Clemson University
Institutional Review Board

Investigator’s Manual
on the Protection of Human Subjects
and Submission of Research Protocols

Office of Research Compliance
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This Investigator’s Manual is also posted on the IRB website.
www.clemson.edu/research/orcSite/indexcomply.htm

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Clemson University (otherwise known as CU or the Institution) is committed to adhering to the highest ethical standards in the conduct of all its research. This manual describes procedures and policies that have been instituted to protect those who voluntarily participate as research subjects in order to help advance the frontiers of human knowledge and contribute to the betterment of the human condition.

The Office of the Vice President for Research and Economic Development (OVPRED) is the administrative office that is responsible for the University’s system of protections for research participants. University policy requires that all research involving human subjects be reviewed and approved by the University’s Institutional Review Board (IRB) for the Protection of Human Subjects in Research prior to initiation of the research. This requirement applies to all human subjects research conducted by faculty, staff, and students, on- and off-campus, regardless of the funding support, if any, for the project.

On behalf of Clemson University, the Office of the Vice President for Research and Economic Development has entered into a Federal Wide Assurance (FWA00004497) with the Department of Health and Human Services committing CU to abide by Federal regulations applicable to human research subjects protection. This assurance is provided to all research funded by Federal agencies that have adopted Title 45 C.F.R. 46 U.S. Department of Health and Human Services (DHHS) / Office for Human Research Protections (OHRP) Regulations, including the “Common Rule” regulations and Subparts B, C, and D of the U.S. Code of Federal Regulations (C.F.R.). Research that is not funded by these Federal agencies is covered by policies and procedures of the Clemson University OVPRED, the Office of Research Compliance (ORC) and the IRB. These policies and procedures provide equivalent review and human research subjects protections, as specified in this Standard Operating Procedure Manual.

The Vice President for Research and Economic Development is responsible for the establishment and support of the university-wide Institutional Review Board (IRB) and the Office of Research Compliance. The Office of Research Compliance is responsible for the initial and continuing education of all those involved in the human research (i.e., investigators, key research personnel, IRB members and IRB administrators), initial and continuing review of research protocols involving human subjects, and monitoring of research investigators for adherence to federal regulations and institutional policies and procedures.

I. Authority under which the Human Subject Protection System is Established and Empowered

Federal Regulations. Clemson University’s Institutional Review Board (IRB) and the University’s human research subject protection program are based upon both ethical principles and Federal law. The guiding ethical principles are embodied in the **Belmont Report**: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of 1979 (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research). The principles of respect for persons, beneficence and justice are accepted as absolutely essential requirements for the ethical conduct of human subjects’ research. In
1) Title 45 C.F.R. 46 U.S. Department of Health and Human Services (DHHS) / Office for Human Research Protections (OHRP) Regulations, including the “Common Rule” regulations that have been adopted by multiple Federal agencies.  
2) Food and Drug Administration (FDA) Title 21 C.F.R. 50 and 56,  
   a) Investigational New Drug Applications – IND (312)  
   b) Radioactive Diagnostic Drugs (361)  
   c) Investigational Device Exemptions IDE (812)  
3) Health Insurance Portability Accountability Act (HIPAA)  

**Assurance.** The CU Assurance for Protection of Human Research Participants document has been renewed through April 8, 2006. The Assurance certifies that CU will comply with the DHHS regulations for the protection of human research subjects, 45 CFR 46, as amended.

Clemson University has additional agreements with:  
1) Greenville Hospital System  
2) University of South Carolina (USC)  
3) Medical University of South Carolina (MUSC)  
4) University of Kentucky  
5) University of Connecticut Storrs  
6) Palmetto Health Alliance  
7) Spartanburg Regional Healthcare System

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**II. Role and Purpose of the Institutional Review Board (IRB)**

**Purpose of the IRB.** The purpose of the IRB is the protection of human participants in research. The IRB is the final authority for safeguarding human research subjects. Failure to have human research reviewed and approved by this University’s IRB or the IRB of record of an institution which Clemson University has an Inter-Institutional Agreement is a violation of University policy, federal regulations and the Assurance. The IRB assures protection of human subjects by it’s adherence to good clinical practices, federal regulations, and institutional policies and procedures.

**Types of Studies that Must Be Reviewed.** All studies that qualify as “research” involving “human subjects” must be reviewed by the IRB. Research is defined as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” Human Subject refers to a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.
Clemson University’s IRB reviews research sponsored by Clemson University; any research under the direction of Clemson faculty, students, staff; any research that involves the use of non-public information maintained by Clemson University, and student conducted research.

Clemson University has an Inter-Institutional Agreement with Greenville Hospital System to review biomedical research for Clemson University. Some health related research studies may still be reviewed by Clemson University. This will be decided in the Office of Research Compliance with consultation of the IRB Chair.

**Authorities to Approve, Disapprove, or Modify Research.** The IRB has the statutory authority to take any action necessary to protect the rights and welfare of human subjects in the CU research program. The IRB has the authority to approve, require modifications in, or disapprove any research protocols and informed consent procedures.

**Authority to Require Progress Reports, Annual Reports, and Research Oversight.** The IRB may require progress reports from the investigators at any time and may determine a need to oversee the conduct of the study. The IRB has the authority to observe and/or monitor human subject research to whatever extent it considers necessary to protect human subjects.

**Authority to Restrict, Suspend, or Terminate a Study.** The IRB may require progress reports more frequently. The IRB has authority to place necessary restrictions on a research study. Examples of when this may apply include non-compliance of the principal investigator, new information regarding risks to subjects, unexpected and / or serious adverse events. Any suspensions or terminations by the IRB are reported to the Office of the Vice President for Research and Economic Development, who in turn will notify the appropriate individuals, agencies and institutions.

### III. Lines of Communication

For matters relating to the execution of its duties and responsibilities, the IRB reports directly to the Authorized University Official (the Vice President for Research and Economic Development), or his/her designee, Director of Research Compliance.

