Procedure Title: Vulnerable Populations

Associated Policy:	Human Research Protection Policy (OSA Policy 1.0)		
Responsible Unit:	Office of Scholarly Activity		
Created:	03/20/2018	**Executive Lead:**	Chief Research Officer
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Approved by:	Institutional Review Board		
Procedure Number:	128.03		
Key Words:	Vulnerable; Homeless; Children; Tribal; Indian Health Service; Students		
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 protecting vulnerable populations.

General Information:
Federal regulations require the IRB to give special consideration to protecting the rights, safety, and welfare of vulnerable subjects. The regulations at 45 cfr 46 define vulnerable populations as children, prisoners, pregnant women, neonates, and fetuses. There are other individuals that may be considered vulnerable. These individuals may be prone to undue influence or coercion, may be compromised in their ability to give informed consent, or may be part of a convenient population.

Investigators must include additional safeguards in the research design when some or all of the subjects are likely to be vulnerable to coercion or undue influence.

Responsible Parties

The Institutional Review Board (IRB) is responsible for:

- Ensuring that the principal investigator (PI) identifies the potential to enroll vulnerable subjects in the proposed research and provides the justification for their inclusion in the study.
- Ensuring that the PI provides appropriate safeguards to protect the subject's rights and welfare.

- Considering and requiring as needed, the inclusion, either as members or ad hoc consultants, of individuals who have experience with the vulnerable populations involved in the proposed research.
    - Prisoner representatives must be IRB members, not consultants.
- Reviewing the PI's justifications for including vulnerable populations in the proposed research.
- Ensuring that additional safeguards have been included in the proposed research to protect the rights and welfare of vulnerable subjects, and assesses the adequacy of additional protections for vulnerable populations provided by the PI.
- Evaluating the proposed plan for consent and, as needed, assent of the specific vulnerable populations.
- Evaluating the proposed research to determine the need for additional safety monitoring.
- Documenting a risk and benefit assessment for each cohort involved in the protocol in the general comments section of the reviewer checklist. Documentation for vulnerable populations (children, PNWU students, prisoners, pregnant women, fetuses, employees, indigenous persons, tribal members, immigrants and/or individuals unable to provide consent) should also include protocol-specific findings that support and justify the risk and benefit assessment.
- Reviewing existing safeguards, for an amendment to an existing protocol, to protect the rights and welfare of vulnerable subjects in the protocol to ensure that they continue to be adequate
- Determining whether current or past subjects, for an amendment to an existing protocol, must be informed of the amendment and, if so, how they will be informed (verbally and/or in writing). Current and past subjects must be notified if the study amendment affects their safety and welfare, and current subjects must be re-consented if the amendment changes future study procedures

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

- Monitoring compliance with this SOP
- Posting this SOP for the PNWU community
- Providing the necessary support to investigators and the IRB
- Obtaining medical ethics or legal consultation to the IRB as needed

Investigators are responsible for:

- Identifying and ensuring compliance with all Federal Regulations, applicable laws and guidance on human subjects' research in the country or nation where the research will be conducted
- Documenting and declaring in the submitted protocol specific recruitment of vulnerable populations
- Seeking support from OSA and the IRB on proper procedures involved with vulnerable populations
- Ensuring communication and training of the research team on proper protocols for the protections of vulnerable populations
- Refraining from unduly influencing their own students who serve as research subjects

Definitions

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

- Children
- Guardian
- Health Information Portability & Accountability Act (HIPAA)
- Human Research Protection Program (HRPP)
- Human subject
- Indigenous
- Institutional review board (IRB)
- Investigator
- Parent
- Principal investigator (PI)
- Prisoner
- Tribal
- Vulnerable population

Procedure:

1. The PNWU Human Research Protection Program (HRPP) abides by federal regulatory requirements to provide appropriate additional protections for vulnerable subjects (Department of Health and Human Services [DHHS] and Food and Drug Administration [FDA]). The HRPP is multidimensional and includes the Office of Scholarly Activity, the members of the Institutional Review Board, the Institutional Official, as well as the policies and procedures for research with human subjects.

