

University and Medical Center Institutional Review Board

Policy and Procedure Manual

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SCOPE AND PURPOSE OF THE UMCIRB

East Carolina University, IORG0000418, has provided an assurance to the Department of Health and Human Services that it will follow procedures to assure the protection of all participants involved in human subjects research projects through submission of a Federalwide Assurance (FWA). The FWA applies to all human subject research conducted at the designated institution.

Each institution engaged in human subject research must contact the Office of Human Research Protections (OHRP) to discuss the appropriateness of obtaining their FWA. Any institution that relies on the University Medical Committee Institutional Review Board (UMCIRB) for review of a research study must complete and execute the appropriate agreements. The FWA numbers for ECU is FWA00000658.

Scope:

East Carolina University has established the Biomedical UMCIRB (IRB00000705 East Carolina U IRB #1 Biomedical) to review biomedical research projects involving human subjects, and the Behavioral and Social Sciences UMCIRB (IRB00003781 East Carolina U IRB #2 Behavioral/SS) to review behavioral and social sciences projects involving human subjects. In addition, there is a Prisoner UMCIRB (IRB00004171) to review research involving those individuals meeting the definition of prisoners, and the Behavioral and Social Sciences Summer IRB (IRB00004973) which reviews behavioral and social science research during the breaks in an academic year.

The UMCIRB consist of representatives from a variety of scientific disciplines, non-scientists and community members. The primary function of the UMCIRB is to protect the rights and welfare of human subjects and to assist investigators in this process. Investigators bear the primary responsibility for the conduct of the research study and ensuring that research meets the standards established by Federal regulations and the

UMCIRB. The UMCIRB office and committee strive to have open lines of communication and wide accessibility for everyone involved in research.

Purpose:

Before any research project involving human subjects is initiated, it must first be reviewed and approved by the UMCIRB, and once approval is granted, the research must then be conducted according to the guidelines set forth in this handbook. All ECU faculty, staff, and students must seek UMCIRB approval for any human subject research conducted at the university or elsewhere in connection with their institutional responsibilities. This compliance is a crucial element of the UMCIRB process, because it is the collective effort of individual investigators in this area that ensures the integrity of the university as a research institution.

Anyone transferring research studies from their previous place of employment, or performing ongoing research from an educational experience (i.e. thesis, dissertation work) from an institution other than ECU, must seek advice regarding approval from the UMCIRB before continuing any aspect of the research.

Investigators not affiliated with ECU or PCMH conducting research involving the use ECU or PCMH resources or facilities (faculty, staff, students and/or patients) must complete an Unaffiliated Investigators Agreement and submit the appropriate paperwork for UMCIRB approval.

The UMCIRB complies with the “Common Rule” published at [45 CFR 46 Subpart A](#), along with Subpart B (pregnant women, human fetuses, neonates), Subpart C (prisoners) and Subpart D (children), FDA 21 CFR 50 and 56, sections applicable to the IRB included in the International Conference on Harmonisation Good Clinical Practices (section 3: Institutional Review Board/Independent Ethics committee, section 4.8: Informed Consent of Trial Subjects, and other relevant portions), federal/state/local laws, and institutional policy. All human subject research studies must comply with ethical

principles as outlined by the Belmont Report, as well as applicable regulations as requested by the sponsor or federal agency, regardless of the funding source. It is important to realize that all research must meet [45 CFR 46](#) as a minimal standard, even when being conducted under supervision of another department such as the FDA. While most regulations are similar, there are currently some significant [differences](#) between such bodies as the FDA and DHHS.

ETHICAL PRINCIPLES GUIDING THE UMCIRB

The cornerstone for conducting human subject research is the application of ethical principles. The history of unscrupulous research practices has resulted in passing congressional acts and the creation of important documents such as Declaration of Helsinki and the Nuremberg Code to provide ethical guidance. One of the most important documents, the Belmont Report, is outlined below.

Belmont Report:

In 1974, the National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission published the [Belmont Report](#), which sets forth the following three basic ethical principles guiding the conduct of research with human subjects as outlined below.

Respect for Persons:

In consideration of respect for persons, investigators are required to seek voluntary informed consent from potential subjects. Voluntary informed consent means that subjects are given free choice to decide about participation, and the study is fully described in terms that are easy to understand. The consent form document should include adequate information about the study risks and benefits to assist subjects in deciding whether to participate in the research. In addition, respect means honoring the privacy of individuals and maintaining the confidentiality of data obtained. Respect for minors and mentally disabled persons requires taking extra precautions to protect those individuals who are immature or incapacitated, perhaps even to the extent of excluding them from participation in certain research. The extent of protection depends upon the level of autonomy the person possesses.

Beneficence:

The principle of beneficence requires that researchers maximize the potential benefits to the subjects and minimize the risks of harm. Benefits to the subjects, or generalized knowledge gained from the research, should balance or outweigh the risks.

Justice:

The principle of justice means that subjects are selected fairly and that the risks and benefits of research are distributed equitably. Investigators should take precautions not to select subjects simply because of the subjects' availability, their compromised position, or because of social, racial, gender, economic or cultural biases. Investigators should base inclusion criteria on those factors that most effectively and soundly address the research problem.

UMCIRB COMMITTEE

Leadership:

The major leadership force for the UMCIRB office is the Administrative Director, appointed on authority of the Vice Chancellor for Research and Graduate Studies to an unlimited term. The major leadership forces for the UMCIRB committees are the Biomedical Director/Chair and Behavioral and Social Sciences Director/Chair, appointed on the authority of the Vice Chancellor for Research and Graduate Studies to an unlimited term. The Directors/Chairs must be faculty in good standing at East Carolina University, and have training and education consistent to perform the duties of the position. The Directors/Chairs must have an ongoing commitment to engage in educational opportunities specifically related to human subject protection, and should seek professional certifications recognizing such accomplishments.

The Directors/Chairs report directly to the Administrative Director regarding administrative matters. The Administrative Director reports directly to the Vice Chancellor for Research and Graduate Studies for East Carolina University, but has open lines of communication to all levels of institutional officials, human protection administrators, deans, department chairs and with other individuals outside of the institution. The Administrative Director appoints the Human Protections Administrator for East Carolina University, who functions as the primary contact between OHRP, ECU and other institutions utilizing the UMCIRB services.

The Biomedical Committee, Behavioral and Social Sciences Committee, Prisoner Committee and Summer Behavioral and Social Sciences Committee Chairs routinely preside over the scheduled UMCIRB meetings, and perform expedited reviews of research studies within the office. The Chairs have the authority to appoint UMCIRB members to act as their designee in the review of human subject research, based on appropriate experience and training, and to make other appointments as necessary to ensure the committee's function. The Administrative Director has the authority to appoint a designee to act in his/her place for the purposes of conducting the business of the UMCIRB and to appoint ad hoc committees to address issues as required in consultation with the Directors/Chairs.

The Directors/Chairs may be removed for failure to adequately perform the duty to provide leadership in research related human protections oversight by the Vice Chancellor for Research and Graduate Studies, or if continued services is no longer in either parties best interest.

UMCIRB office purpose and responsibilities:

The UMCIRB office exists to support the work of the UMCIRB committee in its duties related to the protection of human subjects. The Administrative Director serves as the Department Chair for the UMCIRB office, and collaborates directly with the Vice Chancellor for Research and Graduate Studies in ensuring adequate resources, both financial and human, are available to adequately perform the day-to-day office functions

and human protection duties as required by federal regulations. Financial resources are generated by fees set through institutional authority, by contractual agreements between institutions we serve as the IRB of record, and from funds generated by East Carolina University. All budget and accounting records, as well as other records required for the daily operations, will be maintained in the UMCIRB office in accordance with institutional policy.

The Associate Director reports directly to the Administrative Director. The Associate Director has the authority to act on behalf of the Administrative Director to conduct office business in his/her absence. The Associate Director is primarily responsible for the daily office operations, participating in policy and procedure development, supporting the UMCIRB committee members and interacting with research investigators and their staff.

The UMCIRB office exists to support the work of the UMCIRB committee and the research investigator in his/her mission to protect the safety and welfare of human subjects involved in human subjects research. The UMCIRB will facilitate open lines of communication for all interested parties. General files will be kept and retained indefinitely to document significant correspondence that occurs between the investigator, institutions, institutional officials, sponsors and federal regulatory agencies.

Communication to officials from each institution regarding the UMCIRB work and actions will routinely occur through distribution of the minutes. Any significant additional communications will occur via letters specifically addressing issues from the office by the Administrative Director or his/her designee.

The UMCIRB office will be responsible for maintaining a current roster reflecting the members name, gender, highest earned degrees, primary scientific or nonscientific specialty, affiliations with institutions where research is routinely conducted, and replacement designation for alternate members. The designation of alternate members must be based on similar expertise or functions of the absent full member. An institution utilizing the UMCIRB for purposes of the routine review and approval of research must appoint an institutional representative who has knowledge of the institution or research being conducted at the institution to serve as ex-officio. The UMCIRB roster will be

updated as changes occur, but not more frequently than just prior to each meeting. The office will submit the updated roster to the Office of Human Research Protections as needed for updates. UMCIRB member information will be maintained in a file for the current committees and updated accordingly, for example current CVs or resumes will replace the outdated version and the outdated versions will be discarded. Any additional relevant information will also be maintained as needed.

The UMCIRB office will house hardcopy reference materials and make them available to committee members, researcher staff, and institutional officials. Additionally, the UMCIRB office will make resource links and other materials available on the web site at timely intervals.

The office will be responsible for preparing and maintaining adequate records of research study activities and procedures:

- Maintenance of Research Files: All items received into the office from investigators regarding a specific research proposal will be maintained in a folder designated for the study, and filed numerically by the UMCIRB number. Research study files are expected to contain all submission requirements, consent documents, reported adverse events, report of significant new findings reported to participants, continuing review activities, all study specific correspondence via hardcopy or contact log, and all internal office review and evaluation documents. All significant forms of research related correspondence will be maintained in the study specific binder, for example completion of a contact log, e-mail copy, and letter. The committee's discussion of the research study will be maintained in the corresponding UMCIRB minutes. Investigators or key research staff are invited and encouraged to make an appointment to visit the office for a regulatory review between the investigator and UMCIRB folders. All active research records will be maintained in the UMCIRB office. Research records taken from the UMCIRB office for designee review will be tracked. Active research studies where any portion of the file is maintained in a contracted university storage facility for easy retrieval will have a memo to file describing the contents in storage and its

location, for example large volumes of non-local adverse events may be stored in this fashion. Research studies that have been closed and are no longer active will be sent for confidential storage at the university contracted storage facility, where they are easily retrievable when needed. All records will be maintained for no less than 3 years after the study closure date. Records from research studies involving FDA regulated test items will be retained for at least 3 years after completion of the studies. Research records on studies receiving an exempt status classification will be retained for no less than 3 years after the date of review. The research files are available for review and copying by institutional officials when carrying out their institutional responsibilities and federal agencies as required during an UMCIRB audit.

- Maintaining Committee Meeting Records: The UMCIRB office will be responsible for constructing minutes in sufficient detail to show attendance at the meetings in categories of full member, voting alternate members, guests, consultants, non-voting alternate members, ex-officio attendance, and absent members; actions taken by the UMCIRB; the vote on these actions including the number of members voting for, against, abstentions, and the number of recusals; the basis for requiring changes in or disapproving research unless otherwise obvious on their face such as an incompletely answered question or misspelled words; and a written summary of the discussion of controverted issues and their resolution. The minutes will also serve to report all expedited actions performed between meetings, including the expedited approval of new research studies with requested modifications as granted authority by the committee, exempt studies, and all other actions not requiring approval by a convened UMCIRB committee. The minutes will serve to communicate the UMCIRB committees' actions or actions taken on behalf of the committee to the ECU signatory official, as he/she will receive a copy of the past meeting minutes along with a copy of the upcoming meeting agenda. The minutes for each meeting will be maintained indefinitely.[45 CFR 46.115](#)
- Quality Improvement: The UMCIRB complies with federal regulations governing the conduct of human subject research. The UMCIRB office conducts

evaluations of the office and committee according to the FDA self assessment checklist and OHRP compliance assessments in order to measure compliance with regulations, which are retained in the general office files. The UMCIRB is subject to internal or external auditing by relevant institutional offices as directed by the ECU signatory official. The UMCIRB is also subject to audit, both routine and for cause, by outside regulatory agencies. The audit system for the conduct of FDA inspections and OHRP oversight provides a valuable tool for ongoing quality improvement for the protection of human subjects in research. The results of these inspections may be viewed at the site for FDA warning letters and OHRP determination letters.

UMCIRB Committee:

The UMCIRB committee is duly constituted according to federal regulations [45 CFR 46.107](#) and [21 CFR 56.107](#) in order to review human subject research. The UMCIRB must be comprised of at least 5 individuals, including men and women, varied professions and diversity of life experiences. There must be one scientist, one non-scientist, an institutionally affiliated representative and unaffiliated members on the committee. The committee must have sufficient expertise to review and approve studies that are routinely submitted. Membership diversity is encouraged and valued. It is vital to have members representing experiences or expertise with vulnerable populations, such as children and prisoners, because they require special safeguards to protect them from undue influence and coercion. This safeguard requires a membership that includes advocates to ensure vulnerable subjects are treated with the ethical principles as outlined in such documents as the Belmont Report. The committee size and make-up is controlled by the Administrative Director and respective Chairs, in order to best accomplish the work and workload of the committee.

Committee member duties:

Committee members should plan to attend at least half of the meetings in order to maintain a current understanding of guidelines and their application. However, some very experienced members may be able to contribute meaningfully with less frequent attendance. Full and alternate members planning to attend a meeting should review and be prepared to discuss all meeting related information, and apply the regulations, laws and ethical principles through the reviews process. The members reviewing research studies are expected to utilize the reviewer checklist and to provide a rationale for the basis of change requested in a research project unless the changes are otherwise obvious on their face such as incompletely answered question or misspelled words. Reviewing members will send reviews in to the UMCIRB office for upcoming meetings in a timely fashion so that the investigator may be contacted prior to the meeting regarding issues and/or concerns raised by the reviewer. Members should assist with meeting scheduling by cooperating with the office to provide anticipated attendance. All members are required to treat all materials, discussion and information pertaining to the work of the UMCIRB committee in a confidential manner.

Types of UMCIRB committee members:

There are two types of voting committee members: full and alternate.

Full members have all the duties and responsibilities of the UMCIRB committee. An alternate member serves in all the capacities of a full member at the UMCIRB meeting only during the absence of his/her designated full member.

The **alternate member** will be designated on the UMCIRB roster to serve for a specific full member based on some similar aspect of his/her training, education or experience. For example, an alternate member may be both a physician scientist and unaffiliated, so he/she may serve as an alternate for either a physician or unaffiliated member. The alternate member is not required to regularly attend meetings, unless his/her designated member is absent and he/she has been invited by the office to attend. The alternate may

not count toward quorum or vote if his/her designated full member is also present and voting on a particular study.

Ex-officio may not vote or have primary and secondary reviewer responsibilities. Examples of ex-officio include institutional counsel, Office of Sponsored Program staff members, and institutional representatives. An ex-officio may attend meetings and receive the meeting material at his/her request.

Committee member qualifications:

Members must be 18 years old or older to be appointed to the UMCIRB committee. There are no educational or professional requirements as long as the committee is properly constituted. Members must complete either the biomedical or behavioral and social sciences UMCIRB required education modules based on his/her committee every three years. Arrangements for alternate education may be made as needed to accommodate unique circumstances, such as a lack of access to a computer or for a disability. A member must submit a CV or other summary of his/her experience.

Becoming an UMCIRB member:

The Vice Chancellor for Research and Graduate Studies appoints full and alternate UMCIRB members, in consultation with the Administrative Director. The Administrative Director recommends a new member after consultation with the Associate Director and UMCIRB Chairs. A letter will be issued confirming membership to the UMCIRB committee with a copy forwarded to the department chairs of East Carolina University employees or managers of other affiliated institutions. Members, full and alternate, will be appointed for an unlimited term. A member may request to be removed from the roster at any time, for example when time constraints make meaningful contributions unmanageable. A departmental Chair, supervisor/manager or other institutional official may also excuse a member from UMCIRB service if it is felt their continued participation does not serve in the best interest of the concerned parties.

The UMCIRB is a voluntary committee, and members will not receive compensation for their service; however, lunch is provided during regular meetings and parking passes are provided for unaffiliated members if needed.

