Section 2: Process of Review

2.1 Submission for Items for Review by the IRB

1.0 Purpose

The purpose of this policy is to describe Organization's requirements for submission and pre-review of all applications and research related forms and reports.

2.0 Policy

It is the policy of the Organization that all submissions will be processed efficiently by the Office of Regulatory Affairs (ORA) for review in accordance with applicable HRPP policies.

3.0 Submission Requirements

- **3.1.** All applications and research related forms and reports will be submitted using the online Research Support System RSS, except as below:
- **3.2.** CRs and certain other forms related to research protocols approved prior to January 16, 2012 may continue to be submitted on paper. All necessary forms are available on the UNMC IRB website and the IRB will maintain paper files for the duration of these studies.
  - **3.2.1.** Research protocols remaining in paper format will continue to be transitioned to RSS as appropriate.

4.0 Deadlines for Submission

- **4.1.** The deadline for submission of any materials requiring review by IRB-01, -02, and -04 is 10 working days prior to each meeting. The deadline for submission of any materials requiring review by the IRB-05 is 6 working days prior to each meeting. The deadlines are published on the IRB website.
  - **4.1.1.** All new applications and re-submissions of tabled protocols will undergo pre-review to the greatest extent possible in consideration of the submission date, and ORA workload.
  - **4.1.2.** Exceptions to the above deadline may be made on a case-by-case basis by the IRB Executive Chair or his/her designee.

- **4.1.3.** Items that qualify for expedited review in accordance with HRPP policy 2.3 (Expedited Review) have no deadlines for submission.
- **4.1.4.** Items that qualify as exempt in accordance with HRPP policy 2.6 (Exempt Research) have no deadlines for submission.

5.0 IRB Review Limits

- **5.1.** The IRB will normally review no more than 10 protocols (new submissions and previously tabled protocols) at each full meeting. Assignment to the IRB meeting are made on a first-come, first-served basis. Protocols in excess of 10 will be assigned to the following IRB meeting.
- **5.2.** The IRB will review reports of internal Adverse Events, Requests for Change, Incident Reports and Special Review Items at the earliest possible full IRB meeting without review limits.

6.0 Determination of Required IRB Review

- **6.1.** Protocols and other action items submitted through RSS will be triaged to the appropriate IRB administrator and processed in accordance with ORA SOPs.
- **6.2.** The IRB Administrator, in consultation as necessary with the IRB Executive Chair, will determine whether or not a protocol or other action item requires review by the full IRB or qualifies for expedited review in accordance with HRPP policies 2.2 (Full IRB Review) and 2.3 (Expedited Review.)

DOCUMENT HISTORY:

? Written: 4/4/2016 (Approved: 4/4/2016) - original author not recorded

? Revised: 2/5/2018 - revision not documented

? Revised: 7/19/2022 - Deleted list of types of forms for review; clarified which items allowable for submission in paper format; corrected deadlines for submission; clarified maximum number of protocols to be reviewed {Approved Chris Kratochvil (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

? Board Notified: 11/16/2022

2.2 Full IRB Review

1.0 Purpose

The purpose of this policy is to describe the Organization’s requirements for: 1) submission of items required for full IRB review; 2) organization, scheduling, and conduct of full IRB meetings; 3) IRB approval criteria; 4) IRB actions; and 5) IRB documentation of actions.

2.0 Policy

It is the policy of the Organization that:

- 2.1. IRB review will be conducted in accordance with HHS regulations at 45 CFR 46.109; FDA regulations at 21 CFR 56.109; and will satisfy the criteria for IRB approval described in HRPP policy 2.5 (Criteria for Approval) and in 45 CFR 46.111 and 21 CFR 56.111, as applicable.
- 2.2. The HRPP will apply equivalent protections to non-federally funded research. These protections will be based upon the ethical principles in the Belmont Report. In addition, the requirements in 45 CFR 46, Subpart A, B, C, and D will be applied to the greatest extent possible in consideration of the nature of the research.
- 2.3. The Organization that will apply the ICH-Good Clinical Practice (GCP) E-6 Guidelines to studies where the sponsored agreement requires compliance with ICH GCP for clinical trials conducted internationally in accordance with HRPP policy 1.13 (Compliance with ICH-GCP Guidelines).
- 2.4. The IRB will conduct continuing review of research at intervals appropriate to the degree of risk, in accordance with 45 CFR 46.109 and HRPP policy 2.7 (Continuing Review of Research).

3.0 Definitions

- 3.1. Controverted issues are issues that cause controversy and dispute among the IRB membership during a convened meeting. Controverted issues that arise during the convened meeting may be the result of opposition to some aspect of the proposed research or may regard applicability or interpretation of ethics or regulation.

4.0 Procedures

- 4.1. All IRB applications are submitted to the ORA and processed in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).
- 4.2. IRB Meeting Schedule
  - 4.2.1. The schedule of IRB meeting dates is posted on the IRB website.
    - 4.2.1.1. IRB-01 meets the first Thursday of every month (except January and July), and IRB-02 meets the third Thursday of every month.
    - 4.2.1.2. IRB-04 (Joint Pediatric IRB) meets the fourth Tuesday of every month (unless such date conflicts with a University holiday).
    - 4.2.1.3. IRB-03 (Rapid Response IRB) meetings are held on demand and convened as soon as possible, as per HRPP policy 1.30 (Use of the Rapid Response IRB).
    - 4.2.1.4. IRB-05 (Single IRB) meets the second Friday of every month, as required, based on items for review.
- 4.3. Quorum
  - 4.3.1. A full IRB meeting cannot be convened without the presence of a quorum. A quorum must represent a majority of the voting membership of the IRB, including at least one member whose primary concerns are in nonscientific areas.
  - 4.3.2. Each IRB includes one member that is not affiliated with the Institution. It is expected that least one unaffiliated member will be present at each meeting of each IRB as per HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).
  - 4.3.3. IRB meetings may be conducted in person, or via video conferencing, as appropriate. Members will have access to all relevant materials prior to the meeting and will be able to participate actively and equally in all discussions.
  - 4.3.4. When the IRB reviews any research involving children, or cognitively impaired persons, an IRB member who is knowledgeable about and/or experienced in

working with that specific population will be present in accordance with HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).
    - 4.3.5. When the IRB reviews any research involving other vulnerable populations, an IRB member who is knowledgeable about and/or experienced in working with vulnerable populations (preferably but not exclusively the particular population in question) will be present in accordance with HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).
    - 4.3.6. When the IRB reviews any research involving prisoners, a prisoner representative must be present in accordance with HRPP policy 4.3 (Research Involving Prisoners).
    - 4.3.7. Any IRB member who abstains from voting for reasons other than a COI (as defined in HRPP policy 1.7) is included in the quorum. This is recorded as an abstention in the minutes.
    - 4.3.8. Any IRB member who has a COI will be recused in accordance with HRPP policy 1.7 (IRB Member, Consultant, Staff COI Identification & Management). This is recorded in the minutes as “recused due to conflict of interest” and the quorum is decreased accordingly. The name of the individual recused will be recorded in the minutes.
    - 4.3.9. A designated IRB Analyst is responsible for determining quorum requirements, monitoring attendance at the meeting to verify maintenance of quorum, and recording the actions taken on all protocols and other items under review.
    - 4.3.10. If attendance at a convened full IRB meeting falls below quorum (including losing all non-scientist members, or another required member), the meeting will be immediately suspended and no official business will be conducted until a quorum is re-established. If it is not possible to re-establish the quorum, the meeting will be adjourned and the remaining reviews will be conducted at the next available full IRB meeting.
- 4.4. Assignment of Reviewers and Creation of the Agenda
    - 4.4.1. Reviewers will be assigned by the IRB analysts with advice from the IRB Executive Chair/designee as necessary.
    - 4.4.2. For new IRB Applications and tabled IRB Applications, at least a primary and secondary reviewer, and usually a non-scientist reviewer, will be assigned. At least one of the assigned reviewers will have relevant scientific, medical, or other expertise in order to perform an in-depth review of the protocol.
        - 4.4.2.1. For IRB-03 (Rapid Response IRB) a non-scientist reviewer may not be specifically assigned; however, a non-scientist is always present during the meeting.
        - 4.4.2.2. For IRB-04 (Joint Pediatric IRB), a pharmacy reviewer is generally also assigned to research involving drugs.
    - 4.4.3. For applications for continuing review, one reviewer will be assigned, unless it is determined by the IRB Executive Chair/designee that more than one reviewer is necessary.
        - 4.4.3.1. Continuing review of protocols in which subjects are in standard follow-up (all research interventions are completed) may be assigned to a non-scientist, provided there is a scientist present during the meeting with relevant scientific, medical, or other expertise.
    - 4.4.4. For requests for change in protocol and/or ICF, reviews of internal adverse event reports, incident reports (including potential unanticipated problems involving

risk to the subject or others, or noncompliance or complaints), or other special review items, one reviewer will be assigned, unless it is determined by the IRB Executive Chair/designee that more than one reviewer is necessary.
    - 4.4.5. If during the pre-review process, the IRB Analyst or reviewer determines that the board will require additional expertise, the services of an expert consultant will be obtained prior to the meeting, as described in HRPP policy 1.6 (IRB Composition, Leadership, Qualifications, & Responsibilities).
    - 4.4.6. All IRB members will be notified by email that a detailed agenda is available in RSS. This agenda contains: 1) education, policy, and informational items; 2) a categorized list of review items; 3) IRB reviewer assignment for each of the items under review, 4) notification of items approved by expedited review (in accordance with HRPP policy 2.3 Expedited Review) and per requirements of 45 CFR 46.110(c), 21 CFR 56.110(c), 5) IRB approval criteria, and 6) description of IRB actions.
- 4.5. Review Materials Distributed to IRB Members
    - 4.5.1. All members and alternates scheduled to attend an IRB meeting (in person or by videoconference) will have access through RSS to all submitted items described in HRPP policy 2.1 (Submission for Items for Review by the IRB), as well as all previously submitted materials, correspondence and IRB determinations related to protocols under consideration by the board.
    - 4.5.2. Materials will be available at least 7 days prior to the meeting with the following exceptions:
        - 4.5.2.1. Materials for IRB-03 (Rapid Response IRB) will be made available as soon before the meeting as is feasible.
        - 4.5.2.2. Occasional review items may be presented to the board at the time of the meeting. In all cases, the reviewer of these items (usually the Executive Chair, or other chair/vice-chair) will have had access to these items in advance of the meeting.
    - 4.5.3. At least two days prior to each meeting, all members and alternates of all Boards will have access through RSS to the following:
        - 4.5.3.1. IRB minutes of the last meeting of that Board
        - 4.5.3.2. Education, Policy and Information items
        - 4.5.3.3. Full agenda for that meeting
- 4.6. IRB Member Review Procedures
    - 4.6.1. All IRB members must be satisfied that they have sufficient information to make the determinations required for IRB approval in accordance with 45 CFR 46.111; 21 CFR 56.111, and HRPP policy 2.5 (Criteria for IRB Approval).
        - 4.6.1.1. IRB members must be satisfied that they have the appropriate expertise to review the protocol. If they do not, then the reviewer or any IRB member may request that the review be deferred and a consultant with appropriate expertise be obtaining, in accordance with HRPP 1.6 (IRB Composition, Leadership, Qualifications, and Responsibilities) section 3.1.3.
    - 4.6.2. IRB members are expected to consult the IRB study files in RSS (including but not limited to the IRB application, full protocol, investigator's brochure, questionnaires and surveys, recruitment and other subject facing materials, and consent documents), applicable regulations, and HRPP policies, as necessary during their review of the protocol.
    - 4.6.3. IRB members are expected to submit written reviews, as early as possible, to ORA.

