Guidelines for Researchers

Portland Area Indian Health Service Institutional Review Board

Portland Area IHS IRB Contact Information:

Francine C. Romero, PhD, MPH, Chair

Portland Area IHS IRB

c/o Northwest Portland Area Indian Health Board

527 SW Hall Street, Suite 300

Portland, OR 97201

Phone: (503) 416-3286 **Fax: (503) 228-8182**

E-mail: fromero@npaihb.org

The Portland Area IHS IRB

Institutional Review Boards (IRBs) play a central role in protecting human subjects who are enrolled in research programs. The Portland Area Indian Health Service (IHS) IRB has the responsibility to review all research activities that use IHS facilities, data, staff resources, or funding in the Portland Area (Idaho, Oregon, and Washington).

The Portland Area IHS IRB reviews research proposals to assess the risks and benefits for the Portland Area American Indian and Alaska Native (AI/AN) population and tribes involved in the research project. Each proposal is reviewed using criteria described in the Office for Human Research Protections (OHRP), *Protection of Human Subjects*, Title 45 Code of Federal Regulations (CFR), Part 46, 1991. The research proposals are reviewed for safety, confidentiality (information about individuals is not released to anyone), degree of benefit, and the need for and quality of informed consent.

Research proposals must also be reviewed concurrently by the Headquarters-Albuquerque Area Combined IHS IRB (also known as the National IHS IRB), unless the Portland Area IHS IRB determines that the research is exempt. For more information about the National IHS IRB, please contact Phil Smith, MD, Chair, National IHS IRB, at (301) 443-6528.

The Portland Area IHS IRB meets once a month. The remaining Portland Area IHS IRB 2002 meetings are scheduled for:

- August 15, 2002
- September 19, 2002
- October 17, 2002
- November 19, 2002, and
- December 19, 2002.

In order to ensure that your research proposal is on the next Portland Area IHS IRB meeting agenda, you must submit your research proposal no less than two weeks before the next regularly scheduled meeting. These guidelines for researchers are designed to answer questions about the ethical principles that govern research, the responsibilities of researchers, and the process and requirements for an IRB review.

The Belmont Report: Ethical Principles that Govern Research

Like all other IRBs, the Portland Area IHS IRB helps ensure that all research in AI/AN communities observes basic ethical principles that underlie acceptable conduct of research involving human participants. The principles that govern research were set forth in a report submitted by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1978. This report titled, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, outlines the three principles, *respect for people*, *beneficence*, and *justice*, that are now accepted as the three quintessential requirements for the ethical conduct of research involving humans:

1. ***Respect for people*** involves a recognition of the personal dignity and autonomy of individuals, and special protection of those people with diminished autonomy.
2. ***Beneficence*** entails an obligation to protect people from harm by maximizing anticipated benefits and minimizing possible risks of harm.
3. ***Justice*** requires that the benefits and burdens of research be distributed fairly.

Specifically, the principle of *respect for people* underlies the need to obtain informed consent; the principle of *beneficence* underlies the need to engage in a risk-benefit analysis and to minimize risks; and the principle of *justice* requires that participants be fairly selected. All of these principles apply to individual participants as well as to the tribal communities of the participants.

Respect for People

Required by the principle of respect for people, ***informed consent*** contains three elements: information, comprehension, and voluntariness. First, **participants must be given sufficient information** on which to decide whether or not to participate, including the research procedures; their purpose, risks, and anticipated benefits; alternative procedures (where therapy is involved); and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Even when some direct benefit to the participants is anticipated, the participants should understand clearly the range of risk and the voluntary nature of participation. Incomplete disclosure of information is justified only if it is clear that: (1) the goals of the research cannot be accomplished if full disclosure is made; (2) the undisclosed risks are minimal; and (3) when appropriate, participants will be debriefed and provided the research results.

Second, **participants must be able to comprehend the information** that is given to them. The presentation of information must be adapted to the participant's capacity to understand it; testing to ensure that the participants have understood may be warranted. Where persons with limited ability to comprehend are involved, they should be given the opportunity to choose whether or not to participate (to the extent that they are able to do so), and their objections should not be overridden, unless the research entails providing them a therapy unavailable outside the context of research. Each such class of people should be considered on its own terms (e.g., minors, people with impaired mental capacities, the terminally ill, and the comatose). Respect for people requires that the permission of a third party also be given in order to further protect them from harm. Finally, consent to participate must be voluntarily given. The conditions under which an agreement to participate is made must be free from coercion and undue influence. IRBs should be especially sensitive to these factors when particularly vulnerable participants are involved.

