# Western Carolina University
# Office of Research Administration
# Institutional Review Board Standard Operating Procedures

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SOPs adapted from The University of New Mexico Office of the Institutional Review Board:
https://irb.unm.edu/library

## I. Purpose

This procedure sets forth the process for determining whether the scope of a project meets the definition of human subjects research.

## II. Definitions

The Common Rule/Department of Health and Human Services (HHS) (45 CFR 46)

**Human Subject** means a living individual about whom an investigator conducting research:

1. Obtains information or biospecimens through intervention or interaction with the individual and uses, studies, or analyzes the information or biospecimens; OR
2. Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

**Biospecimen** is a sample of material, such as urine, blood, tissue, cells, DNA, RNA, and protein from a human.

**Intervention** includes both physical procedures by which information or biospecimens are gathered and manipulation of the subject or the subject's environment that is performed for research purposes.

**Interaction** includes communication or interpersonal contact between investigator(s) and subject.

**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, as well as information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public.

**Identifiable private information** is private information where the identity of the subject is associated with the information or where the identity of the subject may readily be ascertained by the investigator.

**Identifiable biospecimen** is a biospecimen where the identity of the subject is associated with the biospecimen or where the identity of the subject may readily be ascertained by the investigator.

**Research** means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

The following activities are deemed not research:

1. Scholarly and journalistic activities (e.g. oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focuses directly on the specific individuals about whom the information is collected.

2. Public health surveillance activities, including the collection of information, the collection or testing of biospecimens – or both that is, conducted, supported, requested, ordered, required, or authorized by a public health authority.
3. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
4. Authorized operational activities as determined by each agency in support of intelligence, homeland security, defense or other national security missions.
5. Projects that involve human subjects but are conducted within a classroom, in order to achieve an educational learning objective, and where the results will not be shared or disseminated outside the classroom are not considered human subjects research. It is the responsibility of the faculty member overseeing these projects to use good ethical judgement to evaluate the appropriateness of these projects.

Food and Drug Administration (FDA)(21 CFR 56)

If the research involves any of the following, FDA regulations 21 CFR 50 & 56 apply and require IRB approval prior to implementation:

- Any use of a drug in research other than the use of an FDA approved drug for standard medical practice;
- Any use of a medical device in studies where the purpose is to determine the safety or effectiveness of the device; OR
- Data will be submitted to or held for inspection by FDA as part of a marketing permit.

**Human Subject or "subject"** means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.

**Clinical investigation** means any experiment that involves a test article and one or more human subjects, and that either A) must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or B) need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of that experiment are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

The term "clinical investigation" does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies [21 CFR 56.102(c)]. If the activities involve use of an FDA regulated test article (i.e. drug, device, food substance, or biologic under the purview of the FDA), WCU applies the FDA definition of "human subject."

## IV. Procedure

1. Investigators are responsible for assessing their own projects to determine whether they meet the definition of human subjects research. However, the IRB has the authority to over-rule a investigator's self-determination.

2. Projects that do not meet the definition of human subjects research do not need be submitted to the IRB.
3. If an investigator is unsure as to whether their project meets the definition of human subjects research, they should consult with the IRB administrator, chair or other IRB representative informally by phone or email.
4. Investigators may request a formal letter determining a project is not human subjects research from the Office of Research Administration.
5. All projects that meet the definition of human subjects research must be submitted to the IRB, including collaborative project that may have also undergone review at another institution.

## V. Responsibilities

IRB administrators, Investigators

## VI. References

21 CFR 56.102
45 CFR 46.101, 46.102(e)

## I. Purpose

This sets forth the procedures for processing IRB projects in IRBNet prior to assigning review.

## II. Definitions

Each project submitted to IRBNet undergoes pre-review by the IRB administrator to assess completeness of the package. The IRB administrator communicates with the investigator(s) as needed. Once the submission is complete, the IRB administrator makes a preliminary assessment of review type required.

## III. Procedure

1. All projects submitted in IRBNet are first received by the IRB administrator.

2. The IRB administrator conducts an initial administrative review for the following items, utilizing the Project Intake Form:
    a. The Principal Investigator (PI) listed on the project is a full-time faculty or staff member at WCU,
    b. The project has been electronically signed by the PI,
    c. All research personnel have completed the CITI human subjects training modules,
    d. All research personnel have achieved the minimum score required in the human subjects training modules,
    e. All required documents are included in the package, AND
    f. If research takes place off-site, an appropriate permission letter is included.

3. If any of the elements listed above are missing, the IRB administrator contacts the investigator(s) in writing to request clarification or further documentation. The project is then un-locked in IRBNet so the investigators may edit the package. Once an investigator completes the needed updates they select “Mark Revisions Complete” in IRBNet, which notifies the IRB administrator the package is ready.

4. The IRB administrator conducts an initial review of the project and makes a preliminary assessment of type of review required.

