Procedure Title: Review and Approval of Non-Exempt Studies

Associated Policy:	Human Research Protection Policy (OSA Policy 1.0)		
Responsible Unit:	Office of Scholarly Activity		
Created:	7/13/2017	**Executive Lead:**	Chief Research Officer
Effective:	7/13/2017	**Revision History:**	.01 – 10/13/2017; .02 – 01/09/2018; .03 – 06/05/2018; .04 – 11/14/2018; .05 – 10/04/2019; .06 – 12/11/2019; .07 – 05/19/2020; .08 – 05/25/2021; .09 – 3/29/2023
Approved by:	Institutional Review Board		
Procedure Number:	124.09		
Key Words:	Review, Actions, Approve, Modifications Required, Major Modification, Minor Modification, Withhold, Tabled, Disapprove, Suspension, Termination, Continuing Review, Closure		
Purpose:	To meet the responsibilities for protecting human subjects as issued by the Office for Human Research Protections (OHRP) requirement for individuals involved in the conduct or review of human subjects research at institutions holding OHRP-approved Federal Wide Assurances (FWAs)		

Process:
This SOP serves to inform all agents, offices, departments, and affiliate sites of PNWU regarding approval of human subject research studies.

This SOP must be used as a guide in parallel with OSA Policy 1.0, to comply with human subject research protections. SOPs are not intended to supersede existing institutional policies, and local, state, and federal laws and regulations.

General Information: Criteria for IRB Approval of Research:

The PNWU IRB will apply the criteria for IRB approval described in the PNWU SOPs to research subject to the revised Common Rule (45 CFR 46.111).

- Within criterion 45 CFR 46.111(a)(3), the text describing vulnerable subjects is replaced with the following:
    - *The IRB 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.*
- Likewise, within criterion 45 CFR 46.111(b), the description of vulnerable subjects is updated and now reads:

- *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.*

While pregnant women are no longer described as vulnerable within the above criteria, the IRB shall continue to apply Subpart B "Additional Protections for Pregnant Women, Human Fetuses and Neonates" as described in the PNWU SOP. The revised Common Rule does not eliminate or modify Subpart B.

NOTE: Studies approved prior to January 21, 2019 will continue to follow Pre Revised 2018 Common Rule policies and SOPs until the studies are closed.

Responsible Parties

The Institutional Review Board (IRB) is responsible for:

- Reviewing applications in a timely fashion.
- Assessing risk and other considerations per federal regulations.
- Communicating with the investigator as to the application status and modifications needed to ensure protection of human subjects.

The Office of Scholarly Activity (OSA) is responsible for:

- Monitoring compliance with this SOP.
- Posting this SOP for the PNWU community.
- Notifying the investigator, no earlier than 60 and no later than 30 days prior to the current IRB approval expiration date and providing them instructions for submitting a request for continuing review or a closure report.
- Ensuring all required information is received prior to forwarding a request for continuing review to the convened IRB and IRB Reviewer conducting the review.

The Investigator is responsible for:

- Completing all forms required by the IRB when requesting review and approval of research (initial applications and revisions).
- Providing adequate justification based upon the requested category on which their application request is based (investigators may not make their own determinations).
- Distributing revised consent forms and other revised study documents to collaborators and members of the study team along with relevant instructions from the IRB.
- Reviewing closure reports for impact on any related studies.
- Ensuring no ongoing research activities occur once the study is closed.

Definitions

Please reference the Glossary for complete definitions of the following terms and additional terms not listed.

- Expedited
- Family Educational Rights and Privacy Act (FERPA)
- Full Board
- Health Information Portability and Accountability Act (HIPAA)
- Human Subject
- Non-Exempt

- Principal Investigator (PI)
- Quorum
- Standard Operating Procedure

Procedure:

1. Please review PNWU OSA SOP 103 Activities Subject to Human Protections, which defines the institution's process for determining Health and Human Services (HHS) conducted or supported research studies qualify as exempt or non-exempt from the HHS regulations.

