an expedited review. If the study does not meet the criteria for an expedited review, the PI submits a full review application and requests that the ORRC schedule a full review.

- IRB records for all exempt determinations include the citation of the specific category justifying the exemption.

- When the IRB has certified a research study as exempt, the IRB does not require CRs. The exemption approval is in effect for a six-year period. Approximately three months prior to the end of the six-year period, the Investigator must submit a new exemption application if the project is to continue.

- If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit the concerns to the IRB in writing, including a justification for changing the IRB decision. The PI may send the request to the reviewer and/or the IRB Chair or Vice Chair for final resolution. If the investigator is still dissatisfied with IRB decision, he/she may send the study to the full IRB for review.

19.8 REFERENCES

45 CFR 46.101(b)
45 CFR 46.102(i) 21
CFR 56.104(d)

20.0 INITIAL FULL REVIEW by THE INSTITUTIONAL REVIEW BOARD (IRB)

20.1 OBJECTIVE

To describe the policy and procedures for initial full review by the Institutional Review Board (IRB).

20.2 GENERAL DESCRIPTION

The IRB conducts initial review for non-exempt research at convened meetings unless the research is eligible for expedited initial review. See the procedures for conducting a convened meeting, the definition of *quorum*, and the requirements for conducting a full review meeting in the Conduct of IRB Meeting SOPP. Investigators must submit studies that do not meet the federally mandated criteria for exempt or expedited initial review for full review (See Exempt and Expedited Initial Review SOPPs). The IRB only approves research that meets the federal criteria for approval as specified in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. Also, during initial full review the IRB reviews the informed consent process and documentation as specified in the Informed Consent SOPP.

20.3 RESPONSIBILITY

Execution of SOPP: IRB Chairs, IRB Members, Principal Investigator (PI)/Study Personnel, Office of Regulatory Research Compliance (ORRC) Staff, ORRC Research Compliance Officer (RCO).

20.4 PROCEDURES

20.4.1 Submission and Screening

- The PI or designee completes an application for IRB review of a research protocol for initial full review and submits it to the ORRC.

- ORRC staff schedule the IRB application on the agenda for the next available meeting. Each IRB usually meets approximately once every two weeks. ORRC staff schedule protocols for review based on published submission deadlines.
- ORRC staff screen the application to determine whether it is complete (e.g., includes all pertinent forms and appropriate signatures). If it is not complete, ORRC staff sends an incomplete notification email to the investigator to request the missing items.

- ORRC staff screen the IRB application to ensure coordination with other university committee reviews as outlined in the applicable standard operating policies and procedures or to ensure compliance with pertinent federal requirements. Examples of screening include, but are not limited to, the items listed below.
    - If the investigator checks items on the application which indicate Institutional Biosafety Committee (IBC) approval is necessary, the investigator must include IBC provisional approval materials. ORRC staff checks to ensure that the PI has submitted the materials. ORRC staff does not schedule the application for review and notifies the PI if these materials are missing. ORRC staff may check

with the Institutional Biosafety Officer for advice. The Institutional Biosafety Officer has the authority to make the final decision as to whether the project requires IBC approval.

- ORRC staff screen to determine whether the PI addressed off-site issues following procedures outlined in the Off-site Research SOPP.
- If the investigator indicates that the research involves prisoners, ORRC staff sends the protocol to a prisoner representative for review.
- ORRC staff determines whether the U.S. Department of Education has funded the research and/or whether the proposed research involves surveying children in the public schools. If so, ORRC staff informs the IRB of specific U.S. Department of Education requirements (e.g., “No Child Left Behind”).
- ORRC staff determines whether the research is supported by other federal agencies which have specific requirements such as the U.S. Department of Defense (DoD) or U.S. Department of Energy (DOE). If so, ORRC staff informs the IRB of specific agency requirements for the review and conduct of the research.
- If the investigator indicates that the research involves an investigational new drug (IND) or investigational device exemption (IDE), ORRC staff confirms the validity of the IND or IDE number by ensuring that the investigator has included a copy (containing the number) of the detailed protocol from the sponsor and/or verification statement from the sponsor or the Food and Drug Administration (FDA).
- ORRC staff screens submitted forms to determine whether the investigator also is serving as the sponsor in accord with FDA regulations.
- ORRC staff screen submitted forms to determine whether research involves vulnerable subjects and/or sensitive types of research/procedures (e.g., HIV screening). If so, ORRC staff adds a notation on the agenda for the meeting referring IRB members to the pertinent Protocol Specific Training (PST) materials, which are included in the ORRC Investigator’s manual.
- ORRC staff screen the application to determine if the investigator has answered “yes” on the questions in the Research Financial Interest Disclosure Form. If so, ORRC staff and the IRB follow procedures outlined in the Investigator Conflict of Interest/OSPA/IRB/ORRC Coordination SOPP.