5. The IRB administrator screens the project to determine if HIPAA, FERPA, FDA, or other regulatory requirements apply based on the scope of the project. Once assigned, the IRB administrator notifies the application reviewer of any identified concerns in writing with suggestions for compliance.

6. The IRB administrator screens the project to determine the funding source, if any, and to determine if any additional regulatory requirements apply based on the funding sponsor. Once

assigned, the IRB administrator notifies the application reviewer of any identified concerns in writing with suggestions for compliance.

7. The IRB administrator screens the project to ensure compliance with other university review committees, including Conflict of Interest Committee, Institutional Animal Care and Use Committee, and Institutional Biosafety Committee.

8. Once the pre-review items are complete, the IRB administrator assigns the project to a reviewer or to the full-board, as appropriate.

## IV. Responsibilities

IRB administrators, IRB members, Investigators

## V. References

## I. Purpose

This sets forth the process for the determining whether a project meets the criteria for exempt determination and conducting limited review, if applicable.

## II. Definitions

Certain categories of research described in the federal regulations may be exempt from IRB review and approval. However, exempt research is still subject to institutional review by an individual reviewer and subject to the ethical principles outlined in the *Belmont Report*.

Projects may be determined exempt if the only involvement of human subjects in a study meets one or more of the following criteria (45 CFR 46.104(d)):

1. Research conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies as well as, research on the effectiveness or comparison among instructional techniques, curricula, or classroom management methods.

2. Research that includes only interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observations of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

    i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
    ii) Any disclosure of the responses outside the research would not reasonably place the subject at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; OR
    iii) The information is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination (as required at 46.111(a)(7)) that there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data.

3. Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
ii. Any disclosure of the responses outside the research would not reasonably place the subject at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement or reputation; OR
iii. The information is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination (as required at 46.111(a)(7)) that there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data.

For the purposes of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing.

If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
   i) The identifiable private information or identifiable biospecimens are publicly available;
   ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects and the investigator will not re-identify subjects;
   iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); OR
   iv) The research is conducted by, or on behalf of, a federal department or agency using government generated or government collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 55sa, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

5. Research and demonstration projects that are conducted or supported by a federal department or agency, or otherwise subject to the approval of department or agency heads, and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.

6. Taste and food quality evaluation and consumer acceptance studies,
   i) If wholesome foods without additives are consumed; OR
   ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA, EPA or USDA.

WCU is not currently implementing exemptions listed at 46.104(d)(7) and 46.104(d)(8) regarding storage and conduct of research where broad consent is required.

Projects that involve FDA regulated articles are only eligible for exempt category 6.

Research must also meet the following institutional criteria:
1. Research must present no more than minimal risk to participants
2. Projects that involve direct interaction with participants must
   - Adequately inform participants about the research project and obtain prospective agreement to participate - including a description of the project, a statement that participation is voluntary, and whom to contact for questions
   - Use methods that will minimize coercion or undue influence in recruitment
   - Include provisions to protect the privacy and confidentiality of participants

Research not eligible for exemption include:
1. Projects involving prisoners as subjects
2. Projects involving the use of surveys, interview procedures, observations of public behavior, or benign behavioral interventions where participants are minors
3. Research involving deception, unless participants are prospectively notified that they are not being informed about the full purpose of the research
4. FDA regulated research

## III. Procedure

**Submission and Screening**

1. Investigators must submit a completed project package in IRBNet. Investigators may request an exempt review through the "*Request for Initial Review of Research*" application form. The requirements for submission are listed on a checklist on the first page of the application.

2. The IRB administrator receives the package in IRBNet. The project is reviewed for completeness. The IRB administrator will conduct a preliminary assessment to determine which review category is most appropriate for the project.

**Assigning Reviewers**

1. Qualified IRB members or qualified IRB staff may conduct exempt reviews. IRB staff must undergo initial training to conduct reviews.

**IRB Exempt Determination**

1. The exempt reviewer will be assigned the project in IRBNet by the IRB administrator and all materials will be shared.
2. The reviewer will conduct an in-depth review to determine that all research procedures fit into one or more the exempt categories and meet all institutional requirements for exempt research.
3. The reviewer may request additional information to determine exempt status or may require modifications to the project before granting exemption. Requests for modification to the project will be sent in writing to the investigator via IRBNet and email.