2. Please review PNWU OSA SOP 115 Functions of the IRB, which defines the IRB's Function on determining exempt and non-exempt study designations.

3. At a convened IRB meeting, the committee will acknowledge and review the list of studies reviewed via expedited process (initial reviews, renewals, amendments, and deviations). Any IRB member can call for a full board review of any submitted protocol.

4. Full Board Review: After Full Board review, a motion must be made for one of the following actions:
    1. Approve (with a specific continuing review interval for initial or continuing review): Made when all criteria for approval are met. The period of approval is typically one year but may be more frequent depending on the level of risk.

    2. Modifications (Conditions) Required to Secure Approval (with a specific continuing review interval for initial or continuing review): Made when IRB members require specific modifications such that an IRB support staff member can determine whether an investigator has made the required changes without judging whether a change meets the regulatory criteria for approval. When making this motion, the assigned primary reviewer restates the modifications required by the IRB members and the IRB member's reasons for those changes. If reviewers don't agree, the study is not approved. The investigators must address the reviewer comments that determination of approval approved with conditions; not approved and didn't meet regulatory criteria.

    3. Withhold: Made when the research does not qualify for Approval or Modifications Required to Secure Approval and the IRB has recommendations that might make the protocol approvable. When making this motion, the assigned primary reviewer describes the IRB member's reasons for the decision and describes recommendations to make the research approvable. All deferred submissions must go back to the same reviewers, primary and secondary reviewers, and committee that conducted the initial review.

    4. Tabled (No Action): Made when the IRB cannot approve the research at a meeting for reasons unrelated to the research, such as loss of quorum. When taking this action, the IRB automatically schedules the research for review at the next available meeting.

    5. Disapprove: Made when the research does not qualify for Approval or Modifications Required to Secure Approval and the IRB has no recommendations that might make the protocol approvable. When making this motion, the assigned primary reviewer describes the IRB member's reasons for the decision.

    6. Suspension or Termination: Made when current approved research does not qualify for Approval or Modifications Required to Secure Approval. When making this motion, have the IRB Chair or Vice Chair to advise the convened IRB through a discussion of what actions

are needed, if any, to protect subjects. The IRB Chair or Vice Chair assigned describes the reasons for the decision.

7. Open the floor for additional discussion.

8. Review any modifications (conditions) required to secure approval to ensure that the IRB staff has recorded them.
    1) Ensure that the required modifications include any necessary review considerations in the Pre-Review activity.
    2) For a pending financial interest review indicate that a determination that the financial interest is not a conflict of interest or has been eliminated can be verified by the IRB staff, but if there is a management plan that includes anything more involved than simple disclosure of the financial interest in the consent document, it must return to the convened IRB for review.

5. Full Board Review: After a motion is made for one of the above actions, the chair will call for a vote:
    a. Quorum must be in place to count the meeting as official.
    b. Only eligible IRB members present via in-person, teleconference, and/or video/web conferencing may vote.
    c. If a member and an alternate are both present, only one may vote.
    d. Consultants may not vote.
    e. IRB members with a conflict of interest are excused for the vote.
    f. For a motion to be approved, it needs the approval of more than half of the members present at the meeting. (If there are 10 or 11 members present at the meeting, 6 votes are required for approval, which is greater than 5 and 5.5, respectively.)
    g. Re-invite IRB members with a conflict of interest back into the meeting.
    h. Provide any written information provided by a member or consultant to the IRB staff.
    i. Adjourn the meeting when notified by IRB staff that quorum has been lost or when there is no further business.