    - 4.6.4. Deficiencies and/or major points of clarification which require revision of the IRB application or other review item should be described fully, and referenced to sections of the submitted application, to the Reviewer Template, or to the Criteria for Approval at 45 CFR 46.111.
    - 4.6.5. Deficiencies, errors, inadequate explanations, and excessively high readability level should be described sequentially according to the section of the ICF.
- 4.7. IRB Meeting Procedures
    - 4.7.1. When a quorum of the Board is present, the IRB meeting is called to order by the IRB Executive Chair, Chair, Vice Chair, or designee (subsequently referred to as “Chair” in this policy) and each item on the agenda is acted upon.
    - 4.7.2. The Primary Reviewer will present the review followed by the other assigned reviewers (secondary reviewer, non-scientist reviewer, pharmacy reviewer) as applicable. The protocol is then open for discussion by all IRB members. When the discussion is completed, a separate vote will be taken on each application or other item under consideration.
    - 4.7.3. When appropriate, IRB staff will present submitted materials from RSS or information from other sources (including applicable federal, state, and local regulations, and HRPP policies) to assist IRB members in their deliberation.
    - 4.7.4. Relevant regulatory information, including criteria for IRB approval, Subpart B, C, and D determinations, will be available to members, as part of the agenda, or when meeting in person, as placemats or other physical items, to assist IRB members.
    - 4.7.5. Whenever a controverted issue arises during an IRB meeting, or when the vote is less than unanimous, members will be asked if they wish to submit written comments or minority opinion. These items will be appended to the minutes of the meeting.
- 4.8. Voting Requirements
    - 4.8.1. The Primary Reviewer will recommend an action which must be seconded by another IRB member, normally the Secondary Reviewer.
    - 4.8.2. IRB voting on each motion will be recorded as the number of members in favor, the number against, and the number of abstentions. Separate votes for each action will be recorded.
    - 4.8.3. Except as specified in other sections of this policy, no motion shall pass unless two-thirds of the IRB members which constitute the quorum are present during the discussion and vote in favor of the motion.
    - 4.8.4. If a member must leave the meeting temporarily before the vote is taken, the vote can be delayed. If the vote is not delayed, the name of the absent member will be recorded in the minutes.
    - 4.8.5. Only those members physically in the room or attending by videoconference may vote. Absentee voting is not permitted.
    - 4.8.6. If a motion fails to pass by a two-thirds vote, other motions will be entertained. If no further motions are made, the protocol or issue under discussion shall automatically be deemed to have been tabled and shall be referred, as needed, to an IRB subcommittee for further study.
    - 4.8.7. If a protocol or issue has been referred to an IRB subcommittee, the Chair or a member of the subcommittee will present the results of the subcommittee meeting at any subsequent full Board meeting.
    - 4.8.8. The Chair will abstain from voting, except as needed to break a tie vote.
- 4.9. Criteria for IRB Approval and Other Determinations

- 4.9.1. During all reviews, the IRB must determine whether the criteria for IRB approval have been (or continue to be) met, per HRPP policy 2.5 (Criteria for IRB Approval).
- 4.9.2. As appropriate and as relevant to specific board reviews (such as review of new protocols, continuing reviews, review of requests for change in protocol or ICF or other types of IRB reviews as described previously) the IRB must also determine:
  - 4.9.2.1. Whether the research requires continuing review more often than annually, as required at 45 CFR 46.108(a)(3)(ii); 21 CFR 56.109(a)(2), as appropriate to the degree of risk. In making this determination the IRB may consider factors including but not limited to: the nature of the risks associated with the research; the degree of uncertainty regarding the risks involved; the vulnerability of the participants; the experience of the investigator in conducting the research; the IRB's previous experience with that researcher or sponsor; the projected rate of enrollment.
  - 4.9.2.2. Whether the research should have a third party observe the consent process in accordance with HRPP policy 1.2, Section 2.7 (Authority Granted to the IRB by the Organization).
  - 4.9.2.3. If the research involves an FDA regulated investigational device, the IRB will also determine and document the basis for determination that the investigation involves a significant risk device or non-significant risk device (in accordance with 21 CFR 812.66 and HRPP policy 6.2 (Research involving Investigational and Marketed Devices)).
  - 4.9.2.4. Whether the research needs verification from sources other than the PI that no material changes have occurred since the previous IRB review, as required at 45 CFR 46.108(a)(3)(ii) and 21 CFR 56.108(a)(2).
  - 4.9.2.5. Whether the current consent form is still accurate and complete.
  - 4.9.2.6. Whether the research requires an audit of research records in accordance with HRPP policies 1.21 (Post Approval Monitoring of Research) and 8.4 (Review of Noncompliance Involving Risk to the Subject or Others).
  - 4.9.2.7. Whether there are any significant new findings that arise from the review process that might relate to a subject's willingness to continue participation in the study.
  - 4.9.2.8. When the PI is the lead researcher of a multi-site trial, whether the management of information to the protection of human subjects is adequate, such as reporting of unanticipated problems, interim results, and protocol modifications.
- 4.9.3. The IRB may determine that some components of the research have met the IRB criteria for approval whereas other components require minor or substantive changes, or are unacceptable. In this case, the IRB may choose to approve or conditionally approve those components that satisfy the IRB approval criteria. For those components that do not meet the IRB approval criteria the IRB may table or disapprove that component (as per IRB actions described below).

- 4.10. IRB Actions
  - 4.10.1. Approval; initiation of the research is authorized (when institutional requirements are satisfied).
    - 4.10.1.1. All of the criteria for IRB approval are satisfied and no changes are required.

- 4.10.2. Conditional approval; final IRB approval contingent upon IRB Executive Chair/designee review and acceptance of specified modifications and/or submission of additional documents.
  - 4.10.2.1. All of the criteria for IRB approval are satisfied provided the investigator makes the specified changes. The IRB requirements for final approval and release are considered minor and not substantive in nature.
- 4.10.3. Tabled, full IRB re-review required.
  - 4.10.3.1. The IRB requires additional information in order to determine whether the criteria for approval have been satisfied, and/or the IRB had concerns which warrant re-review by the full IRB.
  - 4.10.3.2. If the protocol and application are revised by the investigator in response to the IRB's comments, the protocol will be returned to the full convened IRB for re-review.
- 4.10.4. Disapproved
  - 4.10.4.1. Applications may be disapproved if (1) the IRB finds serious ethical concerns that cannot be resolved after discussions with the investigator, or (2) the protocol does not meet regulatory criteria for approval or institutional policy or requirements, and the investigator is unable to make modifications to meet the criteria or requirements.
  - 4.10.4.2. The investigator shall have an opportunity to appeal before the Board; however, the IRB has the final authority to act on any appeals and the decision of the Board cannot be overturned.
- 4.10.5. Suspension of IRB approval
  - 4.10.5.1. The IRB requires all research activities be halted immediately in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination). This action may be taken in relation to continuing review, complaints, noncompliance, adverse events, and unanticipated problems involving risk to the subject or others.
- 4.10.6. Termination of the research
  - 4.10.6.1. The IRB requires the study be terminated in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination). This action may be taken in relation to continuing review, complaints, noncompliance, adverse events, and unanticipated problems involving risk to the subject or others.

- 4.11. IRB Review Letters
  - 4.11.1. IRB review letters, which reflect the deliberations and decisions of the Board, are developed by the IRB Analysts, in consultation with the IRB Executive Chair/designee and reviewers as appropriate.
  - 4.11.2. IRB review letters must be written in a clear, explanatory, and facilitative fashion in order to assist PIs in understanding the rationale for any IRB concerns, clarifications and mandated changes to the IRB application, ICF(s)/information sheet(s) and/or other associated documents.
  - 4.11.3. The IRB review letters will clearly document the following:
    - 4.11.3.1. The decision to approve, require modifications, table, or disapprove.
    - 4.11.3.2. A list of any modifications or clarifications required by the Board.
    - 4.11.3.3. If the IRB disapproves the action, a statement providing the rationale for the disapproval, and an invitation for the investigator to appeal.
  - 4.11.4. Review letters are signed by the IRB Analyst in accordance with HRPP policy 1.19 (IRB Signature Authority).

- 4.12. IRB Meeting Minutes
  - 4.12.1. Basic Information
    - 4.12.1.1. The IRB minutes are based upon the actions of the IRB recorded in detail by the assigned IRB Analyst. The minutes are then developed after the meeting by the IRB Analysts in consultation with the IRB Executive Chair/designee.
    - 4.12.1.2. The IRB minutes consist of the core minutes and addenda (which contain the detailed review letters provided to the investigator for all protocol related activities).
    - 4.12.1.3. Copies of the core IRB minutes and addenda are available on RSS to IRB members (including alternates) and the Institutional Official, before the next meeting of the board.
    - 4.12.1.4. IRB members for each board have the opportunity to review and correct minutes for the previous convened meeting of that board.
    - 4.12.1.5. The complete IRB minutes will be provided to OHRP, FDA, auditing groups, and other entities in accordance with all applicable federal, state, and Organizational requirements.
  - 4.12.2. The minutes (core and addended review letters) will contain the following information, as appropriate:
    - 4.12.2.1. Identification of the individuals present at the meeting: IRB members, non-voting IRB member alternates, consultants, IRB administrative staff, and guests.
      Note: If consultants are present, a brief description of the consultant expertise will be noted as well as documentation that the consultant did not vote on any actions.
    - 4.12.2.2. Identification of IRB members classified as non-scientists.
    - 4.12.2.3. If the meeting was conducted in-person, the minutes will note by name any IRB members, non-voting IRB member alternates and consultants who attended videoconferencing. If the entire meeting was conducted via teleconferencing, the minutes will so note.
    - 4.12.2.4. Identification of alternate IRB members and the IRB member for whom they are substituting.
    - 4.12.2.5. The names of IRB members who have a COI and are recused at the time of the discussion and vote on each board action.
    - 4.12.2.6. The names of IRB members who do not have a COI but are absent from the room for other reasons at the time of the vote on each board action.
    - 4.12.2.7. IRB special notification items per IRB minutes template.
    - 4.12.2.8. Documentation of quorum for each separate vote count for all board actions (in favor, opposed, and abstentions).
    - 4.12.2.9. In the event a consultant provided an in-depth review of research the agenda will document the information provided by the consultant and verify that the consultant did not vote.
    - 4.12.2.10. Verification that all IRB members who attended through videoconferencing were able to actively participate in all discussions and votes.
    - 4.12.2.11. A written summary of the discussion and resolution of controverted issues.
    - 4.12.2.12. A written summary of the discussion and resolution of actions taken with regard to significant new findings either provided by the investigator or provided by other sources, which may relate to the subject’s willingness to continue participation in the research.

- 4.12.2.13. The reason(s) for disapproval of research.
- 4.12.2.14. A determination of when continuing review is required more often than annually.
- 4.12.2.15. A determination of which projects need verification from sources other than the PI that no material changes have occurred since the previous IRB review.
- 4.12.2.16. A determination of which projects should have a third party observe the consent process.
- 4.12.2.17. A determination of which projects require an audit of research records.
- 4.12.2.18. Rationale for conducting continuing review on research that otherwise would not require continuing review.
- 4.12.2.19. Rationale for an expedited reviewer's determination that research appearing on the expedited reviewer list is more than minimal risk.

5.0 Deadlines for PI Responses

- 5.1. The PI is given 60 days from the date of the IRB review letter to respond to the IRB's review by submitting appropriately revised documents. If no response is received by the end of the 60-day period, or by the expiration of an extension provided granted by the IRB Executive Chair/designee) the study may be withdrawn or closed.

6.0 Review of PI Responses

- 6.1. If the IRB required only minor, directed modifications, the IRB Analyst serves as the designated reviewer and is authorized to review and determine the acceptability of the PI's response. The IRB Analyst will consult with the IRB Executive Chair/designee or IRB reviewers as necessary.
- 6.2. If, on consultation with the Executive Chair, the Analyst determines that the investigator's response to the IRB review is inadequate or incomplete they may correspond with the investigator to resolve those issues or may refer the submission for review by the full convened IRB.
- 6.3. If, on consultation with the Executive Chair, the Analyst determines that the investigator's response to the IRB review contains significant changes not initially reviewed by the IRB, they will refer the submission for review by the full convened IRB.

- 6.4. If the IRB required modifications/clarifications that are more than minor in nature (that is, if the submission was tabled), the investigator's response will be returned to the full convened IRB for re-review. If possible, the revised submission is assigned to both the IRB that performed the initial review and the original primary and secondary reviewers.