**IRB Limited Review for Exemptions 2 & 3**

1. Projects that meet the exemption criteria at 46.104(d)(2)(iii) and 46.104(d)(3)(i)(c) must undergo limited IRB review, conducted by an IRB member, to ensure the research plan makes adequate provisions to protect the privacy of subjects and maintain the confidentiality of data as described in 46.111(a)(7).
2. If the initial exempt review is conducted by IRB staff and is then determined to require limited IRB review, the IRB staff will share the project with an IRB member to finalize the review.
3. Once a project meets all the requirements of the exemption category, the reviewer will notify the IRB administrator that the project is approved. The IRB administrator will issue a record and letter in IRBNet documenting the specific exemption category.
4. Exempt project that required limited review will be listed with review type as “Expedited Review” and action as “Exempt”. Exempt projects that do not require limited review will be listed with review type as “Exempt Review” and action as “Exempt”. No expiration date will apply in either scenario.
5. If the reviewer determines that the study does not qualify for exemption, then the review will proceed as outlined in SOP 204 - Expedited Research.
6. Exempt research is not subject to annual continuing review and it is the responsibility of the investigator to close the study when research is complete by submitting a *Project Closure Form* in IRBNet.
7. Modifications to exempt projects must be submitted to the IRB, prior to implementation, to insure the study continues to meet the exempt criteria.

## IV. Responsibilities

IRB administrators, IRB members, Investigators

## V. References

45 CFR 46.104, 46.111
21 CFR 56.104

| SOP# 204.1 | TITLE: Expedited Review | Date Effective: 1/21/19<br>Last Revision Date: 12/11/18 |
|---|---|---|

## I. Purpose

This sets forth the expedited project review process and criteria for approval.

## II. Definitions

Certain categories of minimal risk research as described by the Department of Health and Human Services (DHHS) may be reviewed by the IRB using an expedited review process. Expedited review allows the IRB to approve research projects without convening the full-board, through the use of designated reviewers. The chair, or an experienced designee from the IRB, may serve as the designated reviewer. Designated reviewers hold all the authority granted to the convened IRB, except that the reviewer may not individually disapprove a project.

Designated reviewers may only approve research that meets the criteria for approval outlined in 45 CFR 46.111 and must ensure the study meets the requirement for informed consent outlined in 45 CFR 46.116 and 46.117 unless the study meets the requirements for waiver of consent or documentation. A list of all projects approved using expedited review procedures will be shared with the entire IRB prior to each convened meeting. Any IRB member may request to review the records of an expedited study.

The expedited review categories as listed by the DHHS are as follows:

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

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   a) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects the amounts drawn may not exceed 550 mL in an 8 week period and collection may not occur more frequently than 2 times per week; OR
   b) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 mL or 3 mL per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

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

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.

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).

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.

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 and investigational new drug application or investigational device exemption where categories two through eight 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

## III. Procedure

**Submission and Screening**

1. Investigators must submit a completed project package in IRBNet. Investigators must complete the "*Request for Initial Review of Research*" application form and include all applicable supplemental documents listed on the checklist on the first page of the application.

2. The IRB administrator receives the package in IRBNet and conducts an initial review for completeness as described in SOP 201. The IRB administrator conducts a preliminary assessment as to whether the project meets the criteria for expedited review.

3. Once all documents have been received and the project is ready for expedited review, the IRB Administrator publishes an *Acknowledgment Letter* in IRBNet, notifying investigators that their project has been forwarded to a reviewer.

4. The IRB administrator evaluates the project topic and selects the IRB member with the most appropriate background and expertise to evaluate the study. If additional expertise is necessary to conduct the review, the IRB administrator will assist the reviewer in finding a consultant with relevant experience.

5. If the project does not qualify for expedited review, the IRB administrator processes the application as a full board review – see SOP 205.

**Assigning Reviewers**

1. Any experienced member of the IRB may serve as an expedited reviewer. Experienced members have served on the board for at least one month and have undergone training with the IRB administrator, chair, or designated IRB mentor.

2. Any reviewer who receives a study may request that it be reassigned for any reason or may request that the project undergo full-board review.

3. Expedited reviewers may not review projects for which they may have a conflict of interest. Examples of a conflict of interest include a situation where the reviewer is a committee member on a student investigator's thesis committee, the reviewer has a romantic relationship with an investigator, or the reviewer has a financial interest in the research.

**IRB Expedited Review**

1. The expedited reviewer is assigned the project in IRBNet and granted access to all submitted materials.

2. The reviewer conducts an in-depth review to determine whether the research meets the regulatory requirements for approval described in 45 CFR 46.111.

3. The reviewer evaluates the informed consent process and documentation to be sure they meet the requirements described in 45 CFR 46.116 and 46.117. If the project involves an FDA regulated device, the informed consent process and documentation will meet the requirements in 21 CFR 50.25 and 50.27.

**Review Outcomes**

1. The expedited reviewer makes one of the following four determinations:
   a) Modifications Required: The reviewer requests additional information or requires modifications to the project before granting approval. Modifications must be directly related to the criteria for approval. Requests for modification to the project will be sent in writing to the investigator via IRBNet and email. Modifications may be requested as many times as necessary to meet the regulatory requirements.
   b) Approved: The expedited reviewer has completed their evaluation and determined that the project meets all criteria for approval. The IRB administrator issues an *Approval Letter* in IRBNet.
   c) Approved with Conditions: The expedited reviewer has completed their evaluation and determined that the project meets all criteria for approval, contingent on minor administrative modifications. The IRB administrator verifies that the investigators complete the modifications and then issues an *Approval Letter* in IRBNet.
   d) Full-Review Required: The expedited reviewer determines that the project requires review by the full-board at a convened meeting. As described in 46.115(a)(3), the IRB reviewer of the expedited application must provide a rationale for the determination that research that appears on the expedited review list presents more than minimal risk.