New members will be supplied with a copy of the Institutional Review Board Member Handbook as a reference and the OHRP educational CD. Support will be provided for those inexperienced members reviewing research proposals. Continuing education will routinely be provided at each UMCIRB meeting on items pertinent to the research proposals outlined on the agenda or otherwise deemed to be appropriate. The committee members may request topics of interest or the topic will be selected by the UMCIRB office staff.

Meetings of the UMCIRB:

Investigator Attendance:

Principal investigators may be invited by the reviewers, committee members, UMCIRB Chair or office staff to attend the meeting for the purposes of answering questions, or to present particularly complex research studies. Additionally, the principal investigator may request to attend the meeting to address the committee. The principal investigator may also choose to have another member of the research team attend the meeting to discuss the study. The investigator's proposed attendance should be coordinated through the office in order to best accommodate the investigator's needs whenever possible. The principal investigator and other research team members are prohibited from participating in the deliberation or vote on the research study. The principal investigator is not required to attend an IRB meeting where his/her study is planned for review.

Guests and Consultants:

Guests may attend the regularly scheduled UMCIRB meetings with prior approval of the UMCIRB office on a limited basis. The role of the guest is primarily as an observer. Guest may observe all discussions, interject any pertinent points into the discussion, and observe the vote, so long as the above does not constitute a conflict of interest. Guests will be educated on the principles of confidentiality for any items discussed during the meetings by their host or by the UMCIRB office. Guests with questions regarding any aspect of the meeting should be forwarded directly to one of the UMCIRB office staff. It is often beneficial for any individual considering a committee appointment to attend at least one meeting as a guest. New research investigators and study staff are encouraged to attend an IRB meeting as a learning opportunity for the conduct of future research.

Consultants may be invited to attend UMCIRB meetings or to provide information on a research topic when the knowledge for a specialty area is not represented on the UMCIRB committee for full review or by the designated reviewer on expedited review. The consultants may also be asked to provide a written response to a specific question or set of questions. A reviewer, the committee, the office or an investigator can request a consultant be involved in the evaluation of a research study.

A consultant's only role is to provide information and answer questions, and he/she is prohibited from serving as a primary or secondary reviewer, or from participating in the deliberation or vote on a research study. The evaluation or summary of the consultant will be captured in the UMCIRB minutes for full committee review or in the UMCIRB folder for expedited review. Investigators may also submit written information from consultants they have secured on behalf of their research study when appropriate to provide information to the UMCIRB committee or reviewer. The UMCIRB office will maintain a list of individuals who have agreed to serve in a consulting capacity and update the list as needed.

Communication to members regarding meetings:

The Biomedical Committee is routinely scheduled to meet on the 2nd and 4th Wednesday of every month, however, the committee meeting may be cancelled if there are no

research studies requiring full committee actions or other unavoidable problems arise. The Behavioral and Social Sciences committee is routinely scheduled to meet on the 1st and 3rd Wednesday of every month, however, the committee meeting may be cancelled if there are no research studies requiring full committee actions or other unavoidable problems arise. UMCIRB members and other appropriate individuals will be notified promptly if a regularly scheduled UMCIRB meeting is cancelled with the rationale provided. The Prisoner Committee and the Summer Behavioral and Social Sciences Committee meet on an as-needed basis. Members of UMCIRB committees that do not regularly meet will be notified of a need to meet by the UMCIRB office, and a mutually acceptable meeting time for all parties will be scheduled. Meetings may be conducted utilizing strategies such as conference calling as set forth in the regulations. UMCIRB members can be convened on an emergency basis if necessary by the Administrative Director or respective Chair.

All full and alternate members attending regularly scheduled IRB committee meetings are given a copy of the meeting agenda, minutes, continuing education, and materials for the research studies to be considered. All full and alternate members attending the as-needed scheduled IRB committee meetings will receive a copy of the agenda, and materials for the research studies to be considered. The Prisoner IRB committee members will also receive continuing education materials. The previous meeting minutes and upcoming meeting agenda are distributed to all full and alternate members. The meeting materials will be circulated by the office approximately one week before the scheduled meeting. All research folders with items to be reviewed during the meeting are available to all UMCIRB members in the office prior to and after the meeting, as well as, immediately available during the meeting. The meeting minutes since 2003 have been converted to an electronic storage device and are readily available during the meeting, while meeting minutes from previous years are accessible through the office.

Communication with other Institutions Relying on the UMCIRB as the IRB of record:

The relevant agenda will be sent electronically or via hard copy to all human protections administrators from institutions relying on the UMCIRB approximately one week before the scheduled meeting of interest. Each of the actions listed on the agenda includes the research site to more easily allow the various institutions to identify committee actions or proposed studies affecting his/her institution. Human protection administrators may raise questions regarding any specific issues through the UMCIRB office, individually contact the investigator, or make plans to attend the UMCIRB meeting. The minutes from the previous meeting will also be circulated electronically to the human protections administrators at institutions relying on the UMCIRB. The minutes serve to reflect the actions taken by the committee on the meeting date and the expedited actions taken by the chair or his/her designee between meetings. Representatives from institutions relying on the UMCIRB as the IRB of record may also receive any materials they request. The Signatory Official at PCMH will receive a copy of the upcoming meeting agenda and the previous committee meeting minutes in addition to the human protections administrator.

UMCIRB Review System:

The Chair or his/her designee initially reviews all protocols submitted to the UMCIRB office requiring any action by, or on behalf of, the committee. A list of these designees will be maintained in the UMCIRB office and updated as necessary.

New Studies Requiring Full Review:

The UMCIRB utilizes a primary and secondary reviewer system for new studies requiring full committee review. A primary or primary and secondary system is employed for all full committee reviews on requested modifications and tabled studies. A primary and secondary reviewer system means that two individuals receive a complete set of all the items for consideration on a research study and then present a summary of the action to the committee members for discussion, review and approval. All other members attending the meeting receive (at a

minimum) the internal processing form that includes a protocol summary and informed consent materials (including advertisements). Other tools and/or supporting documents may also be distributed to the committee as needed

Continuing Review Requiring Full Committee:

The UMCIRB utilizes a primary reviewer system for continuing reviews requiring approval by the full committee. A primary reviewer system means that one individual receives a complete set of all items for consideration on a research study, and then presents a summary of the action to the committee for discussion, review and approval. All other members attending the meeting receive (at a minimum) the internal processing form that includes a protocol summary and the informed consent materials (including advertisements). Other tools and/or supporting documents may also be distributed to the committee as needed.

Revisions Requiring Full Committee:

The UMCIRB utilizes a primary reviewer system for revisions requiring approval by the full committee. A primary reviewer system means that one individual receives a complete set of all items for consideration on a research study, and then presents a summary of the action to the committee for discussion, review and approval. All other members attending the meeting receive the revision application, a protocol summary, and relevant documents being considered for change.

Reviewers:

Reviewers are assigned administratively by the Administrative Director or his/her designee based on the reviewer's availability, experience, training, or the special needs of the study, and via consultation with the chair if needed. A reviewer must

be either a full or alternate member listed on the most currently approved roster to perform a review of research-related materials submitted to the IRB. Investigators are prohibited from selecting or assigning reviewers for either full committee or expedited review procedures. If the Chair has a conflict of interest because he/she is an investigator or otherwise affiliated with a research study, then the Administrative Director or his/her designee will assign the review to an IRB member with sufficient expertise to review the study. UMCIRB members must identify a conflict of interest as soon as possible after receiving the meeting materials in order for the office to assign another reviewer. Reviewers are encouraged to contact the investigator to clarify any questions that will facilitate review at the convened meeting in order to improve efficiency and foster a collaborative environment. The reviewers receive all information submitted to the UMCIRB office for consideration. A research study that has been assigned to, and subsequently reviewed by, a member that is unable to attend the meeting will not be reassigned to another member. If a reviewer is unable to attend an IRB meeting as scheduled before completing a review of the materials, then another UMCIRB member will be assigned to review the study. If a new study has been assigned to both a primary and secondary reviewer and one of the reviewers is unable to attend the meeting or submit a review for the meeting, then the member attending the meeting will function as the primary reviewer. The UMCIRB office staff will read any reviewer's comments to the committee on his/her behalf if he/she is unable to attend the meeting. While this reviewer's recommendation will be read to the committee and documented in the minutes, the reviewer's recommendation is not counted in the total vote as proxy votes are prohibited.

Every effort is made to assign continuing reviews or revisions of existing studies to the members who previously reviewed a protocol.

Member Voting Procedures:

Quorum:

The Chair or his/her designee will certify a quorum at the start of the meeting, and the meeting cannot be called to order until quorum is established. A quorum is required and must be maintained at all times in order to conduct the business of the UMCIRB. It is defined as a majority of members ($\geq 51\%$) or their designated alternates present, which must include a scientist and non-scientist, on each vote. The quorum must also be composed of any additional members required, as dictated by the nature of the research study, such as a physician on biomedical research involving test items regulated under FDA jurisdiction, or a prisoner representative involving prisoner research.

A meeting may achieve quorum by using the flexibility of telephone conferencing as permitted under the regulations. When this method is employed, all members will have received the relevant meeting materials and two-way conference calling will be established. The minutes will reflect when this mechanism is utilized and identify the phone conferenced member(s).

The UMCIRB committee may take no action on a research study at any time there is a loss of quorum. An unaffiliated member is not required to be in attendance in order to call a meeting to order, however, it is expected that unaffiliated members will have regular attendance habits. Only individuals listed on the roster may vote on UMCIRB actions. The Chair or his/her designee is responsible for certifying the existence and maintenance of a quorum. Only full members, or their designated alternate as identified on the roster, are eligible to count towards quorum and participate in voting. Only members participating in the entire presentation, discussion, and deliberation are eligible to count towards quorum and place a vote. Members that join the meeting after a discussion is underway on a study may not be counted towards quorum, and will be recused from the vote, and the reason for their recusal will be documented in the minutes. Members that leave the room during these activities will be recused from the vote, and the reason for their recusal will be documented in the minutes. Members participating in the presentation, discussion and deliberation that are unable to render a “yes” or “no” vote will be counted in the vote as an abstention. Because an abstention is counted towards quorum and the person will be reflected in the total number of votes, the individual’s name will not be documented in the minutes.

Conflict of Interest:

Any member attending a meeting that serves as an investigator, a research team member or otherwise identifies a potential or actual conflict of interest will be excused from both the deliberation and vote on a research study, and will be required to leave the room during these actions. This recusal will be reflected in the minutes. Committee members may abstain from voting without revealing the nature of his/her abstention; however, he/she should not abstain in the place of a “no” vote. The Chair may also recuse a member from the vote if he/she judges that there is a potential conflict of interest.

Recusals are a tool used to manage conflict of interest whereas abstentions are used when the member genuinely does not feel able to render a “yes” or “no” vote. Recusals for conflict of interest are noted on the letter sent to the principal investigator. An ex-officio is not eligible to vote because of his/her actual or potential conflict of interest. Full or alternate members that would have been recused from a vote if they had attended a meeting will be indicated in the UMCIRB committee determination letter sent to the principal investigator as not participating in the deliberation and vote on the particular study. Similarly, any member appearing on the roster who has a conflict of interest will have a notation on the committee’s determination letter to the PI that the person was not present for the vote on a specific study. The approval letters for new research studies undergoing expedited review will also contain a conflict of interest statement.

Voting:

After certification of quorum, the chair or his/her designee will indicate the members or their alternates who will be voting during the meeting. Each research study action will be discussed and voted on separately. The vote will be obtained by calling for a verbal yes vote, no vote and abstentions, with recusals announced. The vote will be captured in the minutes to reflect the “total=number, for=number, opposed=number, abstention=number, recused=number (name – reason)” on each protocol. The total

number will reflect all members eligible for voting at that meeting, and will be the sum of all the for/opposed/abstention votes noted. Recusals do not count toward the total number of votes. Members are prohibited from submitting proxy votes, either in writing or by telephone. If a meeting is held where conference calling is employed, the minutes will document the member that is attending the meeting and registering a vote via two-way conference calling. The member attending the meeting via phone conference must be available to hear the discussion during the presentation and deliberation.

An action will be carried if it gains the majority of the total number of votes, for example, there must be $\geq 51\%$ of total votes recorded as “for” to approve an action. If the majority of the total number of attending members abstains on a particular vote, then there will be an insufficient number of “yes” votes to approve the action at that time.

REVIEW ACTIONS

Full committee review:

The UMCIRB office will communicate the committee decisions to the investigator in writing as soon as possible after the UMCIRB meeting, and outline any additional information or changes that may be requested. [45 CFR 46.109](#) and [21 CFR 56.109](#) Written letters of communication from the UMCIRB committee will be routinely initialed by the UMCIRB office staff typing the letter, and will not routinely be signed by the UMCIRB chair. Forms or letters requiring a full signature may also be signed by UMCIRB staff as designated. The UMCIRB office will maintain documentation of designees for these activities.

1. **Approval:** If a study is approved as submitted, a letter of approval is sent to the principal investigator stating the date of approval and the approval period. The investigator is responsible for providing notification of UMCIRB approval and the approval period expiration to funding agencies or other entities.

2. **Modifications Required:** If a study cannot be approved due to minor revisions or requested modification by the committee, a letter of required modifications and the basis for these changes will be sent to the principal investigator. Modifications may require full UMCIRB approval. The Chair/designee may be granted the authority from the committee to approve the study upon receipt of the requested modifications, only if an exact prescription was constructed and exactly met by the investigator. If the principal investigator does not agree with or cannot accept the requested modifications of the Committee, the study will have to return to the full UMCIRB meeting. If the committee is unable to make an exact prescription and can not formally state all items that require modification, then the committee will request that the study return for full committee review. After the modifications are approved, a letter is sent to the principal investigator stating the date and duration of approval. The approval date for a research

study requiring modifications will be the date of review by the convened committee. If modifications are expeditable by the Chair, the approval date will remain the date of the last review by a convened UMCIRB.

3. **Tabled:** A research proposal may be tabled when more substantive issues regarding the protocol and/or consent form must be addressed. Clarifications or requested revisions may have a significant impact on subject safety or understanding. Full board review of the investigator's response to a tabled proposal is required prior to approval.

4. **Disapproved:** A research proposal may be disapproved when questions regarding the rights and welfare of the subjects are of such significance that the UMCIRB committee feels approval of the study to be unwarranted.

The UMCIRB committee may raise issues outside of the UMCIRB jurisdiction and communicate those issues to the investigator or appropriate institutional official.

Expedited review:

The UMCIRB Chairs are generally responsible for conducting expedited reviews within the office. The Chairs may perform expedited review for either behavioral & social science studies or biomedical studies given the nature of the study or review activity. Expedited review activities requiring medical judgment must be performed by a Chair or designated reviewer prepared through training or experience to exercise the required judgment. A "no more than minimal risk" research study eligible for expedited review that involves a FDA regulated test item must receive initial and continuing review by a biomedical committee Chair or designee. If the Chairs are unavailable or an alternate reviewer is required, the Administrative Director or his/her designee will assign the review to an UMCIRB with sufficient expertise to review the study. If the Chair has a conflict of interest because he/she is an investigator or otherwise affiliated with a research study, then the Administrative Director or his/her designee will assign the review to an IRB member with sufficient expertise to review the study. Investigators are prohibited from selecting or assigning reviewers for expedited review procedures. The

Chair or designated reviewer for expedited review activities may approve a study or request modifications in order to gain approval. The requested modifications may be communicated via e-mail, phone or by other mechanisms. The rationale for the basis in change will be communicated to the investigator unless otherwise obvious on the face of the request, for example completing unanswered questions or correcting misspelled words. The Chair or designated reviewer may not disapprove a research study, and must send the study to the appropriate full committee for review.

The approval period for a research study on expedited review begins on the date the reviewer gives approval or final approval if modifications have been required.

The UMCIRB office will communicate the Chair or designee's decision to the investigator in writing within three to five business days. Approval letters will be routinely initialed or signed by the UMCIRB office staff.

Appeals Process:

Principal Investigators may question or appeal any decision by the UMCIRB. The principal investigator should submit a written notice of appeal to the UMCIRB office. The UMCIRB Chairs and Directors will meet with the principal investigator, and any additional individuals the investigator wishes to attend such a meeting. At this time, a study may be returned to full committee for reconsideration, or the investigator may withdraw the appeal, or the appeal may be further explored. An ad hoc committee consisting of UMCIRB committee members and other individuals may be appointed to further investigate the appeal. The UMCIRB Chairs and Directors will seek advice from regulatory agencies and other relevant sources as needed. Approval of a previously disapproved study or action may only be given at a convened UMCIRB meeting. No body or individual may override the UMCIRB full committee's decision to disapprove, suspend or terminate a research study.