Beneficence

Ensuring beneficence entails conducting risk-benefit analyses, which involve **weighing the probability and magnitude of possible harms against the anticipated benefits**. This further involves defining the nature and scope of the risks and benefits and systematically assessing the risks and benefits. All possible harms, not just physical or psychological pain or injury, should be considered. The principle of beneficence requires both

protecting individual participants against risk of harm and consideration of not only the benefits for the individual, but also the societal and community benefits that might be gained from the research.

Five basic principles or rules apply when making the risk-benefit assessment: (1) "brutal or inhumane treatment of human subjects is never morally justified;" (2) risks should be minimized, including the avoidance of using human participants if at all possible; (3) IRBs must be scrupulous in insisting upon sufficient justification for research involving "significant risk of serious impairment;" (4) the appropriateness of involving vulnerable populations must be demonstrated; and (5) the proposed informed consent process must thoroughly and completely disclose relevant risks and benefits.

In determining whether the balance of risks and benefits results in a favorable ratio, the decision should be based on a thorough assessment of information with respect to all aspects of the research and systematic consideration of alternatives. To achieve this, the Report recommends that the IRB and the investigator communicate and that the IRB insists upon precise answers to questions directed at the investigator. The IRB should: (1) determine the "validity of the presuppositions of the research;" (2) distinguish the "nature, probability, and magnitude of risk...with as much clarity as possible;" and (3) "determine whether the investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies."

Justice

The principle of justice mandates that the **selection of research participants must be the result of fair selection procedures and must also result in fair selection outcomes**. The "justness" of participant selection relates both to the participant as an individual and to the participant as a member of a social, racial, sexual, or ethnic group.

With respect to their status as individuals, participants should not be selected either because they are favored by the researcher or because they are held in disdain (e.g., involving "undesirable" people in risky research). Furthermore, "social justice" indicates an "order of preference in the selection of classes of participants (e.g., adults before children) and that some classes of potential participants (e.g., the institutionalized mentally infirm or prisoners) may be involved as research participants, if at all, only on certain conditions."

Investigators, institutions, or IRBs may consider principles of distributive justice to determine if the proposed methods of selecting research participants may result in unjust distributions of the burdens and benefits of research. Such considerations may be appropriate to avoid the injustice that "arises from social, racial, sexual, and cultural biases institutionalized in society."

You can obtain a copy of the full Belmont Report on the web at http://ohsr.od.nih.gov/mpa/belmont.php3, or you may request a copy by contacting the Portland Area Indian Health Service Institutional Review Board at (503) 416-3286.

Researcher Sensitivity and Responsibility

Researchers must be sensitive to the local culture, traditions, research priorities, and lifestyle of AI/AN communities. Furthermore, researchers must be responsible and accountable to the tribal government where the research is being conducted. Tribal communities are sovereign nations. Listed below are suggestions for improving research sensitivity and responsibility to tribal governments and communities:

Researcher Sensitivity

- Ensure understanding and good communication
- Respect tribal culture and traditions
- Respect tribal sovereignty and self-determination
- Respect concerns and opinions of community

- Respect local research priorities and needs
- Respect individuals, families, and communities
- Respect human participants' rights and dignity
- Exclude over-studied populations from participation
- Demystify research
- Be accessible
- Provide feed-back and findings in a timely manner
- Respect a tribe's right to decline participation
- Respect the autonomy and decisions of the tribe

Researcher Responsibility

- Communicate and coordinate with tribal leaders
- Negotiate tribal and community consent to participate
- Maximize benefits and minimize risks
- Protect human participants and sensitive data
- Comply with informed consent process
- Obtain service unit director, tribal, IHS research committee, and IRB approval
- Do not begin research until all approvals are obtained
- Share results of the research with the tribes
- Protect participant and tribal identity
- Build capacity within the community
- Comply with the agreed-upon protocol specifications
- Comply with tribal and IHS publication clearance

Components of the Research Proposal

The Portland Area IHS IRB's assessment of your research proposal involves a series of steps: (1) identifying the risks associated with the research, as distinguished from the risks the participants would experience even if not participating in the research; (2) determining that risks will be minimized; (3) identifying the probable benefits to be derived from the research; (4) determining that risks are reasonable in relation to the benefits to the participants, if any, and the importance of the knowledge to be gained; (5) ensuring that potential participants will be provided with an accurate and fair description of the risks or discomforts of the anticipated benefits; and (6) determining the intervals of periodic review.

