1. PURPOSE

The IRB, through its review of new protocols and its oversight of ongoing protocols, protects the safety of human research subjects by ensuring that, in general, the criteria under 45 CFR 46 and 21 CFR 56 are met found on hhs.gov. This process applies to all human subject research except for research that has been determined to be exempt from these codes of federal regulation under 45 CFR 46.104 (see IRB Policy, "Exempt Research").

2. WHEN IS IRB REVIEW REQUIRED?

2.1. To determine whether the proposed activity requires review by Creighton University IRB, answer the following three questions:

2.1.1. Is the proposed activity research?

2.1.2. Does it involve human subjects?

2.1.3. Will it be authorized and conducted under the jurisdiction of Creighton University?

3. IS THE PROPOSED ACTIVITY RESEARCH?

Research means a systematic investigation including research development, testing and evaluation designed to develop or contribute to generalizable knowledge. If, according to this definition, the proposed activity is not research, IRB review is not required. [45 CFR 46.102(l)]

4. DOES THE PROPOSED RESEARCH INVOLVE HUMAN SUBJECTS?

4.1. Investigators, with the assistance of the IRB administrative staff, shall determine whether their proposed research will involve human subjects. The regulations define *human subject* as a "living individual about whom an investigator (whether professional or student) conducting research;

Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens" [45 CFR 46.102(e)(1)(i)(ii)].

The regulations extend to the use of human organs, tissues, and body fluids from individually identifiable human subjects, as well as to graphic, interventional, written, or recorded information derived from individually identifiable human subjects. The use of autopsy materials is governed by applicable state and local laws and is not directly regulated by the DHHS or the FDA regulations. Investigators may use the following tools to aid in their determination:

4.1.1. IRB Document, "Definitions for Human Subjects Research"

4.1.2. IRB Document, "Human Subject Regulation Decision Charts"

4.1.3. IRB Document, "Guidelines for Quality Assurance Projects vs. Research"

4.2. If the research does not involve human subjects, IRB review is not required. If the research does involve human subjects, IRB review is required. If it is not clear whether the research involves human subjects, the IRB administrative staff (irb@creighton.edu) should be contacted for assistance.

4.3. If the Principal Investigator requests a letter stating that a project does not require IRB oversight, the Principal Investigator shall complete the online application for Not Human Subject review and submit a copy of the full protocol via the electronic system. The IRB administrative staff shall review the protocol and release a determination letter.

5. WHICH TYPE OF IRB REVIEW IS REQUIRED?

5.1. Projects that involve human subjects in entirely noninvasive activities, such as educational surveys, may be eligible for exempt status review (see IRB Policy, "Exempt Research"). Projects that involve human subjects only in minimally invasive procedures, involving minor risk, may be eligible for expedited review (see IRB Policy, "Expedited Categories"). In all other cases, research projects that involve human subjects, require review at an IRB convened meeting; this includes all prisoner research (unless it is existing data review only).

6. SUBMISSION REQUIREMENTS AND REVIEW PROCESS

6.1. After the required review type has been determined for the project, the Principal Investigator shall prepare the submission to the IRB accordingly, as described in the electronic system.

7. GUIDANCE NOTES FOR RESEARCHERS

7.1. Failure to follow these requirements can result in delay of review and approval by the IRB.

7.2. Throughout the review process and subsequent administration of the project, Principal Investigators and investigators shall comply with all IRB decisions, conditions and requirements. If revisions in the proposed protocol, application, or informed consent document are required by the IRB, the Principal Investigator or designee shall submit them to the IRB for approval before the research project can begin.

7.3. Undergraduate student Investigators shall not be listed as the Principal Investigator on any project. The Principal Investigator on undergraduate student projects shall be the student's advisor or professor for the research course. Graduate students may be listed as the Principal Investigator; however, their faculty advisor must be listed on the project and provide approval of the project in the electronic system. Residents, fellows, postdoctoral students and graduate students shall be allowed to act as Principal Investigators, but a faculty member shall be listed on the project.