2. 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. Examples may include children and prisoners who are approached by an authority figure to participant in research or economically disadvantaged individuals being offered a large monetary incentive to participate in research.

3. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards must be included in the study to protect the rights and welfare of these subjects.

4. The PNWU HRPP expects the IRB to use their judgment when determining if subjects enrolling into particular protocols are considered vulnerable and if additional protections are warranted. These populations include, but are not limited to, the following:
   - Critically ill patients
   - Children
   - Decisionally incapacitated
   - Economically disadvantaged
   - Educationally disadvantaged
   - Homeless persons
   - Indigenous persons
   - Individuals with substance use disorder
   - Migrant populations (migrant and seasonal farmworkers)
   - Non-English-speaking subjects
   - Nursing home residents or others living in institutional settings
   - Patients in emergency situations

- Pregnant women, fetuses, and neonates
- Prisoners
- Students or employees
- Tribal members or self-identified tribal members
- Undocumented immigrants

5. If the PNWU IRB regularly reviews research that involves vulnerable participants, it shall give consideration to the inclusion of one or more members who have knowledge about and experience with subjects (45 CFR 46). In some cases, additional membership or consultation may be necessary.
   - Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
   - Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
   - Subpart D - Additional Protections for Children Involved as Subjects in Research

6. The PI will complete the electronic IRB application and ensure that the protocol contains the information described in the specified areas relevant to the subjects to be enrolled, i.e., children, prisoners, pregnant women, etc. Additional safeguards must be included in the research design to protect the rights and welfare of these subjects. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The IRB considers for approval research projects, if one of the following conditions is met:
   - The research does not involve more than minimal risk to the subject
   - The research is likely to benefit the subject directly, even if the risks are considered to be more than minimal
   - The research involves greater than minimal risk with no prospect of direct benefit to individual participants, but is likely to yield generalizable knowledge about the subject's disorder or condition
   - Requests for approval of any research that exposes vulnerable populations to risks that do not meet one of the above criteria must be submitted to the Secretary of the DHHS for review and approval (federally funded only)
   - All privacy and confidentiality steps are detailed in the protocol

Research Involving Students and PNWU Employees :

1. If researchers wish to enroll their own students, students in partner programs, employees, and/or people they directly supervise into one of their studies, there are special provisions that need to be considered and implemented so that the students or employees do not feel obliged or pressured to participate in the study. They are a potentially vulnerable subject population because they may feel some pressure to participate, especially if the requesting investigator is their supervisor or instructor, or someone who might be in a position to influence their future. Investigators should carefully consider the appropriateness of enrolling individuals they directly supervise or instruct and will require explicit justification in the IRB application. For this SOP a student is defined as a person who is studying at a school, college, or university. A student shall only be deemed a “vulnerable population” when they are being recruited for participation specifically because they are a student and/or part of a specific course requirement.

2. If researchers wish to recruit in the classroom, they must make it very clear that research is voluntary and will not be tied to grades or ~~extra~~ credit. It must be clear that there will be

no stigmatization or ostracizing of students who decline to participate. If class time will be taken for research participation, alternative activities should be provided for those who decline (especially in pre-college levels).

- Considerations for use of research, extra, or course credit as compensation.
    - Researchers are advised to follow the appropriate student recruitment, compensation, and enrollment
    - The schedule of disbursement and amount of credit;
    - Appropriate non-research alternatives to study participation; and notifying professors about their students' participation in a study.
    - Students cannot be required to participate in research for extra or course credit.
    - If extra or course credit is offered for research participation, a comparable non-research alternative must also be discussed in the proposal and course syllabus.
    - The alternative to participating in the research must be comparable to the research participation in time, effort, and amount of credit or fulfillment of course requirements.
- The IRB will seek to determine that:
    - Alternative non-research activities offered for credit are approximately equivalent in time and effort to participating in the research activity
    - If extra or course credit is discussed during recruitment, then that the recruitment material(s) specifies the amount/value and type of credit that may be earned
    - The informed consent materials adequately describe the conditions for earning the credit whether for the research or the alternative activity
    - Explain how and when professors will be notified of their students' research participation (when applicable), and
    - Where research credit is provided as compensation
    - The informed consent materials clearly state that research credit is still awarded either as partial or full credit despite partial participation or early withdrawal
    - The course director does not pose any undue influence to the student's overall course grade as a result of participation or nonparticipation in a study
    - The course director of which the credit is being given does not implement the informed consent form process.

