promote understanding of the ethical principles that guide research and the informed consent process, and the processes of submitting documents to the WVSOM Office of Research and Sponsored Programs and the IRB.

1.4.3 Record Keeping & Reporting Responsibilities

The HRPP ensures that records are maintained for a minimum of three (3) years in accordance with HHS regulations with records accessible upon request to authorized HHS officials. The HRPP ensures that any changes to approved research are not initiated without prior IRB review and approval, except when necessary to eliminate harm to human subjects. The HRPP ensures prompt reporting to the IRB,

appropriate institutional officials, OHRP, and any sponsoring Federal department or agency of any unanticipated problems involving risks to subjects or others, serious or continuing noncompliance with regulations or IRB requirements, and any suspension or termination of IRB approval.

1.4.4 Monitoring, Evaluation, and Continual Improvement Responsibilities

Appropriate monitoring is provided to maintain compliance with IRB determinations and all applicable regulations in accord with WVSOM's commitment to quality improvement, efficiency, and research integrity. The HRPP ensures that all personnel or performance sites participating in HHS-conducted or supported research conducted primarily under the direction of WVSOM investigators are covered under appropriate OHRP-approved assurances. Cooperative IRB review arrangements are documented in writing. All independent investigators that rely on the WVSOM IRB document their commitment to WVSOM's human research protections requirements and agree to adhere to all WVSOM IRB determinations.

1.5 Human Research Protections Program Organization

The HRPP consists of individuals and committees that include the IO, the IRB, and other committees or subcommittees that address human subjects research (e.g., Biosafety, Conflict of Interest in Research, Research Committee), investigators, IRB staff, and research staff.

1.5.1 Relationship between Components

The Office of Research and Sponsored Programs (ORSP) ensures that communication is maintained between the compliance entities. The IRB functions independently of, but in coordination with, other institutional regulatory entities, making determinations to approve or disapprove each research project with jurisdiction over all research involving human subjects. The Financial Conflicts of Interest Committee monitors any identified potential financial conflicts of interest by investigators and advises the HRPP regarding any compliance concerns related to financial conflicts of interest identified within the research community. 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 by the IRB.

1.5.2 Research Project Coordination

The Project Initiation Request form (ORSP 1), submitted for each research project, requires the investigator to indicate any institutional support that will be required for the research project, including laboratory, medicine, educational facilities, or other resources.

1.5.3 Principal Investigator (PI) / Project Director (PD) Eligibility

Since the PI/PD bears responsibility for the proper conduct of research, only investigators with the background and training in scientific and administrative oversight necessary to conduct and manage the research project may serve as the PI/PD. The PI/PD must be an employee of WVSOM or a designated investigator at a non-WVSOM entity with appropriate agreements in place. For students doing research at another site, the PI/PD may be an investigator at another institution. This person must have the appropriate background and training to conduct and manage the project and student (see 1.5.4).

1.5.4 Student Involvement in Research

Students may not serve as the PI/PD. Students involved in research projects must work with a WVSOM employee who will help guide the student through the approval process and ensure that the

required permissions are in place. This employee may or may not be the PI/PD. For example, if a student works with a PI at a remote clinical facility, the PI at that facility is entirely responsible for proper conduct of the study. In consultation with the PI, the WVSOM Regional Assistant Dean or other designated WVSOM employee will assist the student in obtaining required institutional permissions and will monitor the educational aspects if the work is being done as part of a research rotation. Procedures and reporting requirements for research rotations are described in the Clinical Education Manual.

1.6 Human Research Protections Program Reporting & Resources

The HRPP reports to the Assistant Vice President of Research and Sponsored Programs, who is responsible for its operations. Personnel in the ORSP may liaise between investigators, the IRB, the IO and the Business Affairs Office. The ORSP is equipped with necessary office, meeting, and storage space along with appropriate equipment to perform the functions of the HRPP. The adequacy of personnel and other resources are assessed annually by the Assistant Vice President of Research and Sponsored Programs. The institutional Signatory Official provides resources to the IRB and HRPP, including adequate space and staff for IRB business. Resources provided for the IRB and HRPP are reviewed during the annual budget review process.

1.7 Quality Assurance/Quality Improvement

Processes for assessing and improving HRPP effectiveness and compliance are overseen by the ORSP.

1.7.1 Internal Post-Approval Monitoring and Evaluation (PAME)

PAME is part of the continuing review process to monitor quality and assist the IRB in protecting human subjects. Directed ("for cause") monitoring is conducted in response to identified concerns and periodic (not "for cause") compliance reviews are conducted randomly to assess investigator compliance with federal, state, and local law, as well as HRPP policies. Monitoring is intended to identify areas for improvement and the provision of education.

1.7.2 External Post-Approval Monitoring and Evaluation

Audits and periodic compliance reviews may also be conducted at non-WVSOM sites when the WVSOM IRB serves as the "IRB of Record," to assess compliance with federal, state, and local law, research subject safety, and IRB policies and procedures.

1.7.3 Reporting and Disposition

Results are reported to the IRB, HRPP and IO. If deficiencies are identified, a corrective action plan is developed by the HRPP in collaboration with the investigator. Any noncompliance or unanticipated problem is handled in accordance with Federal, state and local regulations and HRPP policies.

1.7.4 HRPP Internal Compliance Reviews

Internal directed monitoring and compliance reviews are conducted to assess current practices and may reveal the need for additional educational activities. The HRPP will review the results of internal compliance reviews with the IRB Chair and IO. If deficiencies are noted, an improvement plan will be developed and implemented by the HRPP. On an annual basis, the IRB Chairperson, in consultation with the Institutional Compliance Officer, will make an assessment and prepare a report that will be submitted to the WVSOM President by Oct. 1 of each year outlining any additional changes or improvements that need to be addressed by the ORSP.

1.8 Collaborative Research Projects

When a cooperative agreement exists, WVSOM may enter into a joint review arrangement, provide IRB review for another institution, rely on the review of another qualified IRB, or make similar arrangements to avoid duplication of effort. A formal relationship must be established between WVSOM and the other institution through an IRB Authorization Agreement (IAA) or a Memorandum of Understanding (MOU). This relationship must be established before the WVSOM IRB will review research projects from another institution or rely on the IRB review of another institution. All facilities participating in a human subjects research must receive adequate documentation about the study to protect the interests of study participants. Before a study can begin, it must be approved by the IRB of record in accordance with the established IAA or MOU. The PI must identify all participating institutions, any responsible IRB(s), and procedures for disseminating project information (initial and continuing approvals, reports of unanticipated problems, protocol changes, and interim reports) to all participating institutions. When WVSOM relies on another IRB, the ORSP will review the policies and procedures of the IRB to ensure that they meet WVSOM standards. If the other IRB is part of an accredited organization, then WVSOM may assume that HRPP standards are being met. WVSOM may also extend the applicability of its FWA to cover collaborating independent investigators or collaborating institutional investigators using a collaborating investigator agreement.

2. IRB Organization & Structure

2.1 Institutional Review Board Authority

The WVSOM IRB operates under the authority of its Federalwide Assurance (FWA00007632) with one IRB (00003217) to review all human research protocols. The HRPP has opted to limit the application of its FWA to research funded by HHS or federal agencies that have adopted the Common Rule. WVSOM also provides IRB review for human subjects research conducted by other institutions, where appropriate. The IRB serves as the Privacy Board for matters involving identifiable information in research. If the IRB is asked to grant a waiver of HIPAA Authorization, IRB members serve as privacy guardians under HIPAA.
The IRB has the authority to:

- Approve, modify, or disapprove research projects conducted under the auspices of WVSOM, including exempt research activities under 45 CFR 46.104 for which limited IRB review is a condition of exemption;
- Suspend or terminate approval of research projects that are not being conducted in accordance with IRB requirements or result in unexpected serious harm to participants;
- Require progress reports from investigators and oversee the conduct of each research project;
- Place restrictions on a research project; and
- Observe, or have a third party observe, the consent process and the conduct of the research.

Research involving prisoners, unless the population only incidentally includes prisoners, and clinical trials using drugs or medical devices are not reviewed by the WVSOM IRB. Research that has been approved by the IRB may be subject to review and disapproval by officials of the institution. However, those officials may NOT approve research if it has not been approved by the IRB. WVSOM officials may strengthen requirements and/or conditions, or add other modifications to secure WVSOM approval or approval by another WVSOM committee. Previously approved research proposals and/or consent forms must be reviewed and approved by the IRB before any changes or modifications are initiated.

2.2 Institutional Review Board Roles and Responsibilities

2.2.1 Institutional Review Board Membership Qualifications and Training

IRB Membership is voluntary with members sufficiently qualified through experience, diversity, and expertise to include consideration of race, gender, cultural backgrounds, and sensitivity to community attitudes that promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. IRB members must complete the IRB Member training curriculum provided by the Collaborative Institutional Training Initiative (CITI) to learn the history, regulations, applicable laws; standards of professional conduct and practice; and community attitudes that are relevant to their role as IRB members. Members also receive ongoing training via publications and other resources that are provided by the HRPP. Members are expected to attend all IRB meetings. If an IRB member will be absent for an extended period, he or she must notify the IRB so that an appropriate replacement can be obtained or the alternate can serve during the primary member's absence. The HRPP maintains a current membership roster describing the qualifications of individual members.

2.2.2 Composition of the Institutional Review Board

The IRB is composed of at least five individuals of diverse backgrounds to promote complete and adequate review of research activities commonly conducted by WVSOM. The IRB includes at least one member whose primary concerns are scientific and at least one member whose primary concerns are non-scientific. The IRB includes at least one member who is not otherwise affiliated with the institution and who is not an immediate family member of a person affiliated with WVSOM.

2.2.3 Appointment of Members & Alternate Members

The IRB Chair and the HRPP review IRB membership composition to determine the need for new members at least annually. Changes in membership are promptly reported to the OHRP and the ORSP by the IRB Chair. IRB members, Department Chairs and others may forward nominations to the IO, the HRPP, or the IRB Chair. The decision to select new members is made by the IRB Chair in consultation with the IO and the HRPP. Appointments are made for a renewable four-year period with any reappointment or removal made by written notification. Members may resign by written notification to the Chair. When there is a need for particular expertise, the appointment and function of alternate members will be the same as IRB members. The role of the alternate member is to serve as a voting member and attend meetings when the regular member is unavailable. When an alternate member substitutes for a primary member, the alternate member will receive and review the same materials prior to the IRB meeting. The IRB roster will identify the primary member(s) for whom each alternate member may substitute. The alternate member will not be counted as a voting member unless the primary member is absent. IRB minutes will document when an alternate member replaces a primary member.

2.2.4 Institutional Review Board Member Conflict of Interest

No regular, alternate, or ex officio member may participate in review (initial, continuing, or modification) of any research project in which the member has a conflict of interest (COI), except to provide information as requested. It is the responsibility of each IRB member to disclose any COI in a study and recuse him/herself from any deliberations and vote by leaving the room. If a member responds affirmatively to a potential conflict, the COIR Officer is notified. If the Conflict of Interest status of an IRB member changes during the course of a study, the IRB member is required to declare this to the IRB Chair.

2.2.5 Chair and Vice-Chair of the Institutional Review Board

The IO, in consultation and approval with IRB members and the HRPP, appoints a Chair to serve an unlimited term. The Vice-Chair is appointed by the IRB Chair from amongst the IRB members. Any change in appointment, including removal, requires written notification. The IRB Chair is responsible for determination of engagement in research, level of review required, coordination of IRB reviews, and conducting IRB meetings. The IRB chair is also the signatory for IRB correspondence. The IRB Chair may designate other IRB members to perform duties for review, signature authority, and other IRB functions. The IRB Chair advises the IO and the HRPP about IRB member performance and competence. The performance of the IRB Chair is reviewed by the Assistant Vice President of Research and Sponsored Programs and the IO. Feedback from this evaluation will be provided to the Chair. If the Chair is not acting in accordance with the IRB's mission or not fulfilling the responsibilities of the Chair, he/she may be removed. 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 Chair.

2.2.6 Use of Subcommittees & Consultants

The IRB Chair may designate subcommittees and appoint IRB members or seek consultations to perform duties and/or make recommendations to the IRB related to research projects. The IRB Chair will indicate whether any subcommittee is a standing or ad hoc IRB Subcommittee. When necessary, the IRB may solicit individuals from WVSOM or the community to provide scientific or scholarly expertise beyond or in addition to that available on the IRB. The need for a non-member reviewer is determined by the Chair. Written consultations will be kept in IRB records and documented in the minutes. Written reviews from the non-member reviewer will be filed with the protocol. Consultants must verbally confirm to the IRB Chair that they do not have a conflict of interest prior to review. Individuals who have a conflicting interest will not be asked to provide consultation.

2.2.7 Responsibilities of Institutional Review Board Members

IRB members review assigned research projects to ensure that any risks to human subjects are minimized, that informed consent forms include all the required elements and any advertisements contain appropriate information that does not include any undue influence or misrepresentation. IRB members also evaluate privacy and confidentiality plans to determine the need for HIPAA authorization and to ensure confidentiality of information. Research project materials and documents are provided to members a minimum of five (5) days prior to the date when their review is expected to be completed. Members are required to maintain the confidentiality of all research projects, protocols, and supporting data, which are maintained in a secured database. All study documents are distributed via this database and meeting materials are distributed to members via email.

2.2.8 Liability Coverage for Institutional Review Board Members

WVSOM's insurance coverage applies to employees and any other person authorized to serve within the scope of IRB authorized activities.

2.2.9 Review of Institutional Review Board Member Performance

IRB members will be reviewed on an annual basis by the IRB Chair and receive formal feedback on the results of this review. Members who are not acting in accordance with the IRB's mission or policies and procedures or who have an undue number of absences may be removed.

2.2.10 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 or she shall make a confidential report to the IO. The official receiving the report will conduct a thorough investigation with appropriate corrective action as necessary.

3. Institutional Review Board Review Process

All human subjects research conducted under the auspices of the WVSOM IRB must meet the criteria for one of the following methods for review:

- Exempt
- Expedited Review
- Full Committee Review

The IRB ensures that the research meets regulatory requirements for initial and continuing review and any modifications of approved research.

3.1 Definitions

Minimal Risk, defined in 45 CFR 46.102, 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 means that there is no substantial alteration in the:

1. Level of risks to subjects
2. Research design or procedures
3. Qualifications of the research team
4. Facilities available to support safe conduct of the research.

Suspension means a directive from the IRB to temporarily stop some or all previously approved research activities. Suspended protocols remain open and require continuing review.

Termination means a directive from the IRB to permanently stop all previously approved research activities. Terminated protocols are considered closed and no longer require continuing review.

3.2 Human Subjects Research Determination

The responsibility for initial determination as to whether an activity constitutes human subjects research rests with the investigator. The investigator should make this determination based on the definitions of "Human Subjects Research" in Section 1. Since WVSOM will hold the investigators responsible if the determination is not correct, investigators are urged to consult the Office of Research and Sponsored Programs and/or the IRB, providing sufficient documentation for a determination.

3.3 Exempt Research Projects

All research must be approved by the institution with initial review by the ORSP and determination of exempt status made by the IRB Chair or his/her designee. WVSOM does not allow investigators to make the exemption determination.

3.3.1 Categories of Exempt Research

Research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from regulatory requirements for approval described in 3.6 except where limited IRB review is noted as a requirement of exemption. Studies in the following categories require institutional review and IRB Chair or designee determination of exemption, as indicated in 3.3:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices that are not likely to adversely impact students' opportunity to learn required content or the assessment of educators who provide instruction, such as (a) research on regular and special education instructional strategies; or (b) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods. Prospective assignment of students to a group receiving an experimental educational intervention and a control group receiving no intervention is not considered exempt research.
2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior (including visual and audio recording), if at least one of the following criteria is met:
    a. The information is recorded in such a manner that the identity of the subjects cannot be readily ascertained directly or through identifiers linked to subjects.
    b. Any disclosure of the 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.
    c. The information obtained is recorded by the investigator in such a way that the identity of the human subjects can be readily ascertained directly or through identifiers and an IRB conducts a limited IRB review to make the determination that adequate provisions are in place to protect the privacy of subjects and to maintain the confidentiality of the data as required by 45 CFR 46.111(a)(7).

    See Section 3.3.2 for limitations to this exemption.
3. Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses 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.
    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 that adequate provisions are in place to protect the privacy of subjects and to maintain the confidentiality of the data, as required by 45 CFR 46.111(a)(7).

    Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant 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 interventions include having the subjects play an online game or solve puzzles under various noise conditions.

    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 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:
    a. The identifiable private information or identifiable biospecimens are publicly available;
    b. 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 subjects, the investigator does not contact the subjects, and the investigator will not re-identify the subjects;
    c. The research involves only information collected 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
    d. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government collected information obtained for non-research activities, if the government 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 522a 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, 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 agreements, 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.

    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, as list of the research and demonstration projects that the Federal department or agency conducts or supports under the provision. The research 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, (a) if wholesome foods without additives are consumed; or (b) 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.

WVSOM currently does not allow exempt category studies requiring broad consent.

3.3.2 Limitations on Exempt Research

Research involving survey or interview procedures or observations of public behavior do NOT apply to research with children, except observations of public behavior when the investigator does not participate in the activities being observed 45 CFR Part 46, Subpart D. The WVSOM IRB does not review or approve research with prisoners unless the population incidentally includes prisoners (see 45 CFR 104(b)(103)). Research involving children that involves identifiable information and requires limited IRB review is not eligible for exemption.

3.3.3 Exemption Determination

The IRB Chair (or designee) reviews requests for exemption to determine whether the request meets the criteria for exempt research and if limited review is required. The IRB Chair may designate an IRB member or trained ORSP staff member to review and grant requests for exemptions. Exempt studies requiring limited IRB review must be reviewed by an IRB member. Individuals involved in making a determination cannot be involved in the research to ensure that there is no conflict of interest. The reviewer will assess any need for additional protections, and document the exemption categories after determining that the research involves no more than minimal risk to subjects. As appropriate, the review may include materials that will assist the IRB in determining that risk is minimal and meets the criteria for exemption as described in 45 CFR 46.101(b). As appropriate, materials may include:

1. Recruitment materials, surveys, questionnaires, and instruments to ensure that selection of subjects is equitable;
2. If identifiable information is recorded, adequate provisions are in place to maintain confidentiality of the data;
3. If there is interaction with subjects, a consent process must disclose that the activity involves research, a description of procedures, participation is voluntary, and contact information for the investigator;
4. Provisions to maintain the privacy of subjects;
5. If sponsored, one copy of the grant application(s) and/or contract;
6. Verification of Significant Financial Conflicts of Interest and human research protection training for all members of the research team, including the faculty advisor;
7. Letter(s) of permission and/or support from non-WVSOM performance site.

Investigators are notified by email with the determination communicated to the IRB at the next convened meeting. Since protocols that are exempt from IRB review are not approved by the IRB, there is no approval period. Investigators are contacted every three (3) years to verify that the research is ongoing and remains exempt. If the research is completed prior to the three (3) year period, investigators are requested to notify the IRB of study closure.

3.4 Expedited Review

If a protocol has been determined to be minimal risk, it may be considered for expedited review if it meets one or more categories authorized by 45 CFR 46.110 for expedited review.

3.4.1 Categories Eligible for Expedited Review

Expedited review may be used to approve research involving no more than minimal risk or minor modifications to ongoing research that involve no more than minimal risk to human subjects. Activities listed here should not be deemed to be of minimal risk simply because they are included on

the list. Inclusion on this list merely means that the activity is eligible for review through the expedited procedure. All categories apply regardless of age, except as noted. Expedited review may not be used when subjects are identified and/or when their responses might place them at risk for criminal or civil liability or be damaging to their financial status, employability, insurability, or reputation unless reasonable and appropriate protections would be implemented to ensure that privacy and confidentiality risks are minimal. Expedited review may not be used for governmental classified research with human subjects. Requirements for informed consent waiver, alteration, or waiver of documentation of consent apply to expedited review. Categories one (1) through seven (7) pertain to initial and continuing IRB review:

1. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture (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. Children are defined in the DHHS regulations 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. [45 CFR 46.402(a)]
2. 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.
3. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

4. 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)(4). This listing refers only to research that is not exempt.]
5. Collection of data from voice, video, digital, or image recordings for research purposes.
6. 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. This listing refers only to research that is not exempt.]
7. Continuing review of research previously approved by the convened IRB (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.
8. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories one (1) through seven (7) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

3.4.2 Expedited Review Procedures

Expedited review may be carried out by the IRB Chair or an IRB member designated by the Chair based upon his or her expertise to review the study. The IRB Chair or Designee will review all research-related materials and documents using the review form within the IRB database. Reviewers will indicate approval, any required modifications, or whether the study should be reviewed at a convened IRB meeting. If modifications are required, the IRB Chair or staff will inform the investigator by e-mail. In the event that expedited review is carried out by more than one (1) IRB member and the expedited reviewers disagree, the IRB Chair will make a final determination or determine that the protocol will be submitted to the full IRB for review.