7.0 IRB Approval Periods

- 7.1. The approval period for protocols for which continuing review is required is based on the date that the convened IRB gave conditional approval of the research. Studies approved with annual continuing review are valid for 364 days from the date of conditional approval; the approval period expires on the 365th day.

8.0 Final IRB Approval Letter

- 8.1. Once all modifications or clarifications required by the Board (as per section 4.11) have been satisfied, and all outstanding Institutional Requirements have been met (section 9.) the ORA will inform the PI that the research may commence.
- 8.2. The final approval letter from ORA will document the following determinations:
  - 8.2.1. Pertinent dates:
    - 8.2.1.1. Date of full Board review.
    - 8.2.1.2. Date all conditions set by the IRB were determined to be met and the study was granted IRB approval.
    - 8.2.1.3. Expiration Date for which continuing review is required (per section 7.1 above).
  - 8.2.2. Compliance with applicable HHS and FDA regulations, HRPP policies and Institutional Requirements.
  - 8.2.3. Documentation of the level of risk (minimal risk or greater than minimal risk).
  - 8.2.4. Documentation that the IRB determined that the research satisfies the requirements of 45 CFR 46, Subpart B and the designated category (46.204; 46.205; 46.206). Per Section 2.2 of this policy the IRB will apply Subpart B as required for federally funded research and for non-federally funded research to the greatest extent possible. Any alteration of Subpart B requirements as applied to non-federally funded research will be documented.
  - 8.2.5. Documentation that the IRB determined that the research satisfies the requirements of 45 CFR 46, Subpart C (46.305) and is appropriately classified under

the designated category {46.306(2)(i); 46.306(2)(ii); 46.306(2)(iii); 46.306(2)(iv)}, as applicable. Per Section 2.2 of this policy the IRB will apply Subpart C as required for federally funded research and for non-federally funded research to the greatest extent possible. Any alteration of Subpart C requirements as applied to non-federally funded research will be documented.
    - 8.2.6. Documentation that the IRB determined that the research satisfies the requirements of 45 CFR 46, Subpart D and has met all the requirements for the designated category (46.404; 46.405; 46.406; 46.407), as applicable. Per Section 2.2 of this policy the IRB will apply Subpart D as required for federally funded research and for non-federally funded research to the greatest extent possible. Any alteration of Subpart D requirements as applied to non-federally funded research will be documented.
    - 8.2.7. Documentation that the IRB determined that the research satisfies the requirements of 21 CFR.50, Subpart D and has met all the requirements for the designated category (50.51, 50.52. 50.53, 50.54), as applicable.
    - 8.2.8. Documentation that the IRB considered protocol specific findings for research involving decisionally impaired subjects, as per HRPP policy 4.6 (Review of Research Involving Subjects with Impaired Decision-Making Capacity).
    - 8.2.9. Documentation of the nonsignificant or significant risk device determinations.
    - 8.2.10. Documentation that the IRB determined that the research satisfies the requirements for waiver of informed consent/ HIPAA authorization as per HRPP policy 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).
    - 8.2.11. Documentation that the IRB determined that the research satisfies the requirements for waiver of child assent as per HRPP policy 4.4 (Research Involving Children).
    - 8.2.12. Documentation that the IRB determined that the research satisfies the requirements for waiver of signed consent as per HRPP policy 5.4 (Waiver of the Requirement to Obtain Signed Consent Form).
- 8.3. The Final approval letter from ORA will note that the determinations were made by the convened IRB, and the specific justifications for the determinations can be found in the approved IRB application, accompanying submitted materials, and/or minutes.

9.0 Review by Other Organizational Committees

- 9.1. Before the ORA will grant final approval and release, the ORA must receive verification of approval or completion of review by components of the HRPP as described in HRPP Policy 1.10 (Scientific and Other Committee Review of Research) and as required by the organization.

DOCUMENT HISTORY:

? Written: 4/4/2016 (Approved: 4/4/2016) - original author not recorded

? Revised: 3/29/2018 - revision not documented

? Revised: 6/2/2021 - Added IRB-05; added definitions (section 3.0); simplified overall by referencing other policies where appropriate; revised procedures to reflect activities during teleconference meetings; clarified when meeting materials will be available (especially for RR-IRB and special review items); revised to delete references to paper copy distribution of materials (all materials available thru RSS); clarified assignment of reviewers; added that chair may vote to break a tie vote; clarified types of other IRB determinations (section 4.9); deleted list of types of items for which documentation of quorum required (section 4.12); revised deadlines for PI responses to be consistent with Policy 2.3. (Expedited Review); clarified that IRB administrator authorized to communicate with investigator to resolve inadequate or incomplete responses to request for minor modifications or clarifications; revised description of contents of condition approval and final approval letters; deleted references to pre-2018 Common Rule and corrected regulatory citations.

? Revised: 10/13/2022 - Modified definition of “controverted issues”; revised throughout to reflect meetings by video conference; clarified identification of members recused; deleted list of materials supplied to members and clarified that materials available in RSS; deleted 20 minute discussion time limit; clarified that IRB approval is distinct from ORA release; deleted IRB action “decline to review”; clarified criteria for disapproval; combined descriptions of contents of core minutes and addended letters; revised policy to require documentation of findings and determinations in the final ORA approval letter as opposed to the initial IRB review letter. {Approved Chris Kratochvil (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

? Revised: 10/13/2022 - amended section numbers due to removal of 4.10.5, amended 8.1.1 to align with heading 8.2, amended 8.2 sequentially to 8.3 (Robert Lewis - IRB Assoc)

? Board Notified: 11/22/2022

? Revised: 11/30/2022 - corrected language in 4.3.3 from: “IRB meetings may be conducted in person, or via video conferencing, as appropriate. In either case If meetings are conducted by video conference, Members will have access to all relevant materials prior to the meeting and will be able to participate actively and equally in all discussions.”, to: “IRB meetings may be conducted in person, or via video conferencing, as appropriate. Members will have access to all relevant materials prior to the meeting and will be able to participate actively and equally in all discussions.” (Robert Lewis - IRB Assoc)

? Revised: 7/31/2023 – revised sections 4.4.5 and 4.6.1.1 to more fully describe the assessment of the need for an expert consultant; added description of items to be reviewed (section 4.6.2); revised 4.10.3.2 to state explicitly that tabled protocols will be returned to the convened IRB for further review. {Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

? Revised 3/29/2024 – revised criteria for disapproval (section 4.10.4). {Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

2.3 Expedited Review

1.0 Purpose

The purpose of this policy is to describe the Organization’s requirements for using expedited review procedures for consideration of:

1. new research proposals;
2. continuing review of previously approved research;
3. minor changes in protocol;
4. minor complaints; and
5. non-serious noncompliance.

2.0 Policy

It is the policy of the Organization that

- 2.1. Expedited review will be conducted in accordance with HHS regulations at 45 CFR 46.110; FDA regulations at 21 CFR 56.110; and will satisfy the criteria for IRB approval described in HRPP policy 2.5 (Criteria for Approval) and in 45 CFR 46.111 and 21 CFR 56.111, as applicable.
- 2.2. Protocols initially reviewed and approved by the expedited method must:
  (1) be no more than minimal risk;
  (2) involve only activities listed in one or more of the categories specified in the OHRP Expedited Review Categories (63 FR 60364-60367, November 9, 1998); and
  (3) meet all the criteria specified in HHS regulations 45 CFR 46.111, FDA regulations at 21 CFR 56.111 (as applicable), the HIPAA Privacy Rule (as applicable), and UNMC HRPP policies.
- 2.3. Expedited review will not be used for initial or continuing review of:

(1) classified research (per OHRP Expedited Review Categories (1998), section D); or (2) research involving prisoners.

- 2.4. Minor changes in IRB-approved research qualify for expedited review in accordance with HRPP policy 2.4 (IRB Review of Changes in Previously Approved Research).
- 2.5. Continuing review of research previously approved by a convened IRB where no subjects have been enrolled and no additional risks have been identified may undergo expedited review.
- 2.6. Continuing review of research which satisfies the requirements of OHRP Expedited Review Categories (1998) category 9 (“research not conducted under an investigational new drug application or investigational device exemption where {expedited} categories 2 through 8 do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified”) may undergo expedited review.
- 2.7. Continuing review of research which has been previously approved by the full IRB prior to the effective date for the Revised Rule, when the research meets the requirements of OHRP Expedited Review Categories (1998) category 8, is eligible for expedited review.
- 2.8. Complaints which are considered minor, unexpected incidents involving no more than minimal risk to subjects or others, and noncompliance which is neither serious nor continuing is eligible for expedited review in accordance with HRPP policies 8.2 (IRB Review of Study Related Complaints) and 8.4 (IRB Review of Noncompliance Involving the PI and Study Personnel).

3.0 Definitions

- 3.1. Expedited Review: review of research involving human subjects by one or more experienced reviewers designated by the Chair from among members of the IRB in accordance with the requirements set forth in 46 CFR 46.110; 21 CFR 56.110.
- 3.2. Minimal Risk: the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (per 45 CFR 46.102(j)), and 21 CFR 56.102(i)).

4.0 Expedited Review Categories

- 4.1. The following categories of research may be eligible for review through the expedited review procedure. Research activities must be no more than minimal risk. For research subject to the Common Rule, inclusion of research activities on the list of OHRP Expedited Review Categories (63 FR 60364-60367, November 9, 1998) is presumed to mean that the activity is minimal risk (FR 82 (12):7206, 2017) unless the reviewer determines and documents the rationale for considering the activity greater than minimal risk.
    - 4.1.1. Category 1: Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
        - 4.1.1.1. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.

      Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.
        - 4.1.1.2. Research on medical devices for which:
            - 4.1.1.2.1. An investigational device exemption application (21 CFR Part 812) is not required; or
            - 4.1.1.2.2. The medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
    - 4.1.2. Category 2: Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
        - 4.1.2.1. From healthy, non-pregnant 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
        - 4.1.2.2. 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.
    - 4.1.3. Category 3: Prospective collection of biological specimens for research purposes by noninvasive means.

      Note: Examples of such biological specimens include but are not limited to
      (a) Hair and nail clippings in a non-disfiguring manner;
      (b) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
      (c) Permanent teeth if routine patient care indicates a need for extraction;
      (d) Excreta and external secretions (including sweat);
      (e) Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
      (f) Placenta removed at delivery;
      (g) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
      (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
      (i) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
      (j) Sputum collected after saline mist nebulization.

- 4.1.4. Category 4: Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing.
  Note: Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.
  Note: Examples of such non-invasive procedures include but are not limited to:
  (a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
  (b) Weighing or testing sensory acuity;
  (c) magnetic resonance imaging;
  (d) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography;
  (e) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
- 4.1.5. Category 5: Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis).
  Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. This listing refers only to research that is not exempt.
- 4.1.6. Category 6: Collection of data from voice, video, digital, or image recordings made for research purposes.
- 4.1.7. Category 7: Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
  Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. This listing refers only to research that is not exempt.
- 4.1.8. Category 8: Continuing review of research previously approved by the convened IRB as follows:
  - 4.1.8.1. 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
  - 4.1.8.2. Where no subjects have been enrolled and no additional risks have been identified; or
  - 4.1.8.3. Where the remaining research activities are limited to data analysis.
- 4.1.9. Category 9: Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) above 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.