3. PNWU Employees - An individual employed for wages or salary. While not considered a vulnerable population per regulations, they may perceive that they are under some pressure from their superior to agree to participate.
    - If researchers wish to recruit from the workplace, they must make it very clear that research is voluntary and will not be tied to evaluations or work performance or bonus pay. It must be clear that there will be no stigmatization or ostracizing of employees who decline to participate. If work time will be taken for research participation, supervisor permission should be sought by the employee to ensure time away is approved for the volunteer study.
        - In order to avoid undue influence or pressure on a prospective subject, researchers should not directly ask employees to be research subjects. It may be difficult to refuse such a request. Rather, researchers should post flyers or provide information sheets that allow volunteers to initiate contact about the study.

- University employees, such as staff, lab technicians, and faculty, are similar to students in that they are vulnerable to perceived, even if not intended, pressures to appear to supervisors and/or colleagues as cooperative and supportive of their unit's work. Such pressure may manifest itself with respect to both the initial decision to participate and any subsequent decisions to continue or discontinue participation. Participation in research conducted by one's unit may also pose unique confidentiality considerations.
- Many of the same procedures (described above) to reduce the likelihood of coercion in recruiting student volunteers apply equally to PNWU employees. The IRB will seek to determine that:
    - Investigators who wish to recruit employees:
        - Provide justification
        - Outline procedures to be followed to minimize the appearance of coercion or undue influence of the employees
        - Maintain privacy and confidentiality

<u>Research Involving Pregnant Women, Human Fetuses, and Neonates (Subpart B):</u>

1. Research Involving Pregnant Women, Human Fetuses, and Neonates. For review of research involving pregnant women, fetuses, and neonates by the convened IRB, in addition to the regulatory criteria for approval documented in the reviewer comments section, the reviewer checklist is used to assist the IRB in making the necessary determination of which category of research is appropriate for the study. The checklist also assists the IRB in making all other necessary determinations related to this research. The IRB meeting minutes will document:
    - That regulatory criteria for approval have been met, and
    - Protocol-specific information that justifies the IRB determination of the regulatory category of research deemed appropriate for the given study.

2. For review of research involving pregnant women, fetuses, and neonates, the expedited procedure and reviewer checklist will be used to determine which category of research involving pregnant women, fetuses and neonates is appropriate for the study.

3. Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities. In addition, if an investigator intends to conduct research using a placenta, dead fetus, or fetal material, the PNWU HRPP will contact the Food & Drug Administration (FDA) to determine whether an Investigational New Drug Application (IND) is required.

4. If information associated with material described above is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent regulations apply.

5. If a woman becomes pregnant while participating in a study that has not been approved for inclusion of pregnant women, the IRB must be notified immediately so that the IRB can determine whether the subject may continue in the research, whether additional safeguards are needed, and to make the determinations required by the regulations.

Research Involving Prisoners (Subpart C):

1. Research Involving Prisoners. At PNWU, expedited review is not permitted for any research involving prisoners. A full board review is required with a prisoner representative present on the IRB committee for initial, amendment, and continuing reviews.
    - Exception: minimal risk, meets expedited categories, and the review is done by the IRB committee prisoner representative OR
    - Research involving no interaction with prisoners (e.g., existing data, record review) does not require prison representative
    - Any studies involving emergency research cannot enroll prisoners

2. Parolees who are detained in residential treatment (i.e., residing in a treatment center) as a condition of parole (which is an alternative to incarceration in a penal institution) are prisoners, for purposes of research taking place within that facility. However, persons living in the community and sentenced to court-supervised monitoring or treatment, regardless of whether they are described as parolees or probationers, are not prisoners. Persons wearing monitoring devices are generally not considered to be prisoners; however, situations of this kind frequently require an analysis of the particular circumstances of the planned subject population.