The following are reported to the Office of the Vice President for Research and Economic Development, who in turn communicates with the appropriate individuals, agencies and institutions:

- Changes in IRB membership.
- Serious or continuing noncompliance with federal regulations.
- Any unanticipated problems involving risks to subjects or others.
- Any suspension or termination of IRB approval for a project.
IV. Responsibilities of the Principal Investigator and Research Team

Principal Investigators. The principal investigator (PI) must ensure that:

- All members of the research team comply with the findings, determinations, and requirements of the IRB.
- All research conducted has received prospective review and approval from the IRB.
- Continuing review and approval of the research has been accomplished within the time frame stipulated by the IRB.
- Prompt reporting to the IRB of any changes in research activity including any changes to the protocol, and/or consent form(s), completion or termination of the study, and in the event the project was never started. No change in approved research may be initiated without the IRB’s approval except under conditions where it is necessary to eliminate apparent immediate hazards to human participants.
- No research may be continued beyond the designated approval period.
- Any unanticipated problems involving risk to subjects and others, and any serious adverse events are reported immediately to the IRB.
- Any serious or continuing non-compliance with applicable regulatory requirements or determination is reported immediately to the IRB.
- The protocol number and title of the research are cited in all correspondence to the IRB.
- Any significant new information that may affect the risk/benefit ratio is submitted promptly to the IRB.
- For every IRB protocol, all pertinent research records, regardless of media type (i.e., validated protocol, all raw data, amendments, correspondence, continuing reviews, original stamped consent form(s) and signed consent form(s) for each research participant [if applicable], and other pertinent documents) are retained on file for at least three (3) years after completion of the study and available for Office of Research Compliance staff to review.
- Only consent/assent/parental permission forms with stamped approval/expiration date may be presented to the research participants.
- A signed, hard copy with signature of appropriate Department Chair is submitted to the IRB.

This information is addressed through orientation programs for PIs, printed materials for investigators, information provided in approval letters to investigators, random audits of research records, and site visit by the IRB staff.

Members of the Research Team. Co-investigators, research assistants, students, and all other key research personnel must have IRB training and have a strict obligation to:

- Comply with research ethics and the protection of human subjects.
- Comply with all IRB determinations and procedures.
- Adhere rigorously to all protocol requirements.
- Inform investigators of all adverse subject reactions or unanticipated problems.
- Ensure the adequacy of the informed consent process.
- Take measures necessary to ensure adequate protection for subjects.
Researchers and administrators at every level are responsible for notifying the IRB promptly of any serious or continuing non-compliance with applicable regulatory requirements, or determinations of the designated IRB of which they become aware, whether or not they themselves are involved in the research.

**Research Training in Human Subjects Protection.** To meet federal regulations, the Clemson University IRB requires PIs and members of the research team to have completed appropriate training in the protection of human subjects. Research protocols will not receive approval until verification of training has been completed. The training requirement may be met by successful completion of the Clemson University track of required modules available through online CITI course in the protection of human subjects. Completion of additional modules may be required when relevant to the research being proposed. Those individuals who completed other forms of CU-IRB-approved training prior to December 31, 2004 are grandfathered for the completion of basic training.

**Research Records.** Students are not permitted to be PIs. Only faculty member or selected staff members may serve as the PI on student projects.

The PI must maintain all research records (including a copy of the entire protocol, consent form(s), amendments, all communications between the IRB and the PI, and original copies of signed consent form(s) for each research participant (if applicable) in the laboratory or office of the investigator.

**Closing a Protocol.** Investigators should close a protocol when human subjects are no longer being followed or studied. As long as subjects are still being followed and data are being analyzed, a protocol is considered active and annual reviews must be completed. When research has been closed, the responsible investigator must notify the Office of Research Compliance. Investigators are encouraged to notify the IRB by memo as soon as a study should be closed.

The records will be accessible for inspection and copying by authorized representatives of the DHHS, the FDA (if applicable), and/or the university IRB staff at reasonable times and in a reasonable manner.

When a PI leaves the University, he or she should terminate his/her protocol(s), or notify the IRB in writing that the protocol(s) should be transferred to another investigator who will take responsibility for the research prior to the original PI’s departure. This letter should be co-signed by the new investigator recognizing that he/she is now responsible for the study. In some cases, this transfer may require an amendment and/or further IRB review and approval. Appropriate changes to consent forms, advertisements, etc. must be submitted to the IRB for review when the protocol is transferred.

**V. Educational and Other Requirements of Research**

The IRB will help to educate investigators regarding their responsibilities to comply with IRB policies and procedures. The IRB staff normally will communicate directly with the PI of each
study. However, in the conduct of its responsibilities, the IRB may query, require responses from, or otherwise communicate directly with any personnel involved with a human subjects research protocol, whether they are listed as investigators or not, and or with subjects themselves.

The IRB will consider proposals submitted by qualified investigators. The investigator’s professional development is taken into account and related to the degree of protocol complexity and risk(s) to human subjects. The IRB may require less experienced research investigators to be sponsored by more experienced researchers. Proposals that, in the estimation of the IRB, require skills beyond those held by a PI may need to be modified to meet the investigator’s skills, have additional qualified personnel added, or be disapproved.

VI. Functions of the IRB

The IRB will conduct initial and continuing review of all research involving human subjects if the project meets the federal definitions for both “research” and “human subject” and if one or more of the following apply:

- This institution sponsors the research.
- The research is conducted by or under the direction of, any employee or agent of this institution in connection with his or her institutional responsibilities.
- The research is conducted by or under the direction of, any employee or agent of this institution using any property or facility of this institution.
- The research involves the use of this institution’s non-public information to identify or contact human research subjects or prospective subjects.
- The institution has an agreement in place to review a protocol from a non-institutional source.

Reporting Findings and Actions to the Investigator and Institution. The following are reported to the investigator:
- Decision of the IRB.
- Reasons for its actions or stipulations.
- Requests for information in order to secure IRB approval.

The IRB will notify investigators in writing of its decision to approve, approve pending revisions, table for major changes or disapprove a research protocol. The IRB will include the reasons for its decision.

Determining which Projects Need Verification from Sources Other than the Investigators. Ordinarily, the IRB places trust in the PI of an approved research project. However, certain situations may be encountered that would lead the IRB to require verification of data or interpretation of data related to the research project from sources other than the investigator(s). Examples of such situations would include: allegations of misconduct by an investigator, complaints from a subject or a third party “whistle-blower”, or as part of a random compliance audit by IRB staff. The IRB may also consider the need for independent verification of data or
interpretation of data in cases where, due to the leading edge nature of the research and/or the potentially high risk to subjects, the IRB decides that more than the investigator’s report is needed to allow the IRB to make an informed determination with respect to the research.

Consideration is given to:
- Complex projects involving unusual levels or types of risk to subjects.
- Projects conducted by investigators who previously have failed to comply with the required DHHS regulations or the requirements or determination of IRB.
  And
- Projects where concern raised about possible material changes occurring without IRB approval based upon information provided in the continuing review report or from other sources.