3.4.3 Informing the Institutional Review Board

IRB members are apprised of all expedited review approvals by means of a list at each scheduled meeting. Any IRB member can request to review the full protocol by contacting the IRB Chair.

3.5 Convened Institutional Review Board Meetings

Except when an expedited review procedure is used, the IRB will conduct initial and continuing reviews of all non-exempt research at convened meetings. The IRB meets on an as needed basis. Meetings may be called at any time when the IRB Chair determines the need to convene an ad hoc full board meeting.

3.5.1 Distribution of Meeting Documents

The agenda is distributed to IRB members via email prior to the meeting along with materials that require full board review. Meeting materials are distributed at least five (5) business days prior to the scheduled meeting to allow sufficient time for review.

3.5.2 Materials received by the Institutional Review Board

For full-board reviews, each IRB member reviews all study-related documents as assigned, including:

- Research application form
- Grant application (sponsored projects only)
- Consent / Assent Form(s)
- Recruitment materials / letters of support
- Data collection instruments (surveys / questionnaires)

At least one primary reviewer must review all study materials. A secondary reviewer may be assigned by the IRB Chair to review a study in which their expertise and experience is needed or if a PI/Co-PI is an IRB member. Any IRB member may request access to study materials. If an IRB member requires additional information, he or she may contact the investigator directly. IRB reviewers use the Initial Reviewer form within the IRB database to complete their review.

3.5.3 Meeting Procedures

The IRB Chair, or Vice-Chair when the IRB Chair is absent, will call the meeting to order when a quorum is confirmed. Quorum is defined as at least 50% of the committee members and at least one member who is primarily concerned with non-scientific content. The Chair or Vice-Chair will remind IRB members to recuse themselves from discussion and voting by leaving the room when there is a conflict of interest. The IRB will review the prior meeting minutes to determine if revisions/corrections are needed. If no changes are needed, the minutes will be accepted as presented and considered final. If revisions/corrections are needed, the minutes will be amended accordingly. Primary and secondary reviewers present a synopsis of the research with review of regulatory criteria that provide the basis for their approval, disapproval, or request for modifications. IRB members present at a convened meeting have full voting rights, except in the case of a conflict of interest. In order to be approved, the full-board reviewed research project must receive the approval of a majority of voting members. At the meeting, all actions approved by expedited review since the previous IRB meeting are presented. Minutes are recorded by the ORSP secretary.

3.5.4 Guests

The Principal Investigator may be invited to answer questions, but may not be present for the discussion or vote on his or her research. Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair. Guests may not speak unless requested by the IRB.

3.6 Criteria for Institutional Review Board Approval of Research

In order for the IRB to approve human subjects research, either by expedited review or full board review, it shall determine that all of the following requirements are satisfied:

- 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.
- 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.

- 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 a category of subjects who are vulnerable to coercion or undue influence, such as children, pregnant women, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.
- 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.
- Informed consent will be appropriately documented, or appropriately waived, in accordance with, and to the extent required by the Federal Regulations.
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- For purposes of conducting limited IRB review, the IRB need not make the determinations regarding items 1 through 6 in this section and shall ensure that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of those subjects.

3.6.1 Risk/Benefit Assessment

The IRB aims to ensure that risks to human subjects posed by the research are justified by any anticipated benefits to the subjects or society gained through new knowledge or improved health for research subjects or disapproves research in which the risks are judged unreasonable in relation to anticipated benefits. Assessment of risks and benefits includes:

1. Identify risks associated with the research, distinguished from risks of therapies that subjects would receive if they were not participating in research;
2. Determine whether risks are minimized to the extent possible;
3. Identify any probable benefits to be derived from the research;
4. Determine whether potential risks are reasonable in relation to potential benefits to subjects, and assess the importance of the knowledge to be gained;
5. Ensure that potential subjects will be provided an accurate description of risks, discomforts, and anticipated benefits.

Risks to subjects should be minimized:

1. By using procedures that are consistent with sound research design and do not unnecessarily expose subjects to risk; and
2. Whenever appropriate, by using procedures already being performed for diagnostic or treatment purposes.

3.6.2 Scientific Review

The IRB must determine that:

1. The procedures must be consistent with sound research design to reasonably expect the research to answer its proposed question;
2. Knowledge expected to result from the research is of sufficient merit to justify the risks.

Additionally, any departmental or committee scientific review should be documented by the investigator in the initial research application.

3.6.3 Equitable Selection of Subjects

The IRB determines that the selection of subjects is equitable with respect to gender, age, class, and will not approve a study that does not provide equitable selection of subjects unless the investigator has provided appropriate scientific and ethical justification for excluding persons from the research. At the time of the continuing review, the IRB will determine that the investigator has followed the subject selection criteria as originally set forth during initial IRB review and approval.

3.6.4 Informed Consent

The IRB will ensure that informed consent is sought from each prospective subject or the subject's legally authorized representative, in accordance with 45 CFR 46.116 and Public Law No: 113-240, "Amendment 12") unless waived by the IRB. The IRB will ensure that informed consent will be appropriately documented in accordance with 45 CFR 46.117 unless the IRB has waived documentation. See Section 5 below for detailed policies on informed consent.

3.6.5 Safety Monitoring

For research that is greater than minimal risk, the investigator must include a safety monitoring plan in the protocol application, describing procedures for reporting of unanticipated problems involving risks to subjects or others, descriptions of interim safety reviews and procedures for transmitting findings to the IRB. The plan should include information regarding an independent Data and Safety Monitoring Board or Data Safety Monitoring Committee, if one exists, or an explanation as to why an independent data safety monitor is not necessary. The IRB will determine whether the safety monitoring plan makes adequate provision for monitoring and collection of data to ensure the safety of subjects. The IRB will consider whether monitoring is timely and appropriate for the nature, complexity, size and risks of the study.

3.6.6 Privacy

The IRB will determine whether adequate provisions are in place to protect the privacy of subjects. Privacy is defined as having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. Private information is defined as information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record). The IRB must obtain information regarding how the investigators gain access to subjects' private, identifiable information and expectations of privacy in the situation. Investigators must have authorization to access private information and the IRB must consider:

1. Methods used to identify and contact potential participants;
2. Settings in which an individual will be interacting with an investigator;
3. Methods used to obtain information about participants and the requested information;
4. Information obtained about individuals;
5. Minimal information needed to complete the study.

3.6.7 Confidentiality

The IRB will determine whether adequate provisions are in place to maintain confidentiality of data based on the definition of confidentiality. Confidentiality pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure. Confidentiality and anonymity are not the same. If anyone, including the investigator, can ascertain the identity of subjects from the data, then the research is not anonymous and the IRB must determine if appropriate protections are in place to minimize the likelihood that the information will be inappropriately divulged. The level of confidentiality protections should be commensurate with the potential of harm from inappropriate disclosure.

The IRB assesses whether there are adequate provisions to protect subject privacy and maintain confidentiality. The IRB does this by evaluating methods:

1. Used to obtain information about subjects;
2. Used to obtain information about individuals who may be recruited to participate;
3. Related to the use of personally identifiable records; and
4. Used to protect the confidentiality of research data.

In some cases, the IRB may require a Certificate of Confidentiality be obtained to protect research data. In reviewing confidentiality protections, the IRB will consider the nature, probability, and magnitude of harms that might result from disclosure of information and evaluate the effectiveness of proposed de-identification procedures, coding, encryption, storage, access, and other relevant factors in determining the adequacy of confidentiality protections.

3.6.8 Vulnerable Populations

At the time of initial review the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research to determine whether additional safeguards should be put in place for vulnerable subjects. Such considerations will including, but may not be limited to, subjects who are decisionally impaired.

3.6.9 Significant New Findings

During the course of research, significant new knowledge or findings must be reported to the IRB by the PI. The IRB will review the significant new knowledge or findings with regard to the impact on the subjects' rights and welfare. Based on this review, the IRB may require the investigator to contact currently enrolled subjects, require that the informed consent be updated, and/or require that currently enrolled subjects be re-consented to acknowledge receipt of this new information and affirm their willingness to continue participation. The IRB will communicate this to the PI. If additional information affecting participant safety is submitted on a closed sponsored protocol, the IRB must be notified immediately. The information should be attached to the study with an explanatory letter to the IRB. The IRB will review the information and determine whether the investigator should contact subjects to inform them of the new information. If the IRB determines that a letter to subjects is required, the investigator will submit the letter for IRB review.

3.6.10 Advertisements

The IRB must approve all advertisements prior to distribution, including information about the mode of communication and a printed narrative of the advertisement. This information must be submitted with the initial application or as an amendment to the protocol. The IRB reviews materials to ensure accuracy, the absence of coercive or exculpatory language, or any unduly influencing statements that

may inappropriately influence subjects to participate such as implying favorable outcome or benefits beyond what is described in the consent document and protocol. Any advertisement should be limited to information required to determine eligibility and interest. When appropriately worded, the following information may be included:

1. The name and address of the clinical investigator and/or research facility.
2. The condition being studied and/or the purpose of the research.
3. In summary form, the criteria that will be used to determine eligibility for the study.
4. The time or other commitment required of the subjects.
5. The location of the research and the person or office to contact for further information.
6. A clear statement that this is research and not treatment.
7. A brief list of potential benefits (e.g., no cost for health exam).

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

3.6.11 Additional Considerations during Institutional Review Board Review and Approval of Research

At the time of initial review and continuing review, the IRB will determine the frequency of IRB review. Meeting minutes will reflect IRB determination of review frequency. Unless the IRB determines otherwise, continuing review of research is not required in the following circumstances:

1. Research eligible for expedited or limited IRB review.
2. 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.
    a. Data analysis including analysis of identifiable private information or biospecimens.
    b. Accessing follow-up clinical data from procedures that subjects would undergo as a part of clinical care.

The rationale for conducting continuing review of research that otherwise would not require continuing review will be documented in the reviewer notes and approval letter

3.6.11.1 Review More Often Than Annually

Unless specifically waived by the IRB, research that meets any of the following criteria will require review more often than annually:

1. Significant risk to research subjects (e.g., death, permanent or long lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects.
2. The involvement of especially vulnerable populations likely to be subject to coercion (e.g., terminally ill).
3. A history of serious or continuing non-compliance on the part of the PI.

3.6.11.2 Additional Factors Used to Determine Which Studies Require More than Annual Review

1. The probability and magnitude of anticipated risks to subjects.
2. The likely medical condition of the proposed subjects.
3. The overall qualifications of the PI and other members of the research team.
4. The specific experience of the Responsible Investigator and other members of the research team in conducting similar research.
5. The nature and frequency of adverse events in similar research at this and other institutions.
6. The novelty of the research making unanticipated adverse events more likely.
7. 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 subjects either studied or enrolled. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed one year and that the number of subjects studied or enrolled determines the approval period only when that number of subjects is studied or enrolled in less than one year. If an approval period of less than one year is specified by the IRB the reason for more frequent review must be documented in the minutes.

3.6.12 Payment to Research Subjects

Research subjects may be compensated for time required, transportation costs, or as an incentive for continuing participation when return visits are required by the research design. Payment for participation is not considered a research benefit and investigators must take care to avoid coercion or undue influence of subjects. Payments should reflect and be proportional to the costs of participation, inconvenience, or discomfort associated with participation. Investigators who wish to compensate research subjects must indicate this and provide justification within the research project application. Justification should include:

1. Information indicating the proposed payments are reasonable and commensurate with the expected contributions of the subject;
2. The terms of the subject participation agreement and the amount of payment in the informed consent form; and
3. How/why the payments are fair and appropriate and do not (or do not appear to constitute) undue pressure on the patient to volunteer for the research study.

The IRB must review compensation amounts and the proposed method of disbursement to avoid coercion or undue influence. Compensation should accrue periodically without being contingent upon completing the entire study. Any bonus amount paid for completion of the entire study should not be so great that it would constitute coercion. The consent form must describe the terms of payment and the conditions under which subjects would receive partial payment or no payment (e.g., if they withdraw from the study before their participation is completed). Unless the study is confidential, the WVSOM Business Affairs Office and the Purchasing Department require identifying information to issue checks, cash, or gift certificates to subjects. The consent form must inform subjects that they will be asked to provide their Social Security Number and verification of U.S Citizenship or Permanent Resident Status to receive payment. For confidential studies, only the name and address are required, but the investigator MUST keep an identity key in a secured place.

3.7 Post-Approval Monitoring and Evaluation

In accordance with 45 CFR 46.109(e) and (g), "An IRB shall conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk, not less than once per year and shall have authority to observe or have a third party observe the consent process and the research." The IRB employs a comprehensive approach to post-approval monitoring through continuing study review at least annually, as well as through HRPP internal and on-site study monitoring aimed at improving human research protections and regulatory compliance through education and oversight. Unless the IRB determines otherwise, continuing review is not required if conditions described in section 3.6.1.1 (45 CFR 46.109(f)) are met. Any IRB-approved research project may be subject to study audit determined by random, for-cause, or investigator-initiated selection. Monitoring and evaluation may include review or study files, consent documents, observation of the consent process and review of training for those who recruit subjects or obtain consent. For-cause monitoring may result from non-compliance, lack of

adherence to study protocol, or subject safety concerns coming to the attention of the IRB, to evaluate risks or assess the need for suspension/termination (see 45 CFR 46.113). Investigator-initiated review of records and procedures may be requested to ensure compliance with federal regulations, IRB policies, or prepare for an external audit by a federal agency.

3.7.1 Selection of Studies

Criteria for the selection of studies include, but are not limited to studies approved by the full board or by expedited review, studies that involve greater than minimal risk to subjects, including risks related to the loss of privacy or confidentiality, vulnerable populations (see 45 CFR 46, Subparts B and D – pregnant women/fetuses/neonates and children), or subjects vulnerable to undue influence including the cognitively, economically, or educationally disadvantaged, unanticipated problems or protocol deviations, or previous audit findings.

3.7.2 Monitoring Notice

Except in cases where the safety of subjects is a concern, written notification of an audit will be sent from the ORSP to arrange a visit at least two (2) weeks prior to a monitoring visit for random monitoring, at least 24 hours prior to for-cause monitoring, and as mutually agreed for investigator – initiated monitoring.

3.7.3 Purpose of Monitoring Visits

HRPP and the WVSOM Institutional Compliance Officer audits focus on the safety of human subjects, adherence to the IRB-approved protocol, compliance with relevant laws, regulations, policies and procedures, conformity to inclusion and exclusion criteria, special provisions for vulnerable subjects, observation of the consent process, provisions to safeguard the confidentiality of data, and compliance with reporting requirements, including unanticipated problems.

3.7.4 Report of Findings & Recordkeeping

Findings of monitoring visits will be reported to the investigator, the IRB Chair, IRB members and the IO, as appropriate. A corrective action plan will be requested from the research site for any identified concerns that result from the monitoring visit. Records and reports are retained within the ORSP. If an audit or review finds that subjects in a research project have been exposed to unexpected serious harm, the reviewer will promptly report such findings to the IRB Chair for immediate action.

3.8 Investigator Conflicts of Interest

Researchers at WVSOM must complete a Conflict of Interest in Research (COIR) disclosure form and conflict of interest training in accordance with WVSOM's Institutional Policy: R-04, Conflict of Interest in Research. The research application asks whether investigators and senior/key personnel have any conflict of interest that might compromise the integrity of the study. As part of its review process, the IRB confirms that the investigator has completed the COIR disclosure form and the conflict of interest training and that no conflicts of interest were reported. If a conflict of interest exists, final IRB approval of a protocol cannot be given until an approved management plan that protects human subjects in the protocol has been approved by the Conflicts of Interest in Research Committee.

3.9 Deception

Deception occurs when an investigator provides false or incomplete information to participants. The IRB accepts the need for certain types of behavioral and social science studies to employ strategies that

include deception. An investigator proposing to use deception or incomplete disclosure should justify its use in the research application. Studies that use deception as part of their experimental design must meet all the requirements of 45 CFR 46.116(d) and include a post-study debriefing, unless an exception is granted by the IRB. If, in the judgment of the IRB, the participant may have declined to participate had he or she been informed of the true purpose of the research, then the study may not be approved.

3.10 Use of Data and Tissue Repositories

When the intended purpose of a database containing identifiable private information includes research, any collection, storage, sharing, or use of the information is considered human subject research that requires oversight by the IRB. Research databases containing identifiable private information are used for the purposes and in the manner specifically described in the IRB-approved protocol and informed consent document under which the information was collected. Investigators wishing to use identifiable database information for research that differs from that described in an applicable protocol approved by the IRB must submit a new or amended protocol for IRB review before initiating the new project. WVSOM currently does not allow exempt category studies requiring broad consent.

Though the creation or operation of non-research databases or repositories does not involve human subject research or require IRB oversight, IRB oversight is required for research use of identifiable private information or identifiable human specimens from databases and repositories, including data or tissue banks and registries. When research involves identifiable private information or identifiable human specimens, each research use must receive prospective IRB review and approval and continuing IRB oversight, unless the research satisfies the criteria for exemption as defined in Federal Regulation 45 CFR 46.101(b). Examples of activities that involve the research use of information or specimens that require IRB review, approval, and oversight include:

- Use of a medical provider's patient database to identify and recruit potential research subjects.
- Use of quality assurance data containing identifiable private information for an activity designed to develop or contribute to generalizable knowledge.

Researchers who wish to use information or specimens from a database or repository including data/tissue banks and registries should submit an application for IRB review and receive IRB approval before initiating the research. The application should include any available information about the circumstances under which the information or specimens were originally collected. In addition, HIPAA regulations may apply, including any requirement for an authorization from subjects for the research use or disclosure of PHI. The WVSOM Informed Consent template includes wording to assist investigators in obtaining permission for the use of information or specimens as well as obtaining HIPAA Authorization.

3.11 Incidental Medical Findings from Research Studies

An incidental finding is an unexpected finding about a research participant that has potential health or reproductive importance that was discovered while conducting research, but is beyond the aims of the study. Before a subject is informed of an incidental finding, the investigator must clearly establish whether the finding is medically important. Any research that may reveal incidental findings that affect the health and welfare of subjects must be considered by investigators and the IRB. Since disclosure of incidental findings can potentially save lives, cause alarm, or reveal potential harm, the decision to disclose is an important consideration. If findings involve a medical condition that is beyond the expertise of the investigator, a physician should be contacted to determine the likelihood of benefit or harm. The subject should be informed by the investigator. If warranted and the subject agrees, the contacted physician should examine the subject after the subject is informed and agrees that any medical information should be sent to the consulting physician or to the patient-subject's personal physician unless the patient-

subject objects. If the subject indicates that he/she does not wish to be informed of the incidental findings, additional considerations may be warranted. In this case, without revealing the information, the researcher should attempt to confirm whether the participant wants to refuse information that may have serious consequences. If the participant indicates that he/she does not wish to be informed, the wishes of the participant should be honored. If this occurs, a notation should be made in the participant's research record and transmitted to the IRB in a timely fashion. Notification of the personal physician if approved by the patient-subject is the extent of WVSOM's responsibility in the matter.

3.12 Institutional Review Board Actions

Research may be approved, disapproved, or tabled pending receipt of details or modifications. IRB decisions are communicated to the investigator in email. IRB determinations are documented in the minutes of the IRB meeting for full board review or in the file for expedited review. Following approval of each study, a letter of approval is sent from the IRB Chair to the Principal Investigator. The approval letter notes the type of review, duration of approval and date of next continuing review, and a summary of investigator responsibilities. The summary reminds investigators that any changes in research activity may not be initiated without IRB review and approval except when necessary to eliminate immediate hazards to subjects. IRB approval letters specify the expiration date. Study approvals lapse at midnight on the expiration date.