2. The expedited reviewer may alternatively determine that the project is eligible for exemption or does not qualify as human subjects research. The expedited reviewer will notify the IRB administrator who will issue the appropriate documentation.

3. The investigator is notified of the outcome of the review in writing. The Office of Research Administration retains all records and correspondence related to the project.

4. Expedited research approval is not required to undergo continuing review. However, the IRB may, at its discretion, choose to require continuing review for certain projects. If continuing review is required, a rationale for this decision will provided to the investigator in writing.

5. Modifications to expedited projects must be submitted to the IRB, prior to implementation. Modifications may be reviewed using the expedited review process, or may require full-board review.

## IV. Responsibilities

IRB administrators, IRB members, Investigators

## V. References

45 CFR 46.109, 46.110, 46.111, 46.115, 46.116, 46.117
21 CFR 56.110, 56.111
21 CFR 50.20, 50.25, 50.27

| SOP# 205.1 | TITLE: Full-Board Review | Date Effective: 1/21/19<br>Last Revision Date: 12/11/18 |
|---|---|---|

## I. Purpose

This sets forth the full-board review process and criteria for approval.

## II. Definitions

The IRB has the authority to approve, require modifications, or disapprove all human subjects research. The IRB reviews all research projects at a convened meeting, except where the project qualifies for expedited or exempt review.

Full board review may only be conducted when a quorum of IRB members is present. A quorum consists of a majority of the members of the IRB, and must include at least one non-scientific member. Quorum must be met prior to initiating any discussion of a research proposal and must be maintained through the entire discussion and voting. Maintenance of quorum must be documented in meeting minutes. All members present at a meeting have full voting rights, unless they have recused themselves due to a conflict of interest. Meetings will be held in person, but members may teleconference into the meeting if necessary.

The IRB meets once a month throughout the academic year. The IRB does not perform full-board reviews during the summer months (May – July). Investigators must submit proposals two weeks prior to a scheduled meeting. Meeting dates are published at the beginning of the semester on the WCU IRB website.

## III. Procedure

**Submission and Screening**

1. Investigators must submit a completed project package in IRBNet. Investigators must complete the "*Request for Initial Review of Research"* application form and include all applicable supplemental documents listed on the checklist on the first page of the application.

2. The IRB administrator receives the package in IRBNet and conducts and initial review for completeness as described in SOP 201. If the project does not meet the criteria for expedited or exempt review, the project is assigned to the next convened meeting with available capacity to review the application.

3. After all documents have been received and the project is ready for full-board review, the IRB administrator will publish an *Acknowledgment Letter* in IRBNet, notifying investigators that their project has been assigned for full board review and the planned review date.

4. If the project meets the criteria for one of the expedited review categories, but the IRB determines the project requires full-board review, the rationale describing why the project involves more than minimal risk must be documented.

5. The IRB administrator screens the project to determine whether additional expertise may be required to adequately evaluate the project. If additional expertise is needed, the IRB administrator coordinates with the chair in identifying an appropriate consultant. The consultant is granted access to the project materials and asked to evaluate the study. Consultants do not need to attend the meeting, but their comments must be shared with all IRB members.

**Assigning Reviewers**

1. The chair of IRB serves as the primary reviewer for the project. They are granted access to the project at least two weeks before the scheduled meeting. The primary reviewer is responsible for conducting an in-depth review and presenting an overview of the project to the other members at the convened meeting. The IRB chair may delegate the vice chair - or other designee - as the primary reviewer for full board reviews. This may occur when the IRB chair has a conflict of interest, is unavailable for the meeting, or if several full board reviews are planned for the same meeting.

2. Each IRB member is granted reviewer access to the project at least one week before the scheduled review and has access to all submitted documents. All members should review the package in enough depth to be able to discuss the project at the meeting.

**IRB Full-board Review**

1. The primary reviewer briefly summarizes the project and identifies any initial items for discussion.

2. All IRB members have the opportunity to discuss each project on the agenda. The board discusses issues related to the approval criteria (45 CFR 46.111) and determines the risk level. The board also evaluates any additional protocol-specific criteria to determine whether the project meets the federal requirements (e.g. waiver of informed consent).

3. The IRB determines the approval period. Projects must undergo continuing review at least annually, unless the project has progressed to a point that it involves only data analysis (may include identifiable data) or accessing clinical data that a subject undergoes as part of normal clinical care. The board must provide justification if the approval period will be shorter than a year.