6. Expedited Review: Studies meeting one or more of the expedited review categories may be reviewed under an expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. Expedited review is carried out by two members of the IRB. IRB members take the following actions approve, require modifications, withhold approval (see the descriptions above), or bump the review up to a Full Board Review. IRB reviews of expedited studies are assigned to a primary and secondary reviewer and are conducted on a rolling basis.
    a. Limitations Expedited Review:
        i. Research activities must present no more than minimal risk and involve ***only*** procedures listed in one or more of the expedited categories (e.g, if one of the research procedures is more than minimal risk or is not listed in one of the expedited categories, the study must undergo full board review).
        ii. Expedited review procedure may not be used for classified research involving human subjects.
        iii. Review of research involving prisoners is not permitted via expedited review procedures.
        iv. Blood draws in children 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.
        v. Expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects= financial standing, employability,

insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

7. Revisions to Approved Projects (Note: A revision may also be referred to as an "amendment," a "modification," or a "change.")
    a. Approved research projects involving human subjects are required to report revisions to the IRB.
    b. The federal regulations require review and approval by an IRB before an investigator initiates any modification to a study. A revision includes, but is not limited to:
        i. A change in study design, study methods, or procedures, including removal of a procedure.
        ii. A change in the study title or sponsor.
        iii. A change in recruitment strategies, populations to be enrolled or procedures.
        iv. A change in the IRB-approved informed consent process or consent form, questionnaires, recruitment materials, e.g., advertisements, contact letters or postcards, scripts, or other study-related documents.
        v. A change in investigators, including the addition or withdrawal of sub-investigators, co-investigators, and key members of the study team.
        vi. A change in study sites or sub-sites, including the addition or removal of sites.

    c. Major Modification: A proposed change in research-related activities that materially affects an assessment of the risks and potential benefits of the study or substantially changes the specific aims or design of the study.

    d. Minor Modification: A proposed change in research-related activities that does not materially affect an assessment of the risks and potential benefits of the study and does not substantially change the specific aims or design of the study.

    e. A change made to correct a typographical or grammatical error in an IRB-approved document is not considered to be a modification and, thus, a modification request is not required. The IRB may administratively approve a request to correct typographical errors and other non-modification changes.

    f. If the study revisions meet the criteria for expedited review, the application will be reviewed under expedited procedures. If the study does not meet the criteria for expedited review, expedited review procedures may still be used for Minor Modifications. Federal regulations allow IRBs to review requests for minor modifications using an expedited review procedure. To qualify as a minor modification, the proposed change must not materially:
        1) alter the assessment of risks and potential benefits of the study.
        2) increase the level of risk to the physical, emotional, or psychological well-being of participants, including loss of confidentiality.
        3) change the specific aims or design of the study.

    g. A modification request should include the following information:
        1) Description of the modification.
        2) Purpose of the modification.
        3) Party initiating the modification, investigator or sponsor.

4) Enrollment status of the study, e.g., open, closed, or the number of locally enrolled participants.
5) An explanation of the likely effects from the modification on participants in sufficient detail for the IRB to determine the risks and potential benefits of the proposed change.
6) Because investigators must relay information relating to modifications to participants when the changes may affect the participants' willingness to continue with the study, the investigators should, as applicable, address in the modification request whether they will notify the changes to currently enrolled participants.
    - The investigator can recommend to the IRB the method of communication to participants, e.g., whether they should be re-consented, provided with a notice explaining the change, or have the change explained at the next study visit.

h. If the proposed changes affect the study such as, but not limited to, its objectives, design, methods, procedures, targeted population, or inclusion or exclusion criteria, the investigator must append a revised protocol or protocol amendment to the modification request.

i. Revision applications that qualify for expedited review can be submitted at any time to the IRB. Revision applications that qualify for full board review must be submitted by the deadline on the website to be placed on the agenda of the following month's IRB meeting.

j. Following review of the modification request, the IRB will notify the investigator in writing of its decision. Investigators may initiate the modification after they have received final written approval of the requested modification, not approval with stipulations.

k. Notification to IRB Members: Like studies under expedited initial or continuing review, all IRB members will be notified in writing of modifications approved under this procedure. In addition, the approval of a modification request does not affect the expiration date of the study and the procedures related to the expiration date, unless, the request is reviewed at the same time as the continuing review of the study.