7.4. If outside investigators are used on a study for which the Creighton University IRB has oversight, the IRB requires that they submit curricula vitae and completion of training requirements of their home institution to the IRB upon submission of the project.

8. SUBMISSION REQUIREMENTS

8.1. If the project requires IRB review (either expedited or review at a convened meeting), Principal Investigators or designee shall submit the following information, as applicable in the electronic system, to include the online application for IRB review. The specific instructions are listed on the final page of the online application after completion.

8.1.1. Protocol or study design, including the purpose of the research, the scientific or scholarly rationale, procedures to be performed, a description of the procedures being performed already for diagnostic or treatment purposes, the risks and potential benefits of the research to subjects and a list of references

8.1.2. Included in the online application in the electronic system, investigators must address all questions related to data storage and security to ensure the privacy and security rights of study subjects are protected and, if applicable, the confidential proprietary study information as well

8.1.3. Full grant applications

8.1.4. Informed consent document

8.1.5. Information script (for projects that have documentation of consent waived)

8.1.6. Assent document(s) (ages 7-11, ages 12-18)

8.1.7. Parental permission document

8.1.8. Genetic testing consent document(s)

8.1.9. HIPAA Authorization

8.1.10. Questionnaires/surveys

8.1.11. Interview questions

8.1.12. Diary cards

8.1.13. Investigator's Brochure

8.1.14. Any applicable checklists (IND Investigator Decision Checklist / Medical Devices Investigator Checklist)

8.1.15. Signed 1572 form or Investigator Agreement (for pharmaceutical agents or devices)

8.1.15.1. For applications for studies that require oversight by the U.S. Food and Drug Administration, the reviewer is provided with the submission. The Principal Investigator is required to provide a current curriculum vitae

8.1.16. Recruitment materials, if any

8.1.17. Any other documents that will be given to research subjects

8.1.18. If the research project being submitted has been previously reviewed by a local IRB other than Creighton University IRB, a copy of the approval or disapproval letter from the IRB of oversight

8.1.19. A copy of any other documents/or items (e.g., description of items to be given to subject, such as diary cards, small gifts, etc.)

8.1.20. If the project is conducted at a site other than Creighton University and the site does not have an IRB; a contract and/or letter of agreement/approval from the cooperative organization

8.1.21. If the project is a clinical trial in which a contract is required with a third-party sponsor, the contract must be reviewed and approved through the General Counsel's office. If the contract is missing any requirements listed in the AAHRPP elements (the accreditation body of Creighton University IRB) and the project is prospective, requires consent and is deemed more than minimal risk, the Office of General Counsel will attempt negotiations with the third-party sponsor to resolve any discrepancies or conflicts regarding AAHRPP elements. If an agreement between Creighton University and the third-party sponsor cannot be obtained following negotiations, the Office of General Counsel will consult with the Institutional Official, or his/her designee, for a final determination on the contract in relation to the research protocol. The General Counsel's office will inform the IRB administrative staff in a timely manner regarding any finalized contracts that deviate from the University required language consistent with the AAHRPP elements.

9. REVIEW PROCESS

Once all study related materials are submitted and the training requirements are complete, the project shall be scheduled for the next available meeting if necessary (the current meeting schedule is posted on the IRB website).

10. PRESENTING AT THE IRB MEETING

At the IRB meeting, the Principal Investigator or an investigator listed on the application, shall be asked to explain the purpose for, risks of, and alternatives to the proposed research, including subject selection and exclusion criteria. IRB members then shall be encouraged to ask clarifying questions concerning the protocol, application and consent process.

10.1. For studies involving a drug, the person presenting shall be licensed to prescribe or dispense the product (such as a medical doctor, an advanced practice nurse or a pharmacist).