4. After all controversial issues have been discussed, an IRB member motions to vote on one of the four review outcomes listed below. Each IRB member casts one of the following votes – yes, no, abstention. The outcome must receive a "yes" vote from the majority of the members present to pass. All votes (including abstentions and recusals) are recorded in the meeting minutes.

**Review Outcomes**

1. The IRB makes one of the following four determinations:
   a) Approved: The study is approved as submitted. The IRB administrator issues an *Approval Letter* in IRBNet. The start of the approval period is the date of the convened IRB meeting.
   b) Approved with Conditions: The study requires minor changes or clarification as detailed in the minutes. These items are communicated to the investigators in writing within 10 days of the meeting. A designated reviewer or subcommittee grants final approval once verifying the investigator has satisfactorily addressed the comments. Once the designated reviewer grants

approval, the IRB administrator issues an *Approval Letter* in IRBNet. The start of the approval period will be the date of the final approval.

c) Deferred: The study requires major changes or clarification before the IRB can make a determination on the study, as detailed in the minutes. These items are communicated to the investigators in writing within 10 days of the meeting. The investigator responses are evaluated by the convened IRB at a subsequent meeting and a subsequent outcome determined.

d) Disapproved: The committee disapproves the project for reasons outlined in the minutes. This decision and the justification is communicated to the investigators in writing. The investigator has the option to appeal the decision with the IRB. Appeals and re-submissions are evaluated by the convened committee at a subsequent meeting.

2. The investigator is notified of the outcome of the review in writing via formal letter. The letter will specifies the approval period for the project. The Office of Research Administration retains all records and correspondence related to the project.

3. Modifications to projects must be submitted to the IRB, prior to implementation. Modifications may be reviewed using the expedited review process (minor changes) or full-board review.

## IV. Responsibilities

IRB administrators, IRB members, Investigators

## V. References

45 CFR 46
21 CFR 56
21 CFR 50

| SOP# 206.1 | TITLE: Continuing Review | Date Effective: 1/21/19<br>Last Revision Date: 12/11/18 |
|---|---|---|

## I. Purpose

This sets forth the continuing review process and the calculation of project expiration dates.

## II. Definitions

Research approved under full-board review is subject to continuing IRB review at least annually (or more frequently if specified by the IRB based on the degree of risk) until the research involves only data analysis of information (including identifiable information) or accessing clinical data from procedures that the subjects would undergo as part of clinical care. The IRB may require continuing review for projects subject to expedited review but must provide a rationale for this requirement at time of approval.

Prior to the expiration date, investigators must submit a continuing request for review. Once the project has expired, all activity must cease. If there is a lapse in approval while the continuing review is conducted, the investigator must cease activity, unless the IRB has determined that it is in the best interest of the participants for research activities to continue due to an overriding safety or ethical concern. Research activity conducted on an expired protocol constitutes serious non-compliance and is handled in compliance with SOP #302.

Continuing review may be conducted using expedited or full-board review procedures. The IRB may conduct continuing review using expedited procedures, for projects initially reviewed by the full-board under the following circumstances:

1. The project is closed to enrollment of new participants, all participants have completed research related interventions, and continuing interaction with participants is limited to long term follow-up; OR
2. The project is still active, but no additional risks have been identified

Continuing review must be conducted at least annually. At the discretion of the IRB, projects may require review at more frequent intervals. Reasons for more frequent review may include, but are not limited to:

1. The project presents a significant risk to participants without the possibility of a direct benefit to the participant.
2. The project involves a vulnerable population likely to be at risk of coercion.
3. A history of serious, continuing non-compliance by the principal investigator.

## III. Procedure

**Submission and Screening**

1. At time of initial submission approval, the investigator receives a letter documenting the approval and expiration dates. IRBNet issues project expiration reminder alerts to the investigator 60, 30, and 0 days prior to the project expiration date. It is the investigator's responsibility to submit the "*Request for Continuing Review"* form prior to the project expiration date.

2. If the "*Request for Continuing Review"* form is received more than 30 days after the project expiration date, the investigator will be required to re-submit their project as a new project. Once the project expires, all activity on the project must cease immediately.

3. Investigators must submit the "*Request for Continuing Review"* form as a subsequent package within their initial project submission in IRBNet.

4. The IRB administrator receives the package in IRBNet and conducts an initial review for completeness as described in SOP #202. The IRB administrator determines whether the continuing review request meets the criteria for expedited or full-board review.

5. After all documents have been received and the project is ready for review, the IRB Administrator publishes an *Acknowledgment Letter* in IRBNet, notifying investigators that their project has been assigned for review. Depending on the review type, Continuing Review will be conducted in accordance with either SOP #204 or SOP #205.

## IV. Responsibilities

IRB administrators, IRB members, Investigators

## V. References

45 CFR 46.109(e), 46.109(f)

| SOP# 207.1 | TITLE: Modifications | Date Effective: 1/21/19<br>Last Revision Date: 12/11/18 |
|---|---|---|

## I. Purpose

This sets forth the process for conducting review of modifications to previously approved or determined exempt projects.