Any information generated from this process is unrelated to a specific study will be filed in a separate folder to serve as an action record, and reported at the UMCIRB Chair's discretion.

Additional Approvals:

Additional committees may be required to review and approve a research protocol prior to issuing final UMCIRB approval. ([45 CFR 46.112](#)) Only the UMCIRB may approve human subject research; however, other committees or offices may require modifications or disapprove research based on their expertise. The approval of the UMCIRB does not constitute approval from these committees. Review and approval may need to be obtained other committees or the institutional research site.

Approval of Other Committees:

In addition to UMCIRB approval, a research project may require the approval of other committees or departments (e.g., Radiation Safety Committee, Biological Safety, etc.) before final UMCIRB approval is granted or the study is implemented. These committees should communicate approval to the UMCIRB via a person with authority to represent the committee or by other outlined mechanisms.

Institutional Approval:

In accordance with federal guidelines, research approved by the UMCIRB may be subject to further review and approval or disapproval by appropriate institutional officials. ([21 CFR 56.112](#) [45 CFR 46.112](#)) These officials may not approve the research if it has been disapproved by the UMCIRB. Additionally, the research site's institutional officials may feel the research study is not in the institution's best interest and deny permission for the research study to proceed. Institutional approval must be documented in a manner consistent with the wishes of each institution, either by a signature from a single representative of the institution or signatures from specific departments within an institution when their services are utilized for research. Instructions and forms to obtain institutional approval are housed on the UMCIRB web site. The UMCIRB office participates in this process in a support role by housing forms on the UMCIRB web site,

collecting and distributing forms. The UMCIRB office will not release an approval letter for a new study unless the indicated relevant signatures as identified by the principal investigator or relevant department/resource have been obtained.

Approval of Other Institutional Review Boards:

An institution is permitted, under the regulations, to rely on another IRB to review and approve a research project, once appropriate documents have been completed as required under East Carolina University's Federalwide Assurance with OHRP to reflect the reliance on another IRB. If a research study has been approved by another IRB and the investigator is also seeking the approval of the UMCIRB, the UMCIRB requests that the approval letter from the other IRB be submitted when available along with the UMCIRB application materials for a new research study.

Any institution relying on the UMCIRB or any institution that East Carolina University relies on to serve as the IRB of record must negotiate an IRB Authorization Agreement in accordance with the Federal-Wide Assurance Agreement. IRB authorization agreements will be maintained on file by the UMCIRB office.

The UMCIRB does not currently have provisions for an investigator to rely on another IRB as the "IRB of record" for a research study.

**CRITERIA FOR RESEARCH REQUIRING
UMCIRB REVIEW AND APPROVAL**

Definitions:

Research is a systematic investigation (i.e., the gathering and analysis of information) designed to develop or contribute to generalizable knowledge. ([45 CFR 46.102\(d\)](#))

Human subjects are individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. ([45 CFR 46.102\(f\)](#)) Under the federal regulations, human subjects are defined as: Living individual(s) who may be normal or have a medical condition about whom an investigator conducting research obtains:

1. Data through intervention or interaction with the individual
2. Identifiable private information
3. An individual on whom or on whose specimen an investigational device is used or as a control participant in research, either as a recipient of the test article or as a control
[21 CFR 50.3\(g\)](#)

The above definition excludes non-living humans, research that uses autopsy materials or cadavers is not ‘human subjects research’ and therefore is exempt from review. ([21 CFR 812.3\(p\)](#)) However, all research, even that meeting the exempt criteria, must be submitted to the UMCIRB office for review by the UMCIRB Chair or their designee to confirm that it does not require committee review and approval without exception.

Human subjects means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease. (21 CFR 812.3)

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes. ([45 CFR 46.102\(f\)](#))

In Vitro, literally “in glass” or “test tube” is used to refer to processes that are conducted outside the living body, usually in the laboratory, as distinguished from in vivo. In vitro diagnostic products are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health,

in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. These products are devices as defined in section [201\(h\) of the Federal Food, Drug, and Cosmetic Act](#) , and may also be biological products subject to section 351 of the [Public Health Service Act](#) and [21 CFR 809.3\(a\)](#).

In Vivo, literally “in the living body” processes, such as the absorption of a drug by the human body, carried out in the living body rather than in a laboratory (in vitro).

Interaction includes communication or interpersonal contact between investigator and subject. ([45 CFR 46.102\(f\)](#))

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public. ([45 CFR 46.102\(f\)](#))

Benefit means a valued or desired outcome or an advantage.

Risk means the probability of harm or injury (physical, psychological, social, legal, economic, dignitary) occurring as a result of participation in a research study.

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.102\(i\)](#) and [21 CFR 50.102\(k\)](#) Examples of minimal risk procedures include electrocardiography, collection of blood by venipuncture from healthy adults who are not pregnant, moderate exercise testing, and administration of psychological tests involving a minor level of stress.

Risk Assessment:

The UMCIRB committee is responsible for evaluating the risk to the human subject in the context of what conditions make the research study dangerous. The definition of minimal risk serves as the benchmark to determine the level of review by the UMCIRB. Both the probability and magnitude of possible harm may vary from minimal to significant. The definition for minimal risk differs when referring to prisoners. ([45 CFR 46.303\(d\)](#))

Additionally, the UMCIRB committee considers the potential variation in age and the association of age with risk when reviewing research on minors. The UMCIRB determines if research risk in minors present no more than minimal risk, a minor increase over minimal risk or more than minimal risk. The UMCIRB reserves the right to assign the risk to a research protocol, which may result in elevating the risk previously assigned by the investigator or department chair.

The UMCIRB Chair or his/her designee reserves the right to elevate a study's status and require full UMCIRB review for any research, even if it meets the standard criteria for lesser review. Additionally, the UMCIRB recognizes that a research sponsor may require full UMCIRB review for new research or amendments to existing studies, even if the action would otherwise be in an exempt or expedited category.

UMCIRB Criteria for Review:

The UMCIRB for full committee review, and the Chair or designee for expedited review, must find satisfactory evidence presented for each of the following seven criteria for approval according to [45 CFR 46.111](#) and [21 CFR 56.111](#) as listed below when reviewing research. The UMCIRB internal processing form for new full committee and expedited review research submissions addresses the specific information regarding each

of these items, and satisfactory answers to these questions ensures these requirements have been sufficiently met. The internal processing form or other UMCIRB application materials may seek information that is redundant if a research study also has an accompanying protocol, or the application materials may request information that is not included in the protocol but is viewed as locally important. Additional safeguards or considerations may be required to protect the rights and welfare of vulnerable participants. The internal processing form for exempt research does not address each of these items because of the nature of the research; role of the IRB is limited to concurrence with a finding of an exempt status. The IRB criteria for approval include the following:

1. Risks to the subjects are minimized
 - (a) By the use of procedures consistent with sound research design which do not expose subjects to unnecessary risk.
 - (b) When appropriate, by the use of procedures already being performed on the subjects for diagnostic or treatment purposes.

2. Risks to subjects are reasonable in relation to any benefits that might be expected from taking part in a research study and to the importance of the knowledge that may result.
 - (a) Only those risks and benefits that may result from research as opposed to those which would be received if not participating in the research.
 - (b) Possible long-range effects of applying knowledge gained in research as among those research risks considered.

3. Selection of subjects is fair and equitable. For example, the UMCIRB seeks to determine that no eligible individuals are denied the opportunity to take part in any study, particularly those from which they may benefit, based on arbitrary criteria such as sex, age, social or economic status. Subjects should not be purposefully excluded secondary to such inconveniences as language barriers.

4. Informed consent is obtained from each prospective subject, or where appropriate, from the subject's legally authorized representative, in accordance with [45 CFR 46.116](#).
5. Informed consent will be appropriately documented, in accordance with, and to the extent required by [45 CFR 46.117](#).
6. When appropriate, the research plan provides for monitoring the data collected to protect the safety of subjects.
7. There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Exempt Research Category:

Listed below are the DHHS criteria for protocols classified in the exempt status unless otherwise directed: ([45 CFR 46.101](#))

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices such as:
 - (a) Research on regular or special education instructional strategies or
 - (b) Effectiveness or comparison among instructional techniques, curricula, or classroom management methods
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, and/or achievement), survey procedures, interview procedures or observation of public behavior unless:
 - (a) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subject, e.g. coding numbers, AND

- (b) Disclosure of the subject's response could place the subject at risk of civil or criminal liability or be damaging to the subjects' financial standing, employability, or reputation.
3. Research involving the use of educational tests, (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or the observation of public behavior that is not exempt under #2 above if:
- (a) Subjects are elected or appointed public officials or candidates for public office or
 - (b) Federal or state status exist which require that without exception the personally identifiable information will be kept confidential during and after the research is conducted
4. Research involving the collection of study of existing data, documents, records, pathological or diagnostic specimens if:
- (a) These sources are publicly available or
 - (b) If the information is recorded in such a way that the subject cannot be identified directly or through identifiers linked to the subject, (no names, or code numbers recorded for the subject; no follow-up studies possible on a particular subject)
NOTE: 1) This information must be existing on the date this IRB application is submitted. 2) The data collection tool may not have an identifier or code that links data to the source of the information.
5. Research and demonstration projects which are conducted by or subject to the approval of federal department or agency heads, and which are designed to study, evaluate, or otherwise examine if:
- (a) Public benefits or service programs
 - (b) Procedures for obtaining benefits or services under those programs
 - (c) Possible changes or alternatives to those programs or procedures
 - (d) Possible changes in methods or levels of payment for benefits or service under those programs

6. Taste and food quality evaluation and consumer acceptance studies if:
 - (a) Wholesome foods without additives are consumed or
 - (b) Food is consumed that contains a food ingredient at or below the level and for a use found to be safe by the FDA, EPA or Food Safety and Inspection Service of the USDA

The above exempt categories are applicable to Subpart D, which provides for additional protections of children involved as subjects in research except for #2 above. The exemption regarding educational testing is also applicable to minors. However, the exemption at [45 CFR 46.401](#) for research in minors involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.

The above exempt categories are not applicable for human subject research involving prisoners.

Additional **FDA exempt status** requirements include: ([21 CFR 56.104](#))

1. Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.
2. Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.
3. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.
4. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food

ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the 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.

Exempt Research Submissions to UMCIRB:

The UMCIRB is the only body at East Carolina University that is authorized to make the determination that a research study meets the criteria for exempt status for any research falling under UMCIRB jurisdiction.

There are no submission deadlines for minimal risk studies that meet the category of exempt research. Investigators must submit **one** copy of the exempt form and **one** copy of all research related items. The grant application must be submitted for any exempt research study that is grant funded.

The reviewer may also raise issues outside of the UMCIRB jurisdiction and communicate those issues to the investigator or appropriate institutional official.

Following a submission to the UMCIRB office, the investigator will routinely receive a communication for additional information, or an official determination letter that the study may proceed within three to five working days via mail and fax according to the contact information provided on the processing form.

The UMCIRB does not require any routine exchange of information related to exempt research, nor is routine continuing review performed; however, the principal investigator is responsible for submitting any changes e.g., confidentiality, consent, risk profile, revisions, or any serious and unanticipated risks to participants or others to the UMCIRB. For example, a research study using interviews as a data collection strategy may be found initially to meet Exempt Category #2, however, if audio/video taping is added then the research activity would meet Expedited Category #6 and require ongoing

UMCIRB oversight. The research project may be elevated from exempt to expedited or full UMCIRB review after initial approval based on new information or regulatory guidance changes. The UMCIRB will retain a hardcopy of the records on exempt protocols for a minimum of 3 years after the approval date of the research. ([45 CFR 46.115](#))

Expedited Review Category:

New research studies are eligible for expedited review if they are no more than minimal risk, and fit into one of the expeditable review categories. Listed below are the criteria for expedited review of research studies as noted in [45 CFR 46.110](#) and as available in the [Federal Register](#) (63 FR 60364-60367, Nov 9, 1998).

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met. a) Research on drugs for which an investigational new drug application ([21 CFR Part 312](#)) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.) b) Research on medical devices for which (i) an investigational device exemption application ([21 CFR Part 812](#)) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or (b) from other adults and children², considering the age, weight, and health of the subjects, the collection

procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

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

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength

testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. [45 CFR 46.101\(b\)\(4\)](#). This listing refers only to research that is not exempt.) The UMCIRB has also determined that secondary uses of specimens previously collected under an IRB approved research protocol may also be eligible for expedited review under this category, even if the specimens were originally collected for research purposes. For example, if tissue collected under a more than minimal risk study by muscle biopsy is not completely used by that research study, an investigator may be permitted to seek its use for a second research study under this category even though it was previously collected for research purposes.

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

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

8. Continuing review of research previously approved by the convened IRB as follows: (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been

enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.

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

Additional **FDA expedited status** requirements include: [21 CFR 56.110](#)

1. Some or all of the research appearing on the [Federal Register](#) (63 FR 60364-60367, Nov 9, 1998) list and found by the reviewer(s) to involve no more than minimal risk.
2. Minor changes in previously approved research during the period (of 1 year or less) for which approval is authorized.

Expedited Review Submission to UMCIRB:

There are no submission deadlines for minimal risk studies that meet the criteria for expedited review. Investigators must submit **one** copy of the expedited processing form and **one** copy of all research related items, including one copy of all written materials to be provided to the participants. The grant application must be submitted for any expedited review research study that is grant funded.

The types of information that should be submitted include: internal processing form, consent document, any advertisements, materials provided to participants, research protocol if available, any data collection tools, any support letters, conflict of interest disclosure, and the grant application must be submitted if the study is grant funded. Specific number of copies or other relevant submission details may be found on the UMCIRB web site.

The reviewer may raise issues outside of the UMCIRB jurisdiction and communicate those issues to the investigator or appropriate institutional official. The UMCIRB reviewer must confirm that the protocol meets the criteria for expedited review.

The investigator will receive a communication for additional information or an official determination letter routinely within three to five working days. The research cannot proceed until all requested modifications are met and the principal investigator receives an approval letter. The principal investigator is responsible for submitting all changes, reporting serious and unanticipated risks to participants or others and other related issues to the UMCIRB because they may result in an elevation in classification to require full UMCIRB review.

The approval period on expedited research can be no longer than 365 days, and will extend from the date final approval is granted for the period as set by the Chair or designee. The research project may be elevated from expedited to full UMCIRB review during or after initial approval based on new information or regulatory guidance changes. The UMCIRB will retain a copy of the research records on file for no less than 3 years after the study closure.

Full UMCIRB Review Category

Research studies that are more than minimal risk require full committee review and approval. More than minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research is greater in and of itself than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Examples of some types of risk include: physical, psychological, social, economic, dignitary, professional, and legal.

Full UMCIRB Review Process:

The submission deadlines for full committee review are related to the period of time it takes to prepare the materials for committee reviewers. The meeting materials for reviewers are distributed one week in advance of the meeting; therefore the submission deadlines are by the end of the day on the Monday prior to distribution of the materials or two Mondays before the scheduled UMCIRB meeting.

All research related materials must be submitted to the committee for review.

The types of information that should be submitted include: internal processing form consent document, model consent, any advertisements, materials provided to participants, research protocol, investigator brochure if available, case report forms if available, FDA 1572 if applicable, any data collection tools, any support letters, conflict of interest disclosure and the grant application must be submitted if the study is grant funded. Specific number of copies or other relevant submission details may be found on the UMCIRB web site.

A separate standalone protocol should include relevant information such as: study purpose, hypothesis, study design, procedures, statistical method for data analysis, justification for sample size, duration, population description, recruitment methods, potential risks and steps to minimize the risk, potential benefits, compensation, and payment schedule. Research studies are placed on the first available appropriate agenda for either the biomedical, behavioral and social sciences or prisoner committee.

The investigator will routinely receive a letter documenting the committee's findings within 3 to 5 days. The letters will be mailed and faxed according to the contact information indicated on the processing form. Requested modifications eligible for expedited review may be submitted any time, while requested modifications that require full review should adhere to the meeting deadlines posted on the UMCIRB web site. Newly submitted research studies without an investigator response to requested modifications or additional requested items within 90 days from the date of the last

review may be administratively closed. Research activities cannot proceed and subjects cannot be enrolled until a final approval letter is issued to the principal investigator.