- ORRC staff screen the protocol to determine whether additional expertise is necessary to conduct the review. If so, ORRC staff may ask an ad hoc or cultural consultant who has appropriate expertise in the discipline or with non-English speaking populations or locations to participate in the review.

- The PI may also recommend cultural consultants provided that they are not directly involved in the study. These consultants may review consent forms, provide

verifications of translations, and provide guidance on the impact of the research on subjects and the impact of the culture on the research to be conducted.

- ORRC staff ensures that ad hoc or cultural consultants do not have a conflict of interest in accordance with the IRB Member and Consultant Conflict of Interest SOPP.

- ORRC staff sends the ad hoc or cultural consultants the same information as voting IRB members and a detailed protocol/grant application, if applicable.

- ORRC staff assigns a primary reviewer based on the IRB member's educational background and expertise. ORRC staff document who served as primary reviewer on the applicable reviewer form (i.e., Criteria for IRB Approval Checklist). If no IRB member has the appropriate expertise, ORRC staff asks an ad hoc or cultural consultant to serve as primary reviewer.

- The ORRC RCO screens all initial Medical IRB submissions to determine whether a protocol falls under regulations of the Health Insurance and Portability and Accountability Act (HIPAA) Privacy Rule and/or the Family Educational Rights to Privacy Act (FERPA). The Nonmedical IRB staff conducts the same screening for all initial Nonmedical IRB submissions. The Nonmedical IRB staff forward any protocol regulated by the Privacy Rule and/or by FERPA to the RCO to ensure compliance with the Privacy Rule and/or with FERPA and forwards them to the IRB. See the HIPAA in Research SOPP for additional information regarding HIPAA review procedures.

20.4.2 Submission of Applications to the IRB and Primary Reviewer Responsibilities

- Approximately 5 to 7 days prior to each convened meeting, ORRC staff uploads application materials for voting, and if relevant, alert the appropriate *ex-officio* (Chair, Institutional Biosafety Committee and Biosafety Officer) members for review. The initial full review applications sent to the IRB members include all applicable sections of the application.
  - Application and research description;
  - informed consent/assent process and forms including waiver requests, Department of Health and Human Services (DHHS) approved sample informed consent document (e.g., National Institutes of Health [NIH] cooperative group trial), and translated consent document for non-English speaking subjects;
  - HIPAA forms;
  - additional materials, including advertisements, proposed data instruments, materials/letters for off-site research, Use of Investigational New Drug Form, Use of Approved Drugs for Unapproved Use Form, Use of Investigational New Device Form; Use of Radioactive Materials Form;

- vulnerable populations including forms for research involving individuals with *impaired decision-capacity*, fetuses and/or neonates, prisoners, or children, *and economically or educationally disadvantaged persons*.

- In addition, the member assigned as the primary reviewer of the study receives the following materials, if applicable:
  - Sponsor's grant application;
  - DHHS approved protocol (e.g., NIH cooperative group trial);
  - Contract or device proposal (if the protocol does not involve the administration of drugs);
  - Sponsor's detailed protocol and investigator's brochure (if the protocol involves the administration of drugs);
  - Financial disclosure form(s);
  - Signature Assurance sheet;
  - Other committee review or final approval materials when applicable;
  - All other application materials.

- The primary reviewer is responsible for:
  - Comparing the detailed grant application or industry/DHHS approved protocol with the IRB application;
  - Informing the full IRB of any discrepancies between the detailed protocol and the summary application materials;
  - Determining whether the project involves a DHHS approved protocol (e.g., NIH cooperative group trial) and, if so, comparing the "Risks" and "Alternatives" sections of the DHHS approved sample informed consent document with the HU proposed form to ensure that the DHHS and HU sections of the consent are consistent;
  - Reviewing the financial disclosure form and alerting the IRB if a "yes" disclosure is made; and
  - Conducting an in-depth review.