3.12.1 Modifications

Modifications may be requested at a convened IRB meeting or by designated reviewer(s) of an expedited study. For full board reviews, email correspondence is sent to the investigator detailing requests for revisions, clarification, or additional information as well as information regarding continuing review. For exempt and expedited reviews, correspondence may be made via phone conversation or email. The investigator has 60 days to respond to all requested revisions. If the investigator does not respond within 60 days, the application is withdrawn. If the investigator wishes to conduct any study that has been withdrawn, he/she must submit a new application, incorporating modifications as previously requested from prior IRB review. In order to receive IRB approval, all requested modifications must be described to the satisfaction of the reviewer(s). IRB decisions are communicated to the investigator by letter sent via email and documented in the minutes for full board reviews or in the file for expedited reviews. In order to receive approval for substantive changes by full IRB review, the investigator's response must be reviewed during a subsequent, convened meeting. For expedited review, the investigator's response is typically, but not always, reviewed by the same expedited reviewer(s). Approval will not be granted until all modifications are met to the satisfaction of the IRB or expedited reviewer(s).

3.12.2 Disapproval

Disapproval means that the IRB has determined that the research cannot be conducted at WVSOM by employees or agents of WVSOM, or otherwise under the auspices of WVSOM.

3.12.3 Approval

Approval in principle is granted to satisfy sponsoring agency requirements or to allow investigators to have access to funding to begin aspects of the project that do not involve human subjects. Federal regulation 45 CFR 46.118 describes two (2) circumstances in which the IRB may grant approval without having reviewed all study procedures and consent documents: (1) if study procedures are to be developed during the course of the research, but human subjects approval is required by the

sponsoring agency; or (2) if the involvement of human subjects depends on the outcome of work with animal subjects. The IRB may then grant approval without having reviewed the as yet undeveloped recruitment, consent, and intervention materials. If the proposal is funded, the investigator must submit materials for approval at least 60 days before recruitment of human subjects begins.

3.12.4 Calculation of Approval and Expiration Dates

- For Full Board Review, the approval date is the date of the convened meeting when approval was determined. For studies approved with conditions, the approval date is the date that a designated reviewer confirms that the condition(s) have been met. For Expedited Reviews and exempt studies undergoing limited review, the approval date is the date that notification of approval was sent to the Principal Investigator.
- For Exempt Review, the approval date is the date that notification of exempt status confirmation was sent to the Principal Investigator.
- The expiration date for non-exempt studies is the last day that the study is approved until midnight in the local Eastern Time zone. The IRB has the authority to set approval dates or other limitations as it deems necessary to ensure adequate monitoring, so long as the approval period does not exceed one year.
- Expiration of approval for annual review occurs at midnight one (1) year minus one (1) day from the "approval date". Approval for a specified time period less than one (1) year occurs at midnight of the specified date.
- For exempt studies, investigators are contacted every three (3) years to verify that the research is ongoing and remains exempt. If the research is completed prior to the three (3) year period, investigators are requested to notify the IRB of study closure.

3.13 Study Suspension, Termination and Investigator Initiated Hold

In accordance with Federal regulations 45 CFR 46.103(b)(5) and 45 CFR 46.113, any suspension or termination of IRB approval will be reported by letter within 30 days of the IRB's decision to the ORSP, the Department Chair, the Dean, the President, and the Office of Human Research Protections.

3.13.1 Suspension/Termination

IRB approval may be suspended or terminated if research is not conducted in accordance with IRB or regulatory requirements or is associated with unexpected problems or serious harm to subjects.

- Suspension of IRB approval means a directive of the convened IRB or IRB Chair to temporarily stop some or all previously approved research activities without terminating all previously approved research activities. Suspension by the IRB Chair must be reported to a meeting of the convened IRB. Suspended protocols remain open and require continuing review.
- Termination of IRB approval means a directive of the convened IRB to permanently stop all activities in a previously approved research project. Terminated protocols are considered closed and no longer require continuing review. Termination of research approved by expedited review must be made at a convened IRB meeting.

The IRB Chair will notify the PI in writing of suspension or termination with an explanation of the reasons for this action. Terms and conditions of the suspension must be explicit. The investigator will have an opportunity to respond in person at a convened meeting or by email correspondence. The convened IRB or individual ordering suspension or termination will consider whether withdrawal of enrolled subjects is necessary to protect their rights and welfare. Alternatives to be considered may include: transferring participants to another investigator; arrangements for continuing care or follow-

up outside the research; allowing continuation of some research activities under the supervision of an independent monitor; or requiring follow-up of participants for safety reasons. When study approval is suspended or terminated, the convened IRB or individual suspending or terminating the research will notify currently participating subjects. If follow-up for subject safety is permitted or required, then subjects will be so informed and will also be informed of any adverse events. The investigator MUST continue to report adverse events and unanticipated problems to both the IRB and sponsor.

Note: Suspension or termination of IRB approval can also be determined by WVSOM officials acting outside the HRPP for reasons that are not necessarily related to protecting the rights and welfare of study participants. Such institutional actions may be made by the President, Vice-Presidents, or Dean. Institutional actions may be made in the Institution's best interest provided that the aggrieved investigator is entitled to all rights and procedures afforded to him/her under the Grievance Policy. The investigator must report any suspension or termination of research by institutional officials to the IRB. The IRB will then determine if suspension or termination of IRB approval is warranted.

Note: For procedures on appealing IRB decisions, see Section 3.18.

3.13.2 Investigator Initiated Hold

An investigator may request administrative hold of research activities to temporarily or permanently stop any approved research activities. Investigator-initiated administrative hold is not a suspension or termination. Investigators must notify the IRB in writing that:

- He or she is voluntarily placing a study on administrative hold;
- A detailed description of research activities that will be stopped;
- Any potential harm to subjects that may result from stopping study activities;
- All proposed actions to be taken to protect current participants;
- Actions to be taken prior to IRB approval to eliminate any immediate harm to participants.

Upon receipt, the IRB Chair, in consultation with the investigators, will determine whether any additional procedures are needed to protect the rights and welfare of current participants and determine how and when currently enrolled participants will be notified. Investigators may request modification of an administrative hold by written request to the IRB.

3.14 Continuing Review

Except for research determined to be exempt or to meet the criteria for non-exempt studies that don't require continuing review described in Section 3.6.1.1 above (45 CFR 46.109(f)), the IRB reviews all ongoing research at least annually and may require more frequent review as appropriate to the level of risk of harm to participants. Study activities may also be monitored as part of the continuing review process. Continuing review occurs as long as the research remains active unless it has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

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

Principal investigators are notified of approval duration and/or limitations of approval in their initial review approval letter. Reminder notices may be sent by the ORSP as a courtesy to investigators, but are not to be relied upon.

3.14.1 Continuing Review Process

It is the investigator's responsibility to ensure that the continuing review of research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted. Therefore, continuing review and re-approval of research must occur by 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. Investigators must submit the continuing review form, the currently used informed consent form and protocol as well as a status report that includes:

- The number of subjects enrolled;
- A summary of reportable events since the last IRB review, including but not limited to adverse events, unanticipated problems, and any complaints about the research;
- A summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review;
- Any other relevant information, especially information about risks associated with the research, including any relevant multi-center and/or data safety monitoring reports.

For non-exempt studies that do not require continuing review, investigators must submit a protocol update prior to the expiration date indicating if the study is ongoing and confirming that there have been no changes that would change the status of the study, or must submit a protocol closure form.

3.14.2 Full Board Continuing Review Notes

In conducting continuing review of research not eligible for expedited review, all IRB members are provided the materials listed in Section 3.14.1, including any modifications previously approved by the IRB. At the meeting, the Primary and Secondary Reviewers lead the IRB through the review. When reviewing the current informed consent document(s), the IRB ensures the currently approved or proposed consent document is accurate and complete. Any significant new findings that may relate to subjects' willingness to continue participation must be provided to subjects in accordance with 45 CFR 46.116(b)(5). Though review of currently approved or newly proposed consent documents occurs during continuing review, informed consent documents should be modified and submitted to the IRB for approval whenever new information becomes available. The IRB will consider whether verification is needed from sources other than the investigator that no material changes have occurred since previous IRB review. Examples that may require verification from other sources include: (a) the investigator has a pattern of submitting the wrong version of the protocol or consent document, or (b) the investigator has a pattern of submitting reports of unanticipated problems (UPs) after the deadline for reporting. Approval will only be granted if the study meets 45 CFR 46.111 regulatory criteria for approval of research.

3.14.3 Expedited Status Update Notes

For studies that were initially approved using expedited procedures and do not require continuing review, investigators must submit a protocol status update prior to the expiration date indicating if the study is ongoing and describing any changes that would alter the status of the study. This information will be reviewed by the IRB Chairperson or Designee to confirm that the study still meets expedited criteria and does not require additional continuing review.

3.14.4 Approval Period

The approval period for study continuation is determined by the IRB based on the potential or actual risk of harm to participants. Though all non-exempt studies are reviewed or have their status

confirmed at least annually, more frequent review and/or monitoring may be required if deemed appropriate by the IRB. Revisions to continuing research applications may be required. The approval and expiration date are noted on IRB letters sent to the PI and must be strictly adhered to. Investigators should submit renewal application materials no less than 30 days prior to the study expiration date. Since regulations make no provision for a grace period beyond the expiration date of IRB approval, continuing review and re-approval of research must occur by midnight of the date when IRB approval expires.

3.14.5 Lapse in Continuing Review

When continuing review or status update of a non-exempt research project does not occur prior to the end of the approval date, IRB approval expires automatically, and all research activities must stop, including recruitment, enrollment, interactions and interventions with participants, and data analysis. Investigators who believe that current participants will be placed at risk by stopping research procedures should immediately contact the IRB Chair and/or prepare a written justification for continuation in accordance with the IRB approval letter. The IRB Chair or designee will review the justification, and notify the investigator by email correspondence whether current participants can continue. The IRB will provide a formal notice of expiration of approval on the date that expiration occurs as a clear alert to Principal Investigators. Expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval.

3.15 Amendment of an Approved Protocol

Investigators must report planned modifications in the conduct of research and receive IRB approval PRIOR to implementing these changes, as specified below depending on the review category of the research. At the time a study receives IRB approval, Principal Investigators receive a letter of approval that outlines the requirement to submit any changes in their research project to the IRB for prior review and approval. Modifications that were unplanned and involved deviations from the protocol in order to minimize or eliminate a serious hazard are unanticipated problems that involve risk to subjects or others. Modifications include, but are not limited to, procedural changes to a protocol, requesting additional subjects beyond the approved number, changes in protocol or investigational drug brochure, and any changes in informed consent materials or advertisements. Minor modifications involve no added risk beyond minimal risk and make no substantive change to study design. Determination of whether changes qualify as minor is made by the IRB. Major modifications are modifications that are not minor. Major modification to an expedited review protocol may increase the risk to greater than minimal and thus change the review status to full board.

3.15.1 Modification to Exempt Studies

Changes to an exempt study that may change the risk level or significantly impact the ethical use of human subjects in research should be submitted for institutional review prior to implementing the changes. Such changes to the protocol must be submitted to the IRB for review and approval before the changes are instituted. Changes that do not meet these criteria do not have to be submitted to the IRB. If there is a question about whether a change must be sent to the IRB, individuals should contact the IRB for clarification. Changes that require review may include:

- Change in principal investigator.
- Change that increases the risk to participants.
- Addition of children or wards of the state participants.

- Change in survey or interview questions that alter the level of risk, including the addition of questions related to sexual activity, abuse, illicit drug use, or illegal activities, or questions that may provoke psychological anxiety, make participants vulnerable, or subject them to financial, psychological or medical risk.
- Change that alters the category of exemption or adds additional exemption categories.
- Change that adds procedures or activities not covered by the exempt category(ies) under which the study was originally determined to be exempt.
- Change requiring additional participant identifiers that could impact the exempt category or determination.
- Change in inclusion dates for retrospective record review if the new date is after the original approval date for the exempt study.
- Addition of a new recruitment strategy or change in a recruitment strategy that alters the risk or influence to the participants.

3.15.2 Modification to Expedited Studies

Proposed modifications to research previously approved by expedited review, for which approval has been granted may be reviewed by expedited review unless the change results in the research activity no longer meeting the conditions for expedited review, in which case, the modification request will be referred for full board action.

3.15.3 Full Board Review of Protocol Modifications

Full board proposed modifications to research originally reviewed via full board review are reviewed via full board review unless found to be minor, as defined below:

1. Examples of modifications that MAY be MINOR:
   - Changes to contact information in study documents;
   - Correction of typographic and grammatical errors that do not change the meaning;
   - Modified wording to clarify the original intent of the protocol that does not change its meaning;
   - Personnel changes that do not alter the competence of the research team;
   - Revisions to study instruments that do not impact the intent or risk level;
   - Changes in research procedures that have no more than a minor risk of harm, such as changes in the frequency of blood draws (within expedited criteria levels), addition of a clinic visit that involves no new procedures, or addition of a questionnaire that does not introduce new subject matter;
   - Adding new recruitment materials or modifications to existing recruitment materials.
2. Examples of modifications that MAY or MAY NOT be MAJOR:
   - Changes to study design or methodology;
   - Extending the time of the study for follow-up depending on procedures done in follow-up;
   - Adding a research site.
3. Examples of modifications that are LIKELY MAJOR (the review may be carried out as expedited after consideration by the Chair and/or primary reviewer and the minor criteria above apply):
   - Significant changes in study design;
   - Change in the treatment or intervention;
   - Change in inclusion/exclusion criteria;
   - New risk information and/or changes in risk to participants.

3.16 Closure of Research Projects

Regulations at 45 CFR 46.109(e) require continuing review until a study has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

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

When a study has reached this point, only an annual status update will be required. The IRB acknowledges that data analysis may take years to complete or be accomplished by external parties. These Standard Operating Procedures take these circumstances into consideration. IRB oversight may end following a request from the PI for closure only under the following conditions:

- The research must be permanently closed to enrollment with no further interaction/intervention with subjects or access to personally identifiable information for the purpose of research data collection, AND
  - (a) All data analysis involving the research site(s), under the IRB approval, is complete (with data and/or samples de-identified and will remain de-identified) OR
  - (b) Data has been de-identified, with no codes or keys that allow for the potential of identifying individuals in the future. NOTE: This typically applies to multi-center research where de-identified data is provided to the sponsor and the sponsor authorizes IRB closure.

3.16.1 Requirements for Closure

The PI must submit the IRB Protocol Closure Form, requesting approval to close the study to further IRB oversight. If closure is approved, the following ongoing obligations apply:

- The IRB will retain all pertinent documents in accordance with federal regulations.
- Investigators must retain all IRB correspondence, documents and raw data for the minimum number of years required by State and Federal law.
- If the PI closes a study and then later finds that future correspondence or interaction with human subjects formerly in that protocol is necessary for data collection, the PI must immediately inform the IRB. The PI may request that the IRB re-open the study by continuing review (if less than 11 months have passed) or must request a new initial review by the IRB.

It is the responsibility of the PI to request closure. It is the responsibility of the IRB to review the request and approve (discontinue IRB oversight) or disapprove (require continuing IRB oversight) study closure.

3.17 Reporting Institutional Review Board Actions

All IRB actions are communicated to the PI, or designated primary contact person, in writing usually within ten (10) working days via an email letter prepared by the IRB and signed by the IRB Chair or designee. All relevant documents (informed consent, assent, recruitment, data collection) with the stamped approval date are sent with this notification letter to the investigator. For a deferral or request for modifications, notification will include the modifications required for approval along with the basis for requiring those modifications. For a disapproval, deferment, suspension, or termination, the notification will include the basis for making that decision, copied to the chair of the appropriate department. All letters to investigators are filed in the study files maintained by the IRB. The IRB reports its findings and actions to the institution in the form of its minutes, which are distributed by IRB staff to the IO and are stored permanently in the IRB files.

3.18 Appeal of Institutional Review Board Decisions

When a study is disapproved, deferred, suspended, or terminated, the IRB will notify the PI in writing with specific deficiencies and, if applicable, all modifications that are necessary for IRB approval. Written notification will include a statement of the reasons for the IRB decision and give the investigator an opportunity to respond in person or in writing. If an investigator disagrees with any decision or action, he/she may request reconsideration by appearing before the IRB or requesting an advisory review panel. This request must be made to the ORSP, in writing, within seven (7) calendar days of the investigator's receipt of IRB notification.

3.18.1 Procedure

The appeal process must be completed within 120 calendar days of IRB notification to disapprove, defer, suspend, or terminate the study. The decision of the IRB will be final under any of the following circumstances:

- The investigator does not appeal;
- The investigator fails to notify the ORSP within seven (7) calendar days of IRB notification;
- The investigator fails to appear before the IRB at its next scheduled meeting;
- The investigator fails to request formation of an advisory review panel within seven (7) calendar days after appearing before the IRB;
- The investigator fails to make study documents available to the advisory review panel within seven (7) calendar days of being requested to do so;
- Final decision by the IRB after receipt of advisory review panel recommendation occurs.

The IRB will notify the PI, advisory review panel, ORSP, and the IO of the decision.

3.18.2 Composition of the Advisory Review Panel

An advisory review panel shall consist of three persons:

- One chosen by the IRB Chair, who may not be a current member of the IRB or IRB staff;
- One member chosen by the PI, who may not have had any direct involvement in the research activities in question; and
- One member chosen by the IO, who will serve as Chair of the Advisory Review Panel, may not be a current member of the IRB or IRB staff, and may not have had any direct involvement in the research activities in question.

3.18.3 Advisory Review Panel Meeting and Report

Within 30 calendar days of its formation, the panel will complete its investigation and transmit to the IRB Chair a written report of its findings and recommendations. The panel may involve the office of the institution's General Counsel. The IRB will consider this report at a regular or special meeting held within 30 calendar days of the IRB Chair's receipt of the report. The Board will provide written notice of its decision within seven (7) calendar days to the investigator(s), department chair(s), members of the Advisory Review Panel, the Office of Research and Sponsored Programs, the IO, and others as deemed appropriate.

4. Documentation and Records

WVSOM maintains documentation of the IRB activities that are accessible for inspection and copying by authorized representatives of the OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner in accordance with 45 CFR 46.115.

4.1 Institutional Review Board Records

IRB records include, but are not limited to:

1. Written operating procedures as described in 45 CFR 46.103(b)(4) and 45 CFR 46.103(b)(5);
2. List of IRB members in accordance with 45 CFR 46.103(b)(3);
3. Training records for investigators, IRB members, and IRB staff;
4. Correspondence between the IRB and investigators;
5. Copies of research proposals reviewed, scientific evaluations, approved consent documents, progress reports submitted by investigators, and reports of injuries to subjects;
6. Records of continuing review activities;
7. Statements of significant new findings provided to subjects, as required by 45 CFR 46.116(b)(5);
8. Documentation of exemptions;
9. Minutes of IRB meetings in sufficient detail to show meeting attendance; actions taken by the IRB; the vote on actions including the number of members voting for, against, and abstaining; the basis for requiring research changes or disapproval; and summary of discussion resolution;
10. Federalwide Assurances and IRB Authorization Agreements (IAA) and/or Memoranda of Understanding with documentation of review by another institution's IRB when appropriate;
11. Protocol violations submitted to the IRB; and
12. Post Approval Monitoring documentation.

4.2 Institutional Review Board Study Files

The IRB maintains a file for each research project with a unique identification number and all communication with the IRB that includes, but is not limited to:

1. All documents submitted as part of a new protocol application;
2. All documents submitted as part of a request for continuing review or study closure application (including progress reports, significant new findings, and safety reports);
3. All documents submitted as part of a modification after the study has been approved;
4. Documentation of all IRB review actions and IRB reviewer forms, including instructions to investigators regarding what must be done before a study may begin;
5. Documentation of the type of IRB review conducted, including regulatory justification for determinations related to vulnerable populations and waiver or alteration of the informed consent process;
6. IRB-approved Informed Consent forms and Assent forms;
7. Notification of expiration of IRB approval with instructions for submitting required materials;
8. Notification of termination or suspension of research;
9. Correspondence pertaining to appeals;
10. IRB correspondence to and from research investigators;
11. Reports of unanticipated problems involving risk to subjects or others; and
12. Documentation of monitoring/audits, investigations, and reports from external site visits.

