

Middle Tennessee State University
Institutional Review Board

**INVESTIGATORS' MANUAL FOR HUMAN SUBJECTS
RESEARCH**

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Institutional Review Board

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This manual has been developed to provide the Middle Tennessee State University research community with an overview of the federal regulations and institutional policies governing the use of human subjects in research. These policies and procedures are based on federal regulations published by the U.S. Department of Health and Human Services (DHHS), Office of Human Research Protection (OHRP) and the U.S. Food and Drug Administration (FDA). Where appropriate, relevant portions of the DHHS and/or FDA regulations are referenced.

1.0 Definitions and Acronyms

Assent – an individual’s affirmative agreement to participate in research obtained in conjunction with permission from the individual’s parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Assurance - a contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).

Beneficence - to do no harm and maximize possible benefits and minimize possible harms.

Children/Minors - are “persons who have not attained the legal age for consent to activities or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. In Tennessee, the legal age for consent is 18 years of age.

Cognitively Impaired - having a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorder), an organic impairment (e.g., dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including individuals under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and individuals with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interest.

Dissent – an individual’s negative expressions, verbal and/or non-verbal, that they object to participation in the research or research activities.

Human subject - a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information

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

Informed Consent - assures that prospective human subjects will understand the nature of the research and can knowledgeably and **voluntarily** decide whether or not to participate. Informed consent is an ongoing process.

The informed consent document must provide each subject with the following:

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 the records identifying the subject will be maintained;
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
8. 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.

Justice - fairness in distribution or that benefits and burdens are distributed equally.

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

Legally Authorized Representative - an individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for participation in research activities.

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Minimal Risk - the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. An example of minimal risk is the risk of drawing a small amount of blood from a healthy individual for research purposes (because the risk of doing so is no greater than the risk of doing so as part of a routine physical examination).

ORI – Office of Research Integrity

ORSP – Office of Research and Sponsored Programs

Parent - a child's biological or adoptive parent.

Prisoner - any individual **involuntarily confined or detained** in a penal institution, including individuals detained in other facilities which provide alternatives to criminal prosecution or incarceration, and individuals detained pending arraignment, trial, or sentencing.

Research - a systematic investigation, including development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for the purposes of the policy, whether or not they are supported under a program which is considered research for other purposes.

Respect for Persons or Autonomy - means that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection.

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2.0 About the Institutional Review Board

2.1 Purpose of the Institutional Review Board

The Middle Tennessee State University Review Board (IRB) is charged with the responsibility of reviewing all research involving human subjects to determine:

- Whether human subjects have volunteered for a research endeavor by means of informed consent.
- And whether risks to these subjects are outweighed by potential benefits to them and the importance of the knowledge to be gained by the research endeavor.

The specific evaluation of risk involves estimating the potential for injury to the subject by reason of the subject's exclusion from ordinary standards of practice of care. Rights of subjects regarding confidentiality and access to professional care and counsel are included in IRB deliberations so that human dignity, rights, physical, behavioral, and social welfare are protected.

2.2 IRB Scope and Authority

All human research authorized and conducted under the jurisdiction of Middle Tennessee State University is subject to review by the IRB for risk, benefit, and informed consent without regard to the source of financial, physical (facilities), or logistical support. This review must be conducted before a project is started. Middle Tennessee State University is responsible for any research activity that involves physical, behavioral, or social welfare of human subjects that is:

- Conducted at Middle Tennessee State University
- Conducted by Middle Tennessee State University faculty, staff, or students.

The IRB shall have the authority to disapprove, discontinue, suspend, or limit research involving human subjects and, by its recommendations, can effect action that withholds or withdraws financial support from projects involving human subjects that are not in compliance with University policies or federal regulations.

2.3 Activities Requiring IRB Review and Approval

Any systematic investigation, including research development, testing, and evaluation (research) that involves human subjects must receive approval from the IRB prior to initiation. This applies to funded and non-funded research.

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2.4 Principles Governing the IRB

Middle Tennessee State University is guided by federal regulations and ethical principles regarding all research involving human subjects. DHHS and FDA are the primary agencies that regulate the IRB. In addition, the IRB is guided by *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) and the *World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects* (1964, amended 1996).