3. The definition of minimal risk for research involving prisoners can be found at 45 CFR 46 and PNWU Glossary.

4. For review of research involving prisoners by the convened IRB, in addition to the regulatory criteria for approval documentation, a checklist is used to assist the IRB in making the necessary determination of which category of research involving prisoners is appropriate for the study. The general reviewer checklist also assists the IRB in making all other necessary determinations related to vulnerable populations. The IRB meeting minutes will document:
    - That regulatory criteria for approval have been met, and
    - Protocol-specific information that justifies the IRB determination of the regulatory category of research involving prisoners deemed appropriate for the given study

5. When an IRB is reviewing a protocol in which a prisoner is a subject, the IRB must make sure that, in addition to other requirements under 45 CFR 46, subpart A:
    - Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
    - The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
    - Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
    - The information is presented in language that is understandable to the subject population;

- Adequate assurance exists that parole boards will not consider a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
- Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact

6. When Subjects Become Prisoners During a Research Protocol. This applies whenever any human subject in a research protocol becomes a prisoner at any time during the protocol e.g., after the research has commenced. This is necessary because it is unlikely that review of the research and the consent document contemplated the constraints imposed by the possible future incarceration of the subject.

7. If a subject becomes a prisoner after enrollment in research, the investigator is responsible for reporting this situation to the IRB immediately via a reportable event. All research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must cease until all requirements of subpart C of the DHHS regulations have been satisfied with respect to the relevant protocol.

8. In special circumstances in which the principal investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated, the IRB chair may determine that the subject may continue to participate in the research until the requirements of subpart C are satisfied.

9. At the earliest opportunity after receiving the investigator's notice or otherwise becoming aware of the prisoner status of a subject, the IRB should review the protocol again with a prisoner representative as a member of the PNWU IRB, in conjunction with the other requirements of this policy. The IRB should take special consideration of the conditions of being a prisoner.

10. Upon this review, the PNWU IRB can either:
    - Approve the involvement of the prisoner-subject in the research in accordance with this policy;
    - Determine that this subject must be withdrawn from the research

11. Additionally, the PNWU IRB should confirm that, when appropriate, the informed consent process includes information regarding when subsequent incarceration may result in termination of the subject's participation by the investigator without regard to the subject's consent.

12. The institution (PNWU) must certify to the Secretary of HHS that the additional IRB duties for the protection of prisoners in research contained in 45 cfr 46.305 have been fulfilled by the IRB.

<u>Research Involving Children (Subpart D):</u>

1. Research Involving Children. In PNWU's catchment area, "children," "adolescents," "minors," and "emancipated minors" are defined differently. Thus, applicable state laws must be reviewed by the PI and IRB committee based on where the research is taking

place. Studies involving these participants must meet Sub Part D. Enrolling children in research studies presents especially difficult considerations for IRBs. Arguments for including children in research include:

- The lack of appropriate research in children will increase their risk of harm from exposure to practices and treatments untested in this population.
- New therapies could not be developed for diseases that specifically affect children.

2. It is very important that the language be appropriate to the subject's reading level if the subject population includes a wide range of education levels.
3. As part of the deliberation on the appropriateness of the research and the regulatory considerations relative to approval of the research on children, the IRB will also consider the manner in which the child's assent and the parental permission will be sought and documented during the review.

4. At a convened IRB review, the Primary Reviewer takes the IRB through the determinations of the protocol. The IRB will make the necessary determination of which category of research involving children is appropriate for the study. The IRB meeting minutes will document:
   - That regulatory criteria for approval have been met, and
   - Protocol-specific information that justifies the IRB determination of the regulatory category of research involving children deemed appropriate for the given study.