In making determinations about independent verification, the IRB prospectively requires that such verification take place at predetermined intervals during the approval period, or may retrospectively require such verification at the time of continuing review.

**Determining which Projects Require Review More Often than Annually.** Each project is required to undergo periodic review at least once a year. At the time of initial approval, or any time thereafter, the IRB may require that a project undergo periodic review at more frequent intervals or after a certain number of subjects are enrolled. Protocols that may justify more frequent review may include the following: (1) research that poses extraordinary risk to subjects; 2) medical condition of the proposed subjects; 3) vulnerability of the population being studied; 4) overall qualifications and or specific experience of the PI and other members of the research team; 5) nature and frequency of adverse events observed in similar research at this and other institutions; (6) nature and location of the study, (7) research that involves an investigator who has previously had a study suspended or terminated by the IRB; (8) novelty of research method; and (9) other factors that the IRB deems relevant.

**Conflict of Interest.** IRB approval is contingent upon the report of the PI that there is no conflict of interest or that the conflict of interest can be managed. This applies for all research protocols except those validated as exempt from IRB continuing review. Areas of concern can be referred to the Vice President for Research and Economic Development.

**VII. IRB Meetings**

**Time and Location of Meetings.** The IRB normally meets on the first Thursday of each month at a regular time and location. Information concerning the date, time and location of meetings is available to investigators on the IRB website ([http://www.clemson.edu/research/orcSite/indexComply.htm](http://www.clemson.edu/research/orcSite/indexComply.htm)) or by contacting the Office of Research Compliance.

**Unscheduled Meetings.** The Chair of the IRB may call an unscheduled meeting at any time. A quorum must be present in order to conduct the meeting. Records are kept of any unscheduled meeting. The purpose of the unscheduled meeting can vary and may include, but not be limited
to, presenting protocols requiring full review when the PI needs approval before the next regularly scheduled meeting if negotiated with the Chairperson sufficiently in advance, to allow for appropriate review or for reasons associated with increased risk to research participants, or for non-compliance of a PI, or focusing on issues of concern related to the protection of human subjects.

Types of Votes.

Approval: The IRB votes for approval with no changes or additions requested.

Approval pending minor changes: The IRB may vote to require changes to the protocol and/or consent form(s). If these are considered minor, then implementation of such changes in the protocol may be approved by the Chair / designee but only if the changes made comply with the IRB’s written requirements. Research cannot begin until all changes have been made and approved.

Tabled because of a need for major changes: Research may not commence. There is a need for additional information or major changes. This may include: (1) the protocol is significantly incomplete; (2) there are questions raised that await the response of the investigator; (3) there are related issues that must be addressed, e.g., in the case of significant conflict-of-interest, a determination from the cognizant dean as to whether the conflict can be managed. This action requires full review on resubmission.

Disapproval: The IRB determines that the research cannot be conducted in its present form or that it is inappropriate in its present design. Research may not commence.

Specific IRB Findings and Determinations Are Documented in the IRB Meeting. Certain findings are documented in the protocol files or in the IRB meeting minutes. Documentation shall be provided for the following items when appropriate: (1) level of risk of the research; (2) approval period for the research including identification of research that warrant review more often than at least annually; (3) identification of any research for which there is a need for verification from sources other than the investigator that no material changes are made in the research; (4) justification for waiver or alteration of informed consent; (5) justification for waiver of the requirement for written documentation of consent; and (6) justification for approval of research involving pregnant women, or children, and other special protection warranted in specific research projects for groups of subjects who are likely to be vulnerable to coercion or undue influence.

VIII. Types of IRB Reviews

Protocol Review. The PI submits a properly endorsed protocol on forms provided by the Office of Research Compliance. For faculty and staff, properly endorsed refers to inclusion of the signature by the department head. The exception to this is for exempt protocols. Department heads who submit proposals must obtain signature of their supervisor. Students may not serve as PIs for research activities. However, they may serve as co-investigators.
Exempt from IRB Continuing Review. Protocols that qualify as exempt from IRB continuing review must meet the criteria outlined in the federal regulations and qualify as almost no risk (see Appendix A). A PI submits a research protocol including the appropriate forms requesting an exemption. This request is carefully reviewed to determine if the project ought to qualify for exempt status. This review is designated to identify any potential problems or ethical considerations that may impact on subjects. Each protocol is reviewed by the IRB Coordinator, Chair/designee to determine if the project meets one or more of the six categories having criteria for exempt status which are defined in 45 CFR 46 (Appendix A). For research projects to qualify for this exemption, they must have very little, if any risk, associated with them. Appropriate clarifications or modifications of the protocol are obtained from the investigator. A determination is also made whether an informed consent or other full disclosure with the use of an introductory letter to participants is necessary. If a research protocol qualifies for exempt status, it may still be referred for further study. If the Chair/designee finds that exempt review criteria have not been fully met, the PI will be required to submit the research protocol for an expedited or full review by the IRB.

Documentation for exempt review and approval consists of the Chair’s written concurrence. The Chair/designee reports the outcome of research protocols submitted for exempt review at the next meeting of the full-convened IRB. A list of these projects is submitted to the IRB members at the convened IRB meeting for concurrence. The IRB minutes will contain documentation of the citation of specific permissible categories justifying exemption. A letter (and in some cases another form of written communication) is sent to the PI to validation as exempt or another IRB action.

Expedited Review. Research protocols that qualify for Expedited Review are determined to be less than minimal risk and comply with the categories listed in the federal regulations (See Appendix B). Protocols are submitted on the Expedited Review Form. Clemson University utilizes a primary and secondary review system for research protocols that involve minimal risk. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research is not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations for tests.

If the Chair/designee and/or assigned reviewers finds that a research protocol does not meet the criteria for expedited review, the PI is notified to submit the research protocol for full review.

The Chair reports the outcome of research protocols submitted for expedited review at the next meeting of the full-convened IRB. The IRB minutes will contain documentation of the citation of specific permissible categories justifying expedited review.