Receipt of Items into the UMCIRB Office:

Research studies may be received via mail or by hand delivery to the office. Investigators submitting materials on new research or activity on currently existing studies should use the most currently available forms located on the UMCIRB web site. New research studies will be assigned a unique identifying number that should be used for any business with the office or committee, since all research studies are filed and organized numerically by this number. A letter can be provided or mailed documenting the new research proposal receipt date, materials received and UMCIRB number. All items received into the UMCIRB office will be stamped received, and each item will be logged for tracking.

INFORMED CONSENT

Informed consent process:

Informed consent is one of the basic ethical obligations for researchers and must be prospectively, legally obtained prior to enrollment or participation in any type of research. Informed consent is not a single event or just a document, but an ongoing process of information exchange that takes place between the prospective subject and the investigator before, during and sometimes after the research study. The principal investigator is responsible for conducting the consent process and obtaining documentation of consent from participants, however, he/she may delegate this role to another individual that is knowledgeable about the research study. Any individuals that will be involved in the consent process must be approved by the UMCIRB.

The amount of information that needs to be presented both in writing (i.e., the consent document and related materials) and verbally is directly related to the research risk and complexity. Language for written and oral communication involving the research study

should be in a language understandable to the participant and others involved in the consent process. The manner and context in which information is conveyed is as important as the information itself. There must be no coercion or undue influence for participants to enroll or to continue in a research study, and subjects' entrance into or continuation of the research study must be totally voluntary. Subjects must have sufficient time to decide whether they want to participate in a research study, and should be encouraged to consult with family and/or others if needed. Subjects should feel free to ask questions at any time. The participant or the Legally Authorized Representative (LAR), if applicable, should have all questions answered to their satisfaction prior to signing the consent document. A copy of the signed and dated consent document, along with other written research-related materials must be given to the participant or his/her Legally Authorized Representative for all "more than minimal risk research". The UMCIRB reviewer may require participants or their Legally Authorized Representatives be provided a signed or unsigned copy of the consent document for "no more than minimal risk research" as indicated on the signature page of the approved consent document.

The UMCIRB committee reserves the option for 3rd party witness of the consent process. This option will primarily be employed for concerns regarding conduct of the consent process. The primary purpose of a 3rd party witness by the UMCIRB is to ensure there is an adequate informed consent process. The UMCIRB committee may assign the Chair or another member to perform the 3rd party witness to the consent process. The observer is expected to prepare a summary of the observations, which will be placed in the UMCIRB folder. The evaluation will be shared with the committee, the investigator, and any other relevant institutional bodies.

Additional safeguards for vulnerable populations should be built into the informed consent documents and processes to add further protections.

Informed consent document:

The purpose of a consent document is to provide a written source of baseline information and serve as a reference source during the study, as well as, a place to document that a subject's consent has been given before the start of the study. Therefore, it is important that the consent document is written in language understandable to participants expected within the study population, and must not contain any exculpatory language where a participant is made to waive, or appear to waive, any of his/her legal rights.

Consent documents must be signed and dated by the subject before any research procedures begin. Additionally, the consent document must be signed prior to any screening tests that otherwise would not be performed. Although it is not required to include the time a consent document is signed, it may be an important method to verify that no screening tests exclusively required by the research were conducted prior to signing the informed consent document. For any research study constituting "more than minimal risk" or at the request of the IRB reviewer for "no more than minimal risk research", the person conducting the consent discussion must sign and date the consent document signature page.

Consent documents do not have to adhere to the consent document template on the UMCIRB web site, but the document must contain UMCIRB or institution specific language under the applicable section. The UMCIRB office will stamp each page of the UMCIRB approved consent document and then return that stamped document to the investigator. Only the most currently approved consent document, with each page stamped may be used in the consent process. The dates on the stamp will reflect either the initial approval period, the last approved continuing review approval period, or the date of the most recently revised document through the end of the approval period.

The UMCIRB reviews each consent document to determine that it contains required information in sufficient detail to protect the rights and welfare of human research subjects. The consent document according to federal regulations may be: ([45 CFR 46.117](#) [21 CFR 50.27](#))

1. A **written consent document** that embodies the elements of informed consent required by [45 CFR 46.116](#). This form may be read to the subject or the subject's legally authorized representative, but, in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed.
2. The **short form is a written** consent document stating that the elements of informed consent required by [45 CFR 46.116](#) have been presented orally to the subject or the subject's legally authorized representative in language understandable to the subject. An impartial witness is required and they should be fluent in both English and the language of the subject. The short form used under this procedure should be approved by the UMCIRB prior to its use, unless the investigator is using the most currently approved short form available on the UMCIRB web site. The investigator must also use the previously approved English version of the consent document to serve as the written summary of what is to be said to the participant or representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary and the short form. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.

Although this alternative means of documenting informed consent in research studies should be used only rarely as an investigator unexpectedly encounters a non-English speaking participant, the UMCIRB has approved an English version of a “short form” written consent document. This document is available and may be translated into the appropriate non-English language. When the document is translated into a language other than Spanish, a description of how this translation was performed must be provided to the UMCIRB when there is no time for the short form document to be submitted to the UMCIRB prior to its use.

The short form should be used only for the unexpected encounter of a participant that speaks a language other than English. Repeated use of the short form is prohibited, as the investigator should use a consent document written in a language understandable to the participant.

Elements of the informed consent document:

Although each research study involving human subjects is unique, regulations and the UMCIRB require that all consent documents contain the following elements unless the research meets the criteria for waiver of all or part of the informed consent document. It is important to remember that the UMCIRB or sponsors may require additional information to be included in the consent document above that required in the elements listed below. The consent document must be consistent with the research protocol, the sponsor template consent document and the consent document submitted to a grant-sponsoring agency. All consent documents in FDA regulated trials must also contain wording related to the purpose of evaluating a test item in terms of safety and efficacy.

The 8 essential elements required in informed consent are: ([45 CFR 46.116](#) [21 CFR 50.25](#))

1. A statement that the study involves research, an explanation of the purposes of the research and expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
2. A description of any reasonably foreseeable risks or discomforts to the subject.
3. A description of any benefits to the subject or to others that may reasonably be expected from the research.
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the subject.
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. The possibility that the Food and Drug Administration may inspect the records should be noted.
6. For research involving more than minimal risk, an explanation as to whether there is any compensation for injury, and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

7. An explanation of whom to contact for answers to pertinent questions about the research and research subject's rights, and who to contact in the event of a research related injury to the subject.
8. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

The 6 additional elements of informed consents that should be included whenever possible are: ([45 CFR 46.116](#) [21 CFR 50.25](#))

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

Research studies that follow Good Clinical Practices should also contain the required elements, which may otherwise be considered optional elements under other regulations or guidance. Some of the additional elements are as follows:

1. An explanation of the probability for random assignment to each study arm.
2. The research participant's responsibilities as related to the research study.
3. The important potential benefits and risks for alternative procedures or options that might be available.
4. The anticipated, prorated payment if any as a result of participating in the trial.

Waiver or alteration of some or all of the elements of informed consent:

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

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

Waiver of the documentation of consent:

An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either: ([45 CFR 46.117](#))

1. that the only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;
2. that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
3. the entire consent was waived under 45 CFR 46.110 CFR 46.116(d).

Non-English Speaking Subjects:

To meet the requirements of [21 CFR 50.20](#), the informed consent document should be in language understandable to the subject (or authorized representative). When the study subject population includes non-English speaking people, or the clinical investigator or the UMCIRB anticipates that the consent interviews will be conducted in a language

other than English. The UMCIRB requires a consent document be prepared for non-English speaking individuals when the subject population includes non-English speaking participants, or when the UMCIRB committee or reviewer believes they are likely to be included in the subject population.

The UMCIRB requires that all non-English consents be submitted for review and approval. The investigator should provide the UMCIRB with the name and credentials for the individual performing the consent document translation, and safeguards to ensure the accuracy of the translation given the target population. The UMCIRB cannot provide financial assistance to the investigator for the translation process. Additionally, all materials the participant may be required to complete should be evaluated for need for translation into a language understandable by the participant. Investigators and research staff must remember that informed consent is an ongoing process.

If a non-English speaking potential research subject is unexpectedly encountered, and investigators do not have a written translation of the consent document, an alternative means of consent and documenting consent may be used. The regulations governing research permit investigators to rely on an oral translation of the informed consent information used in conjunction with an approved “short form” written consent document, as well as, a written summary of what is presented orally as discussed under information related to the “short form”.

Use of a UMCIRB approved written translation of the entire consent document is always preferred. If researchers reasonably expect more than an incidental number of subjects speaking the same non-English language will be enrolled, translation of the entire consent form is recommended at initial submission.

Limited or Low Literacy Subjects:

A person that speaks and understands English, but does not read and write, can be enrolled in a study by signing and dating or by "making their mark" on the consent

document. The principal investigator or his/her designee is responsible for determining whether a participant is able to read the consent document or other materials discussed during the consent process. If the principal investigator or his/her designee has any doubt regarding the literacy of a potential participant, then the principal investigator or his/her designee should put the additional protections in place consistent with consenting participants of limited or low literacy under this section. An impartial third party witness should be present during the entire consent discussion and verify the contents of the informed consent document were orally presented and explained. The witness must then sign the consent document signature page attesting that the consent document contents or other materials were accurately explained, that the participant appears to have understood the discussion, and that the consent was freely given. Investigators should carefully formulate plans to ensure additional safeguards are in place for this vulnerable population. The investigator or research personnel should be sensitive to the increased difficulties in understanding complex study schematics and designs when presented orally. Liberal use of drawings and other such tools may prove beneficial for this group, and other groups may benefit from this strategy as well. These subjects may require more frequent reiteration of the informed consent document contents, and when possible a significant other should be included in the research process.

Subjects Unable to Speak or Write:

A person who can understand and comprehend spoken English, but is physically unable to talk or write, can be entered into a study if they are competent and able to indicate approval or disapproval by other means. A competent subject may be enrolled into the research if they are able to evaluate the study concepts and risks and indicate approval or disapproval for enrollment. The consent form should document the method used for communication with the prospective subject and the specific means by which they communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document. It is recommended to have the witness confirm what type of response was given. A video tape recording of the consent interview may be useful.

Use of a Legally Authorized Representative

When an adult participant is unable to provide legally effective consent to participate in a research study, the investigator may obtain permission from a Legally Authorized Representative (LAR). The investigator should document the decision making process used to determine that a research participant lacked the capacity to provide consent and the surrounding circumstances. A participant that is unable to provide consent may still be able to understand elements of the research study, and indicate his/her willingness to be involved in the research. The investigator should document any discussions with the participant, and describe how his/her willingness to be involved in the study was indicated based on the circumstances. The investigator is responsible to ensure that the appropriate person is selected to fulfill the role of LAR according to applicable institutional policies and laws. The information regarding the research study and the accompanying documents must be presented to the LAR in the same manner as outlined for the participant consent process, with the LAR receiving complete set of study-related materials. The LAR should sign his/her own name on a line designated for this purpose on the consent document signature page, as well as, dating the document. If and when the research study participant regains capacity, the investigator is responsible to debrief the participant on the research-related events, and then obtain consent for continued participation in the research study. The discussion and consent process should occur at the earliest appropriate time, for instance at the first follow-up visit after being discharged from the hospital. The LAR must receive any additional information through the course of the study and be apprised of any new findings that might alter a willingness for continued in the research study.

Relying on the use of a LAR should be avoided in non-therapeutic research trials unless the following are met:

1. The objective of the research can not be met by enrolling participants who can provide their own consent.
2. The foreseeable risks are low.
3. The negative impact on the participants' well-being is minimized and low.
4. The trial is not prohibited by law.

5. The investigator provides sufficient justification to obtain IRB approval to target enrolling participants that are unable to provide consent to the IRB and obtain approval. Generally, the study population targeted for enrollment into the study should have a condition supporting the use of the intended research test item.

GUIDANCE ON RECRUITMENT OF HUMAN RESEARCH

SUBJECTS

Participant Compensation:

One of the primary responsibilities of the UMCIRB is to ensure that a subject's decision to participate in research will be truly voluntary. The UMCIRB must review and approve all payment schedules for incentives or reimbursement to ensure there is no undue coercion or influence on participant decision to enroll in the research study; however, a payment schedule may be eligible for expedited review and approval by the Chair or their designee.

Participant payments should not be contingent upon completing the entire study and should be prorated when appropriate. In studies with very short participation windows and involving minor procedures/inconveniences it may be appropriate to provide the compensation in one lump sum at the end of the study. The UMCIRB is particularly sensitive to any effects that recruitment strategies may have on vulnerable populations such as students or the economically disadvantaged. Payment schedules should be outlined in the informed consent document.

It is not uncommon for subjects to be paid for their participation in research, especially in the early phases of investigational drug, biologic or device development. Payment to research subjects for participation in studies should not be considered a benefit and the payment schedule should not appear under the benefits section of the consent document. Financial incentives are often used when health benefits to subjects are remote or non-existent. ([21 CFR 50.20](#)) When involving minors, incentives for participation should be

appropriate to the ages of the subjects and the nature of the study. Incentives (e.g., toys, coupons for food) should usually be given to the minor subjects, not the parents. Parents may be reimbursed or paid for expenses such as travel. Payment to the research subject should not be contingent upon completing the entire study.

Advertising:

The UMCIRB considers advertising as the first step of the informed consent process.

The UMCIRB must review both the information contained in the advertisement, and the mode of its communication. This review determines that the procedure for recruiting subjects is not coercive, and that the recruitment material does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. The investigator may submit a photocopy of the proposed advertisement to be utilized in order to decrease costs; however, the layout and font size may not be altered once the advertisement has been approved.

To submit an advertisement on an already approved study, the investigator should use a revision form with an attached copy of the proposed advertisement. The investigator should submit a script for any commercial that will be used for advertising.

Advertisements and advertising scripts will be stamped with an approval period.

Advertising for recruitment into investigational drug, biologic or device studies should not use terms such as “new treatment” or “new medication” without explaining that the test article is investigational. A phrase such as “you will receive new treatments” incorrectly implies that all study subjects will be receiving newly approved products of proven worth. Advertisements should not promise “free medical treatment” when the intent is only to say subjects will not be charged for taking part in the investigation.

Generally, advertisements should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements:

1. The name and address of the Principal Investigator and the research facility (e.g., East Carolina University) and the person or office to contact for further information.
2. The purpose of the research (e.g., the condition under study or goal of the project)
3. A summary of inclusion/ exclusion criteria that will be used to determine eligibility for the study.
4. The time or other commitment required of the subjects for participation in the study.
5. A brief list of participation benefits, if any. Advertisements may state that subjects will be paid, but they should not emphasize the payment or the amount to be paid.
6. The words “research study” must appear within the advertisement.

An investigative site may post basic clinical trial information to be viewed by the general public, such as: title; purpose of the study; protocol summary; basic eligibility criteria; study site location(s); and how to contact the site for further information according to the guidance issued by the FDA. However, any descriptive information will require consultation with the UMCIRB to determine if review and approval is necessary. Information posted on a website may not promise or imply a certainty of cure or other benefit beyond what is contained in the protocol and the informed consent document. Direct advertising for study subjects is the start of the informed consent and subject selection process. Advertisements require review and approval by the UMCIRB.

An internal web site may be used by an investigative site to keep physicians and other staff within the organization abreast of clinical trial opportunities for potential participants. This practice would simply be an electronic mechanism to provide the necessary information to determine that one of his/her patients may be eligible for an available clinical trial. Such an internal website would not require review and approval by the UMCIRB.

ACTIVITIES ON ALREADY APPROVED RESEARCH STUDIES

Protocol Amendments or Revisions:

Any changes to the protocol, consent form or research process must have UMCIRB approval.

Requests for changes (amendments) to approved studies must be promptly submitted at any time during the approved period, but before the change is implemented it must receive UMCIRB approval. The need for protocol changes to be submitted as revisions includes one-time protocol exceptions issued by the sponsor. The only exception to this order of approval is when a protocol change is required to protect subjects from an immediate hazard.

If a change is required to prevent an immediate hazard, then this action must be submitted to the UMCIRB office as soon as possible after the change is implemented in the single participant, so that it may be approved for the future participants if appropriate. If the change was required for only a single individual under a special circumstance, then the action should be submitted to the UMCIRB following the instructions for a protocol deviation.

A rationale must be supplied by the investigator for any delays in submitting revisions to a research study.

The approval date for a revision does not extend the approval period for the research study. No research study may be approved for greater than 365 days.