5. Children who Are Wards. Children who are wards of the State or any other agency, institution, or entity can be included in research approved under 45 CFR 46, CFR 50.53, or CFR 50.54 only if such research is:
   - Related to their status as wards; or
   - Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards

6. If the research meets the condition(s) above, an advocate must be appointed for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in loco parentis.

7. The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

<u>Research Involving Homeless:</u>

1. Research Involving Homeless. Studies involving these participants must meet specific safeguards for vulnerable populations. Enrolling homeless people in research studies presents especially difficult considerations for IRBs including:
   - The lack of appropriate research in homeless may increase their risk of harm from exposure to practices and treatments untested in this population.
   - The introduction of new therapies should not be developed only on the homeless.

2. Communities may have specific clinics that the homeless population generally frequent. In the Yakima area, these include, but are not limited to:
   - Yakima Neighborhood Health Services

- Yakima Union Gospel Mission
- Yakima Valley Farm Workers Clinic (especially in the Lower Valley)

3. Getting information about recruiting and studying homeless persons:
   - Most homeless do not have reliable transportation; investigators will probably need to go to places the homeless frequent and/or feel safe.
   - There may be a community advocacy group that knows the homeless population and can assist in contacting them. In Yakima, the ALPHA Team, a group of homeless and formerly homeless, is one such advocacy group. Contact them at Entrust, 501 N. 2nd Street, or by phone at 509-453-4756.
   - Most chronically homeless have some form of recognized cognitive, mental, or physical disability.
   - Many homeless have high school and college degrees.
   - They may appear to give informed consent but not fully understand the information given.
   - They may lie to protect themselves or to manipulate.
   - With people in positions of authority, they may be compliant just to get along or they may become defensive; these are survival skills that are developed.
   - Due to frequent harassment by authorities, they have a natural fear of those in position of authority. Developing trust takes a lot of time.

4. It is preferable to have a homeless advocate sit in on the interview, a person they know and trust, to help explain the process. Case managers may not be best since they normally represent a particular program and not the total wellbeing of the individual.
   a. Camp Hope, located behind the former K Mart (now U Haul Center) on Hwy 24, is the recognized homeless encampment/shelter for the greater Yakima area. It is a secure low barrier shelter but does not allow alcohol or drugs on site. They now have housing for up to 200 people with facilities for separate groups: young adults (18-24), families (parents and children), as well as single men and women. Permission is needed to enter the encampment.

5. Testing that might involve discovery of drugs or other chemicals would cause serious unease in the homeless population unless there is a high level of trust that the information will not be shared with authorities. Due to the instability of the homeless population, testing that requires numerous visits over a period of time will lend itself to a higher dropout or no shows at assigned times. From month to month, they may not know where they will be living, or they may experience medical emergencies or other life issues. Keeping track of days and appointments can be a challenge for them.

6. Incentives. Be careful with any form of incentive that can easily be turned into cash, including gift cards. Many homeless have been banned from certain businesses. Items of clothing or food/snack items are reasonable alternatives.

<u>Research Involving Adults With Impaired Decision-Making Capacity:</u>

1. Research Involving Adults with Impaired Decision-Making Capacity. When vulnerable populations are included in research, regulations require that additional safeguards be put in place to protect the rights and welfare of these subjects. Adults who lack or who have impaired, fluctuating, or diminishing decision-making capacity (collectively referred to as "adults with impaired decision-making capacity" in this section) are particularly vulnerable.

Investigators and IRBs must carefully consider whether inclusion of such subjects in a research study is appropriate; and when it is, must consider how best to ensure that these subjects are adequately protected. The principals and procedures outlined in this section are intended to assist PNWU investigators and the IRB with the development and review of research involving adults with impaired decision-making capacity.

2. Decision-Making Capacity. Decision-making capacity refers to a potential subject's ability to make a rational and meaningful decision about whether or not to participate in a research study. This ability is generally thought to include at least the following four elements:
   - Understanding, i.e., the ability to comprehend the disclosed information about the nature and purpose of the study, the procedures involved, the risks and benefits of participating versus not participating, and the voluntary nature of participating;
   - Appreciation, i.e., the ability to appreciate the significance of the disclosed information and the potential risks and benefits for one's own situation and condition;
   - Reasoning, i.e., the ability to engage in a reasoning process about the risks and benefits of participating versus alternatives, and;
   - Choice, i.e., the ability to express a choice about whether or not to participate.