10.2. For studies involving a medical device, the person presenting shall be licensed or certified to use the device.

11. IRB REVIEW RESPONSIBILITIES

The IRB shall review and have the authority to approve, require modification to, table, or disapprove all research activities. Each Board member shall study the protocol under review to ensure that no unnecessary or unacceptable hazards are present and that adequate safeguards are provided for the research subjects (see IRB Policy, "Data Safety Monitoring Plans"). IRB members shall have access to all documents relating to the research protocol, including all information provided by the Principal Investigator and the pharmaceutical company or device manufacturer, as applicable (see IRB Policy, "Duties of IRB Members"). The Chair or designee shall review the full grant application, the Investigator's Brochure, medical device information, and other relevant documents.

12. IRB ACTION

IRB members then shall discuss the project and make determinations regarding the category of risk, risk and benefit issues and whether informed consent procedures are adequate. During convened meetings, this shall be done by the following process:

12.1. All persons with a conflict of interest shall leave the room before

discussion and a vote is called.

12.2. A Board member shall make a motion to approve at a defined risk. Another Board member shall second the motion (if a motion is not made and/or there is no second, the motion dies without a vote).

12.3. Criteria for approval then shall be discussed (see IRB Policy, "Duties of IRB Members").

12.4. After a consensus is reached, or a member calls a motion to close debate as per Robert's Rules of Order, a vote shall be taken (if debate is closed by a motion, a two-thirds majority is required to approve).

12.5. For the motion to pass, it shall be agreed upon by a majority of the voting members present (unless those who recuse are replaced by appropriate alternates, members who must recuse themselves shall not be counted).

12.6. The IRB shall vote on one of the following actions:

12.6.1. **Approval** indicates the protocol or action has been approved as submitted, requiring no changes, additions, or modifications. The IRB shall provide written notice to the Principal Investigator or designee of its approval, along with the approved informed consent document with the IRB's date stamp noted on each page. The Principal Investigator may begin his/her research project upon receipt of the IRB's written approval. All projects shall be approved for an interval as specified by the IRB

12.6.2. **Conditional Approval/Modifications Required** indicates that only minor revisions or simple concurrence to the required elements under 45 CFR 46.111 and 21 CFR 56.111 is required in the submission. The IRB shall provide written notice to the Principal Investigator of its conditional approval, identifying the specific areas of revisions required. The Principal Investigator shall provide the IRB with a revised protocol and/or informed consent document incorporating the revisions or concurrence as requested. When the required revisions have been completed by the Principal Investigator, the IRB Chair or designee may subsequently approve a revised conditional approval/modifications required submission on behalf of the IRB under an expedited review process. The notice of final approval shall include a copy of the approved informed consent document with the IRB's date stamp on each page. The Principal

Investigator shall not begin his/her research project until he/she has received final written approval from the IRB

12.6.2.1. If the revisions requested by the IRB are not received within 60 days after the date of the IRB notification, a warning notice shall be communicated to the Principal Investigator. The warning notice notifies the Principal Investigator that s/he has 15 business days to respond or the project shall be removed from consideration

12.6.2.2. The Principal Investigator may request from the IRB administrative staff an extension to the 60-day submission deadline for revisions to conditional approvals. These extensions are granted on a case-by-case basis

12.6.2.3. Minor revisions are defined as changes requested by the IRB that are administrative, editorial or proscriptive (i.e., Principal Investigator is given specific text or parameters for addressing the changes); or simple concurrence (i.e., Yes or No answers)

12.6.3. **Tabled** indicates that the IRB has requested substantive revisions regarding the protocol or informed consent documents that are directly related to the requirements under 45 CFR 46 and 21 CFR 56. The IRB may also table a project if it determines it needs further expertise to evaluate the project and may request an outside consultant not affiliated with the study to answer any questions the IRB may have. The IRB Chair or designee shall contact the appropriate consultant and consult with him/her or invite him/her to a subsequent meeting. The IRB shall provide written notice to the Principal Investigator of the specific areas requiring revisions. A subsequent review at a convened meeting of the complete protocol with the revised material is necessary to determine approval. The Principal Investigator shall respond in writing specifically to each IRB comment point by point. Additionally, the Principal Investigator shall provide the IRB with a revised protocol and/or informed consent document incorporating the revisions as requested. The Principal Investigator may or may not be required to re-present his/her project; this shall be determined by the IRB at the time of the discussion