2.5 Selection and Composition of the IRB

IRB members are appointed by the Vice-Provost for Research /Dean of Graduate Studies (VPR/Dean). At the discretion of the VPR/Dean, in consultation with the Office of Compliance, IRB members shall be appointed to manage the research workload. Each IRB panel shall consist of at least five (5) members with diverse backgrounds and expertise, at least one of whom represents the community and is not affiliated with the University. In addition, members shall be diversified as to race, gender, cultural background, and sensitivity to community attitudes. At least one member of each gender shall serve on the board.

2.6 IRB Meetings

The IRB will meet once each month. The schedule of regular IRB meeting is available on the web at www.mtsu.edu/~irb. In addition to the regularly scheduled meeting, the IRB Chair may call emergency meetings of the IRB if necessary to address issues of noncompliance or serious and/or unexpected injury to research subject(s).

2.6.1 Quorum

A majority of members must be present to conduct business of the IRB, except for expedited or exempt reviews, and among this majority at least one member must be a non-scientist, and at least one member must be a non-affiliated member. The final approval or disapproval of any research project application will require a majority vote of IRB members present and voting.

If a quorum is lost at any time during the meeting, the meeting shall be adjourned and no further action taken until a quorum is attained.

2.6.2 Members with Conflicts of Interest

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IRB members with a conflict of interest in a particular research project cannot participate in the board's deliberations and voting concerning that project. Those with a conflict of interest may, however provide information requested by the IRB.

2.6.3 Minutes

Minutes of meeting shall include the following information:

- Attendance of members and guests
- IRB actions taken on each research project reviewed, including the level of risk as determined by the IRB, the approval period, and any required modifications for IRB approval.
- Votes on actions, including the number of members voting for or against the action, the number of members abstaining from voting, and notation of members who were not present during deliberations and voting on projects with which they have a conflict of interest.
- The basis for requiring modifications or disapproving research
- A written summary of the discussion and resolution of controversial issues.

2.7 Annual Reviews and Monitoring

Each year the IRB reviews the Middle Tennessee State University IRB Policies and Procedures to assure they are compliance and up-to-date with the Common Rule (45 CFR 46).

Then IRB will perform a quality improvement self-assessment of the Policies and Procedures. This annual evaluation includes the following:

- IRB membership and functions, including protocol review practices
- IRB records and reporting requirements
- Personnel qualifications and training

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3.0 Administrative Roles and Responsibilities

3.1 The Institutional/University Officials

The VPR/Dean serves as the University Official and has the authority to legally commit, on behalf of Middle Tennessee State University the regulatory requirements will be met under the Institution's Federalwide Assurance of Protection for Human Subjects (FWA), which is required by DHHS (45 CFR 46.103). The VPR/Dean is also responsible for appointing members to the IRB.

The Research Compliance Officer will:

- Serve as the Institutional Officer for the Committee and as the liaison between the University, the community, and the IRB committee.
- Keep the Institution's FWA and IRB Membership Roster updated with the OHRP
- Attend committee meetings without voting privileges.
- Keep Institutional Officials informed of IRB activities
- Record the minutes of all Committee meetings.
- Prepare the agenda for all Committee meetings
- Receives all research protocols and supporting documentation, communicates decisions to research investigators, and forwards certifications of IRB approval to appropriate research personnel.
- Serves as a consultant to the Committee and provide assistance to the Chairperson in the conduct and coordination of activities of the Committee.

3.2 IRB Chair

The IRB Chair must be a university faculty member and is elected by the IRB members to serve for one (1) year. The Chair cannot be the Research Compliance Officer. The Chair shall ensure that the IRB carries out its responsibilities in accordance with federal requirements and these policies and procedures.

3.3 The IRB

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The IRB reviews and approves, requires modification in, or disapproves all research activities conducted at Middle Tennessee State University. The IRB conducts continuing review of previously approved research at appropriate intervals based on risk. The IRB has authority to suspend or terminate previously approved research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to research subjects. The IRB has the authority to place any restrictions on an approved project as necessary to ensure the protection of human subjects.

3.4 Principal Investigator

The Principal Investigator (PI) has the primary responsibility for protecting the rights and welfare of human research subjects and for complying with all applicable provisions of the Institution's FWA, federal laws and regulations, and the Institution's policies and procedures as set forth in this manual. Responsibilities of the Principal Investigator include:

- **General**
 - Contact the Office of Compliance to determine if IRB review is required for the proposed research
 - Ensure that all research staff involved with human subjects protocols complete the necessary education training, and provide documentation of such training.
 - Prepare the protocol and address any special issues.
 - Submit all required documentation to the IRB. This includes permission letters from outside institutions where research is conducted, i.e. businesses, schools, etc. If research is conducted at a public school, a permission letter must be obtained from the principal of the school and the Superintendent of the school district.
 - Notify the IRB of any changes in the research protocol.
 - Submit a protocol summary and a status report on the progress of research according to the timeline determined by the IRB.
- **Informed Consent**
 - Ensure eight (8) elements of consent are covered. (See 5.0)
 - Ensure information is presented in a language that is understandable, with an eighth (8th) grade reading level recommended.