3. Decision-making capacity should not be confused with the legal concept of competence. While the court may consider information about a person's decision-making capacity in making a competency determination, the terms are not synonymous. Incompetence is a legal determination made by a court of law. For example, someone who is judged legally incompetent to manage their financial affairs may retain sufficient decision-making capacity to make meaningful decisions about participating in a research protocol. Likewise, people who have normal cognitive functioning and are considered legally competent may be put into circumstances where their decision-making capacity is temporarily impaired by a physical or mental condition or by alcohol or drugs.

4. Decision-making capacity is protocol and situation specific. Thus, a person may have capacity to consent to participate in low-risk research in usual circumstances, but not have the capacity to consent to a higher-risk protocol when under significant stress or faced with unfamiliar circumstances.

5. Inclusion of Adults with Impaired Decision-Making Capacity in Research. Research involving adult subjects without the ability to provide consent or with impaired decision-making capacity should only be conducted when the aims of the research cannot reasonably be achieved without their participation.

6. Investigators must disclose to the IRB both plans and justification for including adults with impaired decision-making capacity in a research proposal. If adults with questionable or fluctuating capacity will be included, investigators must specify procedures for assessing capacity prior to providing informed consent and, if appropriate, for re-evaluating capacity during study participation.

7. If a prospective subject's capacity to consent is expected to diminish, the investigator should consider requesting that the subject designate a future legally authorized representative (LAR) prior to enrollment in the research, including the future LAR in the initial consent process, and obtaining written documentation of the subject's wishes regarding participation in the research. When the study includes subjects likely to regain capacity to consent while the research is ongoing, the investigator should include

provisions to inform them of their participation and seek consent for ongoing participation.

8. Plans for evaluation of capacity should be tailored to the subject population and the risks and nature of the research. In some instances, assessment by a qualified investigator may be appropriate. However, an independent, qualified assessor should evaluate subjects' capacity when the risks of the research are more than a minor increase over minimal or the investigator is in a position of authority over a prospective subject.

9. In all cases, the person(s) evaluating capacity must be qualified to do so and use appropriate, validated tools and methods (e.g., University of California, San Diego Brief Assessment of Capacity to Consent [UBACC], MacArthur Competence Assessment Tool for Clinical Research [MacCAT-CR]). Assessments of capacity should be documented in the research record, and when appropriate, in the medical record.

10. Under some circumstances, it may be possible for investigators to enable adults with a degree of decisional impairment to make voluntary and informed decisions to consent, assent, or refuse participation in research. Potential measures include repetitive teaching, audiovisual presentations, and oral or written recall tests.

11. Other measures might include follow-up questions to assess subject understanding, videotaping or audiotaping of consent discussions, use of waiting periods to allow more time for the potential subject to consider the information that has been presented, or involvement of a trusted family member or friend in the disclosure and decision-making process.

12. Audio or video recordings, electronic presentations, or written materials used to promote understanding must be provided to the IRB for review and approval prior to use.

13. Under no circumstances may an investigator or caregiver override a subject's dissent or resistance. When assent is possible for some or all subjects, the investigator should provide the IRB with an assent plan that describes when and how assent will be obtained, provisions that will be taken to promote understanding and voluntariness, how assent will be documented, and a copy of the assent form. If the investigator intends to use audio or video recordings to document assent, provisions to ensure the security of the recordings should be described to the IRB.

14. IRB Review. The IRB review process will include at least one member, or a consultant, who is experienced with or otherwise knowledgeable about the population when the research involves greater than minimal risk, or the research is minimal risk but includes interactions with subjects, and the proposed subject population includes adults with impaired decision-making capacity.