12.6.3.1. If the revisions requested by the IRB are not received within 60 days after the date of the IRB notification, a warning shall be sent to the Principal Investigator notifying her/him that s/he has 15

business days to respond or the project shall be removed from consideration

12.6.3.2. The Principal Investigator may submit a written request to the IRB for an extension to the 60-day submission deadline for revisions to conditional approvals. These extensions are granted on a case-by-case basis

12.6.3.3. Substantive revisions are defined as changes requested by a convened IRB that relate directly to the criteria for IRB approval and require clarification from the Principal Investigator (e.g., clarifications, explanations, additional information, changes in risk/benefit, external committee approval). **All substantive revisions must be re-reviewed at a convened IRB meeting

12.6.3. **Disapproval** indicates the IRB has found major flaws in the design of the research or other problems so great it determines the study must be redesigned to address the issues. Protocols shall not be disapproved by the expedited process; they shall be reviewed by a convened full board review. If the IRB disapproves a research protocol, the IRB shall provide to the Principal Investigator, in writing, the reasons for the IRB decision and an opportunity for the Principal Investigator to appeal the decision. The appeal process consists of resubmission of the project to the IRB, with or without modification, accompanied by a letter from the Principal Investigator indicating why s/he feels the project should be considered again by the IRB

12.6.4. All actions taken shall be recorded in the minutes. Minutes of the IRB meetings shall be forwarded to IRB members and may be forwarded to other interested parties on request. Specific letters of instruction based on the IRB review shall be sent to each Principal Investigator

13. IRB CONTINUING REVIEW

IRB review of a Progress Report for Continuing Review follows the same process as review of the initial application for Full Board studies and/or FDA regulated studies.

13.1 Unless the IRB determines otherwise, continuing review is not required for projects approved under an expedited category after implementation of the

revised common rule (January 21, 2019) or projects that have progressed to data analysis unless FDA regulated. Instead, an Annual Review (by means of an Annual, Continuing, or Project Termination Form) will be completed by the Principal Investigator or designee and submitted to the IRB to ensure compliance. The IRB administrative staff shall review the Annual Review submission.

14. SUBMITTING A PROJECT PREVIOUSLY REVIEWED BY ONE IRB TO A DIFFERENT IRB

14.1. **Previously Disapproved by Creighton University IRB**
If Creighton University IRB disapproves a research project, subsequently submitted to one or more other IRBs, Creighton University IRB disapproval shall be made known to the other IRB(s). If Creighton University IRB disapproves a project, it shall not be conducted at any Creighton University site.

14.2. **Previously Reviewed by an IRB other than Creighton University IRB**
If the Principal Investigator is submitting a protocol to Creighton University IRB that has been reviewed by one or more local IRBs, Creighton University IRB shall be provided with copies of the approval or disapproval letter(s) along with the Principal Investigator's initial submission.

15. IRB FEE POLICY

Creighton University IRB's overall goal is to support human subjects' research at Creighton University by providing the best possible service and protection to its subjects, to its faculty, and to its public and private sponsors. To support this goal and help the IRB meet increasing demands of human subject regulations, the IRB shall charge a fee for review services (see IRB Fee Schedule).

16. OFFICIALS OF THE UNIVERSITY REVIEW OPTION

Officials of Creighton University may further review and approve or disapprove research projects previously approved by the IRB, with the following exception: the Officials shall not approve any research project that has been previously disapproved or has not yet been approved by the IRB.

17. IRB SUSPENSION OR TERMINATION OF A PROTOCOL

See IRB Policy, "Suspensions and Terminations."