Full Review. Research that is greater than minimal risk is reviewed as Full Review by the IRB. Research is submitted on the Full Review Application. The IRB utilizes a primary and secondary reviewer system to assist in the initial review of research involving more than minimal risk. The primary and secondary reviewers receive: (1) the full protocol and grant application; (2) proposed informed consent form; (3) investigator’s brochure, if applicable; (4) advertisements to be seen or heard by potential subjects or subject information for recruitment, if applicable; (5) subject surveys or questionnaires, if applicable; and (6) applicable research forms. The primary
Primary and secondary reviewers complete an in-depth review of all pertinent documentation regarding scientific merit, protection of human subjects, and level of risk to the subject. The reviewers are responsible for reading the full protocol and all related materials in a detailed manner. The secondary reviewer forwards comments to the primary reviewer who contacts the PI, if needed, with any questions and issues that can be resolved before the meeting. At the convened meeting, the study is presented by the primary reviewer, or the secondary reviewer if the primary reviewer is not available. In some other circumstances, if neither the primary or secondary reviewer is available, the Chair of the IRB can present the research protocol. An external reviewer may be utilized at the discretion of the Chair if the study involves a vulnerable subject population or if the research involves extraordinarily high risk or novel research.

If there are issues that cannot be resolved, the primary reviewer may request the Chair of the IRB to intervene and contact the PI.

Other IRB members receive copies of the protocol application, proposed informed consent form, written reviews by the primary and secondary reviewers, any advertising material intended to be seen or heard by potential subjects, and any other material deemed important for the IRB members by the Chair. These materials are received by the members sufficiently in advance of the meeting date to allow for review of the material. The full protocol and any supplementary materials are available for review in the IRB Office prior to the meeting as well as during the meeting for members of the IRB.

Training Grants, Multi-Project Grants, and Center Grants. Federal regulations require that organizations certify that the human subject aspects related to research funded by an overall grant such as a training grant, multiple project, program project, or center grant have current IRB approval. The following should be submitted to the IRB:

- Research application forms.
- Grant application minus appendices and budget information.
- Cover letter indicating that no funds will be transferred to the individually supported sub-projects proposing to conduct research with human subjects until the sub-project has received current approval from the IRB.
- List of all the human subject related projects supported by the grant. The list should include the following: name of PI(s); title of the project; and current approvals for the project(s).

Review of Request for Approval of Changes/Amendments to Ongoing Research during the Approval Process. The PI will submit, in writing, a request for change to a research protocol and/or consent form. Minor changes proposed for previously approved research may be reviewed in an expedited manner. When a proposed change in a research study is not minor (e.g., procedures involving increased risk or discomfort are to be added), then IRB must review and approve changes at a convened meeting before changes can be implemented. In other rare circumstance, in which a change is necessary to eliminate apparent immediate hazards to the
research subjects, the IRB should be informed as soon as possible of the changes following its implementation as soon as possible and should review the changes to determine that these are consistent with guidelines for the protection of human subjects.

When the consent form is modified and approved, a new approved date is affixed to the consent form. The IRB Office will notify the PI in writing when approval has been granted. This does not change the date for the yearly review.

The Chair of the IRB may review minor changes to an Expedited Review or Full Review Protocol that does not involve increased risk to the subject. This may include, but not be limited to, change in members of the research team, minor changes to data collection tools, additions of other sites, increase in sample size. If no subjects have been enrolled in the study since the last IRB review and there are no additional risks to the study, the Chair and or designee can conduct a continuing review using expedited procedures.

Continuing Review. The IRB conducts a “substantive” and “meaningful” continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. Continuing reviews will be approved by expedited or full review and reported to the convened IRB. If a protocol was initially reviewed by a Full Review and is now in data analysis phase only and no further subjects are being enrolled, a review may be conducted under expedited review basis.

If a protocol was reviewed under Full Review procedures and no new subjects have been enrolled in the study since the last IRB review and there is no change to subject risk, the protocol may be reviewed using Expedited review procedures.

For protocols reviewed under Expedited Review and no new subjects have been enrolled in the study since the last IRB review and there is no change to subject risk, the protocol may be reviewed by either the Chair, Primary reviewer or Secondary reviewer.

PIs will receive notification of annual renewal approximately two months before the anniversary date of the approved protocol. If the approval period has expired and the required documentation for continuing review has not been received, the IRB Office will notify the PI that no further subjects can be enrolled. The PI will be requested to identify if any subjects are still on the study protocol. Continuation of research interventions or interactions in already enrolled subjects will only continue if the IRB finds that it is in the best interest of individual subjects to do so. The IRB will address on a case-by-case basis those rare instances where failure to enroll would seriously jeopardize the safety and well being of an individual prospective subject. If the required documentation is not subsequently received within five (5) working days the project will be administratively closed. If applicable, appropriate University Administration and study sponsors may be notified.

The Continuing Review Form is to be completed by the PI for all protocols that have received full or expedited IRB review. This form includes:
  - Abstract of the study and a current status report.
  - Information on the number of subjects enrolled in the past year and from the start of the research study.
• Information on whether subjects have withdrawn.
• Complaints about the study since the last IRB review.
• Summary of any relevant recent literature which would indicate a need to modify the study.
• Summary of any unanticipated adverse events/complications or Serious Adverse Events (SAEs) that would affect the risk/benefit assessment of the study and any amendments or modification to the research since the last review.

A clean copy of the consent form is also included for review with space for a stamp of the new expiration date upon IRB approval.

The minutes of the IRB meeting document separate determinations, actions, and votes for each protocol undergoing continuing full review by the convened IRB. Continuing reviews for expedited research protocols are presented as a list to the convened IRB.

The IRB will continue to review research projects as long as individually identifiable follow-up data are collected on subjects. This remains the case even after enrollment of new subjects has stopped and protocol-related treatments/interventions have been completed for all subjects.

The IRB reserves the right to re-review research protocols after 5 years of continuing review as if the research study is a new study. This is to insure that subjects are fully protected and that new information, if available, is incorporated into the protocol.

**Review of Reports of Serious Unanticipated Problems or Serious Adverse Events.**
Investigators are required to notify the IRB promptly of any unanticipated problems or serious adverse events involving risks to subjects or others. (Serious is defined as any experience that suggests a significant hazard, contraindication, side effect, or precaution, or a clinical experience that is fatal, life threatening, permanently disabling, requires hospitalization, is a congenital anomaly, cancer, or overdose.)

- All on-site serious adverse events must be reported to the IRB within 72 hours of the PI becoming aware of them.
- All deaths must be reported to the IRB immediately by phone or by fax.

The only exception is for observational studies in which death is the end point. All off-site adverse events must be reported to the IRB office as usual as required by protocol if using Clemson University adverse event form, MedWatch or other similar forms.