## II. Definitions

Modifications to any previously approved or determined exempt projects must be submitted to the IRB prior to implementation, unless there is an immediate hazard to participants. Modifications include any change to the project, including administrative changes such as research personnel changes.

Minor modifications to projects reviewed by the full-board or modifications that involve no more than minimal risk may be reviewed utilizing expedited review procedures. All other modifications must be reviewed by the convened board.

Failure to submit a modification request prior to implementing a change to an approved or a determined exempt project will constitute non-compliance and will be handled in accordance with SOP #302.

## III. Procedure

**Submission and Screening**

1. Investigators must submit subsequent modification documents within their initial project as a new package in IRBNet. Investigators must complete the "*Request for Modification*" application form and include any new or updated documents referenced in the application.

2. The IRB administrator receives the package in IRBNet and conducts an initial review for completeness as described in SOP #202.

3. The IRB administrator and IRB have the authority to determine that a modification request constitutes a change in scope or the addition of major new activities such that a new application is required rather than a modification to an existing application.

4. If the modification is to a previously determined exempt project, the IRB administrator determines whether the modification alters the exempt determination. If it does not, then the IRB administrator issues an exempt determination letter. If the modification causes the project to no longer qualify for exemption, the IRB Administrator notifies the investigators and continues processing the project as a non-exempt review. The entire project must undergo either expedited or full-board review.

5. After all documents are received and the project is ready for review, the IRB administrator publishes an *Acknowledgment Letter* in IRBNet, notifying investigators that their project has been assigned for

review. Depending on content of the modification request, the project is assigned for review in accordance with either SOP #204 or SOP #205.

## IV. Responsibilities

IRB administrators, IRB members, Investigators

## V. References

45 CFR 46.109

| SOP# 301.1 | TITLE: Unanticipated Problems and Adverse Events | Date Effective: 1/21/19<br>Last Revision Date: 12/11/18 |
|---|---|---|

## I. Purpose

This procedure sets forth the process for reporting, reviewing, and correcting unanticipated problems, protocol deviations, protocol violations and adverse events.

## II. Definitions

**Unanticipated Problem** is defined as any 1) unexpected (in terms of nature, severity, or frequency) problem or event and 2) possibly related to the participation in research, given the research procedures described in the IRB-approved protocol and the characteristics of the subject population being studied. Unanticipated problems may or may not place subjects at an increased risk of harm. An unanticipated problem may include subject complaints, protocol deviations or violations, as defined below.

**Protocol deviation** is defined as an inadvertent act in which the approved IRB protocol is not followed. Examples include the accidental loss of consent form or study materials with identifiable information, or an accidental misread of a laboratory value leading to the erroneous inclusion of a participant.

**Protocol violation** is defined as an intentional act in which the approved IRB protocol is not followed. Examples include implementing changes to the protocol without first obtaining IRB approval, enrolling subjects after study expiration, or enrolling subjects who do not meet inclusion/exclusion criteria. A lapse in IRB approval must always be reported to the IRB as a protocol violation.

**Adverse Event** is defined as an event either anticipated or unanticipated that result in direct or actual physical, psychological, economic, or social harm to the participants. Examples include the death of a research participant, a participant experiencing a negative reaction after participating in the research intervention, a change made to the research protocol to immediately eliminate a hazard to participants.

For the purposes of this SOP, any of the four items identified above will be referred to as an event.

## III. Procedure

**Investigator Reporting Requirements and Submission**

1. Any event must be reported to the IRB within 10 business days of the Principal Investigator (PI) becoming aware of the event.
2. An unanticipated study-related death must be reported to the IRB within 24 hours of the occurrence of the event.
3. The PI must submit a written report of the event using either the "*Protocol Deviation/Violation Event"* form or the "*Adverse Event"* form, depending on the circumstances. The PI should submit this form within their project in IRBNet as a new package.