When amendments impact the safety of subjects previously enrolled in the study or those continuing to receive study intervention, then it may be necessary to convey this

information (i.e., to obtain the consent of the subjects) by means of an addendum to the existing consent document or by using a new consent document. The UMCIRB may determine, for example, that such subjects must be notified of new findings or for toxicities not previously noted at the time they were originally enrolled. Such notification is consistent with the view of informed consent as a continuous process, and affords subjects the opportunity to determine whether or not they wish to continue their participation in the research. The UMCIRB will determine on a case-by-case basis when such notification, and its documentation, is required.

Amendments that increase the risk or created as a result of adverse events may require a shorter approval period with a more frequent continuing review interval to protect the safety and welfare of subjects. Amendments that may affect the rights of human research subjects or intended to supply additional safeguards must provide the required information to ensure these safeguards are in place.

If a revision is submitted to place a hold on enrollment for a research study, an investigator may not begin enrolling participants until the UMCIRB approves a revision to commence enrollment. Planned holds on enrollment will not be considered a UMCIRB suspension. For example, an investigator initially planning to hold enrollment after a set number of participants in order to perform and obtain interim analysis would not be considered to have a suspended study.

Expeditable revisions:

Amendments to no more than minimal risk research studies, that were initially eligible for review by expedited process, may also be eligible for expedited review provided they do not change the risk/benefit analysis, or do not increase the risk presented by the research study above minimal risk, or in and of themselves do not present more than minimal risk. ([45 CFR 46.110](#)). The addition of new procedures or tools to a research study that was initially deemed “more than minimal risk” may also be approved under expedited review provided they meet one of the categories eligible for expedited review.

All expedited amendments approved by the Chair or his/her designee will be reported to the UMCIRB committee on the next available meeting minutes. Amendments that in and of themselves involve greater than minimal risk or elevate a “no more than minimal risk” research study to a “more than minimal risk” status will be reviewed at a convened committee. Amendments involving minor changes may be reviewed using an expedited process, for example, editorial/administrative changes. Examples of activities that the UMCIRB interprets as minor changes eligible for expedited review include: additions/deletions that add clarification, revisions that do not increase risk, revisions that do not decrease potential benefit, Data Monitoring Committee reports where “no changes” in the research study are recommended, new Investigator Brochures, or favorable updates on the status of the research project. Additions or deletions of investigators may also be eligible for expedited review by the Chair or his/her designee. The investigator should use the form specifically designed for the revision of investigators found on the web site. All other revision may be submitted on the general revision form.

Only one copy of the form and one copy of all revised materials have to be submitted for review and approval. The chair and his/her designee has access to the entire UMCIRB folder while conducting an expedited review. Investigators submitting revisions to the consent document should submit a copy of the clean consent document for an approval stamp, and a copy illustrating all the changes, unless they have been specifically located and clearly described on the revision form. The Chair and office will complete the bottom of the revision form, which then serves as the documentation for approval of the revision. The revision form will be routinely mailed and faxed to the investigator within 3 to 5 days working days.

Revisions requiring full committee review and approval:

Revisions will require full committee review and approval if they are not eligible for expedited review, or at the discretion of the Chair or his/her designee. Examples of

revisions requiring full committee review are those procedures instituted to minimize risk of the research study but that in and of themselves are more than minimal risk.

Additionally, the sponsor may request that a revision undergo review and approval by the full committee. The UMCIRB prefers that amendments be incorporated into the protocol rather than loosely submitted, which assists to ensure that the protocol on file is valid in its entirety.

The investigator should submit the revision form, protocol summary and revised materials. Specific instructions for submitting revisions are located on the UMCIRB web site.

Protocol Deviations:

Any change in the administration of the protocol or conduct of the study requires prospective UMCIRB approval.

A protocol deviation occurs when changes are made to the protocol, which affects the conduct of the study for a single or all participants. Investigators should institute a protocol deviation when required to protect participant safety and welfare or when medically indicated, as discussed above under the revision section. The UMCIRB does not intend to jeopardize the safety and welfare of any research subject.

The investigator should submit one copy of the protocol deviation form along with one copy of any accompanying materials as soon as possible after the deviation has been identified by the investigator or study staff. The protocol deviation form will not be returned to the investigator, and there will only be communication from the UMCIRB office when additional information is required. The chair and his/her designee has access to the entire UMCIRB folder while conducting an expedited review.

The UMCIRB recognizes the opportunity for a wide range of deviations to occur, from a required visit being conducted outside the window because the visit would be scheduled to fall on a Saturday and the office is closed, to the investigator repeatedly not obtaining protocol required tests built into the research study to minimize risk.

Minor deviations can be characterized as those deviations where there has been no significant effect on the risk of harm or on the potential benefit of a participant, did not interfere with data collection, did not interfere with monitoring the participants or collected data, or did not represent the willful or knowing misconduct on the part of the investigator or study staff. Major deviations can be characterized as those deviations that suggests participants were placed at an increased risk of harm, interferes with or negatively impacts data collection as outlined by the protocol or case report forms, evidence of willful or knowing misconduct on the part of the investigator or study staff, represents serious and ongoing noncompliance with the protocol or IRB procedures, or represents noncompliance with local/state/federal laws.

The Chair or his/her designee will review the protocol deviations submitted to separate those that are problematic from those that are unlikely to be problematic based on the information supplied on the form. The Chair or his/her designee, may request additional information or a corrective action plan before taking further action or a final decision-making. Any protocol deviation that requires medical judgment must be reviewed by an individual with sufficient health care training and education.

The Chair or his/her designee may determine that no further action is needed and the protocol deviation will be forwarded to the committee for information. The Chair may also request that the protocol deviation be sent to the UMCIRB committee for further consideration and action. The Chair or his/her designee will report to the principal investigator, UMCIRB attorney, ECU signatory official, relevant human protections administrator, sponsor, and relevant regulatory agencies prior to review by the UMCIRB full committee, if the event is of a nature where this immediate action is justified for safety. Events of this nature will be forwarded as an agenda item to the UMCIRB

committee. Human protections administrators and the institutional official receive electronic copies of the agenda. Meeting minutes will reflect the UMCIRB committee's discussion and judgments on these referred events, including whether the event was determined to constitute serious or continuing noncompliance, or constitutes an unexpected problem involving risks to participants or others and any subsequent action requested or required. The meeting minutes are circulated to the relevant full/alternate UMCIRB committee members, human protections administrators, and institutional officials. All events satisfying the criteria for serious or ongoing noncompliance or unanticipated problem involving risks to participants or others require reporting. The UMCIRB will promptly report to the appropriate regulatory bodies an event that is determined to be serious or ongoing noncompliance or an unanticipated problem involving risks to participants or others. The UMCIRB may require an investigation by institutional offices or committees of any research study based on the frequency, seriousness or nature of the protocol deviations reported.

Repeated protocol deviations that constitute serious and ongoing non-compliance reflect on the overall conduct and oversight of the research by the principal investigator, which may result in restricting or suspending the investigator's privilege to conduct research. Restrictions over an investigator or a section will be set at the institutional level, while restrictions on a particular research study may be set by the UMCIRB. Repeated and ongoing protocol deviations may result in suspension or termination of a research study and will be reported promptly to the principal investigator, UMCIRB attorney, ECU signatory official, relevant human protections administrator, sponsor and relevant regulatory bodies. Repeated and ongoing protocol deviations may not necessitate suspending or terminating a study if the UMCIRB believes it is in the best interest of study participants to receive continued monitoring or other study related interventions. Protocol deviations may also constitute unanticipated problems involving risks to subject or others involved in the research study, and will likewise be promptly reported as required.

Notifying the UMCIRB of protocol deviations does not replace the investigators obligation to notify other institutional offices or other appropriate officials per institutional policy.

Reporting of Unanticipated Problems to Subjects or Others, Including Serious Adverse Events:

Definitions:

Unexpected (in terms of nature, severity, or frequency) means that:

1. the event was not previously described in the research procedures included in the protocol-related documents, such as the protocol, processing form or consent document, or in other relevant sources of information, such as product labeling or package inserts, OR
2. the event was not previously described given the characteristics of the participant or the participant population being studied such as natural progression of any underlying disease, disorder or condition of the participant experiencing the adverse event, and the participants predisposing risk factor profile for the adverse event.

Related or possibly related to participation in the research means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

Problem suggests that the research places subject or others at a greater risk of harm (physical, psychological, economic, or social harm) than was previously known or recognized.

Unanticipated problems involving risks to participants or others are defined as meeting all of three of the following criteria:

- 1 The event is unanticipated because it is not included in the currently approved research study documents, the event exceeds the described frequency or severity, or it

is unexpected that it would occur given the study population described in the research. AND

- 2 The event is related or possibly or reasonably caused by procedures involved in the research. AND
- 3 The event suggests that the research places the participants or others at a greater risk of harm than previously thought.

Serious adverse event is defined as any event that:

1. results in death
2. is life threatening or places the participant at immediate risk of death from the event that has occurred
3. results in inpatient hospitalization or prolongation of existing hospitalization
4. results in persistent or significant disability or incapacity
5. results in a congenital anomaly or birth defect
6. based upon appropriate medical judgment, may jeopardize the participant's health and may require medical or surgical intervention to prevent one of the outcomes listed in this definition

Investigators conducting human subject research falling under FDA jurisdiction must adhere to the relevant definitions as found in those regulations. ([21 CFR 312.32](#))

Investigators are responsible for reporting to the UMCIRB any unanticipated problems involving risks to subjects or others as soon as possible. Research conducted under the jurisdiction of the FDA also has specifically defined events that require reporting, such as serious or unexpected adverse events. The investigator must report all locally occurring serious adverse events to the UMCIRB office on any participant enrolled in a research study regardless of the relationship to the test item. All deaths of participants enrolled or being followed in a research study must be reported to the UMCIRB. These events should be reported as soon as possible.

Investigators acting as sponsors have all the obligations for adverse event reporting that are associated with an external sponsor of a study. The investigators are also responsible for adhering to reporting requirements as determined by the institution serving as the research site.

Sponsors have definitions for what will be reported as adverse events listed in the research protocol. Investigators must comply with the adverse event reporting plan outlined within the processing form, which must likewise be consistent with the sponsor or investigator prepared protocol for more than minimal risk studies.

The UMCIRB office will accept reporting of unanticipated problems or adverse events after a study is closed at the discretion of the investigator or sponsor. The UMCIRB differentiates between locally occurring events and non-locally occurring events, and places a large priority on the reporting and review of local events since these events may not be reviewed by another group.

Locally Occurring Events:

Adverse events and unanticipated problems are defined as local if they involve research participants that are enrolled and followed by researchers at an institution under UMCIRB jurisdiction for a particular study. For example, if a participant has a reportable event that occurs out of state but is followed for a research study being conducted by an investigator at ECU, then the event is reported as a local adverse event. The investigator should submit one copy of the local event submission form and any related documentation as soon as possible after the event, or after the investigator learns of the event. The chair and his/her designee has access to the UMCIRB folder while conducting an expedited review. The investigator should provide an explanation on the form for any reporting delays. The form will not be returned to the investigator, and there will be no further communication on a report unless additional information is required.

Adverse events and unanticipated problems will be reviewed by the Chair or his/her designee. Any adverse that requires medical judgment must be reviewed by an individual with sufficient health care training and education. The reviewer will specifically evaluate and document whether the three criteria comprising unanticipated problems involving risks to participants or others have been satisfied. The Chair or his/her designee may determine that no further action is needed and the local event will be forwarded to the committee for information. The Chair may also request that the event should be sent to the UMCIRB committee for further consideration and action. The Chair or his/her designee will report to the principal investigator, the UMCIRB attorney, ECU signatory official, relevant human protections administrator, sponsor and relevant regulatory agency prior to review by the UMCIRB full committee if the event is of a nature where this immediate action is justified. Events will be forwarded as an agenda item to the UMCIRB committee. Human protections administrators and the institutional official receive electronic copies of the agenda. Meeting minutes will reflect the UMCIRB committee's discussion and judgments on these referred events, including whether the event was determined to be unanticipated problems involving risks to participants or others and subsequent action. The meeting minutes are circulated to the relevant full/alternate UMCIRB committee members, human protections administrators, and signatory officials. All events satisfying the criteria for an unanticipated problem involving risks to participants or others require reporting. The UMCIRB will promptly report to the appropriate regulatory bodies an event that is determined to be an unanticipated problem involving risks to participants or others. The UMCIRB committee may request an investigation of any research study based on the frequency, seriousness or nature of the adverse events reported.

The UMCIRB Chair may deem it necessary to immediately suspend some part or all of a study in order to protect the safety and well-being of research participants prior to convening a full UMCIRB committee meeting. The UMCIRB committee may deem it necessary to suspend, terminate further enrollment, or hold any interventions of the research study to protect human subject based on materials submitted to the UMCIRB for review of the events. Unanticipated problems involving risks to subjects or others may

result in suspension or termination of a research study and will be reported promptly to the principal investigator, UMCIRB attorney, ECU signatory official, relevant human protections administrator, sponsor and relevant regulatory bodies.

Notifying the UMCIRB of unanticipated problems involving risks to subjects or others does not replace the investigators obligation to notify other institutional offices or other appropriate officials per institutional policy.

Non-Locally Occurring Events:

Non-local adverse events are defined as the events that occur to participants who are enrolled by, or followed by, researchers at institutions outside the jurisdiction of the UMCIRB. The investigator must report to the UMCIRB only those non-local events that represent unanticipated problems involving risks to participants or others. The investigator should submit one copy of the non-local event form and any related documentation as soon as possible after the event or after the investigator learns of the event. The chair and his/her designee has access to the UMCIRB folder while conducting an expedited review. The investigator should provide an explanation on the form for any reporting delays.

The form will not be returned to the investigator, and there will be no further communication on a report unless additional information is required. The Chair or his/her designee will review the event submission form and materials as described above under the local adverse events. The same notification and report processes will be utilized as outlined above under the local event section for non-locally occurring events that constitute unexpected problems involving risks to subjects or others. Non-locally occurring events that do not meet this definition will not be reported to the UMCIRB committee or others. These reports will be filed in the UMCIRB folder after review by the chair or his/her designee.

Continuing Review:

Research studies, excluding those studies with an exempt status, are given an approval period that can extend for no longer than 365 days. ([21 CFR 56.108 and 56.109](#)).

Enrollment **may not** occur in any research study outside of the approval dates.

If some element of the research study must continue in order to protect the safety and well being of human subjects, the UMCIRB must be notified in writing as soon as possible to determine the appropriate course of action. The UMCIRB chair or his/her designee may permit continued research intervention in already enrolled participants, but may prohibit enrolling any new participants into the research until the study has been reapproved. Restrictions may be placed on data collected outside of the UMCIRB approval period. The UMCIRB will not provide retrospective approval for a lapse in study approval. It is not the intention of the UMCIRB to create any situation that would endanger the safety and well being of human subjects or cause harm, but it is vital to the protection of all subjects that research fully comply with federal and institutional policies.

The UMCIRB committee or institutional officials may request an interim report or simple update on the study progress for any active study for reasons such as breaking news items. The following are examples of factors the UMCIRB committee considers when setting the approval period:

- Studies with significant risk medical devices
- Early phase studies such as Phase I and II
- Investigator experience or mentor oversight
- Evidence of previous or current noncompliance
- Studies with vulnerable populations
- Interim data analysis and data monitoring plans
- Non-externally sponsored research studies

- Rate of proposed enrollment or proposed sample size
- Proposed study location

The principal investigator is responsible for ensuring research studies maintain current UMCIRB approval. Notices for an upcoming continuing review interval will be mailed prior to the research study expiration date. Although the UMCIRB office will assist the investigator by communicating the need for continuing review, it is highly recommended for the principal investigator to establish a reliable system within their office to track upcoming expiration dates.

Research studies that are allowed to expire will be reported to the relevant institutional leadership, relevant human protections administrator, ECU signatory official and relevant UMCIRB committee.

It is the goal of the UMCIRB office for studies to undergo review during the month prior to their expiration. This is an effort to minimize studies missing an opportunity for full review if a meeting should be cancelled or other extenuating circumstances should arise. In the case of committee review prior to the expiration date, the UMCIRB will reset the approval date and period. The UMCIRB is aware that this will disrupt the original date of approval.

The UMCIRB does not deem the failure of the investigator to renew a single study as an offense reportable to the regulatory agencies.