4.3 Institutional Review Board Minutes

Minutes of all IRB meetings shall be recorded and, in accordance with 45 CFR 46.115(a)(2), include:

1. Attendance at the meeting;
2. Business items discussed at the meeting, including expedited reviews, adverse events, study closures, emergency use reports or non-compliance reports;
3. Education provided to IRB members and announcements of training opportunities;
4. Notation of any members recused from deliberation and voting due to a conflict of interest;

5. Actions taken by the IRB on each application undergoing initial or continuing review;
6. The vote on each action, including the number of members voting for, against, abstaining, and members absent due to conflict of interest or other reason will be noted by name;
7. The rationale for requiring changes, disapproval, suspension or termination of research;
8. Documentation of all vulnerable groups to be included in the research (children per 45 CFR 46 Subpart D, and pregnant women, fetuses or neonates per 45 CFR 46 Subpart B);
9. Documentation of the rationale for approval of a waiver of consent or waiver for documentation of consent, per 45 CFR 46.116(d) and 45 CFR 46.117(c);
10. Summary of the discussion of any controverted issues and their resolution;
11. Period of approval no greater than one (1) year from the date of the convened meeting;
12. Documentation of any requirement for a data safety monitoring board/committee.

The minutes shall be sent for review and approval via email to the IRB members attending the meeting. Members will be instructed to send any comments, proposed changes or additions to the minutes to the IRB Chair within one (1) week of their receipt. Absence of a response from an IRB member will be considered an approval. After one (1) week, final changes will be made to the minutes. The final version of the minutes will be distributed to the IRB members. Copies of the minutes shall also be sent to the IO. Minutes are retained for at least three (3) years after completion of the research per 45 CFR 46.115(b).

4.4 Institutional Review Board Membership Roster

A roster of IRB members must be maintained, sufficiently describing each member's contributions to IRB deliberations to include the following information:

1. Name;
2. Earned degrees;
3. Affiliated or non-affiliated status (the member nor immediate family member of the member may be affiliated);
4. Area of expertise, including primarily scientific or primarily non-scientific;
5. Research experience including training in research (doctoral degree) and prior or current research (students being trained in research are designated as scientists);
6. Professional experience, including board certification or licenses describing each member's anticipated contributions to IRB deliberations;
7. Whether knowledgeable about or experienced working with vulnerable populations, including children, pregnant women, cognitively impaired individuals, and others;
8. Role as IRB Chair, Vice-Chair, or subcommittee member;
9. Voting status (Ex-officio members are non-voting);
10. Notation of the primary member or class of members for whom an alternate may substitute.

The IRB Chair promptly reports changes in IRB membership to the OHRP and the ORSP. The ORSP maintains the IRB membership roster.

4.5 Access to Institutional Review Board Records

IRB records are kept in a protected electronic system. Paper copies of studies closed prior to the electronic system are kept in a locked cabinet within the ORSP. Doors to the ORSP are locked when the offices are unattended. Access to IRB records are limited to the IRB Chair, members, staff, authorized institutional officials, and officials of Federal and state regulatory agencies. Research investigators are provided reasonable access to their files following written request. Accreditation bodies are provided access as requested. All other access to IRB records is limited to those who have a legitimate need as determined

by the IO and IRB Chair. Records are accessible for inspection by authorized representatives of Federal regulatory agencies during regular business hours. Records may not be removed from the ORSP; however, the IRB staff will provide copies of records for authorized personnel if requested.

4.6 Record Retention

Print-based IRB records, research applications, and research cancelled without participant enrollment are retained for no less than three (3) years after study closure and electronic web-based records are retained indefinitely. Any records stored off-site are stored according to the security and storage policies of the West Virginia School of Osteopathic Medicine.

5. Obtaining Informed Consent from Research Subjects

No investigator conducting research under the auspices of WVSOM may involve a human being as a subject in non-exempt research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative (LAR) unless a waiver of consent has been granted by the IRB. The IRB will evaluate the consent process and procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants.

5.1 Definitions

Legally authorized representative (LAR) 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 (see 45 CFR 46.102(i)). If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research. Federal regulations state that "no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative" (45 CFR 46.116). For the purposes of these Standard Operating Procedures , a legally authorized representative includes a person appointed as a health care agent under a Durable Power of Attorney for Health Care (DPAHC), a court appointed guardian, or next-of-kin in the following order of priority under W. Va. Code §§ 16-30-1 et. seq. (West Virginia Health Care Decisions Act): spouse, adult child (18 years or older), parent, adult sibling (18 years or older), grandparent, or adult grandchild (18 years or older).

Legal guardian means a person appointed by a court of appropriate jurisdiction.

5.2 Basic Requirements for Informed Consent

Legally effective informed consent must be obtained before involving participants in research from each subject or the subject's LAR. The informed consent process involves three (3) key features:

1. Disclosing information needed to make an informed decision;
2. Ensuring that participants understand what has been disclosed; and
3. Promoting voluntariness in the decision to participate or not participate in the research.

Informed consent is more than just a signature on a form. It is a process of information exchange that includes reading and signing the informed consent document as well as communication between the prospective subject and investigator. The informed consent process begins with initial recruitment by an Investigator and continues until the completion of the study. Investigators must answer questions to ensure understanding by the potential study participant. Though information may be conveyed face to face, by mail, telephone, or fax, informed consent must be obtained face to face by the investigator and

potential study participant unless the IRB approves a modified process. Investigators must obtain consent prior to entering a subject into a study or conducting any study procedures unless consent is waived by the IRB. If someone other than the investigator conducts the interview and obtains consent from a patient or subject, the investigator must formally delegate this responsibility, and the person so delegated must have received appropriate training to provide informed consent. The person so delegated must be knowledgeable about the research and the consenting process, and must be able to answer questions about the study. Though draft consent documents may be developed by a sponsor or cooperative study group, the IRB-of-record has the final authority to approve or require modification of informed consent documents. These requirements are not intended to preempt any applicable Federal, state, or local laws that require information to be disclosed for informed consent to be legally effective.

5.3 Informed Consent Process

Informed consent must be obtained in accordance with 45 CFR 46.116 and 45 CFR 46.117:

1. From subjects who have the legal and mental capacity to give consent.
2. From a legal guardian or a legally authorized representative (LAR) for subjects without the legal and mental capacity to give consent.
3. Under circumstances that provide the subject or LAR with sufficient opportunity to discuss and consider whether or not to participate.
4. Under circumstances that minimize the possibility of coercion or undue influence.
5. In language that is understandable to the subject or LAR. To the extent possible, the language should be understandable by a person educated to 8th grade level using layman's terms in the description of the research.
6. In the native language that is understandable to the subject or LAR when the native language is not English. An informed consent conference must include a reliable translator when the prospective subject does not understand the language of the person obtaining consent.
7. Providing information that a reasonable person would want to have in order to make an informed decision about whether or not to participate and an opportunity to discuss that information.
8. In sufficient detail and presented in a way that does not merely provide lists of isolated facts but facilitates the subject's or LAR's understanding or the reasons why one might or might not want to participate.
9. Without any exculpatory language that would require the subject to waive, or appear to waive, any legal rights or through which the investigator, sponsor, WVSOM employees or agents are released from liability for negligence, or appear to be so released.
10. The Principal Investigator is responsible for insuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided.
11. Informed consent must begin with a concise and focused presentation of key information that is most likely to assist a prospective subject or LAR in understanding why one might or might not want to participate in the research. This part of the informed consent document must be organized and presented in a way that facilitates comprehension.

5.4 Basic Elements of Informed Consent

The consent process must provide the following basic elements of information to potential subjects:

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 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 on the research team for answers to pertinent questions about the research or to voice concerns or complaints 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 IRB to obtain answers to questions about the research; to voice concerns or complaints about the research; to obtain answers to questions about his or her rights as a research participant in the event the research staff could not be reached or in the event the subject wishes to talk to someone other than the research staff.
9. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject 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.
10. For applicable PHS-funded clinical trials, the following language must be incorporated verbatim: "A description of this clinical trial will be available on www.ClinicalTrials.gov as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time." (See 21 CFR 50.25(c).)
11. One of the following statements about any research that involves the collection of identifiable private information or biospecimens:
    - 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
    - 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.

Additional elements of informed consent should be included, as appropriate:

1. A statement that the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable.
2. A statement that if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable.
3. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or LAR's consent.
4. Any additional costs to the subject that may result from participation in the research (include any anticipated additional costs to subjects).
5. The consequences of a subject's decision to withdraw from the research (include any adverse consequences that would result from withdrawal from the research).
6. Procedures for orderly termination of participation by the subject.

7. A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.
8. The approximate number of subjects involved in the study (include when the research involves more than minimal risk).
9. 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
10. A statement regarding whether the clinically relevant research results, including individual research results, will be disclosed to subjects and if so, under what conditions
11. 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.

5.5 Documentation of Informed Consent

In accordance with 45 CFR 46.117, except as provided in Section 5.5.1, informed consent shall be documented by the use of a written consent form approved by the IRB and signed (including in an electronic format) by the subject or the subject's LAR. A copy shall be given to the person signing the form. The consent form may be either:

1. A written consent document that embodies the elements of informed consent required by 45 CFR 46.116 (this form may be read to the subject or the subject's LAR; the investigator shall give the subject or the LAR adequate opportunity to read it before it is signed); or
2. A short form written consent document stating that the required elements of informed consent have been presented orally to the subject or the subject's LAR. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the LAR, and that the key information required by Section 5.3.11 above was presented first to the subject, before other information, if any, was provided. Only the short form itself is to be signed by the subject or the LAR. The witness shall sign both the short form and written summary. The person actually obtaining consent shall sign a copy of the summary. A copy of the written summary and short form of the informed consent shall be given to the subject or the LAR.

The IRB must approve all foreign language versions of the short form document. Expedited review is acceptable if the protocol, the full English language informed consent document, and the English version of the short form document have already been approved by the convened IRB.

5.5.1 Waiver of Documentation of Informed Consent

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

1. That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality (each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern); or
2. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-researchers; or
3. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more

than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism documenting that informed consent was obtained.

In cases in which the documentation requirement is waived, the investigator must provide in the application materials a written summary of information to be communicated to the subject. The IRB may require the investigator to provide subjects with a written statement regarding the research.

5.6 Waiver of Informed Consent

In accordance with 45 CFR 46.116(e) or (f), an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

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: (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; and
2. The research could not practicably be carried out without the waiver or alteration.

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

1. The research involves no more than minimal risk to the subjects.
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
3. The research could not practicably be carried out without the waiver or alteration.
4. If the research involves using identifiable private information or biospecimens in an identifiable format, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.
5. Whenever appropriate, the subjects or LAR will be provided with additional pertinent information after participation.

5.7 Special Consent Circumstances

5.7.1 Non-English Speaking Subjects

When the study subject population includes non-English speaking people or the PI and/or the IRB anticipate that consent discussions will be conducted in a language other than English, the IRB shall require a translated consent document to be prepared. In order to assure that the translation is accurate, the IRB may require a certified translation or review of the consent document by an IRB member or other person fluent in that language. When non-English speaking subjects enroll, both the subject and the witness must sign the translated consent document. Subjects are given a copy of the signed consent document.

1. Unexpected enrollment of a non-English speaking subject: If a PI decides to enroll a subject into a protocol for which there is not an extant IRB-approved informed consent document in the prospective subject's language, the PI must receive IRB approval to follow the procedures for a “short form” written consent as described in Section 5.5.
2. Use of interpreters in the consent process: Unless the person obtaining consent is fluent in the prospective subject’s language, an interpreter must provide the IRB-approved summary and should, preferably, be someone other than the subject’s family. The interpreter should receive a copy of the short form and IRB-approved summary 24 hours before the consent

conversation. If the interpreter also serves as the witness, she/he may sign the short form consent document and summary as the witness, noting "Interpreter" under the witness signature line. The person obtaining consent must document that the "short form" process was used in the progress note of the subject's medical record, including the name of the interpreter.

5.7.2 Braille Consent

For blind subjects who read Braille, the IRB may approve a consent document prepared in Braille. In this case, the IRB will require a printed transcription and may require review by an IRB member or other person who reads Braille. If possible, the subject will sign the Braille consent; otherwise verbal consent will be obtained, witnessed and documented as described below.

5.7.3 Oral Consent

When subjects are unable to read a written consent form (blind or illiterate subjects), the IRB may approve an oral consent process, provided the subject is (1) able to understand and evaluate the risks and benefits of the study and (2) able to indicate approval or disapproval to enroll. For research that is no more than minimal risk, documentation of consent may be waived as noted in Section 5.5.
For greater than minimal risk research, the consent form must be read to subjects who must also be given an opportunity to ask questions. An audiotape approved by the IRB may be used. If capable, the subject signs, or marks an X to signify consent. If that is not possible, the subject will provide verbal consent with the person obtaining consent and a witness signing the consent form. A note should be made on the signature page that an oral process was used and the subject gave verbal consent. The consent process must be documented in the medical record. Signed copies of the consent are given to the subject and provided to the subject on audio or video tape if possible.

5.7.4 Informed Consent for Newborn Screening Research

In accordance with Public Law No: 113-240 (Newborn Screening Saves Lives Reauthorization Act of 2014), when federally funded research on newborn dried blood spots is conducted, it shall be considered human subjects research regardless of whether the specimens are identifiable as in 45 CFR 46.102(f)(2). Furthermore, 45 CFR 46.116(c) and (d) (waivers of informed consent) shall not apply and informed consent, in these cases, shall not be waived by the IRB.

5.7.5 Posting of Clinical Trial Consent Form

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 Federal department or agency 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 trial determines that certain information should not be made publicly available, the agency may permit or require redactions to the information posted. The informed consent form must be posted after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subjects as required by the protocol.

5.8 Consent Monitoring

The IRB may determine that monitoring of the consent process by an impartial observer is required to reduce the possibility of coercion and undue influence, ensure that the consent process is being followed, or ensure that subjects are providing informed consent for high risk studies, studies that involve

complicated procedures, vulnerable populations, or study staff with little experience, or other situations deemed necessary by the IRB. Monitoring may also be appropriate as a corrective action when the IRB has identified problems with a particular investigator or research project. In such cases, the IRB Chair and Assistant Vice President will develop a monitoring plan and submit it to the IRB for approval. Consent monitoring may be conducted by IRB members, ORSP staff, or another party. The PI will be notified of the IRB's determination and the reasons for the determination. Arrangements will be for monitoring of a specified number of subjects to assess whether the informed consent process was completed and documented properly, the subject had sufficient time to consider participation, the consent process involved coercion or undue influence, information conveyed was accurate and understandable, and the subject appeared to understand the information and give voluntary consent. Following the monitoring, a report will be submitted to the IRB to determine any appropriate action.

5.9 Subject Withdrawal or Termination

Subjects enrolled in a research study may withdraw from the research or an investigator may terminate a subject's participation. Investigators must anticipate subject withdrawal or termination by including details regarding how this will be handled within the research protocol and informed consent forms.
For research that is not subject to FDA regulations, investigators, in consultation with a funding agency, may honor a subject's request to destroy the subject's data or exclude the subject's data from analysis.
When seeking informed consent from subjects, details regarding data retention and use must be included as follows: For research not subject to FDA regulation, the investigator should inform subjects as to whether the investigator will (1) retain and analyze collected data up to the time of withdrawal; or (2) allow the subject to request that the investigator destroy or exclude the subject's data from analysis.

A subject may withdraw from the primary interventional component of a study, but allow the investigator to continue other research activities as described in the IRB-approved protocol and informed consent form such as: (1) obtaining data through follow-up interviews, physical exams, blood tests, or radiographic imaging; or (2) obtaining identifiable private information from the records or from healthcare providers, teachers, or social workers. When a subject's withdrawal request is limited to discontinuation of the primary intervention, then research activities involving other types of participation for which the subject previously gave consent may continue. The investigator should ask a withdrawing subject whether the subject wishes to continue follow-up and further data collection after withdrawal from the interventional portion of the study. Under this circumstance, the discussion should distinguish between study-related interventions and continued follow-up of clinical outcome information, such as medical or laboratory results obtained through noninvasive chart review, addressing the maintenance of privacy and confidentiality of information. If a subject withdraws from the interventional portion of the study, but agrees to continue follow-up of associated clinical outcome information, then the investigator must obtain the subject's informed consent for any limited participation in the study unless such a situation was described in the original informed consent form. In this case, IRB approval of informed consent documents would be required. If a subject withdraws from the interventional portion of a study, does not consent to follow-up of clinical outcome information, and does not request removal of his or her data, the investigator may not access the subject's medical record or other confidential records for purposes related to the study. An investigator may review data collected prior to the subject's withdrawal from the study and consult public records such as those establishing survival status (death).

6. Vulnerable Subjects in Research

When some or all of the participants in a research project conducted under the auspices of WVSOM 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 those participants. The IRB must ensure that all regulatory requirements for the protection of vulnerable subjects are met and that appropriate protections are in place. Vulnerable participants may include children, pregnant women, fetuses, neonates, or adults who lack the ability to consent, students, employees, or homeless persons. IRB review of potentially vulnerable participants will include one or more individuals who are knowledgeable about or experienced in working with these participants. The WVSOM IRB does not review or approve studies that involve prisoners.

6.1 Definitions

Dead fetus means a fetus that does not exhibit heartbeat, respiration, movement, or umbilical cord pulsation.

Delivery means separation of the fetus from the mother by expulsion or extraction or any other means.

Fetus, as defined by 45 CFR 46 Subpart B, means the product of conception from implantation until delivery.

Guardian means an individual who is authorized to consent on behalf of a child or protected person. In West Virginia, a "Guardian" of a minor means a person appointed by the court to be responsible for the personal affairs of a protected person, to make health care decisions for that minor or protected person, to ensure that a patient's right to self-determination in health care decisions be communicated and protected in accordance with the protected person or minor's expressed values and wishes, or, if those values and wishes are unknown, in the protected person's best interests. (See W. Va. Code §§ 49-1-4, 16-30-2 and 3, 44A-1-1, and 2-3-1.) Research conducted in jurisdictions other than WV must comply with the laws of guardianship in the relevant jurisdictions.

Minors means persons under the age of eighteen years (see W. Va. Code § 2-2-10). Though the WVSOM IRB defines minors as persons under eighteen years of age, certain West Virginia statutes provide minors with "majority" status when a court has declared the minor to be emancipated or a minor over age sixteen who marries is considered emancipated by operation of law with all of the privileges, rights and duties of an adult, including the right of contract (see W. Va. Code § 49-7-27). Absent specific West Virginia case law or statute to the contrary, persons who are eighteen years of age or older and emancipated minors may execute contracts under these laws. If specific issues arise under West Virginia law, the WVSOM IRB will review them on a case by case basis with the WVSOM General Counsel. Research conducted in jurisdictions other than West Virginia must comply with the laws regarding the legal age of consent for that jurisdiction.

Neonate means a newborn.

Nonviable means a neonate after delivery that, although living, is not viable.

Pregnancy is 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.

Surrogate Consent means consent obtained from an LAR on behalf of a participant determined to lack decision-making capacity.

Viable means able to survive after delivery to independently maintaining heartbeat and respiration.

6.2 Responsibilities

1. The PI is responsible for identifying the potential for enrolling vulnerable subjects or subjects at risk for impaired decisional capacity due to age, psychiatric illness, or other cognitive limitation who may be asked to participate in a research study with greater than minimal risk.
2. The IRB shall include representation, as members or ad hoc consultants, individual(s) who have expertise with the vulnerable populations described in the research proposal.
3. The IRB reviews the PI's justifications for including vulnerable populations in the research to assess appropriateness of the research proposal.
4. The IRB must ensure that additional safeguards are included to protect the rights and welfare of vulnerable subjects at the time of initial review of the research proposal.
5. Information reviewed as part of the continuing review process should include the number of participants considered as members of specific vulnerable populations.
6. For studies that do not have or are not required to have a Data and Safety Monitoring Board (DSMB) or a Data Safety Monitoring Committee (DSMC) and have entered vulnerable subjects, the IRB needs to carefully review the safety monitoring plan.
7. The IRB should be knowledgeable about and experienced in working with populations who are vulnerable to coercion and undue influence. If the IRB requires additional qualification or expertise to review a protocol, it should obtain consultation.

6.3 Research Involving Pregnant Women, Human Fetuses and Neonates

For research involving pregnant women, fetuses, or neonates the IRB will approve the conduct of the research only if it finds that the research meets the regulatory criteria for approval addressed under 45 CFR 46, Subpart B (see 45 CFR 46.204, "Research involving pregnant women or fetuses prior to delivery"; 45 CFR 46.205, "Research involving neonates"; and 45 CFR 46.206, "Research involving, after delivery, the placenta, the dead fetus, or fetal material").

6.3.1 Research Involving Pregnant Women

The IRB will document in the minutes that all of the following conditions required under 45 CFR 46.204(a-j) have been met to approve research involving pregnant women or fetuses:

1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant 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, her consent is obtained in accord with the informed consent provisions of subpart A of this part;
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 informed consent

provisions of subpart A of this part, 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 45 CFR 46.204(d) or (e) is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46, Subpart D;
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.