15. In considering the risks of research involving adults with impaired decision-making capacity, the IRB should consider whether any components of the research involve risks that are greater for participants with diminished capacity. For example, whether subjects might experience increased sensitivity or discomfort to certain stimuli or may not be able to verbalize or otherwise demonstrate when they are experiencing discomfort or pain.

16. As appropriate to the research, the IRB will consider the following in evaluating research involving adults with impaired decision-making capacity:
    - Whether the aims of the research cannot reasonably be achieved without inclusion of the population.
    - Whether the research is likely to improve the understanding of the condition, disease, or issue affecting the subject population.
    - Whether any experimental procedure or interventions have undergone preclinical testing or human testing on other populations and whether the data from that testing supports its use in the proposed research.
    - Whether the procedures or interventions that the subject will undergo in the research place them at increased risk and whether appropriate mechanisms are in place to minimize risks, when possible.
    - Whether the data and safety monitoring plan, including any stopping rules, is appropriate given the risks of the research and the vulnerability of the population.
    - Whether the procedures for withdrawing individual subjects from the research are appropriate.
    - Whether the recruitment procedures, consent process, and any plans for financial compensation support voluntariness and minimize the likelihood of undue influence or coercion.
    - Whether the subjects will be exposed to financial or other risks that they might not consider acceptable if they had the capacity to provide consent, and whether appropriate mechanisms have been put into place to minimize these risks.
    - Whether the procedures for determining capacity to provide consent, and for evaluating capacity on an ongoing basis, if applicable, are appropriate.
    - Whether the procedures for informing subjects who regain capacity about their involvement in the research, and for obtaining consent for ongoing participation, if applicable, are appropriate.
    - Whether assent should be required when possible, and, if so, if the proposed procedures to obtain and document assent are appropriate.
    - Whether periodic re-evaluation of capacity and/or periodic re-consent should be required.
    - Whether a research subject advocate or consent monitor should be required, for some or all subjects.

17. In general, the IRB will only approve research involving subjects unable to provide consent or with impaired decision-making capacity when the aims of the research cannot reasonably be achieved without inclusion of the population, and there are appropriate provisions to:
    - evaluate capacity
    - obtain consent (and assent if possible)
    - otherwise protect subjects

<u>Research Involving Indigenous Persons, Tribal Members, and Sovereign Trial Nations:</u>

1. The PNWU HRPP expects the IRB to use their judgment when determining if tribal or indigenous subjects enrolling into particular protocols are considered vulnerable and if additional protections are warranted. For example:
    a. Indigenous Persons
    b. Tribal Affiliation members
    c. Self-Identified Tribal members

2. Research involving indigenous persons, tribal members, and sovereign tribal nations. Tribal laws have additional requirements for prospective investigators using tribal members as research subjects. The PNWU IRB must ensure, through consultation with experts if necessary, that its risk assessment is accurate for the site.

3. Research methods with minimal risk in the United States may have greater than minimal risk if conducted at certain sovereign tribal sites. The IRB must consider the following:
   - Questions that might be inoffensive in the United States could be offensive at certain sovereign tribal sites
   - Confidentiality may be difficult to maintain in those sovereign tribal sites
   - Breach of confidentiality in the research locale can pose dangerous consequences
   - Depending on political and other factors, there may be dangers to the researcher and/or institution conducting the research

4. All proposed research must first have obtained the formal, written approval of the appropriate tribal government(s). This approval must be submitted with the original application to the relevant tribal IRB. A letter of support from the tribal government(s) of the specific tribes involved in the study. This requirement can be fulfilled by a tribal council resolution, or an approval from a tribal research review committee or tribal health official to whom this authority has been delegated by the council. For multi-tribal studies in a group of tribes served by a council of tribal leaders, a resolution from that council may also be accepted.

5. For the Yakama Nation, Mr. Davis Washines (Yellowwash) serves as the tribal elder and liaison to PNWU. The full application including the formal tribal government written approval, the local tribal IRB approval letter, and the PNWU application must be submitted for a PNWU full board review. The PNWU IRB must also consider the requirements under federal and state law related to research involving such prospective research subjects as well as the release of private health information set forth in HIPAA, if applicable. The convened PNWU IRB must meet the following requirements before approving such research studies:
   - The PNWU IRB must consider tribal laws within the context of the research and seek elder council, as applicable.
   - The PNWU IRB must receive approval from the tribal nation's council and respective tribal institutional review boards (IRB).