5.0 Procedures

- 5.1. All IRB applications are submitted to the ORA and processed in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).
- 5.2. Appointment of Designated Expedited Reviewers
  - 5.2.1. An IRB member may serve as an expedited reviewer once they have been judged by the IRB Executive Chair/designee to be sufficiently qualified and experienced. Specifically, the reviewer must have:
    - 5.2.1.1. An acceptable level of knowledge about the area of research under review.
    - 5.2.1.2. An understanding of the categories of research that qualify for expedited review.
    - 5.2.1.3. The ability to apply the IRB approval criteria and determine conditions required for IRB approval.
    - 5.2.1.4. An absence of a COI in accordance with HRPP policy 1.7 (IRB Member, Consultant, and Staff COI Identification & Management).
  - 5.2.2. An IRB Analyst who is also a voting board member may serve as an expedited reviewer, provided they meet the requirements above.
  - 5.2.3. Assignment of an expedited reviewer for a protocol will be made by the Executive Chair/designee. In the absence of a specific decision to the contrary the expedited reviewer will be the IRB Analyst responsible for the protocol, provided they meet the requirements above.
- 5.3. Expedited Review Procedures
  - 5.3.1. The expedited reviewer must be satisfied that they have sufficient information to make the determinations required for IRB approval in accordance with 45 CFR 46.111; 21 CFR 56.111, and HRPP policy 2.5 (Criteria for IRB Approval).
    - 5.3.1.1. The expedited reviewer must be satisfied that they have the appropriate expertise to review the protocol. If they do not, then the reviewer may request that a consultant with appropriate expertise be obtained, in accordance with HRPP 1.6 (IRB Composition, Leadership, Qualifications, and Responsibilities) section 3.1.3.
  - 5.3.2. The expedited reviewer is expected to consult the IRB study files in RSS (including but not limited to the IRB application, full protocol, investigator's brochure, questionnaires and surveys, recruitment and other subject facing materials, and consent documents), applicable regulations, and HRPP policies, as necessary during their review of the protocol.
- 5.4. Criteria for Expedited IRB Approval and Other Determinations
  - 5.4.1. The expedited reviewer must determine that the research falls into one or more of the categories described in section 4.1 above and is no more than minimal risk. If the expedited reviewer finds that the research falls into one of the above categories but constitutes greater than minimal risk the reviewer must document the rationale for considering the activity greater than minimal risk and for review by the

convened IRB.
    - 5.4.2. The expedited reviewer(s) must determine whether the criteria for IRB approval have been (or continue to be) met, per HRPP policy 2.5 (Criteria for IRB Approval).
    - 5.4.3. As appropriate and as relevant to the specific review (such as review of new protocols, continuing reviews, review of requests for change in protocol or ICF or other types of IRB reviews as described previously) the expedited reviewer must also determine:
        - 5.4.3.1. Whether continuing review is required, and if so, whether it is required more often than annually. In making this determination the expedited reviewer may consider factors including but not limited to the nature of the risks associated with the research; the degree of uncertainty regarding the risks involved; the vulnerability of the participants; the experience of the investigator in conducting the research; the IRB's previous experience with that researcher or sponsor); the projected rate of enrollment. If the expedited reviewer determines that continuing review is required, the rationale for conducting continuing review will be recorded in accordance with 45 CFR 46.115(a)(3).
        - 5.4.3.2. Whether the research should have a third party observe the consent process in accordance with HRPP policy 1.2, Section 2.7 (Authority Granted to the IRB by the Organization).
        - 5.4.3.3. Whether the research needs verification from sources other than the PI that no material changes have occurred since the previous IRB review, as required at 45 CFR 46.108(a)(3)(ii) and 21 CFR 56.108(a)(2).
        - 5.4.3.4. Whether the current consent form is still accurate and complete.
        - 5.4.3.5. Whether the research requires an audit of research records in accordance with HRPP policies 1.21 (Post Approval Monitoring of Research) and 8.4 (Review of Noncompliance Involving Risk to the Subject or Others).
        - 5.4.3.6. Whether there are any significant new findings that arise from the review process that might relate to a subject's willingness to continue participation in the study.
        - 5.4.3.7. When the PI is the lead researcher of a multi-site trial, whether the management of information to the protection of human subjects is adequate, such as reporting of unanticipated problems, interim results, and protocol modifications.

6.0 Expedited Review Actions

- 6.1. Approval; initiation of the research is authorized (when institutional requirements are satisfied).
    - 6.1.1. All of the criteria for approval are satisfied and no changes are required.
- 6.2. Conditional approval; final approval contingent upon Expedited Reviewer/designee review and acceptance of specified modifications and/or submission of additional

documents unrelated to the regulatory criteria for approval.
    - 6.2.1. All of the criteria for IRB approval are satisfied provided the investigator makes the specified changes and/or submits the specified documents. The requirements for final approval and release are considered minor and not substantive in nature.
- 6.3. Tabled; re-review required.
    - 6.3.1. The expedited reviewer requires additional information in order to determine whether the criteria for approval have been satisfied.
      Note: Prior to tabling a protocol, the expedited reviewer may continue communication with the investigator to resolve issues related to the protocol that prevent approval (for example that relate to the regulatory criteria for approval).
- 6.4. Refer to full IRB for review
    - 6.4.1. The expedited reviewer is unable to determine that the protocol satisfies the regulatory requirements for expedited review (for example, on closer examination it appears the protocol or the modification constitutes greater than minimal risk); or the expedited reviewer determines that the regulatory criteria for approval are not met; or the expedited reviewer considers the protocol has serious deficiencies which would merit disapproval; or the expedited reviewer believes the research would be more appropriately reviewed by the convened IRB.
      Note: The Expedited Reviewer may not disapprove research. Research which does not satisfy regulatory criteria for approval, or which has serious deficiencies which would merit disapproval must be referred to the full IRB.

7.0 Development of IRB Expedited Review and Final Approval Letters

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- 7.1. Expedited review letters, which reflect the deliberations and decisions of the expedited reviewer(s), are developed by the IRB Analysts, in consultation with the IRB Executive Chair and/or expedited reviewers as appropriate.
- 7.2. The IRB review letters will clearly document the determinations of the Expedited Reviewer and will include:
    - 7.2.1. The decision to approve, require modifications to secure approval, or table.
    - 7.2.2. List any modifications or clarifications required by the Expedited Reviewer.

8.0 Deadlines for PI Responses

- 8.1. The PI is given 60 days from the date of the IRB review letter to respond to the IRB's review by submitting appropriately revised documents. If no response is received by the end of the 60-day period, or by the expiration of an extension provided by the IRB Executive Chair/designee, the study may be withdrawn or closed.

9.0 Review of PI Responses

- 9.1. The IRB Analyst serves as the designated reviewer and is authorized to review and determine the acceptability of the PI's response, in consultation with the IRB Executive Chair, board members and/or other expedited reviewers as appropriate.
  - 9.1.1. If, on consultation with the Executive Chair, the IRB Analyst determines that the investigator's response to the review is inadequate, incomplete, or contains significant changes not initially reviewed by the IRB, the analyst may re-review (or refer back to another expedited reviewer for re-review) and further communicate with the investigator, or may refer the submission for review by the full convened IRB.

10.0 Final IRB Approval Letter

- 10.1. The IRB final approval letter will document the following determinations:
  - 10.1.1. Pertinent dates:
    - 10.1.1.1. Date of conditional approval by expedited reviewer
    - 10.1.1.2. Date all conditions set by the expedited reviewer were determined to be met and the study was granted final approval and release.
    - 10.1.1.3. Expiration Date (per section 11.0)
  - 10.1.2. Compliance with applicable HHS and FDA regulations
  - 10.1.3. Verification that the research is classified as minimal risk
  - 10.1.4. The applicable expedited review category or categories.
  - 10.1.5. Subpart B category for inclusion of pregnant women (as applicable)
  - 10.1.6. Subpart D category for inclusion of children (as applicable)
  - 10.1.7. Waiver or alteration of the requirements for informed consent (as applicable)
  - 10.1.8. Waiver of the requirement for documentation of informed consent (as applicable)

11.0 IRB Approval Periods

- 11.1. The approval period for protocols for which continuing review is required is based on the date that the expedited reviewer gave conditional approval of the research. Studies approved with annual continuing review are valid for 364 days from the date of conditional approval; the approval period expires on the 365th day.

12.0 Documentation of Expedited Review

- 12.1. The IRB Review Checklist: Full and Conditional Approval must be completed and maintained in the protocol file. This checklist will specify: a) the category or categories of research under which the protocol qualifies, b) the risk level as being no more than minimal risk, and c) the IRB approval criteria are satisfied.
- 12.2. IRB members and the IO are advised via email that minutes documenting all actions reviewed and approved by the expedited review procedure are available for review in RSS.
- 12.3. The full convened IRB retains the authority to require modification of the protocol and/or ICF(s) of research reviewed and approved under the expedited process, or to suspend the study or halt accrual if warranted.

13.0 Review by Other Organizational Committees

- 13.1. Before the IRB will grant final approval and release, the ORA must receive verification of approval or completion of review by components of the HRPP as described

in HRPP Policy 1.10 (Scientific and Other Committee Review of Research) and as required by the organization.

DOCUMENT HISTORY:

? Written: 4/11/2016 (Approved: 4/11/2016) - original author not recorded

? Revised: 6/13/2018 - revision not documented

? Revised: 3/17/2021 - Clarified that IRB administrator may re-review “inadequate or incomplete responses” by investigators (or refer back to the expedited reviewer for re-review) and further communicate with the investigator to seek modifications or clarifications; deleted regulatory references to pre-2018 Common Rule; deleted list of “other determinations (section 5.4) and referenced policy 2.2 instead; deleted list of other organizational committees (section 13.1) and referenced policy 1.10 instead.

? Revised: 9/16/2021 - Revised time allowed for investigator to respond (section 8.1) to match policy 2.2

? Revised: 8/4/2023 – generally revised for clarity and for consistency with HRPP 2.2; deleted reference to limited IRB review (section 2.4) since the Organization does not utilize limited IRB review, as per policy HRPP 2.8; revised section 5.3 to better describe Expedited Review Procedures; revised section 5.4 to more fully describe Criteria for Expedited IRB Approval and Other Determinations and to clarify requirement for expedited reviewer to determine and document if research needs continuing review; added description of items to be reviewed (section 5.3.2); simplified section 8.0 (Deadlines for PI Responses; clarified that expedited reviewer may refer a protocol to the convened IRB if they believe it would be more appropriately reviewed by the convened IRB (section 6.4.1); corrected typographic and grammatical errors. {Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

? Revised 1/24/2024 – added section 5.4.1 {Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

2.4 IRB Review of Changes in Previously Approved Research

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization's requirements for IRB review of changes in previously approved research, including single subject protocol deviations.

2.0 Policy

- **2.1.** It is the policy of the Organization that any proposed change in a research activity must be reviewed and approved by the IRB prior to implementation in accordance with the requirements of 45 CFR 46.103(b)(4) (rev 45 CFR 46.108(3)(iii)); 21 CFR 56.108(a)(4) except when: 1) a change is necessary to eliminate an apparent immediate hazard to the subject(s), or 2) a subject needs to be advised immediately of significant new information. Administrative changes do not require IRB review and can, accordingly, be approved by ORA.
- **2.2.** It is the policy of the Organization that protocol changes that are minor are eligible for expedited review under the provisions of HHS regulations at 45 CFR 46.110(b)(2) (rev 45 CFR 46.110(b)(1)(ii)) and FDA regulations at 21 CFR 56.110(b)(2), as applicable.
- **2.3.** It is the policy of the Organization that single subject protocol deviations represent a change in protocol for a single subject and must be reviewed by the IRB prior to implementation; single subject protocol deviations that are minor may be eligible for expedited review by the Executive Chair, IRB Chairs, or designee under HHS or FDA regulations as above.

3.0 Definitions

- **3.1.** ***Major change in protocol*** is a change that, in general, adversely affects the risk-benefit relationship by adding appreciably increasing risks, or appreciably decreasing potential benefits, or impacts the process of consent in a manner that might effect a reasonable person's willingness to participate in the research. Specific activities which constitute major changes are listed in the appendix to this policy.
- **3.2.** ***Minor change in protocol*** is a change that is not characterized as major per 3.1 above. Specific activities which constitute major changes are listed in the appendix to this policy.

- **3.3.** ***Single subject protocol deviation*** is a change in an IRB-approved protocol which is permitted for an individual subject when it is in the best interest of that subject and/or is necessary for research purposes (e.g., data completion).
- **3.4.** ***Administrative change*** is a change where one of the following criteria must be met: 1) the proposed change has no impact on human subject protection, or 2) the proposed change is necessary to clarify or provide only editorial updates to the protocol and/or ICF. These changes can be reviewed and approved by IRB administrators/staff in consultation with the IRB Executive Chair as necessary.
  Examples of administrative changes include: changes in telephone numbers, deletion of study personnel, correction of typographical errors, or minor administrative changes in the protocol by the sponsor.