8. Renewal of an Approved Project

a. Non-Exempt Full Board and Expedited review studies reviewed under the Pre-2018 Common Rule are required to undergo continuing review at intervals appropriate to the level of risk, but not less than once per year for previously approved studies by the IRB to ensure approval criteria, as applicable, are still being met. Investigators must submit sufficient information well before the study expires to allow the IRB to perform a substantial and meaningful review that includes, but not limited to:
    i. Review of the ongoing level of risks and benefits.
    ii. Assessment of the need for special safeguards to protect subjects.
    iii. Review of the adequacy of ongoing protection for potentially vulnerable subjects.

b. Full Board Reviewed studies (Reviewed under the Revised Common Rule) - A continuing review must be submitted at intervals appropriate to the level of risk, but not less than once per year for previously approved studies by the IRB to ensure approval criteria, as applicable, are still being met. Investigators must submit sufficient information well before

the study expires to allow the IRB to perform a substantial and meaningful review that includes, but not limited to:

i. Review of the ongoing level of risks and benefits.
ii. Assessment of the need for special safeguards to protect subjects.
iii. Review of the adequacy of ongoing protection for potentially vulnerable subjects.

c. Expedited Reviewed studies (Reviewed under the Revised Common Rule) - may require Continuing Review. Annual check-in will be required for studies not undergoing continuing review. Annual check-in forms are sent to the investigator 30 days prior to the study anniversary date. Check-in forms are due within 30 days of receipt. For studies that require continuing review, this requirement is based on the IRB reviewer recommendations. These recommendations include, but are not limited to, risk, study status, study population, or funding source. To ensure approval criteria when Continuing Review is required investigators must submit sufficient information well before the study expires to allow the IRB to perform a substantial and meaningful review that includes, but not limited to:
    i. Review of the ongoing level of risks and benefits.
    ii. Assessment of the need for special safeguards to protect subjects.
    iii. Review of the adequacy of ongoing protection for potentially vulnerable subjects.

d. Continuing review approval of research must occur on or before the date when IRB approval expires. This includes a study team making and submitting any modifications required by the IRB during its review and the IRB reviewing and approving them prior to the expiration of the current approval period.

e. Continuing review of research is required if the research remains active for long-term follow-up of participants, even when the research is permanently closed to enrollment of new participants and all participants have completed all research-related interventions. Continuing review is also required if the remaining research activities include collection or analysis of private identifiable information as described in the approved protocol.

f. Documents included in a renewal application may include, but are not limited to the currently approved:
    i. Informed consent document
    ii. HIPAA/FERPA authorization
    iii. Protocol
    iv. Recruiting Materials/Advertisements

g. The interval for continuing review will be at least once per year (not to exceed 365 days) but may be shorter. The new expiration date will be calculated based on the approval date. Continuing Review must be completed within 30 days before the approval expiration.

h. When continuing review is not completed prior to the expiration of the current approval period, there is an automatic lapse of IRB approval. All research must stop unless the IRB Chair or Vice Chair determines that it is in the best interests of individual participants to continue the research interventions or interactions. Approval of an amendment during the current approval period by the IRB does not alter the date by which continuing review must occur.

i. If the investigator wants to re-open a study that lapsed for more than 30 days a new application must be submitted or the investigator can consult with the IRB Chair or Vice

Chair and the Institutional Official (IO) regarding any documentation that may be required, in addition to the continuing review application, for the review to take place.

j. If the investigator submitted all the required documents by the expiration date, but the approval period lapses, all the actions as described above must still take place.

k. Renewal procedures for non-exempt studies vote similar to those outlined above.