Expedited Continuing Review:

Research studies may be eligible for expedited continuing review when:

1. The research study was originally approved by expedited review.

2. The research studies that were previously approved by full committee at more than minimal risk may be eligible for expedited review only if specific categories are satisfied for expedited review, which are outlined below:

- The continuing review of research previously approved by the convened IRB as follows:(a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.
- The continuing review of research, not conducted under an investigational new drug application or investigational device exemption where expedited 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

The types of information that should be submitted include: processing form, protocol summary, consent document, any advertisements, materials provided to participants, and research protocol if available. The UMCIRB Chair and his/her designee has access to the UMCIRB folder while conducting an expedited review. Specific number of copies or other relevant submission details may be found on the UMCIRB web site.

Any research study requiring a revision at the time of continuing review must have a revision form accompanying the continuing review application.

The UMCIRB Chair or his/her designee is eligible to review and approve the study. Any research study requiring medical judgment must have a reviewer with an appropriate health care training or background. A “no more than minimal risk” research study eligible

for expedited review that involves a FDA regulated test item must receive continuing review by a biomedical Chair or designee.

The investigator will receive an approval letter routinely within 3 to 5 days by mail and fax according to the contact information on the processing form. Approved informed consent documents and advertisements will be stamped to reflect the new approval period. Informed consent documents will not be stamped for research studies no longer enrolling participants. The approval period will start from the date of approval by the reviewer or upon completion of any requested changes for a period specified by the reviewer. The expedited approval will be reported to the UMCIRB committee and signatory officials by being placed on the first available agenda and minutes. In the case of review and approval prior to the expiration date, the UMCIRB will reset the approval period. Concerns regarding the truthfulness of the continuing review application related to material changes may create a need for verification of an outside source such as the sponsor or other institutional departments. A request for third party verification may be made of the investigator by the UMCIRB Chair, Director, reviewer or the UMCIRB committee. Only the Chair, Director, or his/her designee should communicate requests on behalf of the UMCIRB committee of external entities for third party verification.

Full Committee Continuing Review:

The types of information that should be submitted include: processing form, protocol summary, consent document, any advertisements, materials provided to participants, and research protocol if available. Specific number of copies or other relevant submission details may be found on the UMCIRB web site.

The investigator will receive a letter describing the committee's decision routinely in 48 hours after the UMCIRB meeting via mail and fax according to the contact information on the processing form. Approved informed consent documents and advertisements will be stamped to reflect the new approval period. Informed consent documents will not be

stamped for research studies no longer enrolling participants. The approval period will start on the date of the last review by full committee for a period specified by the committee. If there are requested modifications on the continuing review that may be eligible for expedited review, then the approval date will also start from the date last reviewed by the full committee. In the case of review and approval prior to the expiration date, the UMCIRB committee will reset the approval date and period.

Study Closures:

A research study may be closed when there is no further participant enrollment, follow-up, data collection or data analysis. Investigators are required to keep a research study active through data analysis, but investigators are prohibited from re-contacting participants to obtain new data without first obtaining UMCIRB approval. Investigators are not required to keep a research study open for UMCIRB continuing review for manuscript preparation and publication only. The investigator must consult the UMCIRB office if a study has been closed and verification of original collected information must be performed by re-contacting the original participants.

The UMCIRB requires a final report for completed research, research studies allowed to expire, or a request to close studies that have not been initiated. A researcher may not collect or perform any protocol required activities on a research study that has been closed. Research studies that are closed to enrollment, but are following subjects are not considered closed for the purposes of UMCIRB review and must undergo continuing review until the time that no subjects are being followed in any fashion and data analysis has been completed. To close a study, the investigator should use the same form as the continuing review since the UMCIRB requires the same information for a review of the past approval period's activities. Study closures are eligible for expedited review; therefore, only one copy of the required materials is needed. The investigator will receive a letter describing the reviewer's decision routinely in 3 to 5 working days via mail and fax according to the contact information on the processing form.

Newly submitted research studies that do not have a response to requested modifications or additional items within 90 days from the date of the initial review may be terminated without the completion of a study closure form. Investigators that have never received UMCIRB approval for their new research studies because of a failure to respond to requested modification are not required to submit closure forms.

An investigator will be required to go through the entire submission process to open a new study once they receive a closure letter for a research study.

REVIEW OF RESEARCH INVOLVING MINORS

Definitions:

Assent: A child's affirmative agreement to participate in research. Mere failure to object should not be construed as assent. ([45 CFR 46.402](#))

Children: Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted. ([45 CFR 46.402](#))

Emancipated Minor: A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self-support, marriage, or procreation. ([NC General Statutes Article 35 7B 3500-3509](#))

Guardian: An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care or participation in research. ([45 CFR 46.402](#)) <http://www.fda.gov/OHRMS/DOCKETS/98fr/042401a.htm>

Permission: The agreement of parent(s) or guardian to the participation of their child or ward in research. ([45 CFR 46.402](#))

Parental or Legal Guardian Permission:

Minors, by definition, cannot give legal ‘consent’ unless they have been granted emancipation by the NC court system. It is important to note the NC laws related to emancipation of minors [NC General Statutes Article 35 7B 3500-3509](#), as well as those related to the ability of minors to consent to medical treatment. ([NC General Statutes Article 1A 90-21.1](#)) Minors are afforded special protections under federal regulations secondary to their vulnerable status. Parental permission should be obtained in accordance with [45 CFR 46.116](#), except when it is not a reasonable requirement to protect the minors such as in the case of neglected or abused children, and provide for an appropriate mechanism for protection consistent with federal, state and local laws. The permission of one or both parents or legal guardian is required based on the research risk and expected benefit knowledge to be gained as outlined in [45 CFR 46 Subpart D](#) and [45 CFR 46.408](#).

Only parents and legal guardians have the authority and responsibility to provide permission. School principals, teachers, clinic personnel, etc. do not have the authority to give ‘blanket’ permission for their students/patients/clients to participate in research.

Minors who reach the age of consent, 18 years old in North Carolina, must provide their consent for ongoing participation in a research study.

Assent Process and Documentation:

Information must be presented in a language and format that is understandable. The minors should have an understanding of the research procedures, and what they may

expect. It should be clear that their participation is voluntary, and they can stop at any time without penalty.

An exception to the assent mechanism is made for children with life-threatening illnesses who are entered into 'open-label treatment protocols' with the expectation of benefit. In these cases, the permission of the parent is sufficient, but the understanding of the minor subject is still desirable. Assent in the sense of agreement, is not sought from the minor subject because if the minor does not agree, the parent's wishes will prevail. It would be disingenuous to ask for agreement when negative responses will be ignored, however investigators must request and justify this exception. Additionally, the UMCIRB may waive assent requirements in those minors capable of assenting in accordance with [45 CFR 46.116](#).

The assent process and documentation must be appropriate to the study as well as the age, maturity and psychological state of the child. It is widely expected that infants cannot assent, and that older adolescents can understand a well-written "adult" consent form in layman's language. The UMCIRB committee will determine the appropriate format for obtaining and documenting assent in the intended study population or for individual subjects. The potential options include documenting verbal affirmation for younger children, signing of a separate assent form for school age children, or signing a minor assent line on a consent form for older adolescents. Documentation of a verbal assent should adequately reflect the assent process, the minor's affirmative response, and the witness. The UMCIRB must approve both the assent process and informed consent documents prior to use in a research study.

Minors that previously provided assent must be consented for continued participation in a research study upon reaching the age of consent, which occurs at 18 years of age in North Carolina. The consent process should be conducted no later than the first regularly scheduled visit after his/her birthday.

UMCIRB responsibilities for review of research involving minors:

In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research that satisfies the conditions of all applicable sections. DHHS will only fund and conduct research meeting these requirements [45 CFR 46.403](#). Research in children involving test items falling under FDA jurisdiction must also adhere to the regulations set forth in [21 CFR 50 and 56](#).

Research involving no more than minimal risk. ([45 CFR 46.404](#))

The following requirements must be met:

1. Adequate provisions must be made for soliciting assent of the children and permission of the parents or guardians.

Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. ([45 CFR 46.405](#))

The following requirements must be met:

1. The risk is justified by the anticipated benefit to the subjects;
2. 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
3. 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. ([45 CFR 46.406](#))

The following requirements must be met:

1. The risk represents a minor increase over minimal risk;
2. 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;

3. 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
4. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians

Research not otherwise approvable (under 45 CFR 46.404,405,406) which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children. ([45 CFR 46.407](#))

DHHS will conduct or fund such research provided that:

1. 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
2. The DHHS Secretary, after consultation with experts in pertinent disciplines (for example: science, medicine, education, ethics, law), has determined either:
 - (a) The research in fact satisfies the conditions of [45 CFR 46.404](#) , [45 CFR 46.405](#) or [45 CFR 46.406](#) 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

RESEARCH INVOLVING WARDS OF THE STATE

Children who are wards of the state or any other agency, institution or entity may participate in research, however, restrictions apply to the types of research where they may be enrolled. Children who are wards may participate in research studies under 46.406 [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 46.407 [Research not otherwise approvable (under 45 CFR 46.404,405,406) which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children] when at least one of the following conditions are met:

- (1) The research study is related to child's status as a ward: OR
- (2) The research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved are not wards.

When a research study does meet the conditions for approval, additional protections must also be added. The UMCIRB requires that an advocate is appointed for each child that is a ward. The advocate serves in addition to any other individuals that might be acting on behalf of the child as a guardian or loco parentis. The person serving as the child's advocate for participation in a research study must have 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. An advocate may be assigned to one or more children. The advocate must not have a potential for conflict of interest, therefore, he/she must not be associated in any other way with the research study, the investigator, or the guardian institution. The advocate may be a member of the IRB.

Principal investigators are responsible for identifying children as wards prior to enrollment or during the course of the research study. Investigators working with children as the target population should implement mechanisms to ensure they fulfill their responsibilities to this vulnerable population. Principal investigators are responsible for notifying the UMCIRB prior to enrolling any child that is a ward into a research study. The principal investigator is responsible for notifying the UMCIRB regarding a child's status as a ward prior to initiating any research-related interventions if a child's status has changed from not being a ward to being a ward of the state.

RESEARCH INVOLVING PREGNANT WOMEN, HUMAN FETUSES, AND NEONATES

Definitions:

Pregnancy encompasses the period of time from confirmation of implantation (through any of the presumptive signs of pregnancy, such as missed menses, or by a medically acceptable pregnancy test), until expulsion or extraction of the fetus. [45 CFR 46.203](#)

Fetus means the product of conception from the time of implantation (as evidenced by any of the presumptive signs of pregnancy, such as missed menses, or a medically acceptable pregnancy test), until a determination is made, following expulsion or extraction of the fetus, that it is viable. [45 CFR 46.203](#)

Neonate means a newborn. [45 CFR.202](#)

Viable as it pertains to the fetus means being able, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration. If a fetus is viable after delivery, it is a premature infant. [45 CFR 46.203](#)

Nonviable fetus means a fetus ex utero, which, although living, is not viable. [45 CFR 46.203](#)

In vitro fertilization means any fertilization of human ova, which occurs outside the body of a female, either through admixture of donor human sperm and ova or by any other means. [45 CFR 46.203](#)

Research involving pregnant women and fetuses is governed by [45 CFR 46. Subpart B](#). Women and fetuses are considered a vulnerable population that requires additional

safeguards. All research should have an equitable selection of subjects as noted [45 CFR 46.111](#), therefore inclusion of women in research studies requires consideration. The following is extracted from the HHS regulations that govern research involving pregnant women and fetuses.

Women and Fetuses ([45 CFR 46.204](#))

No research activity involving pregnant women or fetuses may be undertaken unless all of the following are satisfied:

1. Appropriate studies on pregnant animals and non-pregnant individuals have been completed and provide data for assessing potential risk to pregnant women and fetuses
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.
3. Any risk is the least possible for achieving the objectives of the research.
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with standard informed consent procedures. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
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 standard informed consent procedures, 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. Each individual providing

consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.

6. For children who are pregnant, assent and permission are obtained in accord with the provisions of the regulations applied to minors.
7. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.
8. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.
9. Individuals engaged in the research will have no part in determining the viability of a neonate.

Research involving neonates [46.205](#)

Neonates of uncertain viability may be involved in research if all of the following conditions are satisfied:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
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 standard informed consent procedures, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
3. Individuals engaged in the research will have no part in determining the viability of a neonate.
4. The IRB determines that 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 the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research.

Nonviable neonates may be involved in research if all of the following conditions are satisfied:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
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 standard informed consent procedures, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
3. Individuals engaged in the research will have no part in determining the viability of a neonate.
4. Vital functions of the neonate will not be artificially maintained.
5. The research will not terminate the heartbeat or respiration of the neonate.
6. There will be no added risk to the neonate resulting from the research.
7. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.
8. The legally effective informed consent of both parents of the neonate is obtained in accordance with standard consent procedures, except that the waiver and alteration provisions do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accordance with the regulatory requirements for all research, as well as, those regulations applicable to minors.

Research involving the dead fetus, fetal material, or the placenta ([45 CFR 46.206](#))

Activities involving the dead fetus, macerated fetal material, or cells, tissue, or organs excised from a dead fetus shall be conducted only in accordance with any applicable State or local laws regarding such activities and federal policy on fetal tissue research. If information associated with the biological materials 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, then the research must follow all pertinent regulations under research with pregnant women, human fetuses and neonates.

Research not otherwise approvable by the UMCIRB which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates:

The Secretary will conduct or fund research that the IRB does not believe meets the requirements of Sec. 46.204 or Sec. 46.205 only if:

1. 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.
2. The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and

comment, including a public meeting announced in the Federal Register, has determined either:

(1) That the research in fact satisfies the conditions of Sec. 46.204, as applicable;

or

(2) All of the following apply:

(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.

(iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

RESEARCH INVOLVING PRISONERS

Definitions:

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 ([45 CFR 46 Subpart C](#). [45 CFR 46.303](#))

Minimal Risk regarding Prisoners means risk of physical or psychological harm that is no greater in probability and severity than that ordinarily encountered in the daily lives, or in the routine medical, dental or psychological examinations of healthy persons. ([45 CFR 46.303](#)).

Purpose:

In as much 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 subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable. ([45 CFR 46.302](#)) It is important to note that the UMCIRB should be immediately notified of any human subject currently enrolled in a research study that becomes incarcerated or detained in any fashion for review of their ongoing participation.

Additional duties of the Institutional Review Boards where prisoners are involved
([45 CFR 46.305](#))

In addition to all other responsibilities prescribed for Institutional Review Boards under this part, the UMCIRB Committee shall review research covered by this subpart and approve such research only if it finds that:

1. The research under review represents one of the categories of the research permissible under ([45 CFR 46.306](#))
2. 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.
3. The risks involved in the research are commensurate with the risks that would be accepted by non-prisoner volunteers.
4. 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.

5. The information is presented in language that is understandable to the subject population.
6. 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.
7. 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.

Criteria for UMCIRB approval

Biomedical or behavioral research may involve prisoners as subjects only if: [45 CFR 46.306](#)

1. The Research Subjects Review Board has approved the research under [45 CFR 46.305](#) of this subpart.
2. The proposed research involves solely the following:
 - (a) 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.
 - (b) 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.
 - (c) 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.

- (d) 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 studies require the assignment of prisoners to control groups, which may not benefit from the research, the study may proceed only after the UMCIRB Chair has consulted with appropriate experts, including experts in penology medicine and ethics, and published notice, in the Federal Register, of his intent to approve such research.
- (e) If a participant in a research study becomes incarcerated, a full written description of this must be submitted immediately to the UMCIRB. The Prisoner UMCIRB Committee will be convened to review the participant's ongoing participation in the study.

Additional criteria exist for the approval of Biomedical or behavioral research conducted or supported by DHHS:

- (1) The institution responsible for the conduct of the research has certified to the Secretary that the UMCIRB has approved the research under 45 CFR 46.305 AND
- (2) In the judgment of the Secretary, the proposed research involves solely the following:
 - a) 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 subject;
 - b) Study of the prisoners' 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;
 - c) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine and ethics, and published notice in the FEDERAL REGISTER, of his/her intent to approve such research; OR
 - d) 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 the protocol approved by the UMCIRB to control groups with may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notices, in the FEDERAL REGISTER, of the intent to approve such research.