4.0 Procedures for Change Request in Protocol (other than Single Subject Protocol Deviation)

- **4.1.** The PI must submit a Change Request in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).
- **4.2.** The Change Request will be processed for review in accordance with HRPP policy 2.1 (Submission of Items for Review by the IRB).
- **4.3.** Administrative changes are reviewed and processed by an IRB Administrator or ORA staff.
- **4.4.** The procedure for review via full IRB review or expedited review is in accordance with HRPP policies 2.2 (Full IRB Review) and 2.3 (Expedited Review), respectively.
- **4.5.** The criteria for approval via full IRB review or expedited review is in accordance with HRPP policies 2.2 Section 3.9 (Full IRB Review) and 2.3, Section 5.4 (Expedited Review), respectively.
- **4.6.** The date of continuing review is not changed based on the date of IRB approval of a Change Request.
- **4.7.** Changes in protocol for research classified as exempt per HRPP policy 2.6 (Exempt Research) do not need to be submitted to the ORA provided the changes do not:
  - **4.7.1.** Affect the risk-benefit relationship of the research
  - **4.7.2.** Pose new risks which are greater than minimal
  - **4.7.3.** Constitute a new risk to privacy or confidentiality
  - **4.7.4.** Involve sensitive topics (including but not limited to personal aspects of the subject's behavior, life experiences or attitudes)
  - **4.7.5.** Involve deception
  - **4.7.6.** Target a vulnerable population (as defined in HRPP Policy 4.1; Additional Protections for Vulnerable Populations)
  - **4.7.7.** Include prisoners or children
  - **4.7.8.** Otherwise suggest loss of the exempt status of the research.
    Note: Investigators are encouraged to contact the ORA to discuss whether changes to exempt research requires review by ORA.

5.0 Procedure for Single Subject Protocol Deviation*

- **5.1.** A Single Subject Protocol Deviation Request must be submitted to the ORA and be approved by either the IRB Executive Chair, IRB Chair or designee or the full IRB prior to the initiation of the deviation.
- **5.2.** The PI/authorized study personnel should request approval for the single subject protocol deviation from the study sponsor (if appropriate) in advance of submission to the ORA.
- **5.3.** The IRB Executive Chair, IRB Chair or designee will obtain any additional information required for the review.
- **5.4.** Single subject protocol deviation requests that are more than minor cannot be approved by the IRB Executive Chair, IRB Chair, or designee and will be referred to the full IRB by the designated IRB Administrator for review and approval.
- **5.5.** Single subject protocol deviation requests that are minor will be reviewed and approved by the IRB Executive chair, IRB Chair, or designee.
- **5.6.** All minor single subject protocol deviation requests approved by IRB Executive Chair, IRB Chair, or designee will be submitted to the IRB for their notification.
- **5.7.** Initiation of a single subject protocol deviation without IRB approval represents noncompliance and addressed in accordance with HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).

6.0 Changes in a research activity requiring immediate implementation

- **6.1.** If the change is required to eliminate an apparent, immediate hazard to the subject(s), the PI may implement the change without prior IRB approval in accordance with 45 CFR 46.103(b)(4) (rev 45 CFR 46.108(3)(iii)); 21 CFR 56.108(a)(4).
- **6.2.** The ORA must be notified as soon as possible, but no later than two business days from the time the change was initiated.
  - **6.2.1.** If the change was initiated for all subjects, a Change Request, the revised IRB application and other required documents must be submitted in accordance with this policy.
  - **6.2.2.** If the change was initiated for a single subject, the Single Subject Protocol Deviation Request must be completed and submitted.
- **6.3.** The full IRB will be notified of all changes implemented without prior IRB approval and will take any additional actions necessary to protect human subjects.

7.0 Provision of new information to subjects which requires immediate implementation

- **7.1.** If a change involves immediate disclosure of significant new information (e.g., an important new risk) which is essential to a subject's decision to continue participating in research, the investigator is authorized to implement the change without IRB approval in accordance with 45 CFR 46.103(b)(4) (rev 45 CFR 46.108(3)(iii)); 21 CFR 56.108(a)(4) and HRPP policy 5.1 (Obtaining Informed Consent from Research Subjects).
- **7.2.** The ORA must be notified as soon as possible, but no later than two business days from the time the change was initiated. No new subjects can be accrued without IRB

approval of a revised ICF that includes the relevant information.

- **7.3.** If a Change Request is submitted to the ORA which includes a revised ICF or an addendum ICF containing significant new information involving risk which is germane to a subject's decision to continue participating in the research and the change is not eligible for expedited review, the ORA will submit the RFC for review at the earliest possible full Board meeting.
- **7.4.** The full IRB will be notified of all changes implemented without prior IRB approval and will take any additional actions necessary to protect human subjects.

Appendix to HRPP Policy 2.4 (Changes in Previously Approved Research)

Examples of Major and Minor Changes in Protocol or Single Subject Protocol Deviations (per Sections 3.1 and 3.2)

Examples of Major Changes:

? Changes in inclusion or exclusion criteria that broaden eligibility (i.e., broadening the range of the inclusion criteria or narrowing the range of the exclusion criteria) when risks to new subjects will be different than to previously eligible subjects

? Addition of a vulnerable population (e.g., children, cognitively impaired, prisoners, socially or educationally disadvantaged, students)

? Increase in target accrual of subjects in studies where UNMC. CHMC and/or UNO are the only sites

? Increase in study wide accrual of subjects in a multi-institution study

? Increase in subject payment amount that exceeds criteria in HRPP Policy

? Change in study design, where such change might affect risk, potential benefit to subject or scientific value or validity

? Alterations in the dosage or route of administration of an administered drug

? Addition of research activities that carry greater than minimal risk

? Change in research activities where the change might negatively impact the potential benefit of the research (e.g., change from one questionnaire to another which is not substantively similar, or to a non-validated questionnaire; change from CT-based staging to clinically based staging of a tumor)

? Modification of research questionnaires or data collection instruments/processes to collect sensitive information (e.g., depression, sexuality, illegal activities)

? Addition of an element that may affect subject confidentiality (e.g., specimen banking or genetic testing; addition of focus groups or identifiable surveys)

? Extending substantially the duration of exposure to the test material or intervention

? Deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations

? Addition of serious adverse events, serious UADEs or other significant risks to the Informed Consent process or form

? Addition of a new (additional) consent form

? Addition of a qualified investigator with a disclosable conflict of interest

? Changes, which, in the opinion of the IRB chairperson or his/her designee, do not meet the criteria or intent of a minor modification

Note: Multiple minor changes in the protocol, instruments, and/or consent may, together, be considered a major change subject to convened IRB review

Examples of Minor Changes:

? Changes in inclusion or exclusion criteria that narrow eligibility (i.e., narrowing the range of the inclusion criteria or broadening the range of the exclusion criteria).

Note: such changes should not appreciably reduce the likelihood that the research can be completed in a timely manner

? Changes in inclusion or exclusion criteria that broaden eligibility (i.e., broadening the range of the inclusion criteria or narrowing the range of the exclusion criteria) when the investigator provides evidence that risks to the new subjects will not be different than to previously eligible subjects

? Increase in local enrollment of subjects in a multi-institution study without a change in the overall study wide enrollment target

? Addition of research activities that constitute no more than minimal risk.

Note: addition of clinically indicated procedures where data will be used for research purposes (i.e., where the incremental risk is no more than minimal) are considered a minor change

? Addition of research activities that would be eligible for expedited IRB review (per §_.110(b)(ii)) under categories 1-7 (unless specifically defined as “major” above)

? Alterations in the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug, provided the dose and route of administration are unchanged

? Decrease in the number or volume of biological samples collection, provided that such a change does not affect the collection of information related to safety evaluations;

? Decrease in the length of hospitalization or number of study visits, provided such a decrease does not affect the collection of information related to safety evaluations

? Alternations subject payment schedule, provided such payments remain fairly pro-rated

? Increase in subject payment amount provided such amounts are within criteria in HRPP Policy

? Changes to improve the clarity of statements or to correct typographical errors in the protocol, CF or any questionnaire, provided that such a change does not alter the content or intent of the statement

? Changes in recruitment materials and advertising, provided such items continue to satisfy criteria in HRPP Policy

? Revision of subject identification and recruitment strategy to include use of the Nebraska Medicine Conditions of Treatment Opt-In database.

? Consent form modifications that add or remove information from the consent form so that it is consistent with an already approved IRB requirement

? Updating a consent form using IRB approved boiler plate language

? Addition or deletion of qualified investigators or personnel

? Addition of study sites (that have a valid FWA and Reliance agreement as appropriate); or that serve as performance sites where informed consent will not be obtained; or that serve as performance sites where informed consent will be obtained by a UNMC, CHMC or UNO investigator.

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2.5 Criteria for IRB Approval

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization’s criteria for IRB approval for human subject research, reviewed both by the full convened IRB or thorough an expedited review process.

2.0 Policy

It is the policy of the Organization human subject research must satisfy certain basic ethical and regulatory requirements, including those described in 45 CFR 46.111 and 21 CFR 56.111.

3.0 Criteria for IRB Approval

Each of the following criteria for IRB approval must be satisfied in full accordance with applicable federal regulations and HRPP policies which contain greater detail about how the IRB interprets and applies these criteria. The criteria must be met before the IRB can grant approval of any submission by expedited review or full IRB review.

- **3.1.** Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures, already being performed on the subjects for diagnostic or treatment purposes.
  - **3.1.1.** The IRB will:
    - **3.1.1.1.** Ensure that the PI and other study personnel have the necessary qualifications, experience and medical licensure
      - **3.1.1.1.1.** The credentialing processes at Nebraska Medicine, BMC or CHMC in advance of IRB review will facilitate IRB assessment that investigators and study staff are qualified
    - **3.1.1.2.** Evaluate the research design in order to ensure that it is both sound and does not unnecessarily expose subjects to risk.
    - **3.1.1.3.** Ensuring that the research uses procedures already being performed on the subjects for diagnostic or treatment purposes
    - **3.1.1.4.** Assess whether risks are minimized by using alternative procedures that have less risk, precautions to decrease the likelihood that harms will occur, and contingencies to deal with harms if they occur.

        - **3.1.1.5.** Utilize reviewers (or other members or consultants) who have familiarity with the procedures being performed, and who therefore can more ably assess whether risks are minimized.
- **3.2.** Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
    - **3.2.1.** The IRB will only consider those risks and benefits that may result from the research as distinguished from risks and benefits of therapies (or other interventions) the subjects would receive if not participating in the research.
    - **3.2.2.** The IRB will not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) in determining whether the risk-benefit relationship is acceptable.
    - **3.2.3.** The IRB will carefully evaluate the protocol in order to identify all risks. A risk is a potential harm (injury) associated with the research that a reasonable person in the subject position would likely consider significant. Risks can be generally categorized as physical, psychological, sociological, economic, and legal.
    - **3.2.4.** In evaluating the risk(s) of the research, the IRB will use the criteria that the risk(s) must be “reasonably foreseeable“. This means data exists which indicate there is a reasonable possibility that the subject could experience the harm described. It does not mean that every known risk associated with each research intervention must be addressed. It is also important to consider when a harm may be irreversible.
    - **3.2.5.** The IRB will assess the anticipated benefits to subjects (if any) and the importance of the knowledge that may be reasonably expected to result from the research. In making this assessment, the IRB will consider the background section, the literature citations, and other sections of the IRB application and other related materials (for example, the detailed protocol or the published literature) which support the PI’s statement of anticipated benefits. The IRB does not classify financial compensation to the subject as a “benefit” in the context of the risk-benefit relationship.
    - **3.2.6.** The IRB will assess the risk/benefit relationship of the research and ensure that it is both acceptable and that subjects are not disadvantaged by participating in research as opposed to choosing available alternatives which may be more advantageous.
    - **3.2.7.** The IRB will assess that the research has the necessary resources to protect subjects:
        - **3.2.7.1.** Adequate time for the researchers to conduct and complete the research.
        - **3.2.7.2.** Adequate number of qualified staff.
        - **3.2.7.3.** Adequate facilities.
        - **3.2.7.4.** Access to a population that will allow recruitment of the necessary number of participants.
        - **3.2.7.5.** Availability of medical or psychosocial resources that participants may need as a consequence of the research.
- **3.3.** Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