6.3.2 Research Involving Neonates

6.3.2.1 Neonates of Uncertain Viability and Nonviable Neonates

The IRB will document in the minutes that the following four (4) conditions under 45 CFR 46.205(a)(1-4) have been met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. Individuals providing consent shall be informed of 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. All requirements of 45 CFR 46.205(b) or (c) have been met as applicable.

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by 45 CFR 46, Subpart B, unless the following additional conditions have been met AND the IRB will document in the minutes that conditions under 45 CFR 46.205(b)(1)(i-ii) have been met with legally informed consent provided in accordance with 45 CFR 46.205(b)(2) AND/OR for research involving or could involve nonviable neonates, the IRB will document in the minutes that the following five (5) conditions under 45 CFR 46.205(c)(1-5) have been met:

1. The IRB determines that (a) 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 (b) 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.
2. 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 45 CFR 46, Subpart A, except that the consent of the father or his LAR need not be obtained if the pregnancy resulted from rape or incest.
3. In addition to conditions 1 and 2 noted above, a nonviable neonate may not be involved in research covered by 45 CFR 46, Subpart B, after delivery unless all of the following conditions are met:
    a. Vital functions of the neonate will not be artificially maintained;
    b. The research will not terminate the heartbeat or respiration of the neonate;
    c. There will be no added risk to the neonate resulting from the research;

d. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
e. The legally effective informed consent of both parents of the neonate is obtained in accord with 45 CFR 46, Subpart A, except that the waiver and alteration provisions of 45 CFR 46.116(c) and (d) do not apply. If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent will suffice to meet the requirements, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of an LAR of either or both parents will not suffice to meet consent requirements.

6.3.2.2 Neonates of Certain Viability

The IRB will only allow viable neonates to be included in research in accordance with 45 CFR 46, Subpart A and 45 CFR 46, Subpart D (children) as per 45 CFR 46.205(d).

6.3.2.3 Research Involving the Placenta, Dead Fetus, or Fetal Material

The IRB requires any research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, to be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities. If information associated with material described here 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 subjects and all pertinent regulations are applicable.

6.3.3 Research Not Otherwise Approvable

Under 45 CFR 46.207, there is an option to consider research not otherwise approvable under 45 CFR 46, Subpart B, that presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates. This option requires the IRB to document certain findings and, if the research involves federal funding, to seek approval of the Secretary of the Department of Health and Human Services. In such cases, the Secretary will conduct or fund research that the IRB does not believe meets the requirements of 45 CFR 46.204 or 45 CFR 46.205 only if both (a) and (b) are found:

(a) 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

(b) The Secretary, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:

1. That the research in fact satisfies the conditions of 45 CFR 46.204, as applicable; or
2. 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 informed consent provisions of 45 CFR 46, Subpart A and other applicable Subparts.

6.4 Research Involving Children

The following applies to all research involving children, consistent with 45 CFR 46, Subpart D. The IRB will make the determination that research involving children fits into one (1) of the following four (4) categories described in detail below and document as part of the official record the required findings:

Category 404 - Minimal Risk

The IRB must find and document that the following three (3) conditions have been met:

a. The research is not greater than minimal risk;
b. Adequate provisions for permission are in place from parents or guardians under 45 CFR 46.408; and
c. Adequate provisions for assent are in place.

Category 405 - Greater than Minimal Risk with Prospect of Direct Benefit

The IRB must find and document that the following four (4) conditions have been met:

a. Research greater than minimal risk is presented by a procedure that holds out the prospect of direct benefit for the individual child;
b. The risk is justified by the benefits to the child;
c. Adequate provisions for permission are in place from parents or guardians under 45 CFR 46.408; and
d. Adequate provisions for assent are in place.

Category 406 - Greater than Minimal Risk with No Prospect of Direct Benefit

The IRB must find and document that the following six (6) conditions have been met:

a. Research risk is a minor increase over minimal risk;
b. There is no prospect of direct benefit to the individual child;
c. The research is likely to yield generalizable knowledge about the participant's disorder or condition;
d. The research procedures/intervention is reasonably commensurate with experiences that the research participant is exposed to (during actual or expected medical, dental, psychological, social, or educational situations);
e. Adequate provisions for permission are in place from parents or guardians under 45 CFR 46.408; and
f. Adequate provisions for assent are in place.

Category 407 - Not Otherwise Approvable Potential to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children

The IRB must find and document that the following conditions have been met:

a. The research does not meet the requirements of 45 CFR 46.404, 46.405, or 46.406;
b. The research presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children; and
c. The HHS Secretary (after consultation with a panel of experts in pertinent disciplines and following public review and comment) has determined either:
    i. That the research, in fact, is found to satisfy the conditions of 45 CFR 46.404, 46.405, or 46.406, as applicable, or
    ii. The following:
        (1) The research presents a reasonable opportunity to further understand, prevent, or alleviate a serious problem affecting the health or welfare of children;

(2) The research will be conducted in accordance with sound ethical principles;
(3) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 45 CFR 46.408.

Required reporting to DHHS is initiated by correspondence from the IRB Chair or designee who will report directly to the Office for Human Research Protections. The OHRP Guidance Document: Children Involved as Subjects in Research: Guidance on the HHS 45 CFR 46.407 ("407") Review Process will be followed by the IRB and OHRP. Not until the appropriate official has issued determinations in writing back to the IRB as documented in the official record will the IRB be able to fully review the research and consider its approval status.

6.4.1 Parental Permission and Assent

The IRB will assess the process of obtaining and documenting assent/dissent and obtaining and documenting parental permission to determine whether adequate provisions have been made for providing the basic elements of consent and any additional elements as described in Section 5. The IRB may find that the permission of one parent is sufficient for Categories 404 or 405. The IRB's determination of whether consent must be obtained from one or both parents will be documented in the approval letter and meeting minutes. Consent from both parents is required for research under Categories 406 or 407 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 consent from a parent or legal guardian if the research meets provisions for waiver or the IRB determines that the research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect subjects (e.g., neglected or abused children) provided an appropriate mechanism for protecting the children is substituted and waiver is consistent with Federal, State, or local law. The choice of an appropriate mechanism depends upon the nature of the study, the anticipated risk and benefit to subjects, and their age, maturity, and condition. Permission from parents or legal guardians must be documented in accordance with Section 5.

6.4.2 Assent and Documentation of Assent from Children

Assent means that each child gives affirmative agreement to participate in research, actively showing his or her willingness to participate rather than just complying with directions to participate. The process of assent shall include an explanation in language suitable to the age and competence of the children, describing the purpose of the research and an explanation of risks and benefits associated with the child's participation in the research. When judging whether children are capable of assent, the IRB is charged with taking into account the age, maturity, and psychological state of the children involved. The assent procedure may include:

- An oral and/or written explanation of the research presented to the child. Unlike the consent or parental permission process, federal regulations do not specify the elements of assent. The content of the assent process should be developmentally appropriate as to length and content.
- How, and whether, assent is applicable to all, some, or no children. If assent is only applicable to some children, indicate which children are asked to provide their assent to participate.
- The child is asked to assent orally and may be asked to sign the assent or parental permission form, indicating willingness to participate in the proposed research study.
- Although written documentation of the child's assent is not required, the investigator and the IRB will consider providing an assent signature line for children to sign, as appropriate.

The IRB must determine the capacity to assent based on the nature of the proposed research activity. The assent procedure should reflect a reasonable effort to enable the child to understand what his or her participation in research would involve to the degree the child is capable. Unless age-specific waiver of assent is requested and approved, children of age 7 and higher are expected to be part of the discussion. To request a waiver of assent for some or all participants, due to age or anticipated condition, the PI must provide a sufficient justification. Child participants not meeting the age or condition specified in the waiver must give assent to participate in the research. An IRB approved waiver of assent for children below age 7 is not required. The justification for waiver of assent may include, but is not limited to, the following examples:

i. If the PI has determined that some or all subjects over age 7 will not be capable of providing assent based on their developmental status or impact of illness, then the PI will need to support this determination, and the IRB relies upon the professional opinion of the investigator for determining an individual's capacity for assent;
ii. The research offers a prospect of direct benefit not available outside of the research; and/or
iii. The same conditions under which parental permission can be waived apply (see 45 CFR 46.116(c-d)).

- In cases where the IRB has approved a waiver of assent for individual subjects, the PI must provide a clear process for determinations when waiver of assent from the child is appropriate, noting any justification for waiver of assent specific to that individual on the assent/parental permission form.
- If a child's parent or parents give permission for the child to participate and there are grounds for waiving assent, then the assent should be waived. Nevertheless, the child must be informed about the proposed research intervention. Therefore, it is possible that a child may voice an objection (dissent) to participate (even when assent has been formally waived by the IRB). In this case of "waiver of assent" versus "individual objection," the PI (together with the parents) should assess the child's dissent and respect this choice when and if possible. If the PI and the parents determine that the objection cannot be respected, the PI is to consider consultation with the IRB, off-protocol access to identical research therapies, and/or consultation with the results reported to the IRB.

6.4.3 Children Who are Wards of the State

Children who are wards of the State or any other agency, institution, or entity can be included in research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge only if the 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 subjects 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 interest 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.

6.5 Persons with Impaired Decision Making Capacity

The decision-making capacity of a potential research subject should be evaluated when there are reasons to believe that the subject may not be capable of making voluntary and informed decisions about research participation. The investigator and research staff must have adequate procedures in place for assessing and ensuring subjects' capacity to understand and provide informed consent or assent. The IRB evaluates the adequacy of proposed plans for research protocols that involve subjects with cognitive impairments that may affect decision-making capacity. Though it is not necessary to require a formal cognitive assessment by an independent professional for all potential research subjects with cognitive limitations, the IRB may determine that cognitive assessments are necessary for, but are not limited to, the following situations:

- For research that poses greater than minimal risk, the IRB may require investigators to use independent qualified professionals to assess whether potential subjects have the cognitive capacity to give informed consent.
- Even in research involving only minimal risk, the IRB may require cognitive assessment if there are reasons to believe that potential subjects' cognitive ability may be impaired.
- For research protocols involving subjects who have fluctuating or limited decision making capacity, the IRB may require investigators to maintain ongoing communication with caregivers.
- Third party consent monitors may be used during the recruitment and consent process, or waiting periods may be required to allow subjects to consider information provided.
- Investigators may allow persons with decisional impairment to make informed consent decisions or refuse participation in research.
- Cognitive metrics may include repetitive teaching, group sessions, audiovisual presentations, and oral or written recall tests.
- Cognitive assessment may include follow-up questions to assess understanding, videotaping or audio-taping of consent interviews, second opinions, use of independent consent observers, and/or interpreters for the hearing-impaired.
- Trusted family members or friends may be involved in the disclosure and decision-making processes.
- Since decision-making capacity may fluctuate for some subjects, a re-consenting process with LAR (surrogate consent) may be necessary.
- Some persons may resist participating in a research protocol approved by their representative. Under no circumstances may subjects be forced or coerced to participate.

When a research participant experiences impaired decision-making capacity after enrollment, the PI is responsible for notifying the IRB. The PI is also responsible for developing a monitoring plan for impaired decision-making research participants. Research involving persons with impaired decision-making capacity may only be approved when the following conditions apply:

1. Incompetent persons or persons with impaired decision-making capacity are only suitable as research subjects due to the nature of the study. In this case, competent persons are not suitable for the proposed research. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available or easily enrolled.
2. Incompetent persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm. The proposed research must either

entail no significant risks or, if the research presents some probability of harm, there must be a greater probability of direct benefit.

3. Procedures must be in place to ensure that participants' representatives are informed of their roles and obligations to protect incompetent subjects or persons with impaired decision-making capacity. Health care agents (appointed Durable Power of Attorney for Health Care (DPAHC)), next-of-kin, and/or guardians must be given descriptions of the research study along with a description of any obligations they assume as representatives. They must be told that they have an obligation to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the subject's best interest.

The IRB membership must include at least one member with expertise in the research area with consideration given to adding another member, family member of a cognitively impaired person, or an advocacy group member for the population to be studied. The IRB may utilize ad hoc members or consultants to ensure appropriate expertise.

6.5.1 Procedures for Determining Capacity to Consent

Decisional capacity has been interpreted by the American Psychiatric Association as requiring:

1. Ability to evidence a choice,
2. Ability to understand relevant information,
3. Ability to appreciate the situation and its likely consequences, and
4. Ability to manipulate information rationally.

Studies enrolling vulnerable populations who may lack capacity to consent must include someone able to assess the capacity of each potential subject to consent. The consent assessor should be a researcher or consultant familiar with dementia and qualified to assess and monitor subject capacity to consent on an ongoing basis. The IRB will consider the qualifications and any conflict of interest related to assessing capacity to consent. Investigators may determine after medical evaluation that a prospective research subject lacks decision-making capacity and is unlikely to regain it within a reasonable time. If lack of capacity is because of mental illness, a psychiatrist or psychologist must confirm and document this determination in the individual's medical record. A person who has been determined to lack capacity to consent to participate in a research study must be notified of that determination before permission may be sought from his or her LAR to enroll that person in the study. If permission is given to enroll the person, then the potential subject must be notified. If the person objects to participating, then the person may not be enrolled.

6.5.2 Informed Consent, Assent, and Surrogate Assent by the Legally Authorized Representative

When participants have the capacity to give consent as determined by qualified professionals, informed consent should be obtained and documented in accordance with Section 5. When participants lack the capacity to give consent, investigators may obtain consent from the LAR who gives surrogate consent. A person who is incompetent or has been determined to lack capacity to consent to participate in a research study should be informed about the trial to the extent possible, given the opportunity to assent to participate, and to sign and date the written informed consent or a separate assent form. If the person objects to participating, then the person may not be enrolled. Investigators and IRB members must be aware that some subjects' decision-making capacity may fluctuate. For subjects with fluctuating decision-making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary. Although incompetent to provide informed consent, some persons may resist participating in a research

protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

7. Unanticipated Problems Involving Risks to Subjects or Others

Federal regulations require that unanticipated problems that occur during the course of a research study and as defined herein must be reported promptly to the IRB.

7.1 Definitions from the Office of Human Research Protections Guidance

Adverse Events or AE, including on-site and off-site events, means any unfavorable medical occurrence in a human subject, including any abnormal sign (physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse events encompass both physical and psychological harms, occurring most commonly in the context of biomedical research, although they can occur in the context of social and behavioral research.

Promptly means that every effort should be made to report all UPs as soon as possible. Federal regulations require that all UPs involving risks to research participants or others be reported promptly to the IRB. The WVSOM IRB provides a window of five (5) working days (Monday-Friday) for reporting unanticipated problems.

Protocol Deviations means any change to the IRB-approved protocol taken without prior IRB approval.

Protocol Violations means an accidental or unintentional change to the IRB-approved protocol that harmed or increased the risk of harm to participants or others.

Research Setting means the research site and responsible IRB when reporting UPs:

- Internal UP involves a research site under the jurisdiction of the WVSOM IRB.
- External UP involves a research site that is NOT under the jurisdiction of the WVSOM IRB.

Unanticipated problems involving risks to participants or others or UPs means any incident, experience, outcome, or new information that meets all 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 (in these Standard Operating Procedures, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

7.2 Reporting

Investigators must promptly report the following problems to the responsible IRB:

1. Adverse events involving direct harm to participants, which in the opinion of the Principal Investigator meet the criteria for an unanticipated problem involving risk to subjects or others.
2. An unanticipated event related to the research that exposes participants to potential risk but does not involve direct harm to participants.
3. An unanticipated event related to the research that exposes individuals other than the research participants (e.g., investigators, research assistants, students, the public, etc.) to potential risk.
4. New information indicates a change in risks or potential benefits of the research. For example:

a. An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB.
b. A paper is published from another study that shows that the risks or potential benefits of the investigator's research may be different than initially presented to the IRB.

5. A breach of confidentiality.
6. Incarceration of a participant in a protocol not approved to enroll prisoners.
7. Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant.
8. Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team.
9. Protocol violation, in which an accidental or unintentional change to the IRB approved protocol harmed participants or others or indicated participants or others may be at an increased risk of harm. Protocol violations must be reported within thirty (30) days of the PI being made aware of the violation.
10. Protocol deviations or exceptions that result in an increase in risk or a decrease in benefit to participants.
11. Sponsor imposed suspension due to an increase in the level of risk.
12. Any other event that indicates participants or others might be at risk of unanticipated harm that is reasonably related to the research.

7.2.1 Submission of Reports

Investigators must report possible unanticipated problems to the IRB promptly.

- If the event requires immediate intervention to prevent serious harm to participants or others, the investigator must report the event within five (5) days of learning of the event.
- Investigators must report all other unanticipated problems occurring at research sites to the IRB as soon as possible but no later than ten (10) business days from the date of the event or from the date the investigator is notified of the event.

Investigators or the study team must report possible unanticipated problems to the IRB in writing using the Unanticipated Problem Reporting Form. Upon receipt of a report of a possible unanticipated problem from someone other than the investigator or study staff, the IRB director will notify the PI on the study when appropriate.

7.2.2 Institutional Review Board Procedures for Handling Possible Unanticipated Problems

1. The IRB Chair or IRB member designated by the Chair will review the report and make the final determination as to whether the event is an unanticipated problem.
2. The IRB Chair or designee may suspend research to ensure protection of the rights and welfare of participants. Suspension directives made by the IRB Chair or designee must be reported to a meeting of the convened IRB.
3. The IRB or the IRB Chair (or designee) has the authority to require submission of additional context from the PI, the sponsor, the study coordinating center, or Data Safety Monitoring Board/Committee about adverse event occurring in a research protocol.
4. If the reviewer considers that (1) the problem was foreseen OR (2) no participants or others were harmed AND participants or others are not at increased risk of harm, the reviewer indicates that the problem is not an unanticipated problem. The form is filed in the study record, the determination is communicated to the investigator, and no further action is taken.

5. If the reviewer considers that the problem is an unanticipated problem, but that the risk is no more than minimal, the reviewer will review the study protocol, the currently approved consent documents, and any prior reports of unanticipated problems involving risks to participants or others to take any appropriate action related to the nature of the risks involved, including modification of the study protocol or consent documents. The results of the review will be recorded in the study record, communicated to the investigator, and reported to the IRB.

It is the responsibility of the Principal Investigator to follow these reporting requirements and provide the IRB with additional information as requested. The IRB is responsible for assessing risk or harm to subjects or others and whether an Unanticipated Problem constitutes Serious or Continuing Non-Compliance.

7.2.3 Institutional Review Board Determinations Related to Unanticipated Problems

After reviewing the study file, consent documents, current and previous reports of unanticipated problems involving risks to participants or others, and recommendations from the IRB Chair or designee, when appropriate, the IRB determination will be made based on the following:

a. Whether the reported event is an unanticipated problem involving risks to participants or others according to the definition in these Standard Operating Procedures;
b. Appropriate action in response to the report;
c. Whether suspension or termination of approval is warranted; and
d. Whether further reporting to Institutional and/or federal officials is required.

1. If the IRB finds that the event is not an unanticipated problem involving risks to participants or others, the IRB may require any of the following:
    a. No action;
    b. Modifications to the protocol;
    c. More frequent continuing review;
    d. Modification of the consent process;
    e. Modification of the consent document;
    f. Provision of additional information to current participants (e.g. when information may affect participant's willingness to continue participation);
    g. Provision of additional information to past participants;
    h. Additional training of the investigator and/or study staff;
    i. Other actions appropriate for the local context.
2. If the IRB finds that the event is an unanticipated problem involving risks to participants or others, the IRB may require any of the following:
    a. Modifications to the protocol;
    b. More frequent continuing review;
    c. Modification of the consent process;
    d. Modification of the consent document;
    e. Re-consent of current participants;
    f. Provision of additional information to current participants (e.g. when information may relate to the participant's willingness to continue participation);
    g. Provision of additional information to past participants;
    h. Additional training of the investigator and/or study staff;
    i. Reconsideration of study approval;

j. Monitoring of the research;
k. Monitoring of the consent process;
l. Referral to other organizational entities (e.g., legal counsel, institutional officials);
m. Suspending the research;
n. Terminating the research;
o. Other actions appropriate for the local context.

3. If, after reviewing a report, the IRB finds that the event is an unanticipated problem involving risks to participants or others or that suspension or termination of approval is warranted, the IRB will notify the investigator in writing with copies to the Chair of the investigator's department, other affected units and the investigator's supervisor. Findings and recommendations will be reported to the IO and appropriate Federal officials (OHRP and ORI).