Reports to the IRB should contain enough information for the designated IRB reviewer to judge whether the event raises new questions about risks to participants. When the study is part of a multi-site trial, a standard form may already be in use to provide details of the event to the sponsor. If the event occurred at a different site, the information will also be in a standard format. These reports can be forwarded to the IRB to provide information about the event. Principal Investigators will use the form developed by the IRB for reporting adverse events. This form is available on the Website.
The IRB Chairperson/designee reviews all such on-site reports. If the event does not raise new concerns about risks to subjects (for example, the likelihood, severity and specificity are adequately described in the protocol, investigator’s brochure, and informed consent document), the Chair reports this finding to the IRB. Adverse event reports may prompt requests for additional information, follow-up action, revision of the informed consent document, a request for protocol amendment, and/or suspension or revocation of the approval of the study. Suspension or revocation of approval will occur after review and voting by the convened board unless an imminent danger to study patients warrants quicker action by the Chairperson. The Chair reports such actions to the IRB at the next convened meeting. The Chair or designee reports serious adverse or serious unexpected events to the Vice President for Research and Economic Development in writing and reports deaths immediately.

**Monitoring for Compliance.** The IRB monitors ongoing research during the period for which the research is authorized. The monitoring process is part of the performance improvement program for the protection of human subjects and includes routine reviews as well as reviews of complaints, allegations and findings of non-compliance with institutional policies, and scientific misconduct.

Monitoring of ongoing studies will be conducted by the Office of Research Compliance as part of its performance improvement program and may include the following:

- Determining whether the investigator has current, complete copies of all informed consents in his/her files for subjects enrolled in the study.
- Determining whether the investigator has a copy of the current protocol and a blank copy of the most recently approved informed consent document.
- Determining whether the investigator has complete and current copies of correspondence from the IRB and, if applicable, the study sponsor.

**Suspension or Termination of IRB Approval of Research (38 CFR 16.113).** The IRB may vote to suspend or terminate approval of research not being conducted in accordance with university or federal regulatory requirements, or if it has been associated with unexpected problems or serious harm to subjects. The IRB may suspend or terminate approval for any of the following reasons:

- Failure to obtain properly executed informed consent.
- Failure to report possible serious adverse events involving risks to subjects or others.
- Failure to make requested change(s) in a proposal.
- Unauthorized modification(s) to the study or consent form.
- Failure to give copies of the informed consent to the appropriate recipients.
- Failure to provide accurate and/or timely progress reports.
- Any unanticipated problems involving risks to subjects or others.

This suspension or termination may occur during the progress of a study or prior to the onset of a study. All suspensions or terminations initiated by the IRB will be reported to the Office of the Vice President for Research and Economic Development, who in turn will notify the appropriate agencies.
Where the IRB Chairperson determines that such action is necessary to ensure the rights and welfare of subjects, the Chairperson may require an immediate, temporary suspension of human enrollment of new subjects or of continued participation of previously enrolled subjects, pending review of the situation by the convened IRB. The events will be documented in IRB minutes.

The IRB will notify the PI in writing of such suspensions or terminations and shall include a statement of the reasons for the IRB’s actions. The investigator has an opportunity to respond in person to the full IRB board or in writing.

Criteria for IRB Approval. The IRB takes many different factors into account when evaluating a proposal for approval. These factors include, at a minimum:

- **Level of risk.**
- **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, and to the importance of the knowledge that may reasonably be expected to result.
- **Selection of subjects is equitable.** IRB takes into account the purposes of the research and the setting in which it will be conducted and any issues with vulnerable populations.
- **Informed consent is adequate.** Informed consent is sought from each prospective subject or the subject’s legally authorized representative in accordance with policies and federal regulations
- **Research plan** may make provision for monitoring the data collected to ensure safety of subjects.
- Adequate provisions to protect the privacy of subjects and maintain confidentiality of data.
- **Appropriate safeguards** are included in the study to protect the rights and welfare of vulnerable subjects.

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

- Determines whether the anticipated benefit, either new knowledge or of improved health for the research participant, justifies asking any person to undertake the risks.
- Disapproves research in which the risks are judged unreasonable in relation to the anticipated benefits.

Advertisements and Recruitment Incentives. The IRB reviews advertisements and recruitment incentives associated with the research that they oversee. Advertisements and incentives are directly related to the informed consent process and must be consistent with prohibitions on coercion and undue influence. Advertisements will be reviewed and approved by the IRB/Chair or designee, primary or secondary reviewers as part of initial review or as an amendment/change to the protocol. Payment to research subjects for participation is not considered a benefit but a recruitment incentive. If a subject withdraws early, payment must be prorated to reflect the time and inconvenience of the subjects participating up to that point.
Certificates of Confidentiality. Where research involves the collection of highly sensitive information about individually identifiable subjects, the IRB may determine that special protections are needed to protect subjects from risks or investigative or judicial process. The IRB may recommend or require that an investigator obtain a Department of Health and Human Services (DHHS) Certificate of Confidentiality (CoC). If there is an Investigational New Drug Application (IND) or an Investigational Drug Exemption (IDE), the sponsor can request a CoC from the FDA. The CoC was developed to protect against the involuntary release of sensitive information about individual subjects for use in Federal, state, or local civil, criminal, administrative, legislative, or other legal proceedings.

It should be noted that the CoC does not prohibit voluntary disclosure of information by an investigator, such as voluntary reporting to local authorities of child abuse or of a communicable disease. In addition, the CoC does not protect the release of information to DHHS or the FDA for audit purposes. Consequently, these conditions for release should be stated clearly and explicitly in the informed consent document. OHRP recommends a CoC for repositories and tissue banks.

Health Insurance Portability and Accountability Act (HIPAA). HIPAA language is used in consent form documents when protected health information is collected from research participants.

IX. Elements of Informed Consent

The basic elements of informed consent as found in 45 CFR 46.116 include:

1) Statement that the study involves research.
2) Purpose of research and expected duration of the subject’s participation.
3) Description of procedures to be followed.
4) Identification of any procedures which are experimental.
5) Reasonably foreseeable risks or discomforts.
6) Benefits to the subject or to others which may reasonably be expected from the research.
7) Alternative procedures or treatments, if any.
8) Extent of confidentiality of record.
9) Whether any compensation is provided and whether treatment is available in the event of injury, for research involving more than minimal risk.
10) Whom to contact if injured or for answers to pertinent questions about the research.
11) Statement that participation is voluntary participation and the subject’s freedom to withdraw from the study at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Additional elements of informed consent that are required when appropriate to the study. 45 CFR 46.116 also specifies additional elements that should be included where appropriate:

1) Possible risks to the subject (or to the embryo or fetus) which are currently unforeseeable.
2) Circumstances under which the subject’s participation may be terminated.
3) Any additional costs to the subject that may result from participation in the research.
4) The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination.
5) Provision for informing subjects of significant new findings that may relate to their willingness to continue participating.
6) The number of subjects involved in the study both at CU and at other institutions.