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- Ensure that there is no undue coercion or influence.
- Ensure that the informed consent form is adequate.
- Store and manage informed consent documents.
- Submit any changes to the informed consent document to the IRB for review prior to instituting.
- **Recruiting Subjects**
 - Ensure recruitment methods and advertising follow appropriate guidelines for adequate protection of research subjects.
 - If vulnerable research populations are involved, ensure all relevant guidelines are followed.
- **Reporting Requirements**
 - Promptly prepare and submit reports of adverse events to the IRB.
 - Promptly notify the IRB of any procedures performed in variance with the protocol.
 - For all expedited and full review studies, yearly continued review is required if the study is not finished. A study is considered finished when all data is collected and analyzed. A Progress Report and request for continuation must be submitted PRIOR to research expiring. Please allow time for review and requested revisions.
 - Prepare and submit End of the Year Final Reports for all studies.

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4.0 Education and Training

4.1 IRB Members

All IRB members shall receive initial training, to include an overview of the Belmont Report and The Common Rule and how to apply the guidelines to research review. Each member of the IRB shall receive a copy of this manual.

4.2 Research Investigators

MTSU is required by federal regulations to make available training for all investigators involved in a study. According to MTSU Policy, a research investigator is defined as anyone who works with data or has contact with participants. Anyone meeting this definition needs to be listed on the protocol and needs to provide a certificate of training to the Office of Compliance. It is recommended that human subjects research training be made available in the following areas:

- Key historical events and current issues that impact guidelines and legislation on human participant protection in research.
- Ethical principles and guidelines that should assist in resolving the ethical issues inherent in the conduct of research with human participants.
- The use of key ethical principles and federal regulations to protect human participants at various stages in the research process.
- A description of guidelines for the protection of special populations in research.
- A definition of informed consent and components necessary for a valid consent.
- A description of the role of the IRB in the research process.
- The roles, responsibilities, and interactions of federal agencies, institutions, and researchers in conducting research with human participants.

Training can be currently accessed through the Office of Compliance.

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5.0 Informed Consent/Assent

5.1 Informed Consent

§46.116 General requirements for informed consent.

Except as provided elsewhere in this policy, 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. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate, and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in a language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive, or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Basic elements of informed consent consist of the following:

- A statement that the study involves research, an explanation of the purposes of the research, the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
- A description of any reasonably foreseeable risks or discomforts to the subject.
- A description of any benefits to the subject or to others which may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-

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related injury to the subject, which corresponds to both the Principal Investigator and the Office of Compliance.

- 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.

When appropriate, additional elements of informed consent can be provided to the subjects and include one or more of the following elements of information:

- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- Any additional costs to the subject that may result from participation in the research;
- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and
- The approximate number of subjects involved in the study.

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:

- 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:
 - Public benefit or service programs;
 - Procedures for obtaining benefits or services under those programs;
 - Possible changes in or alternatives to those programs or procedures;
 - Or possible changes in methods or levels of payment for benefits or services under those programs; and

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- 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:

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

The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

§46.117 Documentation of informed consent.

Informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative unless the IRB has waived the requirement for consent. A copy shall be given to the person signing the form.

The written consent form may be either of the following:

- A written consent document that embodies the elements of informed consent required by §46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or
- A short form written consent document stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. 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 representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of

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the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

- The Middle Tennessee State University provides an informed consent template, which can be found at the IRB website www.mtsu.edu/~irb/forms

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

- 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
- 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.

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

5.2 Assent

In instances where the participant is not legally capable of giving informed consent (e.g., minors) or where the participant is cognitively impaired, the IRB must find that adequate provisions are made for soliciting the assent of the participant when in the judgment of the IRB, the participant is capable of providing assent.

In determining whether participants are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the participant involved. This judgment may be made for all participants to be involved in research under a particular protocol, or for each participant, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the participants is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the participant and is available only in the context of the research, the assent of the participant is not a necessary condition for proceeding with the research. Even where the IRB determines that the participants are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with IRB Policy.