- All IRB members review all application materials and information in advance of the meeting (including those protocols for which the IRB member is not the primary reviewer) in enough depth to be familiar with the protocol, to be prepared to discuss the protocol at the meeting, and to be prepared to determine whether the research meets the regulatory criteria for approval.

- Ad hoc or cultural consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review. IRB staff maintains documentation of written comments or reports in the protocol file. In cases where the consultant participates in the meeting, the minutes of the meeting document the information provided by the consultant (See Minutes of IRB Meetings SOPP).

20.4.3 IRB Review

- A majority of the voting IRB members (or their designated alternates), including at least one member whose primary concerns are in nonscientific areas, must be present in order to conduct a convened meeting. For the Medical IRB, a licensed physician must be present. In order for the IRB to approve the proposed research, the protocol must receive the approval of a simple majority of those members present at the meeting (See The Conduct of IRB Meetings SOPP).

- When the IRB reviews research that involves categories of human subjects vulnerable to coercion or undue influence, ORRC staff ensures that adequate representation or consultation is present for discussions of research involving vulnerable human subjects (See Protection of Vulnerable Subjects SOPP and Membership of IRB SOPP).

- All IRB members attending the meeting receive materials listed in the Submission of Applications section above, prior to the convened meeting, have the opportunity to discuss each research protocol during the convened meeting, and participate in the determination of whether the research meets the regulatory criteria for approval.

- The IRB reviews each initial full review application with the PI or co-investigator present during the convened IRB meeting unless the ORRC or IRB waives the requirement. After the PI leaves the meeting, the IRB reviews the application and discusses any controverted issues and their resolution prior to voting.

- During discussion, the IRB members raise only those issues that the committee determines do not meet the federal criteria for approval as specified in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. In addition, the IRB determines whether the risk level assigned by the PI is appropriate. Also, the IRB considers whether the PI's preliminary assessment of federally mandated specific findings requirements (e.g., request for waiver of informed consent) is acceptable with respect to meeting federal requirements.

- For research involving a new drug or new device where the PI or the sponsor has not obtained an IND or IDE, the committee determines what action(s) is needed (whether the PI needs to obtain an IND/IDE or whether PI needs to contact the FDA for guidance).

- In conducting the initial review of the proposed research, the IRB utilizes the Criteria for IRB Approval: Reviewer Checklist.

- A member or consultant with a conflict of interest must leave the room during the vote and only participate in the review by providing information in accordance with the IRB Member and Consultant Conflict of Interest SOPP.

20.4.4 Review Outcome(s)

- An IRB member makes a motion while another member seconds the motion, and then the convened IRB votes for or against or abstains from one of the following five actions:
  - APPROVED/ ACCEPTED as SUBMITTED: A vote for Approval indicates that the IRB has concluded that the research and consent/assent forms meet the federal criteria for approval. IRB approval verifies that the IRB agrees with the assessment of the protocol and/or specific findings as described by the PI in the application. ORRC staff sends the investigator an approval notification letter, according to the guidelines in the ORRC Customer Service Standards, accompanied by an informed consent/assent document (if applicable) with the affixed "IRB Approval" validation stamp, which includes valid dates of IRB approval. If the IRB approves a HIPAA Waiver of Authorization Request, ORRC staff sends a separate approval letter as well.
  - REVISIONS and/or ADDITIONAL INFORMATION or ADMINISTRATIVE REVIEW REQUESTED: A vote of Revision and/or Additional Information Required may indicate one of the following:
    - Accept with Administrative Review - That the IRB has approved the protocol pending submission of minor revisions: In this case, the IRB has given the individual chairing the IRB meeting the authority to approve the minor revisions which do not involve substantive concerns. The PI responds to the IRB's suggested revisions in writing and sends the response to the ORRC, and to the IRB chair or member who chaired the meeting for further review. The Chair or designee may forward the responses to the entire IRB for additional review, request additional information, or approve.
    - Revision Requested - The IRB requests a revision and resubmission of the protocol before approval: In this case, neither the IRB chair nor a designated IRB member has the authority to approve the protocol upon resubmission. Instead, the PI responds to the IRB's suggested revisions in writing and sends the response to the ORRC who then place the protocol on the agenda for full board review, at a duly convene and constituted IRB board meeting. Approval of the revised protocol is not guaranteed, especially, if the revision is inadequate or raise new concerns. However, if the committee is satisfied with the revision the protocol is approved.
  - In either of these two scenarios, the ORRC staff sends the investigator a notification letter, according to the guidelines in the ORRC Customer Service Standards.
  - DISAPPROVED/REJECT as SUBMITTED: In this case the application is not approvable with minor revision. However, it can be resubmitted with major revisions.
  - TABLED: Means critical information needed to review the application is missing, and therefore, could not be reviewed.
  - SUSPENSION: Additional alternative actions may include suspension of a protocol (See section 10.5.2 of the HU Policy and Procedures).