8. Investigation and Reporting of Unanticipated Problems, Serious or Continuing Non-compliance, Suspensions, and Terminations

DHHS regulations 45 CFR 46.103(a) and (b)(5) require that institutions have written procedures to ensure that the following incidents related to research conducted under an OHRP-approved assurance are promptly reported to OHRP:

- Any unanticipated problems involving risks to subjects or others;
- Any serious or continuing noncompliance with these Standard Operating Procedures or the requirements or determinations of the IRB; and
- Any suspension or termination of IRB approval.

This section describes circumstances that require reporting of noncompliance and unanticipated problems; the process for evaluating, investigating, and determining serious or continuing noncompliance or unanticipated problems; and preparing and distributing reportable IRB determinations. The convened IRB makes determinations of serious or continuing noncompliance and unanticipated problems involving risk to subjects or others, which are reportable to federal agencies and sponsors. IRB actions such as suspensions or terminations of previously-approved research are also reportable. The IRB Chair facilitates review and determination of the above findings.

8.1 Definitions

Continuing non-compliance means a pattern of non-compliance that, in the judgment of the IRB Chair or convened IRB, suggests a likelihood that instances of non-compliance will continue without intervention. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance.

Non-compliance means a failure to comply with any of the regulations and policies described in this document and failure to follow the determinations of the IRB. Non-compliance may be minor or sporadic or it may be serious or continuing.

Serious non-compliance means a failure to follow any of the regulations and policies described in this document or failure to follow the determinations of the IRB that, in the judgment of the IRB Chair or the convened IRB, increases risks to participants, decreases potential benefits, or compromises the integrity of the HRPP. Research conducted without prior IRB approval or participation of subjects in research activities without prior consent (in studies where consent was not waived by the IRB) is considered serious non-compliance.

8.2 Complaints

The IRB Chair will promptly handle (or delegate) investigation of all complaints, concerns, and appeals received by the IRB from investigators, research participants and others. The identity of any entity bringing a complaint, concern, and/or allegation of non-compliance to the attention of the HRPP shall be kept confidential to the greatest extent possible. All complaints, written or verbal (including telephone complaints), and regardless of point of origin, are recorded on a complaint form and forwarded to the IRB Chair. Upon receipt of the complaint, the IRB Chair will make a preliminary assessment as to whether the complaint warrants immediate suspension of the research project. Within three (3) business days, the IRB Chair will generate a letter to acknowledge that the complaint has been received and is being investigated, providing a follow-up contact name.

8.3 Non-compliance

Non-compliance may be found or alleged in a number of ways, including: (1) an Unanticipated Problem involving risks to subjects or others, including a protocol violation; (2) found during post-approval monitoring visits; or (3) reported by a concerned individual. Reasonable efforts should be taken to protect the confidentiality of any persons who allege non-compliance or file reports or grievances, as well as the confidentiality of the investigator and those interviewed during the investigative process. Investigators and study staff are required to report instances of possible non-compliance. The Principal Investigator is responsible for reporting any possible non-compliance by study personnel to the IRB. Common reports to the IRB that are not serious or continuing are typically protocol deviations.

8.3.1 Review of Allegations of Non-compliance

All allegations of non-compliance will be reviewed by the IRB Chair, who will review:

1. All documents relevant to the allegation;
2. The last approval letter from the IRB;
3. The last approved IRB application and protocol;
4. The last approved consent document;
5. The grant, if applicable; and
6. Any other pertinent information (e.g., questionnaires, Data Safety Monitoring Board/Committee (DSMB/C reports), etc.).

The IRB Chair will review the allegation and make a determination as to the truthfulness of the allegation. He/she may request additional information or an audit of the research in question. If the IRB Chair determines that noncompliance did not occur, then this determination is reported in writing to the PI and any other applicable reporting party. The determination letter will be copied to the IO if the IO was notified at the outset. If the IRB Chair determines that noncompliance did occur, then the non-compliance will be reviewed as outlined in Section 8.3.2. If the IRB Chair determines that any allegation or findings of non-compliance warrants suspension of the research before completion of any review or investigation to ensure the protection of the rights and welfare of participants, the IRB Chair may suspend the research with subsequent review by the IRB. The IRB Chair may determine that additional expertise is required to make determinations and may form an ad hoc committee to review the fact gathering process. When an ad hoc committee assists in the review process, the IRB Chair is responsible for assuring that minutes of the meeting are generated and kept to support any determinations or findings made by the ad hoc committee.

8.3.2 Review of Findings of Non-compliance

- When the IRB Chair determines that the non-compliance occurred but that it does not meet the definition of serious or continuing non-compliance, the determination is reported in writing to the PI and, if applicable, the reporting party. The IRB Chair will work with the PI to develop a corrective action plan to prevent future non-compliance. The report of non-compliance and corrective action is reported to the IRB at a convened meeting. If the PI refuses to cooperate with the corrective action plan, the matter is referred to a convened IRB meeting and the IO is notified.
- When the IRB Chair determines that non-compliance has occurred and that the non-compliance meets the definition of serious or continuing non-compliance, the report of non-compliance is referred for review by the convened IRB. The IRB Chair may call an emergency IRB meeting should the circumstances warrant. All findings of serious or continuing non-compliance will be reviewed at a convened IRB meeting. All IRB members will receive all documents relevant to the allegation, the last approval letter from the IRB, the most recently approved study protocol, and consent documents. The IRB may:
  1. Find that there is no issue of non-compliance;
  2. Find that non-compliance is not serious or continuing with an adequate corrective action plan in place;
  3. Find that there is serious or continuing non-compliance and approve a corrective action plan proposed by the Chair and/or ad hoc committee;
  4. Find that there may be serious or continuing non-compliance and direct a formal inquiry to be held;
  5. Request additional information.

8.3.3 Inquiry Procedures

As noted in Section 8.3.2, the IRB may determine that an inquiry is necessary based on several issues that may include but are not limited to:

1. Subject(s) complain that their rights were violated;
2. Report(s) that investigator is not following the protocol approved by the IRB;
3. Unusual and/or unexplained adverse events in a study;
4. Repeated failure of the investigator to report required information to the IRB.

A subcommittee is appointed consisting of IRB members, and non-members if appropriate, to ensure fairness and expertise. The subcommittee responsibilities may include the following:

1. Review of protocol(s) in question;
2. Review of sponsor audit report of the investigator, if appropriate;
3. Review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files, etc., as they relate to the investigator's execution of her/his study involving human subjects;
4. Interview of appropriate personnel if necessary;
5. Preparation of either a written or oral report of the findings, which is presented to the full IRB at its next meeting;
6. Recommend actions if appropriate.

8.3.4 Final Review

Results of the inquiry will be reviewed at a convened IRB meeting. If the results substantiate the finding of serious or continuing non-compliance, the IRB actions may include, but are not limited to:

1. Request a corrective action plan from the investigator;
2. Require verification that participant selection is appropriate and observation of the actual informed consent;
3. Require an increase in data and safety monitoring of the research activity;
4. Request a directed audit of targeted areas of concern;
5. Request a status report after each participant receives intervention;
6. Modify the continuing review cycle;
7. Request additional investigator and staff education;
8. Notify current subjects, if the information about the non-compliance might affect their willingness to continue participation;
9. Require modification of the protocol;
10. Require modification of the information disclosed during the consent process;
11. Require current participants to re-consent to participation;
12. Suspend the study (see below); or
13. Terminate the study (see below).

In cases where the IRB determines that non-compliance meets the definition of unanticipated problem involving risks to subjects or others, the policy and procedure for review of such events will be followed. The investigator is informed in writing of the IRB determination and the basis for the determination and given a chance to respond. If the IRB determines that the non-compliance is serious or continuing, review will be reported as described below in Section 9.

Note: For procedures on appealing IRB decisions, see Section 3.18.

9. Reporting to Regulatory Agencies and Institutional Officials

Federal regulations require prompt reporting to appropriate officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing non-compliance with these Standard Operating Procedures along with the requirements and determinations of the IRB; and (ii) any suspension or termination of IRB approval. The WVSOM HRPP will comply with this requirement as soon as the IRB takes any of the following actions:

- Determines that an event is an unanticipated problem involving risks to participants or others;
- Determines that non-compliance was serious or continuing;
- Suspends or terminates approval of research.

The IRB Chair or designee will prepare reports or letters that include the following information:

1. The nature of the event (unanticipated problem, serious or continuing non-compliance, suspension or termination of approval of research);
2. Name of the institution conducting the research;
3. Title of the research project and/or grant proposal in which the problem occurred;
4. Name of the Principal Investigator;
5. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
6. A detailed description of the problem including the findings of the organization and the reasons for the IRB's decision;
7. Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.);
8. Plans, if any, to send a follow-up or final report by the earlier of:
   - A specific date when an investigation is complete or a corrective action plan is implemented; or

- When the IRB Chair and IO have reviewed and modified the report as needed.

An official written report must be submitted to the OHRP for NON-EXEMPT research that is:

1. Conducted or supported by DHHS;
2. Conducted or supported by any non-DHHS federal department or agency that has adopted the Common Rule and is covered by an FWA; or
3. Covered by an FWA, regardless of the funding source.

The appropriate OHRP address for sending these reports is available on the OHRP webpage. The reporting timeline for the OHRP is "promptly." For more serious incidents, the report will be filed as soon as practicable (possibly within days). It may be necessary to telephone OHRP in order to alert the agency to a very serious problem. Subsequent written reports should reference the date and time of the initial telephone call. In the case of an urgent written or phone report, the nature of the report, the investigation on the part of the institution, and a pending follow-up report with more information as it becomes known should be indicated.

10. Investigators and Research Personnel

The Principal Investigator (PI) or Project Director (PD) and other research personnel make up the research team. The PI/PD oversees and is responsible for the research team, which may include research assistants who intervene or interact directly with human subjects for recruitment or consent or individuals who analyze identifiable data and/or tissue derived from human subjects, but do not make substantive decisions in relation to the design, conduct, or reporting of the research.

10.1 Definitions

Employees or agents, as defined by the OHRP, means individuals who: (1) act on behalf of the institution; (2) exercise institutional authority or responsibility; or (3) perform institutionally designated activities.
Institution, as defined in 45 CFR 46.102(b), means any public or private entity or agency.
Principal Investigator or PI, as defined by the OHRP, means the individual who directs and appropriately supervises all research activities. This role may also be referred to as the Project/Program Director (PD). The presence of more than one investigator does not diminish the responsibility or accountability of the PI/PD.

10.2 Who May Serve as Principal Investigator?

Since the PI/PD bears responsibility for the proper conduct of research, only investigators with the background and training in scientific and administrative oversight necessary to conduct and manage the research project may serve as the PI/PD. The PI/PD must be an employee of WVSOM or a designated investigator at a non-WVSOM with appropriate agreements in place. For students doing research at another site, the PI/PD may be an investigator at another institution. This person must have the appropriate background and training to conduct and manage the project and student (see 1.5.4).

10.2.1 Investigator Roles and Responsibilities

The PI/PD is entirely responsible for the conduct of the research, though he or she may delegate responsibilities to other qualified members of the research team. Ultimately, however, it is the responsibility of the PI/PD to maintain oversight and of all persons to whom any responsibilities are delegated. The PI/PD must be qualified to conduct the research project or have one or more co-investigator(s) that can fulfill any required skills beyond those held by the PI/PD. Investigators who conduct research involving human subjects, and others identified by the WVSOM ORSP or IRB, accept the following responsibilities:

1. Develop and conduct research in accordance with the ethical principles in the Belmont Report;
2. Develop a research plan that is scientifically sound and minimizes risk to the subjects;
3. Have sufficient resources to protect human subjects, including:
   a. Access to a population that allows recruitment of the required number of subjects;
   b. Sufficient time to conduct and complete the research;
   c. Adequate qualified staff and facilities;
   d. Training for all personnel to ensure their competence in conducting research activities;
   e. Medical or other resources, as needed as a consequence of research participation;
4. Ensure study activities are performed with appropriate supervision and only by individuals licensed and qualified to perform the research activities;
5. Ensure research personnel receive and maintain up to date training about ethical research conduct and procedures;
6. Protect the rights and welfare of prospective research participants;
7. Ensure that risks to subjects are minimized using: (i) sound research design and (ii) procedures that may have been performed for diagnostic or treatment purposes when possible;
8. Recruit subjects in a fair and equitable manner;
9. Obtain and document informed consent;
10. Describe plans to monitor data collection for the safety of research participants;
11. Protect participant privacy and maintain confidentiality;
12. Include safeguards when participants may be vulnerable to coercion or undue influence;
13. Provide a procedure to receive complaints or requests for information from participants;
14. Ensure that all laws, regulations, and institutional procedures are upheld;
15. Ensure that all research involving human subjects receives written IRB approval before commencing;
16. Comply with all IRB decisions, conditions, and requirements;
17. Ensure that projects receive timely continuing IRB review and approval;
18. Report unanticipated problems involving risk to subjects or others to the IRB;
19. Obtain written IRB approval before implementing any changes to any project or consent form;
20. Seek IRB assistance about whether any proposed project requires IRB review.

10.2.2 Student Investigator Roles and Responsibilities

The IRB recognizes that a key component in the mission of WVSOM includes research experience for all interested students. While students/trainees may not serve as the PI on human subject research studies, they are encouraged to work with qualified faculty or staff supervision. Students involved in research projects must work with a WVSOM employee who will help guide the student through the approval process and ensure that the required permissions are in place. This employee may or may not be the PI/PD. For example, if a student works with a PI at a remote clinical facility, the PI at that facility is entirely responsible for proper conduct of the study. In consultation with the PI, the WVSOM Regional Assistant Dean or other designated WVSOM employee will assist the student in obtaining required institutional permissions and will monitor the educational aspects if the work is being done as part of a research rotation. Procedures and reporting requirements for research rotations are described in the Clinical Education Manual.

10.3 Investigator and Research Personnel Training and Education

WVSOM is committed to providing training and an ongoing education for investigators and members of the research team related to ethical principles and regulatory and institutional requirements for the

protection of human subjects. Investigators and research personnel must complete the appropriate CITI training, which is determined on a case by case basis depending upon the nature of the research. These courses are found on the CITI website. New research project submissions including "exempt", continuing reviews, and modifications to research are approved by the IRB only after completion of CITI training has been verified. All research personnel, including the PI, co-investigators, research assistants, and students, are required to complete CITI Conflicts of Interest training. Research staff who are involved with the research project through interaction or intervention with research participants or identifiable data must complete Human Research Protections (Biomedical or Social-Behavioral) and Information Privacy and Security training. The PI/PD must confirm that all research personnel have completed appropriate CITI training. Alternative training programs may be accepted by the IRB on a case-by-case basis and this will be documented in IRB records. CITI Conflicts of Interest training must be completed as required by WVSOM's Institutional Policy: R-04, Conflict of Interest in Research and Human Research Protections refresher training must be completed every four (4) years after initial completion for as long as the PI and research personnel are involved in the research. IRB applications for initial and continuing review will not be approved without evidence of CITI training.

10.4 Investigator Concerns

Investigators who have questions or suggestions regarding WVSOM's ORSP or IRB should convey them to the IRB Chair and/or Assistant Vice President of Research and Sponsored Programs to discuss questions, concerns and suggestions. If such concerns are not addressed, other administrative parties (e.g., Dean, Department Chair) or the IO may be contacted as appropriate. The appropriate party will research the issue as necessary to form a response for the investigator.

11. Conflicts of Interest in Research (COIR)

These procedures are guided by Federal regulation Title 42 Part 50, Subpart F and WVSOM's Institutional Policy: R-04, Conflict of Interest in Research to promote objectivity in research and ensure that conflicts of interest do not adversely affect the protection of participants or the credibility of the WVSOM HRPP. The term Conflict of Interest in Research (COIR) refers to situations in which financial or other personal considerations may compromise, or have the appearance of compromising, an investigator's professional judgment in conducting, analyzing, interpreting, or reporting research, and also in hiring staff, procuring materials, sharing results, choosing protocols, using statistical methods, and training students and fellows. Since any unaddressed conflict of interest has the potential to impact research integrity, the Principal Investigator must identify all COI investigators, including any sub-recipient locations, within the Study Personnel Roster.

11.1 Institutional Review Board Confirmation of Investigator Reporting and Training

All individuals responsible for the design, conduct or reporting of research identified by the PI/PD must report all potential conflicts of Interest and complete COI training prior to engaging in any research project. The IRB will confirm that the Significant Financial Interest Disclosure (SFID) form and CITI training has been completed by all study personnel prior to approving any research project.

11.2 COIR Reporting and Management Plan

If a financial conflict of interests exists that would reasonably appear to compromise the objectivity of the research, a management plan for reducing or eliminating the conflict is required by the COIR Officer and COIR Committee. The management plan may include, but is not limited to: (a) public disclosure of the financial interest, (b) naming another individual to serve as the Principal Investigator, (c) divestiture of the

financial interest, (d) severance of the relationships that create actual or potential conflicts, or (e) WVSOM declining an award. The IRB Chair/designee will review the investigator-signed COIR Committee determination and management plan. Based on this information, the IRB Chair/designee may make recommendations to augment the management plan, including revisions to the informed consent form and process. The IRB will not prepare an approval letter until IRB review of the COIR Committee determination and management plan and subsequent IRB recommendations are completed. If the IRB approves the research activity, an approval letter will be issued. If the IRB disapproves the research activity, the IRB notification letter will include the reasons for this decision and give the investigator an opportunity to respond in person or in writing. (For detailed requirements on COIR reporting and management plans, see WVSOM's Institutional Policy: R-04, Conflict of Interest in Research.)

12. Safeguarding Confidentiality of Research Records/Data

Health Insurance Portability and Accountability Act (HIPAA) regulations created federal privacy standards to protect patient medical records and other health information. These standards provide patients with access to their medical records and more control over how their personal health information is used and disclosed. They represent privacy protections for medical records and other individually identifiable health information, whether on paper, in computers or communicated orally. The Privacy Rule is codified in 45 CFR 160 and 164. WVSOM provides guidelines for using private identifiable information, including, but not limited to Protected Health Information (PHI).

12.1 Health Insurance Portability and Accountability Act in Research

Research involving access or use of protected health information must be in compliance with HIPAA regulations. The WVSOM IRB is designated as a Privacy Board to ensure regulatory compliance requirements are met in the conduct of human participant research. All research activities involving PHI must implement an appropriate pathway for the use or access of PHI in accordance with HIPAA regulations that:

- Protect a subset of individually identifiable information, known as PHI, from inappropriate disclosure;
- Only protect individually identifiable health information held or maintained by covered entities or their business associates that create, use or receive such information in a health care context; and
- Specifically address the use of protected health information for research purposes.

12.1.1 HIPAA 18 Identifiers

All individually identifiable health information is considered protected health information. Health information is identifiable if any of the following 18 identifiers are included:

Names	Electronic mail addresses	Certificate/license numbers
Geographic subdivisions smaller than state, except 3 initial zip code digits	Social security numbers	Vehicle identifiers & serial numbers, including license plate numbers
All over age 89 identifiers and elements of dates except year (birth date, procedure, admission date)	Medical Record numbers	Device identifiers and serial numbers
Telephone numbers	Health plan beneficiary numbers	Web Universal Resource Locators (URLs)
Fax numbers	Account numbers	Internet Protocol (IP) address numbers
Biometric identifiers, including finger and voice prints	Full face photographs and any comparable images	Any other unique identifying number, characteristic or code

12.1.2 Access to Protected Health Information for Research

The WVSOM IRB, designated as a Privacy Board, must approve access to any PHI by investigators prior to accessing PHI through one of the following pathways:

- Signed HIPAA Authorization from research participants;
- HIPAA De-Identified Data;
- Waiver of Authorization;
- Partial Waiver of Authorization for Recruitment;
- Partial Waiver of Authorization;
- Limited Data Set and Data Use Agreement;
- Research on Decedent PHI.