When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

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6.0 The Review Process

Any research that involves human subjects and is authorized and conducted under the jurisdiction of Middle Tennessee State University is subject to review by the Middle Tennessee State University IRB. **No new research project or changes to previously approved research projects may be initiated until approved by the IRB.** The IRB reviews new projects, changes to existing projects, and ongoing projects as followed:

- **Initial Review** – All new research must be submitted for initial review. The three types of review include: Exempt, expedited, and full review and are defined in section 6.1.
- **Review of Changes to Previously Approved Protocols** – Any amendments, addenda, supplements, or other changes to existing projects must be submitted to the IRB for either expedited or full Review.
- **Continuing Review of Approved Research Protocols** – Continuing review of projects previously approved by expedited review is conducted by the original reviewer. Continuing review of projects previously approved by full review is conducted by the full board at its regular meeting. Continuing review of exempt projects is conducted by the Compliance Officer.

6.1 Types of IRB Initial Review

6.1.1 Review for Determination of Exempt Status

Federal guidelines identify those research activities that are exempt from 45 CFR 46 and 21 CFR 56 and therefore do not require full IRB review. If your proposed research falls under one of the exempt categories described below, submit your protocol to the Middle Tennessee State University Office of Compliance, Box 134, located in the Sam Ingram Building 011B for official determination of exempt status.

The following information on exempt categories is from 45 CFR 46.101 (b).

Unless otherwise required by Federal Department or Agency heads, research activities in which the only involvement of human subjects (excluding prisoners, fetuses, pregnant women or human in vitro fertilization) will be in one or more of the following categories.

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

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- Research involving the use of educational test, surveys procedures, interview procedures, or observation of public behavior unless:
 - Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects, and
 - Any disclosure or the human subjects' response outside the research could reasonable place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
- Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to subjects.
- Public Benefit or Service Programs.
- Taste and food quality evaluation and consumer acceptance studies.

For additional questions regarding the exempt categories, please contact the Office of Compliance at irb@mtsu.edu.

6.1.2 Expedited Review

Federal guidelines identify those research activities eligible for expedited IRB review. If your proposed research meets the applicable requirements described below and falls under one of the expedited review categories identified below, submit your protocol to the IRB for expedited review.

The following information on expedited review categories is from 45 CFR 46.110:

Applicability

(A) Research activities that:

- 1) present no more than minimal risk to human subjects, and
- 2) involve only procedures listed in one or more of the following categories.

(B) The categories in this list apply regardless of the age of subjects, except as noted.

Research Categories

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

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(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

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

(a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children², considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

(3) Prospective collection of biological specimens for research purposes by noninvasive means.

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

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d)

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electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. [45 CFR 46.101\(b\)\(4\)](#). This listing refers only to research that is not exempt.)

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

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

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

(a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

(b) where no subjects have been enrolled and no additional risks have been identified; or

(c) where the remaining research activities are limited to data analysis.

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

6.1.3 Full Board Review

Research proposals must be submitted a minimum of two (2) weeks prior to the scheduled meeting in order to receive full review. The dates of the scheduled meetings will be kept on file at the Office of Compliance and on the IRB website (www.mtsu.edu/~irb). **Research protocols will not be approved by the IRB until all policies and procedures have been followed. The IRB will not give “after-the-fact” approval on research involving human subjects.** If your

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project requires Full Board Review, submit an original along with eighteen (18) copies of the protocol.

Written documentation of legally effective informed consent is required for all research involving subjects who have been determined to be "at risk." Research on minors or subjects incompetent to give consent requires permission by a parent or legal guardian. Deception research will only be approved if it meets certain conditions (e.g. debriefing).

Examples of research that would require full review include:

- Research which might put subjects at risk
- Non curricular, interactive research in schools
- Research involving deception that might have adverse effects on the subjects
- Interviews or surveys on sensitive topics
- Research on vulnerable populations; e.g. minors (*except as listed above in expedited review*), prisoners, pregnant females, and the mentally incompetent
- Research conducted outside the United States, unless it is innocuous in nature. International research will not be approved as exempt but can fall under expedited review.

6.1.3.1 Full Review Process

IRB Review Responsibilities – The IRB shall have the responsibility to review and authority to approve, require modification to, table, or disapprove all research activities. Each board member will study the protocol under review to ensure that no unnecessary or unacceptable hazards are present and that adequate safeguards are provided for the research subjects. IRB members shall have all access to all documents relating to the research protocol, including all information provided by the principal investigator.