Other additions are subject to applicable laws and regulations.

Signatures. The consent form must only be signed by the subject or the subject’s Proxy. FDA regulations require that the signature be dated.

Consent. Individuals over the age of 18 are able to give consent. Individuals under the age of 18 are considered minors and cannot give consent to participate in research. This individual can give assent and parents given permission. Other individuals who are cognitively impaired may not be able to give consent.

Proxy/Surrogate Consent. If conditions or special populations require consent from a third party and if proxy consent has been approved by the IRB, consent may be obtained from the legal guardian or next of kin according to an established protocol. These persons include:
- Persons appointed as health care agents.
- Court-appointed guardians.
- Next-of-kin in the following order: spouse, adult child, parent, and adult sibling.

Documentation of Informed Consent. The IRB must determine that informed consent is appropriately documented, unless alteration to selected items and documentation can be waived under the Common Rule, or FDA regulations.

Consent may be documented through use of a written consent document that embodies all of the required elements of informed consent and is signed by the subject.
- Consent may be documented through the use of a written consent document that embodies all of the required elements of the informed consent and is signed by the subject or a legally authorized representative, and a copy must be given to the person signing the form.
- Consent may also be documented through use of a short form consent document, which states that the elements of informed consent have been presented orally to the subject (or the legally authorized representative) in a language understandable to the subject. When this method is used, the following are necessary:
  o There must be a witness to the oral presentation.
  o The IRB must approve a written summary of what is to be presented orally. It includes a statement that the elements of the informed consent have been presented orally. The subject or the representative must sign only the short form.

Or
  o The witness must sign both the short form and the summary.
  o The person actually obtaining consent must sign the summary.
A copy of the summary and the short form must be given to the subject or the representative.

The original signed consent document must be retained in the research (investigator’s) file under conditions of confidentiality and a copy of the signed consent form is given to the research participant.

Obtaining Consent from Non-English Speakers. Informed consent conferences include a reliable translator when the prospective subject does not understand the language of the person who is obtaining consent.

The IRB shall require that appropriately translated consent documents be submitted to the IRB for review and approval prior to their use in enrolling subjects. The IRB can utilize expedited review procedures in approving such documents if the English language consent document has already been approved, and if the investigator attests in writing to the accuracy of the translation. When a short form consent document is used, the short form itself must be written in a language understandable to the subject, although the summary may be in English. The translator who took part in the informed consent conference may serve as the witness.

Waiver or Alteration of Informed Consent. Informed consent is required for all research studies involving human subjects unless specifically waived by the IRB. Under certain conditions, consent requirements may be altered or consent may be waived altogether. The informed consent may be waived if:

1) The research involves no more than minimal risk to the subjects.
2) The waiver or alteration shall not adversely affect the rights and welfare of the subjects.
3) The research could not practically be carried out without the waiver or alteration.
4) Whenever appropriate, the subjects shall be provided with additional pertinent information after participation.

Waiver of Documentation of Consent. The waiver of informed consent should be requested and justified at the time the proposal is submitted to the IRB. It is the responsibility of the investigator to request the waiver. It must be documented in the minutes that a waiver was granted and the justification for its use was approved.

The IRB must find and document either of the following conditions:

1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. In this case, each subject shall be asked whether he/she wants documentation linking them with the research, and the subject’s wishes will govern. (The waiver provision is not applicable to FDA-regulated research).

Or

2) The research presents no more than minimal risk of harm to subjects and involves procedures or activities for which written consent is not normally required outside of the research context. In cases in which the documentation requirement is waived, the
IRB may require the PI to provide subjects with a written statement regarding the research.

All protocol documents for closed protocols are maintained in Records Management. All records shall be accessible for inspection and/or copying by representatives of the appropriate departments or agencies.

X. Behavioral and Social Sciences Research

Social and Psychological Harms. When evaluating behavioral and social science research, the IRB examines the research protocol to evaluate risk of harm to subjects in terms of magnitude/severity, probability/likelihood, duration, and frequency. The nature of risk includes the potential for participants to experience emotional or psychological harm (e.g., stress and anxiety), social harm (e.g., stigma), financial harm (e.g., loss of employment or insurability), legal harm (e.g., criminal or civil liability), as well as invasion of privacy or embarrassment due to breaches of confidentiality. The IRB also considers the probability of “delayed harm” and what might be done to ameliorate it should it occur. For example, counseling referral information can be made available for participants.

To mitigate such risks, the IRB reviews the proposal for appropriate preventive protections through sound research design and procedures to protect the subject from risks, such as debriefings, adequate disclosure of risks in the informed consent information, and the mechanisms to protect the confidentiality and privacy of persons participating in or affected by research.

Privacy and Confidentiality Concerns. In general, identifiable information may not be obtained from private (non-public) records without the approval of the IRB and the informed consent of the subject. This is the case even for activities intended to identify potential subjects who will later be approached to participate in research. However, there are circumstances that are exempt from the regulations, and circumstances in which the IRB may approve a waiver of the usual informed consent requirements.

Safeguarding Confidentiality. When information linked to individuals will be recorded as part of the research design, the IRB ensures that adequate precautions shall be taken to safeguard the confidentiality of the information. The more sensitive the data being collected, the more important it is for the researcher and the IRB to review the mechanisms for protecting confidentiality.

Research Involving Deception or Withholding of Information. When reviewing research involving incomplete disclosure or outright deception, the IRB must apply both common sense and sensitivity to the review.

Where deception is involved, the IRB needs to be satisfied that the deception is necessary and that, when appropriate, the subjects shall be debriefed. (Debriefing may be inappropriate, for
example, when the debriefing itself would present an unreasonable risk of harm without a corresponding benefit.) The IRB also makes sure that the proposed subject population is suitable.