     Indian Health Service Institutional Review Boards (IRB)

     National IRB (NIRB) at IHS Headquarters, Rockville, Maryland: IRB00000646
     Rachael Tracy, Chair, HIS National IRB (NIRB)
     5600 Fishers Lane, MS 09E10D
     Rockville, MD 20857
     Phone: 301-443-2029
     Submit projects electronically to irb@ihs.gov with complete hard copy to Rachael Tracy

     Billings Area IHS/Rocky Mountain Tribal: IRB00000638
     Vernon Grant, PhD, Chair Vacant, Co-Chair
     Karen Manzo, PhD, MPH, IRB Coordinator
     711 Central Ave, Suite 220
     Billings, Montana 59102

Phone: 406-252-2550; 406-697-2436(cell)
Email: irb.coordinator@rmtlc.org

Great Plains Area: IRB 00000635
Dewey Ertz, EdD, Chair, Great Plains Area IRB
Marsha Stevens, GPIRB Coordinator
Phone: 605-226-7493
Toll Free: 1-866-331-5794
Email: marsha.stevens@ihs.gov

Portland Area: IRB00000645
Rena Macy, Co-Chair, Portland Area IHS IRB
Portland Area IHS
1414 NW Northrup St Suite 800
Portland, OR 97209
Phone: 503-414- 5540
Email: pairb@ihs.gov

CAPT Thomas Weiser, MD, MPH, Co-Chair
Portland Area IHS IRB, Northwest Portland Area Indian Health Board
2121 SW Broadway #300, Portland OR 97201
Phone: 503-416-3298
Mobile: 503-927-4467

Alaska Area: IRB00000636
Dr. Shanda Lohse, Chair, Alaska Area IRB
Terry Powell, Administrator, Alaska Area IRB
4315 Diplomacy Drive - RMCC
Anchorage, AK 99508
Phone: 907-729-3924 or 907-729-3917
Email: akaalaskaareaIRB@anthc.org

6. Human participant research to be conducted in Indian Health Service (HIS) facilities or with IHS staff or resources must be approved by an IHS IRB. This includes research done in tribal or urban facilities since IHS, tribal, and urban sites fall under the IHS federal-wide assurance (FWA) #00008894. All proposed research projects planning to collect information for nonclinical purposes from groups of IHS patients should review their protocol with the appropriate IHS IRB Chair.

References:

1. Food and Drug Administration (FDA) Federal Regulations (21 CFR 50, 54, 56, 312, 314, 600, 601, 812 and 814) http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm
2. Department of Health and Human Services (DHHS) Regulations (45 CFR 46 Subparts A, B, C, and D) http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
3. OHRP Database for Registered IORGs and IRBs, Approved FWAs and for Documents Received by OHRP in the Last 60 days Retrieved on March 25, 2019. Accessed at: https://ohrp.cit.nih.gov/search/irbsearch.aspx?styp=bsc
4. Indian Health Service Retrieved on March 30, 2021. Accessed at: https://www.ihs.gov/dper/research/hsrp/instreviewboards/

5. PNWU 107 Informed Consent and Assent Processes
6. OHRP Guidance: Recommendations Regarding Research Involving Individuals With Impaired Decision-Making Capacity

Appendices:
N/A

Version/ Effective Date	Author	Section Changed & Reason for Revision
.00/ 3-20-2018	M. McCarroll	Original SOP
.01 / 4-16-2019	M. McCarroll	Put into new SOP Format
.02 / 8-27-2021	C. Case	Added general information section (page 1); removed the word "transnational" throughout the SOP; updated the tribal IRB contact information; Added subsections for the vulnerable populations and renumbered the sections; moved two numbered items to the appropriate subsections.
.03 – 2-13-2023	C. Case	Check and update Indian Health Services Contact information.