**Review of Events**

1. The IRB administrator receives the project in IRBNet and conducts an initial assessment of the form to make sure all fields are completed and the event is adequately described.
2. The Director of the Office of Research Administration (ORA), the Research Compliance Officer (RCO), and the IRB chair review the form and assess whether the event increases the risks to subjects or adversely affects their rights, welfare or safety, whether there is an ongoing risk of harm to participants, and how any newly identified risks may be minimized.
3. Based on their assessment, they may decide that no additional action is needed, minor corrective actions are needed, or, the issue should be referred to the convened IRB. If the event is referred to the full-board, the PI will be notified in writing within 7 days of the referral.
4. If they determine minor corrective actions are necessary, the RCO and the IRB chair work with the PI to develop an appropriate plan and determine whether any modifications to the study are needed.
5. If the issue is presented to the full-board, the IRB votes to determine whether further action is necessary. Possible actions include but are not limited to:
    a. Acknowledging the event with no further action needed.
    b. Requesting further information from the research team.
    c. Opening a non-compliance inquiry.
    d. Requiring monitoring of research procedures - including informed consent - by IRB members or ORA staff.
    e. Increasing frequency of the continuing review cycle.
    f. Requiring additional education and training for research personnel.
    g. Requiring modifications to protocol and/or informed consent process.
    h. Requiring notification of current participants of the event if the information may affect their willingness to continue participation.
    i. Suspending the study.
    j. Terminating the study.
6. If the event represents a serious risk to the participants or indicates a pattern of increasing risk to participants, the Director, RCO, and IRB chair may determine that a Non-Compliance Inquiry is appropriate without a meeting of the convened board. If an inquiry is initiated, it will follow the inquiry procedures outlined in SOP #302.
7. The RCO and chair communicates the IRB-approved actions to the PI in writing within 14 business days the meeting and notifies them of any additional information or changes needed. If modifications to the study are required, the investigator submits a modification request as described in SOP #207.
8. The PI has 10 days to appeal the IRB actions in writing, if they so choose. The IRB reviews the appeal and decides whether to reject the appeal or to re-open the inquiry.
9. The RCO and Director of ORA will assist the IRB in reporting the event to external sponsors and/or regulatory agencies, if applicable to the study.

## IV. Responsibilities

IRB administrators, IRB members, Investigators

## V. References

45 CFR 46.108(a)(4)
21 CFR 56.108(b)

| SOP# 302.1 | TITLE: Non-Compliance | Date Effective: 1/21/19<br>Last Revision Date: 12/11/18 |
|---|---|---|

## I. Purpose

This procedure sets forth the definition of non-compliance and the IRB process for assessing non-compliance and issuing corrective actions

## II. Definitions

All university personnel conducting research involving human subjects are expected to comply with the highest standards of ethical and professional conduct in accordance with federal regulations and institutional policies and procedures. Any member of the research team (i.e., faculty, students, staff, or anyone conducting research reviewed by Western Carolina University's IRB) may be subject to allegations or inquiries into non-compliance. Categorization of type of non-compliance will be determined by the IRB based on the totality of circumstances surrounding the event.

**Non-Compliance** is defined as a failure to adhere to laws, regulations, policies, and procedures during the course of human subjects research. Noncompliance may range from relatively minor, administrative violations to serious violations that pose risks to subjects or violate the subject's rights and/or welfare.

Non-compliance includes, but is not limited to:

- Conducting research under an expired IRB protocol
- Initiating modifications to the protocol without IRB approval
- Enrollment of participants prior to IRB approval

**Serious Non-Compliance** is defined as a failure to adhere to laws, regulations, policies, and procedures involving human subjects research in such a manner that involves substantive harm or risk of harm to the rights, safety, and welfare of human subjects.

Serious non-compliance may include, but is not limited to:

- Failure to obtain informed consent
- Failure to report adverse events or safety concerns to the IRB
- Purposeful disclosure of confidential information outside the research team

**Continuing Non-Compliance** is defined as a repeated failure to adhere to the laws, regulations, policies, and procedures governing human subjects research.

## IV. Procedure

**Allegations of Non-Compliance**

1. Reports or complaints of non-compliance may be submitted to the IRB or to the Office of Research Administration (ORA) verbally or in writing. Reports may arise internally (e.g., from faculty, staff, investigator self-reports, ORA staff, IRB members, etc) or from external constituents (e.g., participants, regulators). The ORA/IRB will maintain the confidentiality of submitter to the fullest extent possible.

**Assessment of Allegations**

1. The Director of ORA and the Research Compliance Officer (RCO) will review the allegation to determine whether there are any supporting documents or statements.
2. If the allegation is determined to be unsubstantiated, the ORA Director and RCO may consult with the IRB chair or their designee. They may decide that no additional action is needed, further inquiry is necessary, or the issue should be presented to the convened IRB.
3. If the allegation is determined not to involve non-compliance, no further action will be taken.
4. If the allegation is substantiated but only involves minor or administrative issues, the RCO will contact the investigator to resolve the concern. The ORA Director and RCO will notify the IRB chair of the report. They may decide that no additional action is needed, further inquiry is necessary, or the issue should be presented to the convened IRB.
5. If the allegation is substantiated and may involve serious or continuing non-compliance the IRB chair will be notified and an inquiry may proceed. If the allegation involves an increased risk of or actual serious or unexpected harm to a participant, then the chair may immediately suspend the project until the inquiry is complete (as in SOP #303 Suspension and Termination).
6. At the completion of the assessment, and when it is appropriate, the RCO will communicate, the IRB chair's decision to the complainant, through the complainant's chosen mode of communication.