Presenting at the IRB Meeting – At the IRB meeting, the Principal Investigator or co-investigator may be asked to explain the purpose for, risks of, and alternatives to the proposed research, including subject selection and the exclusion criteria. IRB members are encouraged to ask clarifying questions concerning the protocol and consent process.

IRB Action – IRB members then discuss the case and make determinations regarding the category of risk, risk and benefit issues, and whether informed consent procedures are adequate. The IRB then votes and takes one of the following actions.

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Approved – The IRB shall provide written notice to the Principal Investigator. After receiving this notice, the Principal Investigator may begin research. In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

- Risks to subjects are minimized:
 - By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk,
 - And 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 vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. Populations should not be exploited nor underrepresented.
- 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 §46.116.
- Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.
- 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.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

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Approval Subject to Modification – The IRB shall provide written notice to the Principal Investigator of its approval subject to modification, identifying the specific areas of modification requires. The Principal Investigator must provide the IRB with a revised protocol and/or informed consent document incorporating the modifications. The IRB Chair(s) or designated member of the IRB shall review the revised protocol and/or informed consent document. The reviewer will then provide written notice of approval of the protocol if the required modifications have been made.

Tabled – The IRB required additional information and/or has a concern regarding the proposed research project. The Principal Investigator will be notified of the IRB’s decision and will be scheduled to address the issues in question at the next IRB meeting.

Disapproval – If the IRB disapproves a research protocol, the IRB shall provide to the Principal Investigator, in writing, the reasons for the IRB decision and an opportunity for the Principal Investigator to appeal the decision. However, it is the policy of the IRB to not disapprove research but to work with the investigator so that they can obtain approval of their research protocol.

6.2.1 Continuing Review of Ongoing Projects

The research investigator is solely responsible for the timely submission of continuing review materials. The investigator must submit a letter requesting continued review along with a Progress Report. The Progress Report form can be found at the following website: <http://www.mtsu.edu/~irb/irbprogressreport.doc>.

FDA regulations set forth the criteria to be satisfied if an IRB is to approve research [21 CFR 56.111]. These criteria are the same for initial review and continuing review and include a determination by the IRB that:

- risks to subjects are minimized;
- risks to subjects are reasonable in relation to anticipated benefits;
- selection of subjects is equitable;
- informed consent is adequate and appropriately documented;
- where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects;
- where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data; and
- Appropriate safeguards have been included to protect vulnerable subjects.

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Process for Conducting Continuing Review

Routine continuing review should include the IRB review of a written progress report(s) from the principal investigator. Progress reports include information such as: the number of subjects entered into the research study; a summary description of subject experiences (benefits, adverse reactions); numbers of withdrawals from the research; reasons for withdrawals; the research results obtained thus far; a current risk-benefit assessment based on study results; and any new information since the IRB's last review. Special attention should be paid to determining whether new information or unanticipated risks were discovered since the previous IRB review. Any significant new findings which may relate to the subjects' willingness to continue participation should also be provided to the subjects in accordance with 21 CFR 50.25(b) (5).

The IRB should determine that the frequency and extent of continuing review for each study is adequate to ensure the continued protection of the rights and welfare of research subjects. The factors considered in setting the frequency of review may include: the nature of the study; the degree of risk involved; and the vulnerability of the study subject population. Note that 21 CFR 56.108(a) (2) requires the IRB to follow written procedures for determining the frequency and extent of continuing review.

The continuation of research after expiration of IRB approval is a violation of the regulations [21 CFR 56.103(a)] and MTSU Policy and Procedure. If the IRB has not reviewed and approved a research study by the study's current expiration date, i.e., IRB approval has expired, research activities should stop. No new subjects may be enrolled in the study. However, if the investigator is actively pursuing renewal with the IRB and the IRB believes that an over-riding safety concern or ethical issue is involved, the IRB may permit the study to continue for the brief time required to complete the review process.

When study approval is terminated by the IRB, in addition to stopping all research activities, any subjects currently participating should be notified that the study has been terminated. Procedures for withdrawal of enrolled subjects should consider the rights and welfare of subjects. If follow-up of subjects for safety reasons is permitted or required by the IRB, the subjects should be so informed and any adverse events or outcomes should be reported to the IRB and the Office of Compliance.