Deception can only be permitted when the IRB documents that a waiver of the usual informed consent requirements is justified under the criteria present in the Common Rule and 38 CFR 16.116(d). Specifically, the IRB must find and document that all four of the following criteria have been satisfied:

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

In making the determination to approve the use of deception under a waiver of informed consent, the IRB should consider each criterion in turn, and document specifically (in the minutes of its meeting and/or in the IRB research protocol file) how the proposed research satisfies that criterion. *(Note: The regulations make no provision for the use of deception in research that poses greater than minimal risks to subjects.)*

**XI. Biomedical Research**

Clemson University has an Inter-institutional Agreement with Greenville Hospital System (GHS) to be the IRB of Record and review biomedical research from Clemson University faculty, staff, and students. It is important to note the Clemson University’s IRB will still review some health related research protocols that are mainly in the area of social and behavioral sciences and that include, but are not limited to, the use of surveys. If the research protocol involves the use of GHS, Bon Secours St. Francis Hospital or Oconee Memorial Hospital patients, it will be reviewed by GHS.

**Procedures.** Listed below are the steps needed to prepare your application for submission:

1) To effectively facilitate submission and review of research protocols, Principal Investigators (PIs) should contact the Clemson University’s IRB Coordinator, Ms. Laura Moll, at 656-6460 or the Chair of the IRB, Dr. Joel Greenstein (656-5649) to discuss the nature of the project and to determine whether the research protocol comes under the Inter-Institutional Agreement and should be reviewed by GHS. This will impact on the timely review and selection of which research application forms need to be completed by the PI.

2) The Clemson University IRB Coordinator will inform the PI, of the appropriate forms that need to be completed, and the time frames for review for either the Clemson University IRB or GHS IRB, which is called the IRC.

3) All investigators submitting research protocols to GHS must complete IRB education for Human Subject Research before the study can begin. If investigators have not completed the education, please contact Laura Moll, IRB Coordinator, Office of Research Compliance, Clemson University, (656-6460) for training.
4) As directed by the Clemson University IRB Coordinator, you may contact the Institutional Review Committee (IRC) at Greenville Hospital. The IRC Coordinators are:
   - IRC-A Coordinator, Kelly Stephens at 864-455-4984 for all types of research except oncology.
   - IRC-B Coordinator, Glyn Hamilton at 864-455-4360 for pediatric oncology research.
   - IRC Coordinator, Jean Winter at 864-455-6607 for oncology research.

5) In order to provide for adequate review time, the IRC can only review six (6) new studies at each meeting. Items are placed on the agenda on a first-come, first-served basis. Deadline dates are enforced to allow for a substantial and meaningful review. There may be consideration given to this number of protocols reviewed at any one time on a case-by-case basis.

6) If your study utilizes a consent form, it must be pre-screened prior to submission to the IRC for approval. The CU IRB Coordinator will assist you in the development of your consent form. This pre-screening process will identify any omissions and help streamline the review process.

7) Principal Investigators are invited to attend the IRC meeting at GHS when their protocols are scheduled for Full Committee Review.

8) Principal Investigators must submit to the Clemson University Office of Research Compliance, IRB Coordinator, a copy of the application approved by GHS as well as the GHS approval letter.

9) Principal Investigators must also submit copies of amendments to the protocol, continuing reviews, consent form changes; current consent forms with approval and expiration dates, and GHS approval letters to the CU IRB Coordinator for our research files.

XII. Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (45 CFR 46 Subpart B)

To what does this policy apply?
(A) Except as provided in paragraph (B) of this section, this policy applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates conducted by faculty, staff, or students of Clemson University.

(B) The exemptions in Appendix A are applicable to this policy.

Definitions. As used in this policy:
Dead fetus means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

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

Fetus means the product of conception from implantation until delivery.
Neonate means a newborn.

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

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

Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of XI, XII, XIV, XV, XVIII, and Appendices A and B.

Duties of the IRB in connection with research involving pregnant women, fetuses, and neonates. Each IRB shall review research covered by this policy and approve only research which satisfies the conditions of all applicable sections of this policy.

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

(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 or behavioral 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 or behavioral knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of XII;
(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 XII, except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
(6) Each individual providing consent under paragraph (4) or (5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
(7) For children who are pregnant, assent and permission are obtained in accord with the provisions of the policy given in XVIII;
(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.

Research involving neonates.

(A) Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:
(1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
(2) Each individual providing consent under paragraph (B)(2) or (C)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
(3) Individuals engaged in the research will have no part in determining the viability of a neonate;
(4) The requirements of paragraph (B) or (C) of this section have been met as applicable.

(B) Neonates of uncertain viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this policy unless the following additional conditions have been met:
(1) The IRB determines that:
   (i) 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
   (ii) The purpose of the research is the development of important biomedical or behavioral knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
(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 legally authorized representative is obtained in accord with XII, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

(C) Nonviable neonates. After delivery nonviable neonate may not be involved in research covered by this policy unless all of the following additional conditions are met:
(1) Vital functions of the neonate will not be artificially maintained;
(2) The research will not terminate the heartbeat or respiration of the neonate;
(3) There will be no added risk to the neonate resulting from the research;
(4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
(5) The legally effective informed consent of both parents of the neonate is obtained in accord with XII, except that the “Waiver and Alteration of Informed Consent” section does not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

(D) Viable neonates. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of XI, XII, XIV, XV, XVIII, and Appendices A and B.

Research involving, after delivery, the placenta, the dead fetus or fetal material.

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

(B) If information associated with material described in paragraph (A) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent policies are applicable.

Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates. Faculty, staff, or students of Clemson University will conduct research that the IRB does not believe meets the requirements of the sections on “Research involving pregnant women or fetuses” or “Research involving neonates” only if:

(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 IRB, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) has determined either:

(1) That the research in fact satisfies the conditions of the section on “Research involving pregnant women or fetuses”, as applicable; or

(2) The following:

(i) 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;

(ii) The research will be conducted in accord with sound ethical principles; and

(iii) Informed consent will be obtained in accord with XII and other applicable policies.
XIII. Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects (45 CFR 46 Subpart C)

Applicability. The regulations in this policy are applicable to all biomedical and behavioral research conducted by faculty, staff, or students of Clemson University involving prisoners as subjects.

Purpose. Inasmuch as prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research, it is the purpose of this policy to provide additional safeguards for the protection of prisoners involved in activities to which this policy is applicable.

Definitions. As used in this policy:

*Prisoner* means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

*Minimal risk* is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

Composition of Institutional Review Board where prisoners are involved. In addition to satisfying the requirements in V, the Institutional Review Board carrying out responsibilities with respect to research covered by this policy, shall also meet the following specific requirements:

(A) A majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.

(B) At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity.