RESEARCH INVOLVING INVESTIGATIONAL DRUGS

Definitions:

Investigational drugs may be defined as one of the following:

1. A new drug in any of the clinical stages of evaluation (Phase 1, 2, 3) which has not been released by the FDA for general use or cleared for sale in interstate commerce.
2. Any commercially available drug proposed for a new use.
3. Any commercially available drug to be used in new dosage form or method of administration.
4. Any commercially available drug that contains a new component such as an excipient, coating or menstruum.
5. A new combination of two or more commercially available drugs.
6. A combination of commercially available drugs in new proportions.
7. Any commercially available drug involved in a post-marketing surveillance.

Investigational drugs are governed by the FDA [21 CFR 312 and 314](#). Investigational products are sometimes used for treatment of serious or life-threatening conditions either for a single subject or for a group of subjects. The procedures that have evolved for an investigational new drug (IND) used for these purposes reflect the recognition by the Food and Drug Administration (FDA) that, when no satisfactory alternative treatment

exists, subjects are generally willing to accept greater risks from test articles that may treat life-threatening and debilitating illnesses.

Off-Label Use

Good medical practice and patient interests require that physicians be free to use commercially available drugs according to their best knowledge and judgment. If a physician uses a drug for an indication not in the approved labeling, he/she has the responsibility to be well informed about the drug and to base its use on a firm scientific rationale and on sound medical evidence, and to maintain records of the drug's use and effects. Use of a drug as part of the "practice of medicine" does not require review by the UMCIRB or FDA notification, despite the fact that the use is technically experimental. However, when the principal intent of the investigational use of a drug is to develop information about its safety or efficacy, UMCIRB review and approval are required. Even though the law may not require an IND in all investigational situations, the FDA believes that it is in the best interests of the investigator and the public for one to be submitted.

RESEARCH INVOLVING MEDICAL DEVICES

Definitions:

Implant means a device that is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more. The FDA may, in order to protect public health, determine that devices placed in subjects for shorter periods are also "implants" for purposes of this part.

Noninvasive, when applied to a diagnostic device or procedure, means one that does not by design or intention: (1) Penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or (2) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os. For purposes of this part, blood sampling that involves simple venipuncture is considered noninvasive, and the use of surplus

samples of body fluids or tissues that are left over from samples taken for non-investigational purposes is also considered noninvasive. ([21 CFR 812.3\(k\)](#))

Transitional device means a device subject to section 520(l) of the act, that is, devices that are the object of clinical research to determine their safety or effectiveness governed by FDA regulations. ([21 CFR 812 and 814](#)) Studies undertaken to develop safety and effectiveness data for medical devices involving human subjects must be conducted according to the requirements of the Investigational Device Exemption (IDE) regulations. ([21 CFR 812](#)) Principal investigators are prohibited from representing the investigational device as safe or effective for purposes of which it is being investigated. [21 CFR 812.7\(d\)](#) If the device is to be sold, the amount to be charged and an explanation of why sale does not constitute commercialization of the device should be provided. [21 CFR 812.20\(8\)](#)

Assessment of Risk:

Investigational devices are classified as either significant risk or nonsignificant risk devices [21 CFR 812.3](#). In addition to determining whether a study should be approved, the UMCIRB will also determine whether the device presents significant or nonsignificant risk. A significant risk device is one that presents a potential for serious risk to the health, safety, or welfare of the subject. Such a device is intended as an implant; is to be used in supporting or sustaining human life; or is of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health.

Examples of significant risk devices are catheters (other than urological), ventilators, CPR devices, TMJ prostheses, stents, lithotripters, sutures and absorbable bandages/materials, ECT devices, extended wear contact lenses, pacemakers, contraceptive devices, most laser systems, and most hemodialysis systems. Investigations involving significant risk devices must meet the full IDE requirements including the submission of an IDE application to the FDA. As with nonsignificant risk

devices, UMCIRB approval is required prior to conducting clinical trials of the investigational device.

Examples of nonsignificant medical devices are: most daily wear contact lenses, lens solutions, heel cups, antibacterial surgical garments, incontinence devices, oral training splints, and ultrasonic tooth cleaners. Unless otherwise notified by FDA, an investigation of a nonsignificant risk device is considered to have an approved IDE if the sponsor fulfills the abbreviated requirements of the IDE regulations. These regulations require, in part, that UMCIRB approval be obtained and maintained throughout the investigation and that informed consent be obtained and documented.

In deciding if a device presents significant or nonsignificant risks, the UMCIRB will consider the device's total risks, and not compare these with the risks of alternative devices or procedures. If the device is used in conjunction with a procedure involving risk, the UMCIRB will consider the risks of the procedure in conjunction with the risks of the device.

UMCIRB Review:

The UMCIRB must determine the degree of risk involved in device studies. Some studies involving nonsignificant risk devices may also be considered no more than minimal risk studies, and thus may be reviewed through the expedited review procedure established by the UMCIRB. The FDA considers studies of all significant risk devices to be greater than minimal risk; thus, UMCIRB review at a convened meeting is required for all studies involving a significant risk device.

In considering whether a study should be approved, the UMCIRB will use the same criteria it would use in considering approval of any research involving an FDA-regulated product. The UMCIRB requires that the off-label use of a medical device for the purposes of research must be reviewed and approved by the UMCIRB, however if

intended solely for the practice of medicine UMCIRB approval review is not required. The UMCIRB will consider the risks and benefits of the test medical device compared to the risks and benefits of alternative devices or procedures in deciding to approve of a study.

Humanitarian Use Devices:

A Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year. A device manufacturer's research and development costs could exceed its market returns for diseases or conditions affecting small patient populations. The FDA, therefore, developed and published this regulation to provide an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations. An HDE (humanitarian device exemption) application to the FDA is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market.

An approved HDE authorizes marketing of the HUD. However, an HUD may only be used after UMCIRB approval has been obtained for the use of the device for the FDA approved indication. The labeling for an HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

The UMCIRB utilizes the same review procedures and processes as with other research with two exceptions. Under the regulations, the UMCIRB may waive a consent

document for the participant, and the research study may be eligible for continuing review utilizing an expedited review process.

RESEARCH INVOLVING THE USE OF BLOOD/TISSUES **FOR FUTURE RESEARCH**

Definitions:

Unlinked Samples are sometimes termed “anonymized” because these samples lack identifiers or codes that can link a particular sample to an identified specimen or a particular human being.

Coded Samples are sometimes termed “linked” or identifiable” because these samples are supplied by repositories to investigators from identified specimens with a code rather than with personally identifying information such as name or Social Security number.

Identified Samples are supplied by repositories from identified specimens with a personal identifier (such as a name or patient number) that would allow the researcher to link the biological information derived from the research directly to the individual from whom the material was obtained.

UMCIRB review:

The UMCIRB requires that all human subject research involving stored human biological materials must be reviewed and approved by the UMCIRB. ([OHRP Human Subject Guidance](#)) The submission and review processes for review of research of this nature are the same as those for all types of all research studies as previously described. The UMCIRB views the standard surgical consent as inadequate for the collection of human biological samples for the purposes of conducting research. Reliance on any document other than the UMCIRB approved consent document or procedures for conducting research is not permitted.

The research study can be classified according to exempt, expedited, or full UMCIRB review as previously discussed, with considerations to the linking of specimens and its risks (physical, psychological, social, legal, economical, and/or dignitary) to the human subject. Again, only the UMCIRB chair or his/her designee may judge a research study as exempt or approve research under an expedited status. Additionally, the Chair or his/her designee reserves the right to elevate a study to full UMCIRB review based on risk to the human subject. ([National Bioethics Advisory Commission reports](#))

EMERGENCY USE REQUIREMENTS

Definitions:

Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted, and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening does not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the UMCIRB is feasible.

Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Emergency use is defined as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain UMCIRB approval. ([21 CFR 56.102\(d\)](#))

An investigator may contact the UMCIRB prior to using an emergency use test item, but notification prior to the use is not required by the UMCIRB or by federal regulations. If the sponsor requires prior notification, the UMCIRB office will issue a letter of

concurrence as soon as possible after the required information has been received so as not to create delays that interfere with the process. The UMCIRB must receive all the required information for notification of the emergency use of a test item within 5 workdays for concurrence, not approval, of the use. A letter of acknowledgement will be sent to the investigator regarding the test item use within three to five working days when the letter reflects concurrence after use of the test item. Any subsequent use of the test article at the institution is subject to prospective UMCIRB review.

The emergency use test items will be reported to the committee and institutions by being placed on the minutes. Although [21 CFR 56.104\(d\)](#) is designed to permit only a single emergency use of a test article for the treatment of one patient by one physician within an institution, the regulation is not intended to limit the authority of a physician to provide emergency care in a life-threatening situation.

If it appears probable that similar emergencies will occur requiring subsequent use of the test article at the institution, every effort should be made either to sign on to the sponsor's protocol, or to develop a protocol for future emergency use of the article at the institution. Either of these protocols would need to be prospectively reviewed and approved by the UMCIRB for future use of the test article. Note that the research sponsor may require full, prospective UMCIRB approval prior to dispensing any additional test items.

Required Documentation for emergency use of a test item:

Listed below are the items that need to be submitted to the UMCIRB office when the investigator is seeking concurrence prior to the research item use:

- The name and title of the investigator.
- The sponsor of the product.
- The IND number for the product. The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not

exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND.

- The protocol or other test item information supplied by the manufacturer.
- A copy of the unsigned informed consent document, so that it can be stamped for a one-time use.
- If the investigator will not be able to obtain informed consent from the potential participant or legally authorized representative, then there should be a statement that if informed consent is not obtained prior to use of a treatment article that the emergency use will not be considered research, nor may any data be used as research. Whenever emergency care is initiated without prior UMCIRB review and approval, the patient may not be considered a research subject. Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity. Simply stated: DHHS regulations for the protection of human subjects do not permit research activities to be started, even in an emergency, without prior UMCIRB review and approval. If the emergency care involves drugs, devices, or biologics that are considered to be investigational by the Food and Drug Administration (FDA), then it may be necessary to meet FDA requirements to use the investigational article for emergency purposes. The sponsor may however require certain pieces of information to be collected and submitted.
- The clinical circumstances for the individual who received the drug.
- The indication for which the drug will be used.
- Documentation that other available treatments are unproven or unsatisfactory by both the investigator and an objective physician from a relevant clinical area.
- A statement that any serious adverse events or unanticipated problems that occur as a result of the emergency use protocol will be reported as soon as possible to the UMCIRB.
- A statement indicating whether additional uses are anticipated, and the plans to submit a research protocol seeking prospective UMCIRB approval.

Listed below are the additional items that need to be submitted to the UMCIRB office within five working days when the investigator secured a letter of concurrence from the UMCIRB prior to research item use:

- The initial response of the patient.
- Any serious adverse events or unanticipated problems that have occurred as a result of the emergency use protocol.
- An update on the patient upon conclusion of the emergency use treatment.

Listed below are the items that need to be submitted to the UMCIRB office within five working days of the research test item use when the investigator is seeking concurrence after the research item use:

- The name and title of the investigator.
- The sponsor of the product.
- The IND number for the product. The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND.
- The protocol or other test item information supplied by the manufacturer.
- Documentation that consent was provided by the participant or his/her legally authorized representative.
- A statement that if informed consent was not obtained prior to use of a treatment article that the emergency use will not be considered research, nor may any data be used as research. Whenever emergency care is initiated without prior UMCIRB review and approval, the patient may not be considered a research subject. Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity. Simply stated: DHHS regulations for the protection of human subjects do not permit research activities to be started, even in an emergency, without prior UMCIRB review and approval. If the emergency care involves drugs, devices, or biologics that are considered to be investigational by the

Food and Drug Administration (FDA), then it may be necessary to meet FDA requirements to use the investigational article for emergency purposes. The sponsor may however require certain pieces of information to be collected and submitted.

- The clinical circumstances for the individual who received the drug.
- The indication for which the drug was used.
- Documentation in the emergency use protocol that other available treatments are unproven or unsatisfactory by both the investigator and an objective physician from a relevant clinical area.
- The initial response of the patient.
- Any serious adverse events or unanticipated problems that have occurred as a result of the emergency use protocol.
- An update on the patient upon conclusion of the emergency use treatment.
- A statement indicating whether additional uses are anticipated and the plans to submit a research protocol seeking UMCIRB approval.

Waiver of Informed Consent Documentation for a single unplanned use:

Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

- The subject is confronted by a life-threatening situation necessitating the use of the test article.
- Informed consent cannot be obtained because the subject's medical or psychological condition precludes an ability to communicate with or obtain legally effective consent from the subject.
- Time is not sufficient to obtain consent from the subject's legal representative.
- No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

If immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the investigator should make the determination and, within five working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

The subject and/or the subject's legal representative must be notified of the use of the experimental procedure and consent to continue should be obtained for those procedures requiring continued/repeated administration. The investigator must notify the UMCIRB within five working days after each use of this waiver.

Waiver of informed consent for planned emergency research in the community

Planned community-based research where it is anticipated that a waiver of consent will be required because subjects will not be able to provide consent or where a Legally Authorized Representative will be unavailable is permissible under the regulations according to 21 CFR 50.24. Research of this nature must meet specific criteria and insert special protections for the research subjects. The UMCIRB will find and document along with the concurrence of a licensed physician the following in order to grant a waiver under 50.24:

- (1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of a particular intervention.
- (2) Obtaining informed consent is not feasible because:
 - a) The subjects will not be able to give their informed consent as a result of their medical condition;
 - b) The intervention under investigation must be administered before consent from the subjects' Legally Authorized Representative is feasible;

- c) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
- (3) Participation in the research holds out the prospect of direct benefit to the subject because:
- a) Subjects are facing a life-threatening situation that necessitates intervention;
 - b) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; AND
 - c) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about risks and benefits of the proposed intervention or activity.
- (4) The clinical investigation could not practicably be carried out without the waiver.
- (5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a Legally Authorized Representative for each subject within the window of time and, if feasible, to ask the Legally Authorized representative for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact Legally Authorized Representatives and make this information available to the IRB at the time of continuing review.
- (6) The IRB has reviewed and approved informed consent procedures and documents consistent with applicable regulations. These procedures and the consent document are to be used with subjects or their Legally Authorized Representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with 7(e) of this section.
- (7) Additional protections of the rights and welfare of the subjects will be provided, including at least:

- a) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be drawn;
- b) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
- c) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population and its results;
- d) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
- e) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a Legally Authorized Representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The UMCIRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a Legally Authorized Representative of the subject, or if the Legally Authorized Representative is not available a family member of the following:

- (1) The subject's inclusion in the clinical investigation, the details of the investigation, and other information contained in the approved consent document.
- (2) The subject's participation may be discontinued at any time without penalty or loss of benefits to which the subject is otherwise entitled.

If a legally authorized representative or family member is informed about the clinical investigation and the subject's condition improves, the subject is informed as soon as feasible. If a subject is enrolled into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be

contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family members, if feasible.

The UMC IRB will retain research-related materials for at least three years after completion of the clinical investigation, and the records will be made accessible for inspection and copying by the FDA or other regulatory bodies.

The UMCIRB requires that a separate Investigational New Drug (IND) or Investigational Device Exemption (IDE) will be obtained even on marketed products regardless of whether the research test items have a current IND or IDE. This separate IND or IDE must clearly state that the protocol may include subject who are unable to consent.

The UMCIRB will document its findings and promptly notify the investigator and sponsor of its decision that the proposed research does not meet the criteria for an exception to informed consent due to regulatory or ethical concerns. This notification will outline rationale for the UMCIRB's decision.

Research regulations are not intended to limit the authority of a physician to provide emergency medical care to the extent a physician is permitted under applicable federal, state and local law.

RESEARCH INVOLVING HIV TESTING

Research involving participants with HIV/AIDS testing must address specific issues and provide specific protections.

Specific issues related to research involving HIV/AIDS must be addressed which include provisions to:

- Provide adequate justifications to the UMCIRB committee for conducting the HIV testing
- A description of who is entitled to see records with identifiers, both within and outside the project, including review by the funding agency and the FDA when applicable. Research participants should be informed who will have access to this information.
- Adequate plans and provisions for pre and post-test counseling for participants that are identifiable. Requirements for pre-test and post-test counseling do not apply in the context of a research protocol if the testing is performed in such a manner that the identity of the test subject is not known and may not be retrieved by the researcher.
- When HIV testing is conducted as part of a research project on individuals whose test results are associated with personal identifiers, such individuals must be informed of his/her own test results in a timely fashion and be provided with the opportunity to receive appropriate counseling. Individuals may not be given the option “not to know” the result, either at the time of consenting or thereafter.
- Consent documents for individuals where specimen HIV results cannot be linked back to the individual in any fashion do not have to contain HIV specific language, but they must be notified of the anonymous nature of the testing.
- Specimens may be tested for AIDS virus infection for research or epidemiological purposes without consent of the person from whom the specimen is obtained if all personal identifying information is removed from the specimen prior to testing.