12.1.2.1 Signed HIPAA Authorization

Signed authorization is the standard mechanism for accessing or using PHI in research. The Authorization describes risks to privacy and explains how, why and to whom PHI may be used or disclosed. When signing an authorization, research participants are directly authorizing the use of their PHI for research. When informed consent is obtained, signed Authorization is typically obtained. Researchers may choose to combine the Authorization and Informed Consent into one document or use separate Informed Consent and Authorization documents. Templates for both are available on the WVSOM IRB website. HIPAA regulations require authorization documents to contain specific elements and statements. WVSOM researchers can ensure that all of the requirements are met by using the template. The required elements of Authorization are:

- Specific description of the PHI to be used or disclosed;
- Names or specific identification of the person(s) or class of persons authorized to release the PHI (e.g., the covered entity);
- Names or other specific identification of the person(s) or class of persons to whom the PHI will be released (e.g., PI);
- The purpose for using the PHI (e.g., purpose of the research);
- Expiration date or event for when use is no longer authorized (for research this may be “end of the study” or “none” in cases where a research registry will be maintained);
- Statement of the individual’s right to revoke the authorization and how to do so, as well as any exceptions to the right to revoke;
- Statement indicating 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;
- Statement of the potential risk that PHI will be re-disclosed by the researcher, and indicating that the disclosed PHI may no longer be protected under the Privacy Rule;
- Signature and date of the participant or LAR (authorization must include a description of the LAR’s authority to act for the individual).

Investigators should submit an Informed Consent document containing authorization elements OR a separate Authorization document with applications to the IRB. The IRB will determine whether signed Authorization is the appropriate HIPAA pathway. When Authorization is combined with the Informed Consent, the IRB will approve the entire document. When the Authorization is a separate document, the IRB will not review the content of the Authorization. The investigator is responsible for ensuring the authorization

contains all required elements. The approved HIPAA pathway will be documented in the IRB record. When combining authorization with informed consent that includes additional permissions, such as a research registry, the HIPAA authorization must make it clear that the subject is not required to provide authorization for both the primary research activity and the registry.

12.1.2.2 HIPAA De-identified Data

Health information that contains none of the 18 HIPAA identifiers is considered de-identified. A code link to identifiers may not be retained when utilizing the de-identified pathway. De-identified data is not subject to HIPAA regulations. The use of de-identified health information would most often apply in secondary data studies (medical chart reviews) or research when the investigator does not record any identifiers and retains no link to identifiable information. The IRB will verify that no identifiers will be recorded such that the de-identified data pathway is appropriate for the study. The approved HIPAA pathway will be documented in the IRB record.

12.1.2.3 Waiver of Authorization

Waiver of Authorization may be requested to use or disclose PHI for research purposes if obtaining a signed Authorization is not feasible. An agreement must be in place with the HIPAA covered entity from which the records will be reviewed and written approval from the covered entity must be submitted with the IRB application. The WVSOM IRB has the authority to approve Waivers of Authorization. Often, a HIPAA Waiver of Authorization is approvable if a Waiver of Informed Consent is approvable. In order to request HIPAA Waiver of Authorization, Investigators must provide justification within the IRB application, explaining why the use or disclosure of PHI involves no more than minimal risk to the privacy of individuals, including:

- Plans to protect health information identifiers from improper use and disclosure;
- Plans to destroy identifiers at the earliest opportunity consistent with conduct of the study;
- Written assurance that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule;
- Why the research could not practicably be conducted without the waiver of authorization; and
- Why the research could not practicably be conducted without the PHI.

The IRB may approve a Waiver of Authorization through full board review or expedited review if all of the criteria above are adequately addressed in the research application and the conditions are satisfied. The approved HIPAA pathway(s) will be documented in the IRB approval letter.

12.1.2.4 Partial Waiver of Authorization for Recruitment

A Partial Waiver of Authorization is required when an investigator intends to identify a pool of potential research participants for recruitment by searching medical records. An agreement must be in place with the HIPAA covered entity from which the records will be reviewed and written approval from the covered entity must be submitted with the IRB application. When it is not practicable to obtain a signature on an Authorization document

(e.g., when a study has an approved waiver of documentation of consent), then a partial waiver of the authorization (to waive the signature) may be sought from the IRB. Within the research application, investigators should provide justification, describing how the use or disclosure of the PHI involves no more than minimal risk to the privacy of individuals, including:

- Plans to protect health information identifiers from improper use and disclosure;
- Plans to destroy identifiers at the earliest opportunity consistent with the conduct of the research;
- Written assurance that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule;
- Why the research could not practicably be conducted without the partial waiver of authorization; and
- Why the research could not practicably be conducted without the PHI.

Though the intent of the Partial Waiver of Authorization is to allow access to PHI for recruitment, all research participants must provide signed authorization to allow the use of their PHI prior to initiating study procedures. Investigators should provide an Authorization form to the IRB within the informed consent form or a standalone Authorization to be signed by potential participants at the time of enrollment. The IRB may approve a Partial Waiver of Authorization by full board or expedited review if all criteria are satisfied with approval documented by letter.

12.1.2.5 Partial Waiver of Authorization

A Partial Waiver of Authorization is required when researchers wish to include all of the required elements of HIPAA Authorization. Though HIPAA Authorization is obtained from each participant, the Authorization may include simplified language or fewer than the standard elements. For example, this may be used to waive the signature in situations where signed consent is also waived by the IRB when the research is of a sensitive nature and the consent and/or Authorization would be the only identifier of the participant. This could also be used for projects where the participants have a language barrier or low literacy level. In the research application, investigators should describe to the IRB which Authorization elements will be waived or altered. The IRB application must include justification for the use or disclosure of PHI that involves no more than minimal risk to the privacy of individuals, including:

- Plans to protect health information identifiers from improper use and disclosure;
- Plans to destroy identifiers at the earliest opportunity consistent with the conduct of the research;
- Written assurance that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule;
- Why the research could not practicably be conducted without the partial waiver of authorization; and
- Why the research could not practicably be conducted without the PHI.

When utilizing a Partial Waiver of Authorization, research participants must still be provided Authorization information or an Authorization document. Investigators should submit an Authorization form/language to the IRB within the informed consent form or as a standalone HIPAA Authorization that will be given or read to potential participants at the time of enrollment. The IRB may approve a Partial Waiver of Authorization by full board or expedited review if all criteria are satisfied with approval documented by letter.

12.1.2.6 Limited Data Set and Data Use Agreement

A Limited Data Set and Data Use Agreement allow for the use of PHI without signed authorization or a waiver of authorization through a written agreement with the HIPAA covered entity that must be submitted with the IRB application. A Limited Data Set may apply when the limited identifiers below are the only identifiers recorded in the data. Limited Data Sets exclude 16 of 18 HIPAA identifiers, but allow for inclusion of the following:

- Geographic information above the street level (e.g., city, state, zip code).
- All dates or elements of dates (e.g., birth date, procedure date, admission date).

When research will utilize PHI and only record the identifiers listed above, researchers are encouraged to use the Limited Data Set pathway, which requires that the investigator enter into a Data Use Agreement with the covered entity that is releasing the PHI. A Data Use Agreement provides assurances to the covered entity that the PHI will only be used for a specific research purpose. A Data Use Agreement must include the following provisions:

- Specific permitted uses and disclosures of the limited data set by the recipient consistent with the purpose for which it was disclosed;
- Identity of who is permitted to use or receive the limited data set;
- Stipulations that the recipient will:
  - Not use or disclose the information other than permitted by the agreement or otherwise required by law;
  - Use appropriate safeguards to prevent the use or disclosure of the information, except as identified in the agreement, and require the recipient to report to the covered entity any uses or disclosures in violation of the agreement;
  - Hold any agent of the recipient (including subcontractors) to the standards, restrictions, and conditions stated in the agreement;
  - Not identify the information or contact the individuals.

The IRB will review the applicability of a limited data set, ensuring that no unallowable identifiers will be used. The approved HIPAA pathway(s) will be documented in the IRB record. The Data Use Agreement will be signed by an authorized signatory and a copy returned to the investigator with study approval documents.

12.1.2.7 Research on Decedent PHI

Research using PHI only of deceased individuals may be conducted without obtaining Authorization from next of kin or a waiver of authorization if assurance from the investigator includes the following:

- Use of the PHI is solely for research on the PHI of decedents;
- The PHI is necessary for the research; and
- Documentation of the death of the individuals from whom PHI will be used.

When research involves PHI from decedents only, the investigator must submit details within the research application.

The investigator will be notified of IRB review and approval.

12.1.3 Accounting for Unauthorized Disclosure

The PI is responsible for maintaining records of any disclosures of PHI to any individual or entity:

- Not identified in a HIPAA Authorization when a signed Authorization is required;
- Outside the research team; or
- Mandated legal reporting when a Waiver of Authorization is required.

When disclosure involves fewer than 50 research participants, the investigator is responsible for documenting and retaining the:

- Names of research participants;
- Dates of disclosure;
- To whom disclosure was made;
- Brief description of what was disclosed; and
- Brief description of why the PHI was disclosed.

When disclosure involves more than 50 research participants, documentation for each participant is not required, though the PI must document the following information pertaining to each disclosure:

- Name of protocol;
- Types of PHI disclosed;
- Dates of disclosures;
- Contact information for recipients to whom PHI was disclosed; and
- Statement that specific individual's PHI may / may not have been disclosed.

Unauthorized disclosure information must be retained for a minimum of six (6) years past study closure.

12.1.4 Minimum Necessary

HIPAA regulations require that investigators access and use only the minimum PHI necessary to conduct the research. Investigators should consider what PHI is required and only request what is absolutely necessary.

12.1.5 Document Retention

HIPAA regulations require that study documents pertaining to HIPAA covered research be maintained for a minimum of six (6) years past the date of study closure with the IRB.

12.1.6 Breach of Protected Health Information

When PHI is disclosed or possibly disclosed to unauthorized individuals or entities (e.g., unencrypted USB drive stolen or lost), the event must be reported to the IRB as an Unanticipated Problem.

12.2 Assessing Study Feasibility

Methods used to determine whether a sufficient number of eligible subjects exist to conduct a research project should not include private identifiable information. IRB review and approval is not required for feasibility determination, which does not include removal of private identifiable information from the premises of the organization responsible for protecting the PHI. Permission must be obtained from the covered entity to review patient records.

12.2.1 Identification and Recruitment of Subjects Preparatory to Research

Identification and recruitment strategies outlined here are not intended to limit investigators, but to provide guidelines for practice. This section does not apply to or limit research activities involving the

identification or recruitment of prospective research participants from public lists or other non-confidential data sources. When an investigator plans to identify, notify, and recruit research participants based on private identifiable information collected or recorded for the purpose of initiating future contact with prospective participants and the investigator has no prior permission from the participant to access his/her private identifiable information (having read the HIPAA Notice of Privacy does not constitute permission), the IRB:

- Discourages "cold calls/contact" where neither the investigator nor his or her representative has prior permission (a) from the subject to access his or her private identifiable information (i.e., no signed consent) or (b) the IRB has not waived consent for the purpose of recruitment.
- Encourages a recruitment strategy that is responsive to an individual's reasonable expectations for privacy. For example, if the research involves information that could be stigmatizing (HIV status, illicit drug use, etc.), additional considerations for privacy may be needed. Investigators should consider the sensitivity of the private, identifiable information needed to prepare for recruitment, the target population, eligibility windows, and plan accordingly.
- Recruitment strategies should not convey the impression of coercion. Some individuals may find it difficult to refuse participation if someone they trust (e.g., physician) is making the request. These same individuals may, however, prefer to have someone known to them tell them about the study. These conflicting concerns can result in differing recruitment strategies.

12.2.2 Identification and Recruitment at Non-WVSOM Sites

Prior to initiating a research project at any non-WVSOM site, the following steps must to be taken to ensure compliance with HIPAA requirements:

- Obtain permission from an authorized official at the Non-WVSOM site to initiate recruitment contact and initiate an appropriate HIPAA pathway to access private identifiable information.
- In the IRB application, describe the recruitment strategy, including what role the Non-WVSOM site will play in facilitating initial contact with prospective research participants.
- Limit collection of private identifiable information for the purpose of recruitment to the minimum data elements needed to effectively carry out recruitment.
- Obtain WVSOM IRB approval, including waiver of informed consent for recruitment to allow for private identifiable information to be used without permission of the individuals as described in Section 5.6.
- If obtaining and recording PHI from a Non-WVSOM site, follow HIPAA compliance procedures as required by the Non-WVSOM site.
- Within the IRB application, describe the recruitment strategy, which may include a combination of approaches, depending upon the study and number of sites. Two approaches include:
    1. OPT IN – prospective subjects receive information (in person, by letter, phone, email, etc.) requesting action if they want contact or information about the project. Prospective subjects may **only** be contacted if they have initiated the process.
    2. OPT OUT – prospective subjects receive information (in person, by letter, phone, email, etc.) requesting action only if they DO NOT want contact or information about the project. To approve this approach, the IRB must approve a waiver of consent, based on the low risk of investigators accessing prospective subjects' personally identifiable information.

13. Research Recruitment

Recruitment should be responsive to an individual's reasonable expectations for privacy. If the research involves information that could be stigmatizing, additional considerations for privacy may be warranted.

Prospective research participants have an assumed expectation of privacy and investigators should consider the sensitivity of any private, identifiable information in preparing for recruitment. Recruitment strategies should be developed to limit the impression of coercion. Some individuals may find it difficult to refuse participation if someone they trust (e.g., physician) is making the request. These same individuals may, however, prefer to have someone they know explain the study. These are conflicting concerns that may require differing recruitment approaches according to the needs of the project, the population, and the setting. The investigator should consider complications that may impact enrollment, including timelines and eligibility windows. The following steps should be taken as appropriate:

- Obtain written permission from the authorized official at the recruitment site, discussing regulations that govern the release of private, identifiable information.
- Describe detailed recruitment strategies in the IRB application, including any role the recruitment site will play in making initial contact with prospective research participants that may include:
  - "OPT IN" if prospective subjects receive information that prompts the individual to take some action for further contact or information about the research opportunity. In this approach, prospective subjects may only be contacted if they initiate the process.
  - "OPT OUT" if prospective subjects receive information prompting them to take action only if they DO NOT want further contact or information about the research. To approve an "opt out" approach, the IRB must approve a waiver of consent after considering any risk related to accessing prospective participants' personally identifiable information.
- Submit a letter of support from the recruitment site, summarizing its role in recruitment with the IRB application.
- Limit recording any private, identifiable information for the purpose of recruitment to the minimum data elements necessary to effectively carry out recruitment plans.
- Obtain IRB approval, including a waiver of informed consent for recruitment to allow for any private, identifiable information to be used without permission. Waiver of informed consent for recruitment may be approved depending upon any risks related to confidentiality and privacy.
- If obtaining and recording PHI, follow HIPAA compliance procedures as required by the recruitment site.

13.1 Recruitment Strategies

Prospective research participants may be introduced to the research opportunity in person, via phone, email, letter, or a mixed approach. The following standard approaches are not exhaustive:

1. Written Introductions: The IRB must review and approve written correspondence including content, format, choice of letterhead, and planned signatures. Although a mailed letter is most frequently employed, electronic communication may be appropriate in some situations. Letters may be signed by a recruitment site authorized official (e.g., administrator, privacy officer, department head, clinician, etc.) or co-signed with the investigator. The site will typically indicate how it prefers to have the introduction carried out. If private, identifiable information is to be removed from the site for the purpose of generating the introductory letters:
   - The IRB must first review and approve a waiver of informed consent for recruitment.
   - The site may have additional required procedures prior to removing private, identifiable information from its premises.
   - Letters should, at a minimum, contain contact information to obtain more information about the research and study team and allow prospective participants to express a lack of interest in participation and request that no further research contact occur.

- In the case of an "OPT-OUT", investigators should wait a reasonable amount of time to allow prospective participants to respond before contacting them. Certain studies may have a brief eligibility window that may justify a shorter wait time. Justification for a shorter wait time must be included in the research application and approved by the IRB.

2. Verbal Introductions: If a service provider verbally informs a prospective participant about a study as part of an office visit, for example, and the participant agrees to participate, then the investigator may contact the prospective participant. The service provider should record and communicate whether each prospective participant agrees or refuses to participate.

13.2 Prospective Participant Questions and/or Complaints

Questions, refusals to hear about the study, and complaints may occur. In anticipation of such occurrences, investigators should describe, within the research application, how the study team will:

- Answer questions (e.g., "How did you get my name?"). Responses should be clear and concise, explaining how permission was obtained.
- Uphold "no contact" requests. What steps will be taken to ensure no further contact occurs with prospective participants who do not want to be contacted? How will these requests for no further contact be reported to the site?
- Respond to and monitor all complaints regarding the recruitment process. Complaints may include concerns over privacy, confidentiality, and trust. How will the investigator and the site work together to respond to complaints and what individual will be responsible for monitoring complaints?
- Inform the IRB of any complaints at the time of continuing review (or sooner if the nature or number of complaints exceeds what is anticipated). A complaint log is suggested.

13.3 Advertising for Subject Recruitment

Recruitment materials, including brochures, flyers, advertisements (print, radio, television, email, and web-based), audio tapes, video tapes, and letters to potential subjects must not contain coercive language or incentives. Information should be an accurate representation of the research purpose and procedures. All materials aimed at recruiting potential participants must be reviewed and approved by the IRB prior to them being used. Guidelines for recruitment materials are as follows:

- Include the purpose and what is expected of participants.
- Include the required time commitment.
- Include the investigator's department affiliation and where the research will take place.
- Provide the contact name and phone number of the PI.
- Do not include the name of sponsors or products.
- Do not include exculpatory language.
- Avoid phrases such as "help needed," instead stating, "participants are invited."

The IRB will review the advertisement and mode of communication to determine that the procedure is not coercive. When advertisements are to be broadcast, the IRB will review the final audio/video. The IRB will review and approve the wording of the advertisement prior to taping with review of the final taped message accomplished through expedited review. The IRB review will ensure that advertisements do not:

- State or imply a favorable outcome or benefits beyond what is in the consent and protocol.
- Include exculpatory language.
- Make claims that any investigational instrument or process is safe or effective.
- Make claims that any test article is known to be equivalent or superior to another.
- Use terms such as "new treatment," without explaining that the treatment is investigational.

- Promise "free medical treatment" when participants simply will not be charged for taking part in the study.

Advertisements may state that participants will be paid or compensated for their time, but should not emphasize payment or the amount by using larger, colored, or bold type.

13.4 Research Participant Compensation

Payment for participation in research may not be offered as a means of coercive persuasion. It should be characterized as compensation for the subject's time, loss of wages, travel, or inconvenience. Compensation may not be withheld contingent on completion of the study. Instead, compensation should be given on a reasonable prorated basis to avoid the impression of coercing the subject to continue in a study or punishing the subject for non-compliance. Payment to research participants may not be considered in the analysis of risks and potential benefits, but rather as a recruitment incentive. The amount and schedule of payments should be presented to the IRB to assure that neither presents undue influence. The IRB will determine whether any amount paid as a bonus for completion is reasonable and not so large as to induce participants to stay in the study when they would otherwise withdraw. Details concerning payment, including the amount and schedule of payment(s), should be provided in the informed consent document. As compensation for participants, investigators should consider using gift certificates from online retailers in lieu of requiring identifiable information to mail compensation.

13.5 Internet Recruitment and Data Collection

The Internet is commonly used for recruitment and research data collection via electronic surveys and/or questionnaires. Advertising for study participants initiates the informed consent and subject selection process and must receive IRB approval. Unlike print, television, or radio, which is passive, the Internet may be passive or active.

13.5.1 Internet Recruitment

Passive electronic recruitment involves electronic advertisements of printed media on a website or pop-up window that must be reviewed and approved by the IRB with a mock-up submitted review. Recruitment tools that use email or electronic solicitations such as text messaging to reach potential research participants are active recruitment methods that require email addresses to be gathered from public sources or with documented permission of the list owner. Recruitment by electronic invitation must allow recipients to ‘opt out” of future contact without any request for a reason and provide an approximate time for contact to be terminated. Recipients may need to be informed of how their electronic address was obtained or permission obtained prior to contact if, for example, the research involves a sensitive subject or issues of confidentiality. The IRB will also evaluate whether the use of electronic media as the only method of recruitment could limit the equitability of subject selection.

13.5.2 Data Collection Using the Internet

Data collection via the Internet may also use passive or active methods. Data mining may be used to identify patterns and relationships using Internet research and research involving the observation and reporting of online behavior. When research involves passive observation of online behavior, the IRB will make every effort to ensure the protection of human subjects, such as online support groups when participants do not intend or agree in advance for the discussion to be used for research. Though most online groups allow persons to join without participating, permissions must be obtained from the list/group/community with an announcement that an observation is taking place for research

purposes after IRB approval and before collecting research data. The investigator may request IRB waiver of documentation of informed consent.