- TEMPORARY HOLD: The Board temporarily stops specific activities/procedures on the protocol. In this case, the Board's concern is not at suspension threshold, but as precautionary measure to ensure the safety of human subjects, while further assessing level of risk.
- TERMINATION: Additional alternative actions may include termination of a protocol (See section 10.5.2 of the HU Policy and Procedures.

- During the convened meeting, the IRB determines the approval period, as appropriate to the degree of risk but not less frequently than once per year. The IRB may set a shorter approval period for high risk protocols or protocols with high risk/low potential benefit ratios.

- When a protocol receives final approval, the ORRC assigns the start of the approval period as the date of the convened IRB meeting. If a protocol has received a vote Revisions and/or Additional Information Required (the IRB requests minor revisions) and the PI completes the revisions, the approval period starts from the meeting date of the convened IRB on which the IRB initially reviewed the protocol. Should there be serious concerns or a lack of significant information requiring the convened IRB to complete its review and issue approval of the study at a subsequent meeting, the approval period starts with the date of the subsequent convened IRB meeting.

- Before issuing the IRB approval letter, ORRC staff confirms that all of the applicable approvals are obtained such as Institutional Biosafety Committee, Radiation Safety Committee, Occupational Safety etc. If applicable approvals are not in place, ORRC staff notify the investigator in writing, requesting the appropriate information. When the investigator submits the information, ORRC staff may put it on an agenda for review by the IRB, if appropriate. ORRC staff only issue the IRB approval letter after obtaining appropriate documentation.

- Before issuing approval, ORRC staff also ensures that all study personnel have completed the required training. If the PI and study personnel have not completed training, ORRC staff notifies the PI in writing. The investigator must send the appropriate certifications of training before the IRB can issue approval. An investigator may submit a request for an exception to submission of certifications before the IRB issues approval. The ORRC Research Compliance Officer, designated ORRC staff person, or the ORRC Director may approve exceptions.

- If the PI is serving as the sponsor in accord with FDA regulations, ORRC staff ensures that the PI has completed the Office of Research Regulatory Compliance Sponsor-Investigator web based training, or equivalent training as approved by the ORRC Director or the IRB Chair or their designee before issuing approval.

- Before issuing approval, ORRC staff verifies that any pending IND or IDE submissions have been approved by the FDA, or have passed the 30 calendar day FDA clearance period, or stipulate in the approval letter that research must not commence until IND or IDE is in place.

- If the research involves prisoners, ORRC staff checks to determine whether the PI submitted the protocol for funding to any DHHS agency. If this is the case and the protocol involves prisoners, ORRC staff, with input from the PI, prepares and submits a prisoner certification report to the Office for Human Research Protection (OHRP) in accordance with OHRP requirements and the Mandated Reporting to External Agencies SOPP.

- Once the IRB approves a protocol, ORRC staff sends an approval letter to the PI, which includes the approval period, a reminder to use only the approved consent/assent form, and a reminder that the IRB must approve any changes to the protocol prior to initiation of the changes.

- Upon request, ORRC staff also sends the PI a funding agency Certification of Approval form (See the Mandated Reporting to External Agencies SOPP).

- At IRB approval, it is the PI's responsibility to request an IRB Statement of Compliance if the protocol falls under the International Conference on Harmonization guidance related to Good Clinical Practice. The ORRC maintains a statement of compliance signed by the IRB Chair and provides that statement upon request.

- If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit them to the IRB via a written document that includes a justification for changing the IRB decision. The IRB reviews the request using the standard procedures.

20.5 REFERENCES

21 CFR 50.25
21 CFR 56.111
21 CFR 312
21 CFR 812
45 CFR 46.108
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117
45 CFR 46 Subparts B
45 CFR 46 Subparts C
45 CFR 46 Subparts D & 21 CFR 50 Subpart D