Any person tested for HIV infection should receive pre and post-test counseling, which may not necessarily be from an individual on the research team. Informed consent and pre-test counseling should consist of:

- An explanation of the test, including its purpose, the meaning of its results, and the benefits of early diagnosis and medical intervention.
- An explanation of the procedures to be followed, including that the test is voluntary, that consent may be withdrawn at any time, and a statement advising the subject that anonymous testing is available.

- An explanation of the confidentiality protections of individuals afforded confidential HIV related information, including the circumstances under which and classes of persons to whom disclosure of such information may be required or authorized.
- An explanation of the nature of AIDS and HIV related illness, information about discrimination problems that disclosure of the test result could cause and legal protections against such discrimination, and information about behavior known to pose risks for transmission and contraction of HIV infection.

At the time of communicating the test result to the subject, the person ordering the performance of the test must provide the subject with mandated post-test counseling. Post-test counseling should consist of information regarding:

- coping with the emotional consequences of learning the test result
- discrimination problems that disclosure of the result could cause
- changes in behavior to prevent transmission or contraction of HIV infection
- available medical treatments
- The test subject's need to notify his or her contacts and notification method for exceptions to this rule when applicable. If disclosure does occur a document must follow warning against any further unauthorized disclosure by the recipient.

RESEARCH CONDUCTED IN FOREIGN COUNTRIES

Because procedures normally followed in foreign countries to protect human subjects may differ from those used in this country, when research takes place in a foreign country the UMCIRB will require additional safeguards to demonstrate equivalency. (45 CFR 46.101) Research involving no more than minimal risk should be approved by a local ethics committee if one is available, and if not, then documentation of local permission or support must be provided. The research must be approved by an appropriately constituted local ethics review committee if a study meets the criteria for more than minimal risk. The local ethics committee must use an acceptable national or international ethical standard as a basis for review, and method must be provided to the UMCIRB

along with their approval letter. Examples of acceptable standards include the World Medical Association Declaration of Helsinki and the Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects. The informed consent document(s) to be used in the foreign country must be submitted. The UMCIRB office will review these to ensure that they are comparable to U.S. standards, especially with regard to the eight essential and six additional elements of informed consent, Good Clinical Practices if relevant, and the Belmont Report. If they are not comparable, changes or appropriate justification will be required. Procedures outlining the consent process must be described, and any alternatives for documentation of consent must be provided. Foreign investigators and co-investigators must agree to provide timely reports on the progress of the research and to report adverse events and unanticipated problems involving risk to participants or others to the UMCIRB (either directly or through the East Carolina University investigator). Federally funded foreign research must also comply with the appropriate agency procedures and regulations. Research in foreign countries that do not have the same or similar projects conducted in this country and/or is not acceptable in this country will not be approved by the UMCIRB. ([International Conference on Harmonisation](#))

RESEARCH RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATORS

Regulatory responsibilities:

The principal investigator is responsible for the conduct of the research study and for overseeing the actions of the research team members. ([Good Clinical Practice 4.01 to 4.13](#)) No human subject research can be undertaken without submission of required research-related materials to the UMCIRB, and review by the UMCIRB chair or his/her designee or the full convened UMCIRB committee. The principal investigator is responsible for determining if an activity involves human subject research, while the UMCIRB is responsible for determining whether the appropriate classification of human

subject research meets the exempt or expedited categories, or requires full committee review. The principal investigator must be competent and have the appropriate training to oversee the research project. The UMCIRB will evaluate an investigator's qualifications through documentation of the Department Chair or Chief of Service signature of approval, by reviewing the CV or other records of training.

A graduate student, resident or fellow may act as a principal investigator only with a responsible faculty or staff support, and in this circumstance the UMCIRB will depend on the faculty or staff's signature of support as documentation that the investigator is capable of fulfilling the role of principal investigator. The support faculty's role is that of mentor, and to ensure compliance with all regulations. A principal investigator is responsible for communication between all relevant parties to the research, such as the sponsor company, the funding agency, the UMCIRB, and any federal regulatory agencies. The principal investigator must ensure that all communication from the UMCIRB regarding its actions or requests is communicated to the study sponsor, funding source or other appropriate individuals. The UMCIRB will communicate disapprovals of research applications directly to the sponsor for research activities.

The principal investigator is solely responsible for the conduct of his/her research study. Additionally, it is important that subinvestigators also agree to follow all the rules and responsibilities for which they are designated by the principal investigator:

- To obtain UMCIRB approval prior to instituting any change in the research study, unless it is necessary to protect the safety and welfare of human participants. An action instituted to protect the safety and well-being requires immediate reporting to the UMCIRB.
- To engage in a continuing exchange of information or advice with the UMCIRB ensuring a continuing review process for the protection of human participants, including submission of a closure form upon completion of the study or study expiration, whichever occurs first.

- To engage in a continuing exchange of information with the appropriate departments within the institutional study site, the institutional officials, the department chairs when appropriate, and the research study sponsor.
- To ensure the research study is conducted only within the periods of UMCIRB approval.
- To inform the UMCIRB, research site institution, sponsor or appropriate federal regulatory agency in writing of any serious adverse events and unanticipated problems involving risks to study participants or others as soon as possible.
- To inform the UMCIRB in writing of protocol deviations as soon as possible.
- To maintain all study records for at least 3 years after completion of the study at all sites or longer if required by a professional organization, sponsor, regulatory body or others.
- To regard participant informed consent as an ongoing process.
- To enroll participants only after obtaining ethically and legally effective informed consent as approved by the UMCIRB, using only the most currently approved UMCIRB stamped consent document, when required.
- To obtain minor assent from children prior to enrollment as outlined.
- To notify the UMCIRB if any relationships develop that may be considered a conflict of interest.
- To abide by the UMCIRB Standard Operating Procedures, all applicable federal regulations, Good Clinical Practice, state laws, and respective institutional policies to conduct this research study. Ethical standards include the Belmont Report and other professional standards for an individual research area.
- To comply with regulatory reviews, data audits, and 3rd party observation for the consenting process by appropriate institutional regulatory officials.
- To notify the UMCIRB prior to relocating employment to provide for the orderly study closure or to transfer the study to another investigator.

Principal investigators must sign all forms intended for submission to the UMCIRB. Subinvestigators listed on the study may sign on behalf of the principal investigator if the principal investigator is away to avoid delays in communicating information to the

UMCIRB. When the principal investigator returns, he or she should submit a countersigned copy of the previously submitted documents, or visit the UMCIRB office to sign the originally submitted documents.

Independent Investigators:

Investigators acting on their own behalf, independent of a hospital, clinic or other facility requiring review through the UMCIRB, and with no internal institutional review board may enter into a formal agreement to rely on the UMCIRB by completing an Unaffiliated Investigator Agreement.

OTHER UMCIRB FUNCTIONS

The UMCIRB Chair or his/her designee reviews HIPAA Waiver of Authorizations and HIPAA Authorizations against a checklist of the criteria for approval. These reviews are reported on the UMCIRB minutes. The approval documents are retained in the UMCIRB folder.

CONFLICT OF INTEREST

Definitions:

Conflict of Interest occurs when financial or other personal considerations might unduly influence or potentially compromise the principal investigator or research team member's judgment in the conduct of human subject research. Conflict of interest may result in undue gain of financial, personal, or professional advantage interjecting bias into the research results.

Immediate Family of a research investigator includes his or her spouse and dependent children or parents.

Significant Financial Interest means anything of monetary value received from a sponsor or affiliated entity exceeding \$10,000 over a twelve month period when

aggregated for the investigator and their immediate family, as determined through reference to public prices or other reasonable measures of fair market value. This definition includes but is not limited to salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); holdings of more than a five percent ownership interest in any single entity; and intellectual property rights (e.g., patents, copyrights and royalties from such rights).

Executive Position refers to any position that includes responsibilities for a material segment of the operation or management of a business, including Board membership.

To participate in research means to be part of the described activity in any capacity, including but not limited to serving as the principal investigator, co-investigator, research collaborator, or persons who are in consistent direct human subject contact for the purposes of research. The term is not intended to apply to individuals who provide primarily technical support or who are purely advisory, with no direct access to the data (e.g., control over its collection or analysis) or, in the case of clinical research, to the trial participants, unless they are in a position to influence the study's results or have privileged information as to the outcome.

Disclosure of Conflicts of Interest by Investigators:

Principal investigators must complete the UMCIRB Conflict of Interest Disclosure Form located on the UMCIRB web site for all sponsored research.

Investigators must disclose conflicts of interest that have the potential to adversely affect his/her judgment in research related matters, to compromise objectivity in conducting the human subject research, or to otherwise compromise his/her ethical principles.

Department chairs will review the conflict of interest disclosure form in addition to other personal information to affirm that there is no apparent, actual or potential conflict of interest with the principal investigator and the research study, or that any conflict of

interest has an appropriate conflict of interest management plan. The Department Chair will review the risk for additional actions or disclosures and indicate his/her recommendation by completing the appropriate sections on the processing form. The research application and relevant documentation will be forwarded by the UMCIRB to the ECU Signatory Official for concurrence when a potential or actual conflict of interest has been identified by the investigator or Department Chair. The enrollment incentives for a research study must be disclosed to the UMCIRB. Enrollment incentives are disallowed for any member of the research team employed by East Carolina University.

Any issues related to conflict of interest must be updated within the continuing review application for the research or as the issues occur when within the approval period. All faculty and staff of East Carolina University must adhere to the Conflict of Interest policy in the Faculty manual. Investigators must also comply with sponsor requirements and FDA regulations for the declaration of conflicts of interest.

Disclosure of Conflicts of Interest during the UMCIRB Review Process:

Investigators are prohibited from participating in the deliberation and voting on a research project during the UMCIRB meeting for which they are an investigator under any circumstance. Any member that attends an UMCIRB meeting must identify any actual or potential conflict of interest for any study being discussed and must be recused from voting. Investigators and all other directly involved personnel for a research study must leave the room during UMCIRB deliberation and vote on the study. The Chair or his/her designee will render a final decision on what actions a member with identified potential conflicts of interest should take during any given meeting. Investigators are prohibited from acting as the Chair's designee in any form of expedited review for a research study where they are involved.

Procedures for Managing Conflict of Interest

Questions regarding a conflict of interest may be reported to the UMCIRB, the university compliance office(s), or directly to the ECU signatory official regardless of the research study site. The report should contain as much information or evidence as possible to facilitate the investigation. The UMCIRB will forward any reports received directly to the ECU signatory official for management at the institutional level through the institution's conflict of interest management processes.

Additional measures instituted to provide human subject protection may require UMCIRB review and approval. These steps may include, but are not limited to, third party witnessing of the informed consent process, informed consent document audits, and a more frequent continuing review interval for Conflict of Interest.

The principal investigator has a clear obligation to ensure compliance with all UMCIRB operating procedures, institutional policies, and federal regulations to disclose and to remove or appropriately manage conflicts of interest or commitment. Listed below are some examples of noncompliance related to conflict of interest:

- Furnishing false, misleading, or incomplete information on the disclosure forms
- Failure to promptly update disclosure forms before the required continuing review update when a significant change in a person's financial or fiduciary status places the individual into an immediate potential or actual conflict of interest situation
- Failure to comply with a prescribed conflict of interest management plan.

RESEARCH COMPLIANCE

Compliance Monitoring:

The compliance office within institutions where research is being conducted may perform compliance monitoring for research studies being conducted within their areas.

Suspensions of UMCIRB Approval:

The UMCIRB has the authority to restrict study activities such as enrollment, require increased supervision of study conduct practices, suspend or terminate approval of research that is not being conducted in accordance with the UMCIRB requirements, sponsor requirements, federal regulations, or where significant new information is available that suggests participants may be placed at an increased risk of harm. Any such suspension of approval shall be reported promptly to the investigator and shall include a statement of the reasons for the UMCIRB action. Such suspension will routinely be made at a convened meeting of the UMCIRB, unless immediate action is indicated. In this case, the UMCIRB Chair may suspend approval. Participants may not be enrolled or receive research interventions during a period of suspension or termination. A restriction on some parts of a research study may be applied, when the UMCIRB chair or committee has determined that it is the best interest for some research activities like monitoring and data collection to continue. The UMCIRB shall promptly notify the principal investigator, UMCIRB attorney, ECU signatory official, relevant human protection administrator, sponsor, and relevant regulatory agencies. Additional notifications to other offices within the institution may be given as directed by the UMCIRB committee or as required by institutional policy. The report shall include the institution's name, title of the research, name of the principal investigator of the research study, UMCIRB number, grant number if applicable, detailed description of the problem, and any immediate actions that have been taken.

Unanticipated Problems Involving Risk

The UMCIRB has the obligation to report unanticipated problems involving risks to participants or others under the regulations. All human subject research studies conducted under UMCIRB jurisdiction are subject to OHRP regulations, while research studies involving FDA regulated items are also subject to FDA regulation.

The UMCIRB Chair will first review and determine whether an event submitted by an investigator meets the criteria for an unanticipated problem involving risks to subject or others. The criteria for this determination includes events that meet all of the following:

1. The event is unanticipated because it is not included in the currently approved documents or it is unexpected that it would occur given the study population described in the research. AND
2. The event is related or possibly or reasonably caused by procedures involved in the research. AND
3. The events suggest that the research places the participants or others at a greater risk of harm than previously thought.

The UMCIRB Chair may take immediate action on an event if necessary in order to protect the safety and well-being of research participants, and then refer the event to the relevant UMCIRB committee. The UMCIRB Chair may refer the event to the relevant UMCIRB committee for a determination of whether an event represents an unanticipated risk to subject or others. The UMCIRB shall promptly notify the principal investigator, UMCIRB attorney, ECU signatory official, relevant human protection administrator, sponsor, and relevant regulatory agencies of the finding for an unanticipated problem. Additional notifications to other offices within the institution may be given as directed by the UMCIRB committee or as required by institutional policy. Other institutional offices may elect to conduct an independent investigation of the event, as they may have additional institutional concerns that fall beyond human subject research. The report will include the institution's name, title of the research, name of the principal investigator of the research study, UMCIRB number, grant number if applicable, detailed description of the problem, and any immediate actions that have been taken. The UMCIRB or institution will provide a follow-up to the original report as needed if additional information is available after subsequent investigation, or upon implementation of a final corrective action plan. Any revisions to the protocol, consent document or procedures previously approved by the UMCIRB will require UMCIRB approval.

Serious or Continuing Noncompliance

The UMCIRB has an obligation to report serious and continuing noncompliance related to the regulations or UMCIRB processes. Serious noncompliance relates to actions that result in increased risk of harm to research participants. Research protocols approved by the UMCIRB include procedures that are required to minimize risks to participants. A failure to follow the research protocol by committing major deviations may constitute an instance of serious noncompliance. Ongoing noncompliance may be related to multiple deviations within a single protocol or evidence of a pattern of failing to follow the research protocol and plan.

The UMCIRB Chair will generally defer a determination of serious or continued noncompliance with a research study to the relevant UMCIRB committee for a determination of whether an event represents an unanticipated risk to subject or others, unless immediate action is necessary to protect the safety and well-being of research participants. The UMCIRB shall promptly notify the principal investigator, UMCIRB attorney, ECU signatory official, relevant human protection administrator, sponsor, and relevant regulatory agencies of the finding of serious and continuing noncompliance. Additional notifications to other offices within the institution may be given as directed by the UMCIRB committee or as required by institutional policy. The report will include the institution's name, title of the research, name of the principal investigator of the research study, UMCIRB number, grant number if applicable, detailed description of the problem, and any immediate actions that have been taken.

Corrective action plans for serious and continuing noncompliance will be crafted at the institutional level. Any revisions to the protocol, consent document or procedures previously approved by the UMCIRB will require UMCIRB approval.

Allegations of Investigator Non-compliance:

Upon submission of a report of the UMCIRB of noncompliance by a third party or if the UMCIRB becomes aware of noncompliance, the UMCIRB will inform the principal investigator to provide information and to submit data and may require him/her to cease

all activity on the study in question. The UMCIRB will forward this information onward to the relevant institutional offices for further investigation and to the signatory official.

[\(45 CFR 46.113 21 CFR 56.113\)](#)