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8.0 REVIEW AND INVESTIGATION OF NONCOMPLIANCE

It is the policy of the MTSU Institutional Review Board that all currently approved research is subject to modification or change in approval status, as deemed necessary by the IRB. The IRB may ask the Investigator to place research on administrative hold to gather information or the IRB may suspend or terminate research due to cause for the research not being conducted in accordance with the IRB's requirements or the Federal regulations or if it has been associated with unexpected serious harm to participants. Examples of a suspension for cause might include:

1. Inappropriate involvement of human subjects in research;
2. Inhibition of the rights or welfare of participants;
3. Serious or continuing noncompliance with Federal regulations or IRB policies; or
4. New information regarding increased risk to human participants, etc.

8.1 Identification of Compliance Issues

Anyone who has concerns or questions about any aspect of human subject research at Middle Tennessee State University, including protocol noncompliance are expected to contact the Office of Compliance at (615) 494-8918. Reports made through the Office of Compliance will be delivered to the IRB Chair for further action. Strict confidentiality will be maintained to the extent possible and allowable by law. No adverse action will be taken against anyone making a good-faith report of noncompliance. The IRB Chair and individual IRB members must also report any suspected incidence of noncompliance for review by the IRB. Such complaints should ideally be made directly to the Office of Compliance.

8.1.1 IRB Chair Suspension of Protocol

In addition to reporting suspected compliance issues, the Chair has authority to immediately suspend IRB approval if he or she has reason to believe that human welfare is being compromised. The IRB Chair shall immediately notify the affected Principal Investigator and the Office of Compliance in writing of any such suspension. The issue or issues that led to suspension shall be investigated as quickly as possible and the IRB Chair shall call an emergency meeting of the IRB to review the suspension.

8.2 Investigation of Compliance Issues

8.2.1 Review of Compliance Issues Prior to an IRB Meeting

Initial investigation of reported compliance issues is normally conducted to the Compliance Officer. Most compliance issues can be handled without the involvement of additional personnel or formal action by the IRB. However, if an issue cannot be resolved without IRB intervention, a subcommittee of the IRB will be appointed by the Chair to continue the investigation. All persons involved shall be informed of the purpose of the investigation and the manner in which it will be conducted. The subcommittee shall evaluate the status of any human subjects involved and the interim status of the Principal Investigator's protocols and shall prepare a report to be

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presented at the next IRB meeting. Prior to the meeting, the individual against whom the complaint is addressed shall be notified in writing by the Chair of the findings and potential necessary, the Chair shall convene an emergency meeting of the IRB to deal with a compliance issues.

8.2.2 Review of Compliance Issues during an IRB Meeting

The IRB shall examine the report of the subcommittee, interview potential participants and the person against whom the complaint is addressed, and decide whether there has been a violation of applicable regulations or procedures. All members shall have the opportunity to present minority views. A majority vote of a quorum of the IRB is required for any findings of the IRB and any action based on those findings. If there is a finding of noncompliance, the IRB must consider whether the noncompliance resulted in harm to animals or personnel, the seriousness of the noncompliance, and the nature of the noncompliance. The final results of the investigation shall be made available to all parties involved, the Dean of the area involved, the appropriate Vice President, the Institutional Official and the Compliance Officer. The IRB may, in its discretion, obtain external review of the matter; however, the IRB shall be the final authority.

8.3 Potential Actions of the IRB

The actions taken by the IRB in response to a finding of noncompliance depend on the seriousness of the violations. IRB actions may include the following:

- If the IRB determines that the allegation also violates the Policy on Misconduct in Scholarly Activities and Research, the allegations will be sent to the Vice-Provost for Research for inquiry/investigation.
- Notify the ORI and ORSP and any other funding agencies involved. This notification is mandatory for any suspended protocols.
- Suspend or continue suspension of some or all of an investigator's study until it is clear that the personnel and procedures have been brought into compliance with federal laws and policies. A majority vote of a quorum of the IRB is required to impose a suspension.
- Require oversight of protocol activities by an IRB member, the Office of Compliance or other designee. Require retraining or additional education for project personnel.
- Implement any other action necessary to protect the welfare of the animals or integrity of the IRB oversight
- Confiscate data and remove publication privileges.

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If a protocol is suspended by the IRB, then the IRB, Compliance Officer and the Institutional Official shall determine appropriate corrective action(s) to be implemented by project personnel and by the university, if appropriate. Relevant federal regulatory and granting agencies will be notified by the Institutional Official of the plan for corrective actions and then the implementation of these actions.

The Office of Compliance is always available to make appointments, etc. should you have any questions or need additional information.

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*Working together, we will promote the highest standard of integrity
and ethics in research and scholarship.*