Procedures must be in place to verify that research participants are adults. The IRB may require additional permissions and/or informed consent depending upon the sensitivity of the discussion, prior disclosure, and confidentiality/anonymity of subjects. Active data collection via direct email, web surveys, or other electronic instruments involves unsecured data that may be vulnerable in transit. Internet data collection is rarely private, anonymous, or confidential. The potential source of risk from breach of confidentiality is more acute if the research involves data that places subjects at risk of criminal or civil liability or could damage their financial standing, employability, insurability, or reputation. An Internet consent document should be provided in the form of a cover letter that includes the elements of signed consent. The consent line should state, "By completing the survey, you are agreeing to participate in the research." Web-based surveys should allow each participant to select whether he/she agrees or not. Online consent may not be appropriate for studies involving highly sensitive information. The investigator must describe the security features of the technology chosen to implement the research and justify the plan based upon the sensitivity of the research. For sensitive data transmissions, the investigator should disclose in the consent process that, "This research involves the transmission of data over the Internet. Although every reasonable effort has been made to ensure data security, confidentiality during transmission cannot be guaranteed." An alternative means for completing the survey should be offered such as printing and mailing the survey. Survey instruments should be designed to allow participants to skip questions or select "I choose not to answer." At the end of a survey, a button should be provided to submit the data and another button to discard the data. The purpose of these buttons is to ensure that subjects may withdraw at any time and to help them understand that if they do withdraw, even after completing the survey, their data can be discarded prior to transmission to the researcher.

13.6 WVSOM Students and Employees as Subjects

When WVSOM students and/or employees are recruited as potential subjects, the investigator must ensure that additional safeguards are in place. The voluntary nature of their participation must be without undue influence. Researchers must emphasize that neither their academic status nor their grades or employment will be affected if they refuse to participate. Being a student can affect making a voluntary decision to participate. The consent form must state that grades or status will not be affected by refusal to participate or withdrawal from the study.

14. Special Requirements

14.1 Certificate of Confidentiality (CoC)

Certificates of confidentiality are issued by the federal government to investigators or institutions engaged in biomedical, behavioral, clinical or other research in which identifiable, sensitive information is collected. The purpose of the COC is to protect the privacy of subjects by limiting the disclosure or identifiable, sensitive information which is defined as information about an individual that is gathered or used during the course of research where an individual is identified or for which there is at least a very small risk 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. COCs will automatically be issued to all research that is ongoing on or after December 13, 2016 that is funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts or other transaction awards that collects or uses identifiable sensitive

information. The NIH will consider requests for COCs for non-federally funded research. Application instructions are provided by the National Institutes of Health.

14.1.1 Statutory Basis for Protection

Protection against compelled disclosure of identifying information about subjects of biomedical, behavioral, clinical, and other research is provided by the Public Health Service Act § 301(d), 42 U.S.C. § 241(d): "The Secretary may authorize persons engaged in biomedical, behavioral, clinical, or other research (including research on mental health, including research on the use and effect of alcohol and other psychoactive drugs) to protect the privacy of individuals who are the subject of such research by withholding from all persons not connected with the conduct of such research the names or other identifying characteristics of such individuals. Persons so authorized to protect the privacy of such individuals may not be compelled in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals." Please note, however, that CoC's are untested in the legal system. There is the possibility that assured protections may be challenged by the courts.

14.1.2 Applicability

NIH considers NIH considers research in which identifiable, sensitive information is collected or used to include:

- Human subjects research including exempt research except for human subjects research that is determined to be exempt from all or some of the requirements of 45 CFR 46 if the information obtained is recorded in such a manner that human subjects cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
- 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 or the use of such data regardless of whether the data is recorded in such a way that the subjects can be identified or readily ascertained.
- 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 identify of an individual as defined in subsection 301(d) of the Public Health Service Act.

14.1.3 Recipient Responsibilities

Disclosure is permitted only when:

- Required by federal, state or local laws excluding instances of disclosure in any federal, state or local criminal, administrative, legislative or other proceeding;
- Necessary for the medical treatment of the individual and made with the consent of such individual;
- Made with the consent of the individual to whom the information, document or biospecimen pertains; or

- Made for the purposes of other scientific research that is in compliance with applicable federal regulations governing the protection of human subjects in research

COC recipients are required to ensure that any investigator or institution not funded by NIH who receives a copy of identifiable, sensitive information protected by a Certificate issued by this Policy, understand they are also subject to the requirements of subsection 301(d) of the Public Health Service Act. In accordance with NIHGPS Chapter 15.2.1, recipients are also responsible for ensuring that any subrecipient that receives funds to carry out part of the NIH award involving a copy of identifiable, sensitive information protected by a Certificate issued by this Policy understand they are also subject to subsection 301(d) of the Public Health Service Act.

For studies in which informed consent is sought, NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

14.2 Genetic Research

The Genetic Information Nondiscrimination Act (GINA) defines genetic testing as analysis of human DNA, RNA, chromosomes, proteins, or metabolites that can detect genotypes, mutations, or chromosomal changes. This includes any test/assay that generates data sufficient to identify an individual by genotype, including by detection of changes in genotype in the form of mutations or polymorphisms. Examples include DNA fingerprinting, Genome Wide Association Studies (GWAS), single nucleotide polymorphism analysis, DNA/RNA sequencing, genomics, and transcriptional profiling by PCR array or microarray formats. Genetic research studies may create risks to participants and their relatives, including employment, insurance, finances, education, and self-perception psychosocial, and economic risks in the near and unforeseeable future should the information not be handled with care. Research participants have the right to make an informed decision regarding current and future uses of genetic information. Privacy and confidentiality related to the procurement, storage, access to and use of genetic information must be carefully maintained and protected to prevent stigmatization, discrimination, or psychological harm. Genetic research can be divided into two broad categories:

1. Research on genetic material common to all bodily specimens, including blood, often described as constitutional, germ-line, or heritable studies. This research may have serious social and economic consequences if confidentiality is breached, since this genetic material can serve as "fingerprint" identification for individuals, be used to predict future diseases, or identify parentage.
2. Research on genetic information from pathologic tissue such as tumor specimens involves sensitive information to the extent that research participants are associated with a particular disease or disorder. Social and economic risks related to this research are less serious than germ-line research.

Routine tests that do not detect genotypes, mutations, or chromosomal changes, such as complete blood counts, cholesterol tests, and liver enzyme tests, are not considered genetic tests under the Genetic Information Nondiscrimination Act (GINA). Also, analyses of proteins or metabolites related to a disease, disorder, or pathological condition that could be detected by a health care professional with appropriate training and expertise in the field of medicine involved are not included.

14.2.1 Institutional Review Board Application Related to Participant Concerns in Genetic Research

Studies that generate information about participants' health risks may provoke anxiety, confusion, damage familial relationships, or compromise insurability and employment opportunities. Though

genetic testing results may not provide a direct correlation to a specific risk, test results have the potential to raise concerns. Investigators play a significant role in minimizing risks or concerns by conducting thorough informed consent and maintaining strict confidentiality when working with genetic information. The research application must include a plan for protecting data and specimens during collection, storage, and transit by electronic or ground delivery. The risk of psychological harm, such as depression or stigmatization, should be adequately described along with how these risks will be minimized. Many genetic studies plan to maintain data for future research purposes. When this information is maintained with identifiers, data collection is considered a research registry that requires the following considerations:

- The research application must describe how specimens and/or genetic data will be collected and what specimens and/or genetic data will be contributed to an existing registry, and/or accessed within an existing registry.
- Investigators may consider obtaining a Certificate of Confidentiality to minimize access to research data. In cases where the risk associated with data access is low, the PI and IRB may agree that a Certificate of Confidentiality is not needed.

14.2.2 Informed Consent Considerations in Genetic Research

The WVSOM informed consent template should be used if genetic research is a component of the research project, which contains sample language for genetic research as well as language for using registries or repositories. The informed consent form should also include information about how data will be stored and any future research that may be conducted. Consider whether participants will be able to designate options for use of collected tissue/specimens such as designating limitations on future research to specific diseases or unrestricted future use. Options should be described in the research application, including the following details:

- How any registry research will track to ensure that future uses of data or specimens are in accordance with the wishes selected within each consent form.
- Choices that participants will have regarding how their samples will be used. Suggested language is included in the informed consent template.
- If participation in the study is contingent upon participants' permission to store data, tissues, or specimens for current or future genetic research, this should be precisely described in the application and informed consent form.
- Disclosure of any potential for commercial profit by the institution, investigator or sponsor from information gathered in the study. The consent form should have a clear statement that the sample/data, any cell lines, profits from data, etc., are the property of WVSOM.
- Description of what will be done with samples when a participant withdraws from the study.
- Participants should be informed of how samples will be handled if they wish to withdraw from the study during active participation or in the future. For example, will samples collected prior to withdrawal be removed or does withdrawal apply to future use only?
- The ability of participants to request removal of samples and/or data from a registry is dependent on whether data will be de-identified (coded) or anonymized. Stripping identifiers with an alpha numeric code does not mean the same as anonymizing data, such that the subject could never be contacted. If identifiers or a code will be maintained with a sample, the prospective subject should be informed that anonymity cannot be guaranteed.
- Consideration of incidental findings that are likely to be found and whether these findings should be shared with research participants. Participants should be informed of incidental findings that

are likely to be sought or may arise from any tests/procedures conducted. Investigators should inform participants about plans for disclosing (or not disclosing) incidental findings.

- Note whether genetic or other incidental findings will be disclosed to participants or another party. In most cases, such information is not disclosed to participants. If the research application and consent form indicates that there will be no disclosure of incidental findings and the investigator later reconsiders, the IRB must give approval for such disclosure before it can occur.
- Inform participants that they have the right to decline receiving the results of genetic testing.
- Any information disclosed must be in a manner consistent with the participant's reading and knowledge level, which may differ for a lay person versus a scientist.
- Indication of the availability of genetic counseling in cases where a study may reveal genetically important information (e.g., genetic defects that could be passed on to progeny).

Note: For informed consent considerations for newborn screening research (i.e., newborn dried blood spots), see Section 5.7.4.

14.2.3 Genomic Data Sharing

The IRB will consider GINA provisions when determining whether genetic research satisfies criteria required for IRB approval, particularly whether the risks are minimized and reasonable in relation to anticipated benefits and whether there are adequate provisions in place to protect the privacy of subjects and maintain the confidentiality of their data. GINA is also relevant to informed consent. The OHRP Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards protects participant genetic data and should be reflected in the consent document's description of risks and provisions for assuring confidentiality of the data. This guidance provides suggested language for informed consent forms.

14.2.4 Genetic Research Involving Minors and Decisionally Impaired Adults

When samples or data collected from a minor or decisionally impaired adult include plans for future research, consideration must be made as to whether waiver of informed consent should be sought, or waiver of informed consent should be sought at the age of majority or when the adult is decisionally capable. This is relevant to research that will require future contact with participants. In some cases, the inability to obtain informed consent may preclude inclusion of the subject's data. Details for obtaining consent in these situations should be described in the research application. Consideration must be made as to whether the results of any genetic analyses will, or should, be revealed to parents or a Legally Authorized Representative. In addition, consideration must be made as to whether this information may be given after the child reaches the age of maturity if the parents had previously refused disclosure. Investigators should consider any risk reducing potential related to genetic counseling.

Note: For informed consent considerations for newborn screening research (i.e., newborn dried blood spots), see Section 5.7.4.

14.2.5 Submitting Genetic Data to Public Repositories

Funding and publication sources are requiring that genetic data be made available for future research. The Genome Wide Association Studies (GWAS) and the Gene Expression Omnibus (GEO) are examples of available genomic repositories in which data may be stored for data sharing. The NIH provides a list of common data repositories. Generally, data that are submitted to repositories is de-identified. Research participants should be notified through the informed consent process of any intent to share data and samples for possible future research, providing a choice of whether they wish to share their

data. A data sharing plan addressing the following elements should be included in the research application that will be reviewed and verified by the IRB:

- Data submission is consistent with all applicable laws, regulations, and WVSOM policies.
- All research uses of data are specifically described within the informed consent form, providing choices to participants related to the nature of current and future research they wish to allow.
- Identities of research participants will not be disclosed to the data repository.
- All plans for submission of data to a repository and subsequent sharing for research purposes is consistent with what is described within the informed consent.
- Plans for de-identifying datasets are described within the research application and informed consent documents.
- Risks to individuals, families, groups/populations associated with data submitted to the repository have been described along with plans to minimize those risks.

Research projects submitting de-identified or anonymous secondary data to a GWAS may not qualify as research involving human subjects. Hence, such a project does not require IRB approval, though WVSOM must certify that the data being submitted to a GWAS fulfills the requirements for submission. Thus, projects of this type must be submitted to the ORSP for review.

Details regarding how to obtain data from the NIH GWAS repository specify requisite security measures. Though data obtained from the NIH GWAS repository are de-identified and generally do not require IRB review, some GWAS databases require IRB review prior to releasing information. Each GWAS database will specify when IRB review is required. Information regarding anonymous or de-identified samples is provided within OHRP Guidance on Research Involving Coded Private Information and/or Biological Specimens and described in Section 14.3 below.

14.3 Research Involving Coded Private Information or Biological Specimens

WVSOM policy is based on OHRP's Guidance on Research Involving Coded Private Information or Biological Specimens, which distinguishes when this research is or is not research involving human subjects and who should determine whether human subjects are involved in research. Coded data assigns a number, letter, symbol, or combination thereof via a key to this coded information that links identifiers to the private information or specimens. Obtaining, receiving, or accessing identifiable private information or identifiable specimens for research purposes constitutes human subjects research. This includes the use or analysis of identifiable private information or identifiable specimens that are already in the possession of the investigator for research purposes. Private information or specimens are individually identifiable when they can be linked to specific individuals directly or indirectly through a coding system. Research involving only coded private information or specimens do not involve human subjects if both of the following conditions are met:

1. Private information or specimens were not collected specifically for the currently proposed research project through interaction or intervention with living individuals;
   AND
2. The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain if:
   a. The key to the codes was destroyed prior to the onset of the research;
   b. The investigator(s) and the holder of the key enter into an agreement prohibiting release of the key to the investigator(s) under any circumstances until research participants are deceased. Note: DHHS regulations do not require IRB review and approval of this data use agreement;

c. IRB-approved written operating procedures prohibit the release of the key to the investigators under any circumstances until research participants are deceased; or
d. Other legal requirements prohibit the release of the key to the investigators until research participants are deceased.

If the investigator(s) unexpectedly/inadvertently learns the identity of a research participant(s) or for unforeseen reasons now believes it is important to identify a research participant(s), then the research activity is then considered to involve human subjects unless the research is determined to be exempt. In this case, IRB review and informed consent would be required unless the IRB approved a waiver of informed consent.

The investigator, in consultation with the IRB Chair, will determine if the research involving coded information or specimens requires IRB review. If the request is verbal (by phone or in person) or by email, it is the investigator's responsibility to maintain documentation of such a decision. If the investigator submits an IRB application, the request must include sufficient documentation to support IRB determination.

14.4 Mandatory Reporting

West Virginia law mandates persons who suspect child or elder abuse or neglect to report this to the West Virginia Department of Health and Human Resources. Research that carries the potential of revealing abuse or neglect should be noted within the informed consent form, advising that mandatory reporting requirements will be upheld under West Virginia law (see W. Va. Code §§ 49-6A-2 or 61-2-29). Investigators should consult the IRB to determine if potential subjects should be advised of mandatory reporting requirements during the informed consent process.

14.5 Case Reports Requiring Institutional Review Board Review

An anecdotal report on a patient or patients seen in clinical practice or a comparison of patients to the existing literature are not research and do not require IRB approval unless data collection constitutes a systematic investigation that contributes to generalizable knowledge, which would require IRB approval. In addition, if the investigator intends to publish case report findings, then the publisher(s) may require a determination letter from the IRB.

14.6 International Research

The OHRP 2014 Edition of the International Compilation of Human Research Standards requires that human subjects outside of the United States who participate in research projects conducted or funded by DHHS receive the same level of protections as research participants inside the United States. All policies and procedures applied to research conducted domestically must be applied to research conducted in other countries. To this end, the WVSOM IRB will ensure review of any international research prior to commencement. Approval of international research is only permitted if the international site holds an Assurance with OHRP and local IRB approval is obtained. Approval of international research at sites that are "not engaged" in research is only permitted if the following circumstances exist:

- The international site has an established IRB or Internal Ethics Committee (IEC) to determine and document that the research meets the OHRP definition of "not engaged" such that approval is not necessary for the investigator to conduct the proposed research at that site.
- When the international site does not have an IRB/IEC, a letter of cooperation must be obtained that provides institutional approval for the research to be conducted at the performance site.

- When approval of international research is conducted at an international site that holds an OHRP Assurance and local IRB approval is obtained, the WVSOM investigator must ensure that policies and procedures are in place for the following:
  - Initial review, continuing review, and review of modification;
  - Post-approval monitoring;
  - Handling of complaints, non-compliance, and unanticipated problems involving risk;
  - The WVSOM investigator will provide documentation of IRB approval, renewal, modification and monitoring by the international IRB; and
  - The WVSOM investigator will notify the WVSOM IRB promptly if a change in research activities alters the performance site's engagement in the research.

The WVSOM IRB will consider the local research context when reviewing international studies as appropriate to the setting, including knowledge of laws and cultural context. When there is no local IRB review, the WVSOM IRB may require expert consultation to evaluate the research. The WVSOM IRB will ensure that all informed consent documents are in a language understandable to participants with documentation of the credentials of the translator detailed within the IRB application. The WVSOM IRB will verify ongoing review of international research through the WVSOM investigator and the international site to ensure compliance with OHRP international standards.

15. Community Based Research (CBR)

Community based research 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, 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, PIs 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.

15.1 Community Based Participatory Research

In some instances, the design and implementation of research can be enhanced when individuals from the community in which the research will be conducted are involved in the design, conduct, and analysis of data from the research. This can occur for an individual study or group of studies.

15.2 Community Based Research Considerations

- Does the community partner have an IRB and/or approval process?
- If community partners are involved in research activities, are the partners considered "engaged" under federal law?
  - If the community partners are considered engaged, they must complete CITI training.
  - Consent forms must be reviewed to ensure the reading level is appropriate for participants. An 8th grade reading level is suggested.
- The IRB application must describe how data will be shared with community partners.

15.3 Institutional Review Board Review of Community Based Research

IRB staff and members receive information about, and guidance regarding, how to address matters that influence the participation of community members in research that are conducted or supported by WVSOM. These include but are not limited to privacy and confidentiality concerns, principles and methodologies involved in Community Based Participatory Research (CBPR), local recruitment challenges,

return of research results, and informed consent. Investigators who are experienced in the design and conduct of community participatory research are available to provide consultation during IRB review of such research protocols, and one or more will serve as alternate IRB members. IRB membership will include members with experience conducting community research when CBR studies are under review. The IRB may consult with a community expert to review any research study for which additional expertise is required.

16. Acronyms Used in These Standard Operating Procedures with Explanatory Links or Definitions

CBR	Community Based Research
CBPR	Community Based Participatory Research
CITI	Collaborative Institutional Training Initiative
CoC	Certificates of Confidentiality
COI	Conflicts of Interest
COIR	Conflicts of Interest in Research
DHHS	U.S. Department of Health and Human Services
DSMB/DSMC	Data Safety Monitoring Board/Data Safety Monitoring Committee
FDA	Food & Drug Administration
FWA	Federalwide Assurance
GWAS	Genome Wide Association Studies
HIPAA	Health Insurance Portability and Accountability Act of 1996
HRPP	Human Research Protections Program
IAA	IRB Authorization Agreement
IEC	Institutional Ethics Committee
IO	Institutional Official
IRB	Institutional Review Board
LAR	Legally Authorized Representative
MOU	Memorandum of Understanding
ORSP	WVSOM Office of Research and Sponsored Programs
OHRP	Office of Human Research Protections
ORI	Office of Research Integrity
PAME	WVSOM Post-Approval Monitoring and Evaluation
PD	Project Director
PHI	Protected Health Information
PI	Principal Investigator

[Approval page to follow]

Procedure Title: Human Research Protections Program Standard Operating Procedures

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APPROVED BY:

Approving Administrator – Vice President for Administration and External Relations:

_____ Date: 18 Jan 2019

Vice President for Legal & Governmental Affairs and General Counsel:

_____ Date: 01-18-19

APPROVED, pursuant to Institutional Policy R-05: Human Subject Research, BY:

Institutional Review Board (IRB) Chair:

_____ Date: 1/18/19

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