    - **3.3.1.** The IRB will assess the IRB application and other related materials (for example, recruitment materials) in order to ensure that the selection of subjects is equitable with respect to age, gender, reproductive status, ethnicity, inclusion of vulnerable populations and any other factors that affect the equitable selection of subjects. No group should receive a disproportionate share of the benefits of the research or bear a disproportionate burden.
    - **3.3.2.** In making this assessment the IRB will evaluate at least the following:
        - **3.3.2.1.** Purpose of the research.
        - **3.3.2.2.** Setting in which the research occurs
        - **3.3.2.3.** Whether prospective subjects will be vulnerable to coercion or undue influence
        - **3.3.2.4.** The selection (inclusion/exclusion) criteria
        - **3.3.2.5.** Scientific and ethical justification for inclusion of vulnerable populations
        - **3.3.2.6.** Scientific and ethical justification for excluding classes of persons who might benefit from the research.
        - **3.3.2.7.** Subject recruitment and enrollment procedures
        - **3.3.2.8.** The influence of compensation to participants
    - **3.3.3.** The IRB's assessment of equitable subject selection will be made at the time of initial review, continuing review, and changes in protocol.
- **3.4.** Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by the Federal Regulations.
    - **3.4.1.** The IRB will review the IRB application and ICFs in order to determine that legally effective informed consent will be sought from each prospective subject or the subject's Legally Authorized Representative (LAR) under circumstances that provide sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence, and which includes information that a reasonable person would want to have in order to make an informed decision about whether to participate. In addition to ensuring that the ICF contains all required elements of informed consent, the Board must also determine there is an appropriate process of informed consent in consideration of the nature of the research, risks associated with the research, and the characteristics of the subject population.
    - **3.4.2.** The IRB will determine which projects should have a third party observe the consent process.
- **3.5.** Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations.
    - **3.5.1.** The IRB will review the IRB application and ICFs in order to determine that all individuals involved in the obtainment and documentation of informed consent have the necessary expertise as well as sufficient knowledge about the protocol and IRB consent requirements.
    - **3.5.2.** Under certain circumstances, the IRB may determine that obtainment and documentation of informed consent by a physician or dentist will be required for some trials.
- **3.6.** When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
    - **3.6.1.** The IRB will review the IRB application and other related materials (e.g., detailed protocol) in order to determine that the safety monitoring plan makes adequate provision for monitoring the involvement of subjects and the collection of data to ensure the safety of subjects.

- **3.6.2.** The overall elements of the monitoring plan will vary depending on the potential risks, complexity, and nature of the research. These may vary from monitoring by the PI in a small, low risk study to the establishment of an independent data and safety monitoring board (DSMB).
- **3.6.3.** The IRB will also determine whether the research requires review more often than annually, as described in HRPP policy 3.1 (Assessing the Need for Increased Monitoring, Interim Continuing Review, and Verification from Sources Other than the PI).
- **3.6.4.** The approval period will be documented in the IRB records and conveyed to the PI.
- **3.6.5.** The IRB will determine which projects need verification from sources other than the PI that no material changes have occurred in the research since the previous IRB review.
- **3.6.6.** The IRB will determine which projects require an audit of research records.

- **3.7.** When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
  - **3.7.1.** Privacy refers to persons and their interest in controlling access to themselves. In order to ensure protection of subject's privacy, the IRB will apply the following criteria:
    - **3.7.1.1.** The methods used to identify and contact prospective subjects is acceptable.
    - **3.7.1.2.** The settings in which the individual will participate in the consent process as well as the research adequately protect privacy.
    - **3.7.1.3.** The personnel involved in the research are appropriate in consideration of their responsibilities.
    - **3.7.1.4.** All necessary procedures are in place during the research to protect privacy.
  - **3.7.2.** Confidentiality refers to protecting data. In order to ensure there is an appropriate plan to maintain confidentiality and minimize the possibility that information will be inappropriately disclosed, the IRB will apply the following criteria:
    - **3.7.2.1.** The reason(s) for disclosing data to individuals, sponsors or other organizations is justified.
    - **3.7.2.2.** The procedures for securing and transmitting data are acceptable.
    - **3.7.2.3.** The potential harm that may result from inappropriate disclosure of research data is minimized.
- **3.8.** When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.
  - **3.8.1.** The IRB will review the characteristics of the proposed subject population in consideration of:
    - **3.8.1.1.** The nature and risks of the research.
    - **3.8.1.2.** Whether the subjects are likely to be vulnerable to coercion, undue influence, or more susceptible to risk.
  - **3.8.2.** The IRB will ensure that additional safeguards are included in the protocol in order to fully protect the rights and welfare of vulnerable subjects in accordance with HRPP policy 4.1 (Additional Protections for Vulnerable Populations).

4.0 Additional Considerations

In addition to the specific criteria described in section 3.0, the IRB will consider other applicable federal, state and local law and regulations, Organization policies, and basic ethical principles (as described in the Belmont Report, or the World Medical Association Declaration of Helsinki) when deciding whether a research proposal is approvable.

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2.6 Exempt Research

1.0 Purpose

The purpose of this policy and procedure is to describe the Organization’s requirements for determining if a research proposal is eligible for exemption under 45 CFR 46.104(d) and 21 CFR 56.104, with appropriate protections in place for research subjects.

2.0 Policy

It is the policy of the Organization that:

- 2.1. All proposed exempt research must be reviewed and approved by the Office of Regulatory Affairs (ORA) prior to initiation.
- 2.2. The ORA has the authority to refer to the full IRB for review and approval any exempt human subject research where such review and approval would meaningfully enhance protection of the rights and welfare of human subjects.
- 2.3. Exempt human subject research must be conducted in accordance with sound ethical standards and all applicable HRPP and institutional policies.

3.0 Categories of Exemption

- 3.1. The following research is exempt from 45 CFR 46:
  - 3.1.1. Category 1: Research which specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods (45 CFR 46.104(d)(1))
    - 3.1.1.1. Per HRPP Policy to be eligible for exemption under category 1
      - 3.1.1.1.1. Study procedures must not involve sensitive subjects (e.g., sex or substance abuse education)
      - 3.1.1.1.2. The research is not regulated by the US FDA.
      - 3.1.1.1.3. Provisions must be made to ensure the existence of a non-coercive environment for those students who choose not to participate
      - 3.1.1.1.4. The school or other institution must grant written approval for the research to be conducted
      - 3.1.1.1.5. Informed consent must be obtained from the prospective subject or their parent or guardian.
  - 3.1.2. Category 2: Research which only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation 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; or (ii) any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or (iii) the information obtained 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 per HRPP policy 2.8 (Limited IRB Review) (45 CFR 46.104(d)(2))
    - 3.1.2.1. Research involving the observation of public behavior of minors is only eligible for exemption if the investigator does not participate in the activities being observed AND if criterion (i) or (ii) above are met.
    - 3.1.2.2. Research involving the use of survey or interview procedures involving minors is not eligible for exemption under this category.
    - 3.1.2.3. Research involving minors is not eligible for exemption under criterion (iii) above.
    - 3.1.2.4. Research regulated by the US FDA is not eligible for exemption under this category.
  - 3.1.3. Category 3: 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; or (ii) any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or (iii) the information obtained 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 per HRPP policy 2.8 (Limited IRB Review) (45 CFR 46.104(d)(1)).
    - 3.1.3.1. Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.
    - 3.1.3.2. Consent of the subject is required, as per section 6.7 below.
    - 3.1.3.3. 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.
    - 3.1.3.4. Research involving minors is not eligible for exemption under category 3.
    - 3.1.3.5. The research is not regulated by the FDA.
- 3.1.4. Category 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; or (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; or (iii) the research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under the HIPAA Privacy Rule (45 CFR 164 subpart E) (45 CFR 46.104(d)(4)); or (iv) The research involves only information collection and analysis, that either involves research conducted by, or on behalf of, a federal department or agency using government-generated or government-collected information obtained for non-research 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 or Privacy Act of 1974, 5 U.S.C. 552a.
    - 3.1.4.1. It is expected that use of this exemption will include, where appropriate, individual's authorization for future, secondary research use of PHI, or waiver of authorization per HRPP policy 5.2 (Waiver or Alteration of Informed Consent and HIPAA Authorization).
    - 3.1.4.2. This exemption does not apply where the PHI originates at an entity subject to HIPAA but is disclosed to an investigator who is not subject to HIPAA.
- 3.1.5. Category 5: Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, 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 (45 CFR 46.104(d)(5)).
    - 3.1.5.1. The research or demonstration project must be listed on a Federal Web site maintained by the department or agency, as per requirements of 45 CFR 46.104(d)(5)(i).
    - 3.1.5.2. The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act). State programs are not included in this exemption unless the Federal Government has contracted or otherwise entered into an agreement with the State to evaluate a program.
    - 3.1.5.3. There must be no statutory requirement that the project be reviewed by an Institutional Review Board (IRB).
    - 3.1.5.4. The research is not regulated by the US FDA.
  - 3.1.6. Category 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 Food and Drug Administration, or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. (45 CFR 46.104(d)(6))
  - 3.1.7. Categories 7 and 8: Storage, maintenance and secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use; and Research involving the use of identifiable private information or identifiable biospecimens for secondary research use (45 CFR 46.104(d)(7 and 8).
    - 3.1.7.1. UNMC does not currently allow investigators within the Organization to use broad consent for storage, maintenance or secondary use of identifiable private information or identifiable biospecimens.
    - 3.1.7.2. Identifiable private information or identifiable biospecimens obtained under broad consent by investigators outside the Organization may be transferred to, and used by an investigator within the organization, provided appropriate Material Transfer Agreements and/or Data Use Agreements are in place, and the ORA has determined that:
      - 3.1.7.2.1. The Broad Consent form obtained by the outside investigator included all the required elements of broad consent per 45 CFR 46.116(d); and
      - 3.1.7.2.2. The research to be conducted within the Organization is within the scope of the general description of the types of research that might be conducted (per 45 CFR 46.116(d)(2)); that is, the broad consent form included sufficient information such that a reasonable person would expect that the broad consent would permit the types of research to be conducted within the Organization.
- 3.2. FDA Category (c): Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days (21 CFR 50.104(c))
  - 3.2.1. This exemption applies only to the first use of the test article within the Organization. Any subsequent use of the test article at the Organization is subject to IRB review per HRPP policy 6.4 (Emergency Use of a Test Article).
- 3.3. FDA Category (d): Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that

contains a food ingredient at or below the level and for a use to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. (21 CFR 50.104(d))

4.0 Limitations on Categories of Exemption

- 4.1. Research involving children where research involves survey or interview procedures or observation of public behavior that qualify under category 2 are not exempt if the investigator(s) will participate in the activities being observed (45 CFR 46.104(b)(3)).
  - 4.1.1. Research involving children may be exempt under category 2 only if the research activities are those involving educational tests or observation of public behavior where the investigators do not participate in the activity being observed. The use of survey or interview procedures is eliminated from this exemption, and so is research involving the observation of public behavior if the investigators participate in the activity being observed. To be exempt, these activities must also meet the condition that the data are recorded without individual identifiers, or the condition that disclosure of the recorded responses would not place the subjects at risk of criminal or civil liability or be damaging to their financial standing, employability, or reputation.
  - 4.1.2. Research involving children is not exempt under category 3 (benign behavioral interventions).
- 4.2. Research involving prisoners is not exempt, except for research aimed at involving a broader subject population that only incidentally includes prisoners (45 CFR 46.104(b)(2)).
- 4.3. Research involving vulnerable populations, sensitive topics (including but not limited to personal aspects of the subject’s behavior, life experiences or attitudes), deception, or greater than minimal risk to subjects, even when allowable under sections 3.0 or 4.0 above, may be deemed not exempt, on a case by case basis. This decision is made by the IRB Administrator in consultation with the IRB Executive Chair or IO.
- 4.4. Any human subjects research where review by the full IRB would meaningfully enhance protection of the rights and welfare of human subjects may be deemed not exempt. This decision is made by the IRB Administrator in consultation with the IRB Executive Chair or IO review.