**Inquiry into Non-Compliance**

1. The ORA Director, RCO, and IRB chair make a determination that an inquiry is necessary based on the nature and seriousness of the complaint.
2. An inquiry may also be initiated by the IRB chair in response to *Protocol Deviations/Violation Event* or *Adverse Event* reports by investigators in situations where multiple reports involving immediate risks to participants have been submitted to the IRB, or at the Chair's discretion.
3. The IRB Chair notifies the Principal Investigator of the inquiry in writing and conveys the nature of the complaint.
4. The IRB chair designates a sub-committee of at least three individuals, consisting of the RCO, IRB members, and non-members as appropriate to constitute the appropriate expertise to assess the complaint.
5. The sub-committee has the ability to review any of the following:
    a. Protocol(s) specific to the complaint.
    b. Review of any sponsor audits, if available.
    c. Review of relevant study records and documents (i.e. consent forms, case reports, data records, etc.).
    d. Conduct interviews with research personnel.
6. If the PI requests or is requested to be present at a sub-committee meeting to be interviewed about the alleged non-compliance, they may be accompanied by a faculty representative, legal counsel, or another member of their department. The role of the individual is to provide support to the PI, they may not engage in the discussion between the IRB and the PI.
7. The sub-committee creates a written report of its findings and recommendations of corrective and/or disciplinary actions.

8. The results of the inquiry are reviewed at a convened IRB meeting where all IRB members will have access to relevant protocol documents and the inquiry report. The sub-committee may provide a report at the convened meeting.
9. If the inquiry suspects research misconduct, the findings are shared with the Research Integrity Officer and further investigation will follow University Policy #56: Ethics in Research.
10. If the inquiry substantiates a finding of serious and/or continuing non-compliance, the IRB votes to determine corrective action(s). Possible corrective actions include, but are not limited to:
    a. Increased monitoring of research procedures including informed consent, by IRB members or ORA staff.
    b. Increased frequency of the continuing review cycle.
    c. Requiring additional education and training for research personnel.
    d. Requiring modifications to protocol or to the consent form.
    e. Notifying current participants of non-compliance if the information may affect their willingness to continue participation.
    f. Requiring re-consent of participants.
    g. Destruction of data.
    h. Preventing release of data to contribute to generalizable knowledge.
    i. Suspension of the study.
    j. Termination of the study.
11. The IRB notifies the Principal Investigator in writing of the determination and basis for determination. The Principal Investigator must implement the corrective actions within the specified time frame determined by the IRB. Failure to fully implement the corrective actions within the specific time frame results in the IRB suspending or terminating IRB approval for the specific study.
12. The PI has 10 days to appeal the decision in writing, if they so choose. The IRB reviews the appeal and decide whether to reject the appeal or to re-open the inquiry.
13. The RCO and Director of ORA assists the IRB in reporting any non-compliance determinations to external sponsors and/or regulatory agencies, if applicable to the study.
14. The IRB Chair is responsible for informing the investigator's department head, dean, and the institutional official of the corrective actions recommended by the committee.

## V. Responsibilities

IRB administrators, IRB members, Investigators

## VI. References

45 CFR 46.103(b)(5), 46.113

| SOP# 303.1 | TITLE: Suspension and Termination | Date Effective: 1/21/19<br>Last Revision Date: 12/11/18 |
|---|---|---|

## I. Purpose

This sets for the process by which the IRB may suspend or terminate an approved project.

## II. Definitions

The IRB has the authority to suspend or terminate any approved research protocol that is not conducted in accordance with IRB requirements or has involved serious or unexpected harm to participants.

**Suspension** is a temporary halt in any ongoing research activities including enrollment of new participants or activities involving previously enrolled participants.

**Termination** is a permanent halt in all ongoing research activities and closure of the project.

## III. Procedure

1. The convened IRB may vote to suspend or terminate a previously approved project if they become aware (via either internal or external report) that a project is not conducted in accordance with IRB requirements. The decision and rationale is documented in the meeting minutes.
2. If the IRB chair becomes aware (via either internal or external report) that a project has involved serious or unexpected harm to a participant, they may immediately suspend the project until the convened IRB is able to meet.
3. If the IRB chair or the convened IRB suspend or terminate a project, the PI must be promptly informed in writing with a statement of the reasons for the suspension or termination.
4. The PI must notify enrolled participants of the suspension or termination of the study and create an appropriate procedure for withdrawal of subjects.
5. The RCO and Director of ORA assists the IRB in reporting any suspension or termination decisions to external sponsors and/or regulatory agencies, if applicable to the study.
6. The IRB Chair is responsible for informing the investigator's department head, dean, and the institutional official of action and the reasons for suspension or termination.
7. If the study is suspended or terminated, the IRB may require the PI take additional actions, including but not limited to:
    - Transferring of participants to another study.
    - Notifying current or former participants.
    - Arranging for care of participants.
    - Requiring follow-up with participants for safety reasons.
8. A suspended study may be re-instated by a vote of the convened board after the PI has provided in writing evidence of the steps taken to rectify the issues that let to suspension.

## V. Responsibilities

IRB administrators, IRB members, Investigators

## VI. References

45 CFR 46.113