Additional duties of the Institutional Review Board where prisoners are involved. The Institutional Review Board shall review research covered by this policy and approve such research only if it finds that:

(A) The research under review represents one of the categories of research permissible under the section on “Permitted research involving prisoners”;

(B) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
(C) The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

(D) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

(E) The information is presented in language which is understandable to the subject population;

(F) Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

(G) Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.

**Permitted research involving prisoners.**

(A) Biomedical or behavioral research conducted by faculty, staff, or students of Clemson University may involve prisoners as subjects only if:

1. The Institutional Review Board has approved the research under the section on “Additional duties of the Institutional Review Board where prisoners are involved”; and

2. The proposed research involves solely the following:
   (i) Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
   (ii) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
   (iii) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the IRB has consulted with appropriate experts including experts in penology, medicine, and ethics; or
   (iv) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners
in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the IRB has consulted with appropriate experts, including experts in penology, medicine, and ethics.

(B) Except as provided in paragraph (A) of this section, biomedical or behavioral research conducted by faculty, staff, and students of Clemson University shall not involve prisoners as subjects.

XIV. Additional Protections for Children Involved as Subjects in Research (45 CFR 46 Subpart D)

To what does this policy apply?

(A) This policy applies to all research involving children as subjects, conducted by the faculty, staff, and students of Clemson University.

(B) Exemptions at Appendix A, Categories 1 and 3 through 6 are applicable to this policy. The exemption in Category 2 regarding educational tests is also applicable to this policy. However, the exemption in Category 2 for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this policy, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.

Definitions. As used in this policy:

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

Assent means a child’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

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

Parent means a child’s biological or adoptive parent.

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

IRB duties. Each IRB shall review research covered by this policy and approve only research which satisfies the conditions of all applicable sections of this policy.

Research not involving greater than minimal risk. Clemson University will conduct research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB
finds that adequate provisions are made for soliciting the assent of the children and the
permission of their parents or guardians.

**Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.** Clemson University will conduct research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject’s well-being, only if the IRB finds that:

(A) The risk is justified by the anticipated benefit to the subjects;

(B) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and

(C) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

**Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition.** Clemson University will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:

(A) The risk represents a minor increase over minimal risk;

(B) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

(C) The intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition; and

(D) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.

**Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.** Clemson University will conduct research that the IRB does not believe meets the requirements of the above three sections (“Research not involving greater than minimal risk”, “Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects”, and “Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition”) only if:

(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 children; and
The IRB, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) has determined either:

(1) That the research in fact satisfies the conditions of the above three sections, as applicable, or

(2) the following:

(i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

(ii) The research will be conducted in accordance with sound ethical principles;

(iii) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

Requirements for permission by parents or guardians and for assent by children.

(A) In addition to the determinations required under other applicable sections of this policy, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with the “Waiver or Alteration of Informed Consent” section in XII.

(B) In addition to the determinations required under other applicable policies, the IRB shall determine, in accordance with and to the extent that consent is required by XII, that adequate provisions are made for soliciting the permission of each child’s parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under the first two categories of research described in this policy (“Research not involving greater than minimal risk” and “Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects”). Where research is covered by the second two categories of research described in this policy (“Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition” and “Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children”) and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
(C) In addition to the provisions for waiver contained in the “Waiver or Alteration of Informed Consent” section in XII, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in XII and paragraph (B) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

(D) Permission by parents or guardians shall be documented in accordance with and to the extent required by the “Waiver or Alteration of Informed Consent” section in XII.

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

Wards.

(A) Children who are wards of the state or any other agency, institution, or entity can be included in research approved under the first two categories of research described in this policy (“Research not involving greater than minimal risk” and “Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects”) only if such research is:
   (1) Related to their status as wards; or
   (2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

(B) If the research is approved under paragraph (A) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child’s participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.
Appendix A: Exemption Criteria

Research activities in the following six categories can be exempt from continuing review of the IRB [45 CFR 46.101]

| CATEGORY #1: | Research conducted in established or commonly accepted educational settings, involving normal educational practices, 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.
| NOTE. | The above exemption is applicable to mentally handicapped individuals only if the research involves no changes in the content, location, or procedures of instruction from those normally experienced by the participant.

| CATEGORY #2: | Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
| | i. the information obtained is recorded in such a manner that human participants can be identified, directly or through identifiers linked to the participants; AND
| | ii. any disclosure of the human participants' responses outside the research could reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, or reputation.
| NOTE: | Survey and interview techniques which include minors are not exempt. Observation of the public behavior of minors, if the researcher is not a participant, is exempt.

| CATEGORY #3: | Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under Category 2, IF:
| | a. the human participants are elected or appointed public officials or candidates for public office, OR
| | b. federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

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

| CATEGORY #5: | Research and demonstration projects which are conducted by or subject to the approval of appropriate Federal Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:
| | a. public benefit or service programs; or
| | b. procedures for obtaining benefits or services under those programs; or
| | c. possible changes in or alternatives to those programs or procedures; or
| | d. possible changes in methods or levels of payment for benefits or services under those programs.

| CATEGORY #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.
Appendix B: Expedited Criteria

Categories of research that may be reviewed by the IRB through an expedited review procedure [63 CFR 60364-60367, November 9, 1998]

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, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

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

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

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

(E) Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

| CATEGORY #1: | Clinical studies of drugs and medical devices only when condition (a) or (b) is met. a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review. b. Research on medical devices for which i. an investigational device exemption application (21 CFR Part 812) is not required; or ii. the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling. |
| CATEGORY #2: | Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: a. from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or b. from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week. |
### CATEGORY #3: Prospective collection of biological specimens for research purposes by noninvasive means.

- hair and nail clippings in a nondisfiguring manner;
- deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
- permanent teeth if routine patient care indicates a need for extraction;
- excreta and external secretions (including sweat);
- 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;
- placenta removed at delivery;
- amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
- 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;
- mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
- sputum collected after saline mist nebulization.

### CATEGORY #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.)

- 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;
- weighing or testing sensory acuity;
- magnetic resonance imaging;
- electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electoretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
- moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

### CATEGORY #5: Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

**NOTE:** Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.

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

### CATEGORY #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.

### CATEGORY #8: Continuing review of research previously approved by the convened IRB as follows:

- where
  - the research is permanently closed to the enrollment of new subjects;
  - all subjects have completed all research-related interventions; and
  - the research remains active only for long-term follow-up of subjects; or
- where no subjects have been enrolled and no additional risks have been identified; or
- where the remaining research activities are limited to data analysis.
| CATEGORY #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. |