5.0 Procedures

- 5.1. Protocols which may be eligible for exemption are submitted to ORA using the following applications:
  - 5.1.1. Exempt Application will be used for the following:
    - 5.1.1.1. Categories 1-3, 5-6, and FDA category (d)
    - 5.1.1.2. Category 4 research which involves only identifiable private information not obtained from medical records.
  - 5.1.2. Human Biological Materials Research Application will be used for the following:
    - 5.1.2.1. Category 4 research which involves identifiable biospecimens, with or without associated medical records.
  - 5.1.3. Medical Records Research Application will be used for the following:
    - 5.1.3.1. Category 4 research which involves only identifiable private information from medical records.

  Note: The Organization does not utilize Exemption categories 7 and 8.
- 5.2. Protocols which appear to be eligible for exemption are reviewed by a designated IRB Administrator. This individual will have no direct involvement in the activity he or she is reviewing or any other conflict of interest that would compromise objectivity as per HRPP policy 1.7 (IRB Member, Consultant, Staff COI Identification & Management).
- 5.3. The IRB Administrator will:
  - 5.3.1. In consultation, as necessary, with the IRB Executive Chair/designee, make the final determination of exempt status.
  - 5.3.2. Determine whether criteria for approval described in section 6.0 are satisfied. If necessary, the IRB Administrator is authorized to require clarification or modification of the IRB Application to determine whether the criteria re satisfied.
  - 5.3.3. Complete the Exempt Research Checklist which includes the category under which the research qualifies for exemption.
  - 5.3.4. Communicate the determination with the PI (or his/her designee)
- 5.4. Projects determined not to be exempt may be referred for expedited review provided the project qualifies under the categories specified at 45 CFR 46.110 or 21 CFR 56.110 (per HRPP policy 2.3: Expedited Review of Research).
  Note: If the Exempt Application was used, the PI will be instructed to fill out the Biomedical Research OR Behavioral and Social Science Research in order to provide the IRB with the information needed to perform a thorough review to ensure that the IRB approval criteria at 45 CFR 46.111 have been satisfied.
- 5.5. If Behavioral and Social Science Research Application is submitted and subsequently determined to be exempt, the PI is notified accordingly.

6.0 Criteria for Approval of Exempt Research

- 6.1. The research must qualify for exemption under the categories specified above (section 4.0)
- 6.2. The research must represent no more than minimal risks to subjects.
- 6.3. Selection of subjects must be equitable.
- 6.4. If identifiable private information is recorded, there must be adequate provisions to maintain the confidentiality of the data.
- 6.5. There must be adequate provisions to maintain the privacy interest of subjects.
- 6.6. The rights and welfare of research subjects must be adequately protected.
- 6.7. If the investigator or his/her staff interacts with subjects, there must be a process of informed consent that will disclose at least (1) a statement that the activity involves research; (2) a statement that participation is voluntary; (3) a description of the procedures; (4) a description of risks if any; and (5) the name and contact information for the researcher.
  - 6.7.1. The ORA and/or the Executive Chair or his/her designee may determine whether this informed consent must be documented by a consent form signed by the subject or his/her LAR, parent or legal guardian.
- 6.8. For exempt research under categories 2 or 3 where 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 (as per 45 CFR 46.104(d)(2)(iii) or 45 CFR 46.104(d)(3)(i)(C)), the IRB must conduct a limited review as described in HRPP policy 2.8 (Limited IRB Review).
- 6.9. For exempt research under category 4 where the research involves only information collection and analysis involving the investigator's use of identifiable health information (as per 45 CFR 46.104(d)(4)(iii)), the ORA must determine that such use is regulated under the HIPAA Privacy Rule (45 CFR 164 subpart E).

7.0 Actions

- 7.1. Approval and full release; initiation of the research is authorized: Criteria in section 6.0 are satisfied. The investigator will be notified of the approval in writing and is authorized to start the study.

- 7.2. Conditional approval; final ORA approval and full release contingent upon IRB Administrator acceptance of specified modifications: Criteria in section 6.0 will be satisfied if specified modifications are made by the investigator. Once the modifications are made, and are accepted by the IRB Administrator, the investigator will be notified of the approval in writing and is authorized to start the study.
- 7.3. Referred for expedited review: The protocol is referred for expedited review in accordance with the requirements of 45 CFR 46.110; 21 CFR 56.110.
- 7.4. Referred for full board review: The protocol is referred for review by the full IRB in accordance with section 4.0 above.

8.0 Review by Other Organizational Committees

- 8.1. Before the IRB will grant final approval and release, the ORA must receive verification of approval or completion of review by the following committees/offices as applicable:
  - 8.1.1. Fred & Pamela Buffett Cancer Center Scientific Review Committee
  - 8.1.2. Conflict of Interest Committee
  - 8.1.3. Sponsored Programs Administration/executed contracts office

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DOCUMENT HISTORY:

? Written: 1/5/2016 (Approved: 1/5/2016) - original author not recorded

? Revised: 2/5/2018 - revision not documented

? Revised: 8/11/2020 - Clarified eligibility of children for exemption category 2, clarified requirement for documentation of informed consent for exempt research

? Revised: 10/7/2020 - Deleted exempt categories from pre-2019 Rule (section 3.1); other minor clarifications and corrections

? Revised: 2/28/2022 - Corrected typographic errors; deleted references to pre-2019 Rule; other stylistic changes {Approved Russell McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

? Revised: 1/7/2024 – Addition of 3.1.4 (iv) to comply with revised Common Rule {Approved Russell McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

2.7 Continuing Review of Research

1.0 Purpose

The purpose of this policy is to describe the Organization’s requirements for continuing review of approved research

2.0 Policy

It is the policy of the Organization that:

- 2.1. Non-exempt research which is subject to the Common Rule or FDA Regulations shall undergo continuing review at intervals appropriate to the degree of risk, but not less than once per year, except as allowed under 45 CFR 46.109(f).
- 2.2. Non-exempt research which is not subject to the Common Rule or FDA Regulations shall undergo continuing review at intervals appropriate to the degree of risk.

3.0 Continuing Review Frequency

- 3.1. Non-exempt research which is subject to the Common Rule or FDA Regulations shall undergo continuing review at intervals appropriate to the degree of risk, but not less than once per year, except as described in section 3.3 below.

    - 3.1.1. The IRB may determine that continuing review is required more often than annually, as described in HRPP policy 3.1 (Assessing the Need for Increased Monitoring, Interim Continuing Review, and Verification from Sources Other than the PI).
    - 3.1.2. Unless the IRB specifically determines at the time of initial review or continuing review that a protocol should be reviewed less often than annually, the research will be subject to review annually
- 3.2. Non-exempt research which is not subject to the Common Rule or FDA Regulations shall undergo continuing review at intervals appropriate to the degree of risk.
- 3.3. Unless the IRB determines otherwise, continuing review of research is not required in the following circumstances:
    - 3.3.1. Research not subject to FDA regulations which underwent expedited review in accordance with 45 CFR 46.110 after January 20, 2019.
    - 3.3.2. Research not subject to FDA regulations which was approved after January 20, 2019 and has progressed to the point that it involves only data analysis, including analysis of identifiable private information or identifiable biospecimens.
    - 3.3.3. Research not subject to FDA regulations which was approved after January 20, 2019 and has progressed to the point that it involves only accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

  Note: For the purposes of this policy, if a particular procedure is specified in the research protocol to occur at a specific time then that procedure is considered a research procedure, and not a procedure "that subjects would undergo as part of clinical care."
    - 3.3.4. If the IRB determines that continuing review is required for research in any of the above categories, the rationale will be recorded in accordance with 45 CFR 46.115(a)(3).
    - 3.3.5. Non-exempt research approved prior to the effective date of the Revised Rule requires continuing review as per sections 3.1 and 3.2.
- 3.4. Unless the ORA determines otherwise, continuing review is not required for exempt research.
    - 3.4.1. If the ORA determines that continuing review is required for a specific research protocol which was eligible for exemption under categories 2 and 3 (45 CFR 46.104(d)(2) and (3)) and had initially undergone limited IRB review after the effective date of the Revised Rule, the rationale will be recorded in accordance with rev 45 CFR 46.115(a)(3).

  Note: The Organization will not utilize exempt categories 7 and 8 (45 CFR 46.104(d)(7) or (8)).

4.0 Criteria for Review

- 4.1. The criteria for continuing approval of all human subject research (either by full board or by expedited review) are described in HRPP policy 2.5 (Criteria for IRB Approval).

- 4.2. In addition to the criteria in HRPP policy 2.5 (Criteria for IRB Approval), during continuing review by the full IRB or by expedited review, the IRB or the expedited reviewer must also determine:
  - 4.2.1. Whether the research requires continuing review more often than annually as appropriate to the degree of risk. In making this determination, the IRB might consider the nature of risks posed by the research, the degree of uncertainty regarding the risks involved, the vulnerability of the participants, the experience of the investigator, the IRBs previous experience with that investigator or sponsor, the projected rate of enrollment, and/or whether the study involves novel therapies.
  - 4.2.2. Whether the research need verification from sources other than the PI that no material changes have occurred since the previous IRB review as required 45 CFR 46.108(a)(3)(ii)), or 21 CFR 56.108(a)(2).
  - 4.2.3. Whether the current consent form is still accurate and complete.
  - 4.2.4. Whether the research should have a third party observe the consent process.
  - 4.2.5. Whether the research requires an audit of research records in accordance with HRPP policy 1.21 (Post Approval Monitoring of Research) and HRPP policy 8.4 (Review of Noncompliance Involving the PI and Study Personnel).
  - 4.2.6. Whether there are any significant new findings that arise from the review process that might relate to a subject's willingness to continue participation in the study.
  - 4.2.7. Whether subject accrual is adequate to achieve the scientific goals of the study.
  - 4.2.8. When the PI is the lead researcher of a multi-site trial, whether the management of information to the protection of human subjects is adequate, such as reporting of unanticipated problems, interim results, and protocol modifications.
- 4.3. During continuing review by an expedited reviewer, if the reviewer believes any of the situations in section 4.2.1 thru 4.2.8 apply, the protocol will be referred to the full IRB.

5.0 Investigator Responsibilities

- 5.1. If continuing review is required (as per section 3.3 above), a continuing review application must be submitted thru RSS prior to expiration date of the approved protocol.
- 5.2. The investigator must update the record in Clinicaltrials.gov as applicable, per HRPP policy 1.29 (Clinicaltrials.gov Reporting).
- 5.3. If the research is completed, the investigator will be responsible for the activities described in HRPP policy 2.9 (Closure of On-Going Research).
- 5.4. If the research is closed because an investigator does not submit a continuing review or a Demographics Reporting form, the investigator will be responsible for the activities described in HRPP policy 2.9 (Closure of On-Going Research).