9. Closure - The completion, suspension, or termination of a project is a change in study activity and must be reported to the IRB. Thus, the investigator is required to inform the IRB using a closure form when a project is closed or terminated.

    a. If the study is terminated by the IRB Chair, Vice Chair, or IO, a letter will be provided to the investigator indicating that all research must stop and provide the reasoning for this termination.

    b. The principal investigator (PI) and/or the IRB administrators may close approved protocols under certain circumstances. The PI is responsible for promptly closing out an IRB approved study if any of the following conditions exist:
        i. All research/clinical investigation activities including data analysis and reporting are complete.
        ii. The PI never initiated the study.
        iii. Subject accrual is finished, all data collection is complete, and the only remaining activity is analysis of the data, the data are de-identified, and there are no identifying links or codes to the de-identified data.
        iv. The PI plans to leave the University and intends to continue the research activities at another institution.
        v. The study has been open for a period of three or more years and the PI has enrolled no subjects in the study, collected no data from records, or collected/received specimens.

    c. The PI cannot close out an active IRB approval if:
        i. He/she is still following subjects or
        ii. He/she is analyzing identifiable data (including data with codes or links to identifiers).

    d. The IRB administrators may notify a PI that IRB approval or active IRB status has expired or that the IRB has inactivated IRB approval after 6-months of non-response from the PI to IRB requests. These requests will be documented in the study files in IRB Manager.

    e. If a study has been open for a period of three or more years and the PI has not enrolled subjects in the study, the IRB requires study closure unless there are extenuating circumstances for keeping the project open (e.g., the study is about a rarely seen condition).

    f. Procedures for closing a study fall into five categories:
        i. Final review
        ii. Non-response from PI to IRB requests
        iii. Closure due to non-enrollment
        iv. Lapse of approval due to non-response to requests for continuation or final review

v. PI initiated withdrawal

g. Regardless of the category for study closure, the expiration date for IRB approval falls on the first day after the approval period end date.

References:

1. Code of Federal Regulations, Title 45, Public Welfare, Department of Health and Human Services Part 46, Protection of Human Subjects, Revised January 15, 2009, Effective July 14, 2009
2. Code of Federal Regulations, Title 42 Policies of General Applicability, Department of Health and Human Services, Part 50 Subpart F – Promoting Objectivity in Research
3. Code of Federal Regulations, Title 21, Food and Drug Administration, Department of Health and Human Services Subchapter A, Part 50 Protection of Human Subjections

Revision History:

Version/ Effective Date	Author	Section Changed & Reason for Revision
.00 / 7-13-2017	M. McCarroll	New Standard Operating Procedure
.01 / 10-13-2017	M. McCarroll	Added "condition" to improve clarity
.02/ 01-09-2018	M. McCarroll	Minor changes to motion to withhold approval
.03 / 06-05-2018	M. McCarroll	Minor changes to quorum at convened meeting
.04 / 11-14-2018	M. McCarroll	Added section regarding closure of a study
.05 / 10-04-2019	C. Case	Put into the new PNWU SOP Format; Updated section 4.a.1-4.a.3 regarding Continuing Review specific to the Revised Common Rule ; Added item 5.e. to excuse members of the IRB with a conflict of interest prior to voting; Number 7.a-d Updated regarding Continuing Review specific to the Revised Common Rule; 7.g.4 Added Recruiting Materials; Number 7.h. updated to reflect the current practice of expiration date being calculated from the approval date.
.06 / 1-24-2020	C. Case	Revised procedure item 4.a.4. adding language for possible review escalation of exempt studies under the Revised Common Rule required to undergo limited IRB Review. The reviewer may request the review level be escalated and require annual continuing review. Annual Check-in language added.
.07 / 05-19-2020	C. Case	Annual Check-in language added.
.08 / 05-25-2021	C. Case	Added timeline language to annual check-in
.09 / 4-13-2023	C. Case	Deleted the information about the L: Drive in the footer of the SOP as all SOPs are now stored in the IRB SharePoint folder and posted in the electronic IRB management system; added General information about Criteria for IRB approval per the revised Common Rule; revised SOP and separated procedures for Exempt vs Non-exempt studies and renamed the SOP from Review and Approval of Studies to Review and Approval of Non-

Version/ Effective Date	Author	Section Changed & Reason for Revision
		Exempt Studies; added language about limitation of expedited review procedures; updated the reference section and the links.

Appendices:
None