6.0 ORA/IRB Responsibilities

- 6.1. Continuing review, when it is required, is conducted by the convened IRB, except under the following circumstances where expedited continuing review is allowed:
  - 6.1.1. Research which satisfies the requirements of OHRP Expedited Review Categories (1998) and HRPP policy 2.3 (Expedited Review), expedited category 8 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 where no subjects have been enrolled and no additional risks have been identified; or where the remaining research activities are limited to data analysis, may undergo expedited continuing review.
  - 6.1.2. Research which satisfies the requirements of OHRP Expedited Review Categories (1998) and HRPP policy 2.3 (Expedited Review), expedited category 9 (“research not conducted under an investigational new drug application or investigational device exemption where {expedited} categories 2 through 8 do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified”) may undergo expedited continuing review.
  - 6.1.3. Research which underwent expedited review in accordance with 45 CFR 46.110 or 21 CFR 56.110 prior to January 20, 2019, may undergo expedited continuing review.
- 6.2. The ORA will send emails to the PI and the Lead Coordinator and/or Regulatory Contact at least 60 days and 45 days prior to the date of expiration.
- 6.3. Protocols initially approved by IRB-01 or IRB-02 will undergo continuing review at either the IRB-01 or the IRB-02 meeting.
- 6.4. Protocols initially approved by IRB-04 (Pediatrics) will undergo continuing review at the IRB-04 meeting. If the Executive Chair determines that earlier review is necessary to minimize risk or inconvenience to subjects, protocols can be reviewed at the IRB-01 or IRB-02 as a “Special Review Item”, provided at least one member of IRB-04 is present at IRB-01 or IRB-02 and can serve as primary reviewer.
- 6.5. Protocols initially approved by IRB-03 will undergo continuing review at the IRB-01 or IRB-02 meeting or at the IRB-04 meeting, depending on the nature of the research and the predominant subject population, at the discretion of the Executive Chair.
- 6.6. Protocols initially approved by IRB-05 (SIRB) will undergo continuing review at the IRB-05 meeting. If the Executive Chair determines that earlier review is necessary to minimize risk or inconvenience to subjects, protocols can be reviewed at the IRB-01 or IRB-02 as a “Special Review Item”, provided at least one member of IRB-05 is present at IRB-01 or IRB-02 and can serve as primary reviewer.
- 6.7. For continuing review by the convened IRB or by expedited review, IRB members (and alternates), or the expedited reviewer, will have access to, and are expected to review, IRB study files in RSS, including but not limited to the CR application (which includes a status report on progress of the research) and any newly proposed consent

forms. The primary reviewer for review by the convened IRB, or the expedited reviewer, is also expected the review any protocol modifications previously reviewed and approved by the IRB.

- 6.8. The expiration date of protocols for which continuing review is required is based on the date that the convened IRB gave conditional approval of the research. Studies approved with annual continuing review are valid for 364 days from the date of conditional approval; the approval period expires on the 365th day.
- 6.9. If a protocol for which continuing review is required has not received full approval by the expiration date, the protocol is considered “expired”, and investigators are no longer authorized to conduct research activities or enroll subjects.
  - 6.9.1. Approval expiration is not study suspension, and the protocol is not subject to reporting as per HRPP policy 8.6 (Study Hold, Suspension, and Termination).
  - 6.9.2. The Investigator and the Lead Coordinator and/or Regulatory Contact will be notified by email or through the RSS Message portal that a study is expired and that investigators are no longer authorized to conduct research activities or enroll subjects.
  - 6.9.3. If the investigator believes that it would be in the best interest of a subject participating in an expired research study to continue research activities, the investigator may submit a “Request to Continue Treatment for Enrolled Subjects on Approval Expired Studies” form in RSS.
    - 6.9.3.1. The Executive Chair or designee has the authority to grant approval of the request for one or more subjects provided (1) the research interventions hold out the prospect of direct benefit to the subjects, or (2) withholding those interventions poses increased risk to the subjects.
    - 6.9.3.2. If the Executive Chair or designee decides that already enrolled subjects should continue to receive the interventions that were being administered to subjects under the research protocol, data collection (especially safety information) should also continue for such subjects.
  - 6.9.4. If the investigator does not respond to the “Approval Expired” notification from the ORA within 30 calendar days, the study will be considered closed.
- 6.10. The convened IRB will conduct continuing review as per section 4.0 above.
- 6.11. For research that requires FPBCC Scientific Review Committee (SRC) review, IRB continuing approval will be contingent of SRC review and approval.
  - 6.11.1. The IRB Continuing Review Analyst, or designee, in consultation with the IRB Executive Chair or designee will be responsible for assuring that no substantive changes have been made to the protocol or the consent forms by the SRC. If substantive changes have been made, re-review by the convened IRB will be required.
- 6.12. The expiration date for the next continuing review will be based on the date that the convened IRB gave conditional re-approval of the research (as per section 5.7 above)
- 6.13. The ORA will keep appropriate records of all continuing review activity in accordance with 45 CFR 46.115(a)(3).
- 6.14. For research that is exempt, or for which continuing review is no longer required per section 3.3, the investigator is required to complete a Demographic Recruiting Numbers form in RSS annually.
  - 6.14.1. If the investigator does not respond to the email requesting demographic information within 20 calendar days, the study will be considered closed. The investigator will be responsible for the activities described in HRPP policy 2.9 (Closure of On-Going Research).

DOCUMENT HISTORY:

? Written: 2/6/2018 (Approved: 2/6/2018) - original author not recorded

? Revised: 9/7/2018 - revision not documented

? Revised: 1/29/2021 - Clarified “procedures that subjects would undergo as part of clinical care” per (45 CFR 46.109(f)(iii)(B)) (section 3.2.3); clarified which IRBs can perform continuing review (sections 5.2 thru 5.5); various minor clarifications and corrections

? Revised: 1/30/2023 – Revised to stress distinction between FDA regulated and non-regulated research; clarified process for submission of demographic information for research that is exempt, or for which continuing review is no longer required (section 6.1.4); deleted requirement that convened IRB be notified of Request to Continue Treatment for Enrolled Subjects on Approval Expired Studies; changed “20 working days” to “30 calendar days”; reformatted; various minor clarifications and corrections. {Approved Chris Kratochvil (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

? Board notified: 1/31/2023

? Revised: 5/17/2023 - Corrected 6.14 to reflect accurate form name, corrected typo of 30 days to 20 days in 6.14.1 (Robert Lewis, IRB Assoc)

? Revised 1/12/2024 - Revised section 4.0 to clarify responsibilities of expedited reviewer; added section 6.1.3 to clarify research approved by expedited review prior to January 2019 may undergo expedited continuing review; revised section 6.7 to clarify materials available to, and expected to be reviewed by, the convened IRB or expedited reviewer; other minor stylistic changes. {Approved Russell McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

2.8 Limited IRB Review

1.0 Purpose

The purpose of this policy is to describe the Organization’s requirements and procedure for limited IRB review.

2.0 Policy

It is the policy of the Organization that the Organization does not utilize limited review as described in 45 CFR 46.104(d)(2, 3, 7 or 8).

DOCUMENT HISTORY:

? Written: 1/24/2018 - (Approved: 1/24/2018) - original author not recorded

? Revised: 6/5/2023 – deleted text; inserted statement that the Organization does not conduct limited review.{Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

2.9 Closure of On-Going Research

1.0 Purpose

The purpose of this policy is to describe the criteria for, and process of, closing an on-going human research study, and to describe the Organization’s requirements of investigators when studies are closed.

2.0 Policy

It is the policy of the Organization that

- 2.1. All research activities, including analysis of identifiable data, must cease when a research study has closed.
- 2.2. Studies may be closed by the PI or sponsor at any time, or by the IRB if subject accrual has been judged to be inadequate to achieve the scientific goals of the study, or by the ORA if the study remains in standard follow-up without additional research interventions or protocol dictated assessments, or by the IRB or ORA if the investigator has failed to respond to the “Approval Expired” notification from the ORA that IRB approval for a study has expired
- 2.3. The investigator is responsible for notifying the IRB when a study is closed, and for making appropriate updates on ClinicalTrials.gov as appropriate, and for posting the consent forms on ClinicalTrials.gov as required.
- 2.4. Studies closed by the ORA or IRB due to inadequate accrual or closed in standard follow-up, may be reactivated under certain circumstances; studies closed by the IRB or ORA for failure to respond to “approval expired” notification require submission of a new application.

3.0. Definitions

- 3.1. Closure of a study means that all research interventions, including analysis of identifiable data, have been or must be ceased. Closure may occur:
  - 3.1.1. When the aims of the study have been satisfied.
  - 3.1.2. As a decision by the investigator before study aims have been met (for example, due to lack of funds, poor accrual, departure of an investigator, demonstration of lack or efficacy or futility).
  - 3.1.3. As a decision by the sponsor or the granting agency.

    - 3.1.4. By the IRB if subject accrual has been judged to be inadequate to achieve the scientific goals of the study.
    - 3.1.5. By the ORA if the study remains in standard follow-up without additional research interventions or protocol dictated assessments.
    - 3.1.6. By the IRB or ORA if the investigator has failed to respond to the “Approval Expired” notification from the ORA that IRB approval for a study has expired, as per HRPP policy 2.7 (Continuing Review of Research).
- 3.2. Expiration means that approval is no longer valid because required continuing review has not received full approval by the IRB by the expiration date, per HRPP policy 2.7 (Continuing Review of Research). Approval expiration is not study suspension (see HRPP policy 8.6 (IRB Study Hold, Suspension and Termination)).

4.0. Closure for Inadequate Accrual

- 4.1. Single site studies where UNMC/UNO/CHMC is the sole participant, or multi-institution studies where UNMC/UNO/CHMC is a participant but there is no external funding, may be closed by the IRB or ORA for low or no accrual.
    - 4.1.1. Low accrual is defined as less than 1/2 of expected accrual based on the total accrual divided by the estimated time to accrue subjects in initial IRB application.
- 4.2. Studies with low or no accrual after two review cycles will be required to provide an explanation and a detailed plan to increase accrual. Plans to increase accrual might include, but are not limited to:
    - 4.2.1. additional sites
    - 4.2.2. additional investigators
    - 4.2.3. additional study personnel, such as coordinators
    - 4.2.4. expanded study populations or less restrictive inclusion or exclusion criteria
    - 4.2.5. augmented education/training of referring practitioners, as applicable
    - 4.2.6. new advertising
    - 4.2.7. extension of the expected time to achieve target accrual
- 4.3. Failure to accrue a minimum number of subjects by the next review cycle, without acceptable justification by the investigator may lead to closure of the study.
- 4.4. The IRB may allow certain studies involving rare conditions to continue despite poor or no accrual.

5.0. Closure of Studies in Standard Follow-Up

- 5.1. Studies may remain in standard follow-up for no more than three review cycles, and then may be closed, unless:
    - 5.1.1. the study is collecting data in any form (such as survival); or
    - 5.1.2. the organization is contractually required to keep the study open; or
    - 5.1.3. the study includes a tissue bank at the organization (UNMC, UNO, CHMC or BMC); or
    - 5.1.4. the investigator can provide adequate justification for the study to remain open.

- 5.2. If later access to study data is needed by investigators or sponsors, a Medical Records application should be submitted to access existing data.

6.0 Closure Procedures

- 6.1. When a study is closed, all research activities must cease. The investigator may not conduct any further research activities (including collection of existing or additional identifiable private information, or new analysis of existing identifiable private information), or allow any other person or organization to conduct any further research activities.
- 6.2. The investigator is responsible for notifying the IRB when a study is closed.
  - 6.2.1. For studies that require continuing review, this is done by submitting a Continuing Review application or a Completion Report.
  - 6.2.2. For studies that do not require continuing review, such as Central IRB applications or expedited research approved under the 2018 New Common Rule, by submitting a message using the message portal in RSS or by completing the annual demographic recruiting numbers form.
- 6.3. When a study is closed, the investigator is responsible for revising the study status on ClinicalTrials.gov, and posting study results as appropriate, as per HRPP policy 1.29 (ClinicalTrials.gov Reporting).
- 6.4. When a study is closed, the investigator is responsible for posting the consent forms on ClinicalTrials.gov as required.
- 6.5. If a study is closed by the IRB or ORA (per section 3.1.4 or 3.1.5. above), the investigator may request reactivation, with adequate justification, within 30 calendar days from the date of completion. Reactivation after the 30 calendar days grace period requires submission of a new IRB application.
- 6.6. If a study is closed by the IRB or ORA for failure to respond to “approval expired” notification (per section 3.1.6 above), investigators wishing to continue the research must submit a new application.

DOCUMENT HISTORY:

? Written: 1/12/2018 (Approved: 1/12/2018) - original author not recorded

? Revised: 1/29/2021 - Added inadequate accrual as reason for closure by IRB (section 3.1.4) and criteria and process for closure (section 4); added prolonged time in standard follow-up as reason for closure by ORA (section 3.1.5) and criteria and process for closure (section 5).

? Revised: 08/10/2023 – clarified that “closure” includes cessation of analysis of identifiable data; deleted definitions of suspension and termination as irrelevant to this policy; clarified possible options for improving accrual; clarified that closure for inadequate accrual, or of studies in prolonged follow-up may (not “must”) occur; clarified investigator responsibilities regarding study closure by the investigator; added that studies closed for failure to respond to “approval expired” notification may not be reactivated, but will require submission of a new application. {Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}