To ensure that the IRB completes their review in a timely manner, your proposal must include the following information, as applicable:

- Cover letter with a list of all investigators and a contact person and telephone number
- Tribal resolution or tribal letter of cooperation and approval from each participating tribe
- IHS Service unit director letter of support
- Letters of IRB approval from collaborating institutions

- Detailed protocol of study design, sampling, analyses, timelines, evaluation, and community involvement
- Informed consent and assent forms
- Other attachments, such as a copy of scripts or survey that will be used, materials that will be distributed, etc.

If your proposal is missing any required items, review of your proposal will be delayed. The following sections describe the protocol and consent forms in detail. See the Appendix for examples of several required materials.

The Detailed Research Protocol

Your research protocol should discuss in detail how you plan to carry out the research, how you will analyze the data that you collect, and what you plan to do with the results. The following are points that you should address in your protocol.

Introduction and Background

- Provide relevant research background and explain why this activity is necessary or important.
- Explain why it is necessary to involve AI/ANs as participants in your research.
- Explain how the burdens and benefits of your research will be equitably distributed. Explain if there are other equally suitable groups who could be recruited for this study.
- Describe the potential impact of the proposed research on AI/ANs.
- If you have not obtained a resolution or support letter from the tribe, describe how and when they will be obtained. The resolution should be forwarded to the IRB when it is received.

Study Design

- Provide a complete description of the study design, sequence, and timing of all study procedures that will be performed. Provide this information for pilot, screening, intervention, and follow-up phases. Include all materials that will be used in the procedure, such as surveys, scripts, questionnaires, etc. Attach flow sheets if they will help the reader understand the procedures.
- Describe how study procedures differ from standard care or procedures (e.g., medical, psychological, educational, etc.).
- If any deception or withholding of complete information is required, explain why this is necessary and attach a debriefing statement.
- Describe where the study will take place
- A letter of approval and cooperation from each participating site is needed. For example, if the study will be conducted in the local school system, an approval letter from the School Board and Superintendent are necessary.

Participants

- Explain how the nature of the research requires or justifies using the participant population.
- Provide the approximate number and ages for the control and experimental groups.
- Describe the gender and minority representation of the participant population.
- Describe the criteria for selection for each participant group.
- Describe the exclusion criteria exclusion for each participant group.

- Describe the source for participants and attach letters of cooperation from agencies, institutions, or others involved in the recruitment.
- Explain who will approach the participants and how the participants will be approached. Explain what steps you will take to avoid coercion and protect privacy. Submit advertisements, flyers, contact letters, and phone contact protocols.
- Explain if participants will receive payments, services without charge, or extra course credit.
- Explain if participants will be charged for any study procedures.

Risks and Benefits

- Describe the nature and amount of risk of injury, stress, discomfort, invasion of privacy, and other side effects from all study procedures, drugs, and devices. Describe the amount of risk the community may be subjected to.
- Describe how due care will be used to minimize risks and maximize benefits.
- Describe the provisions for a continuing reassessment of the balance between risks and benefits.
- Describe the data and safety monitoring committee, if any.
- Describe the expected benefits for individual participants, the community, and society.

Adverse Effects

- Describe how adverse effects will be handled.
- Discuss if facilities and equipment are adequate to handle possible adverse effects.
- Explain who will be financially responsible for treatment of physical injuries resulting from study procedures (e.g., study sponsor, subject, organization compensation plan, etc.).

Confidentiality of Research Data

- Explain if data will be anonymous (no possible link to identifiers).
- Explain if identifiable data will be coded and if the key to the code will be kept separate from the data.
- Explain if any other agency or individual will have access to identifiable data.
- Explain how data will be protected (e.g., computer with restricted access, locked file, etc.).

Consent Forms and Assent Forms

- If the consent form is written, submit copies of all consent and assent forms for each participant group. If an oral consent or assent script will be used, submit written scripts for each group.
- If you will not use a consent form or script, submit written justification of waiver of consent per 45 CFR 66.116(d).

Drugs, Substances, and Devices

- List all non-investigational drugs or other substances that will be used during the research. Include the name, source, dose, and method of administration.
- List all investigational drugs or substances to be used in the study. Include the name, source, dose, method of administration, IND number, and phase of testing. (INDs must be registered with the appropriate institutional pharmacy.) Provide a concise summary of drug information prepared by the investigator, including available toxicity data, reports of animal studies, description of studies done in humans, and drug protocol.

- List all investigational devices to be used. Provide the name, source, description of purpose, method, and Food and Drug Administration IDE number. If no IDE is available, explain why the device qualifies as a non-significant risk. Attach a copy of the protocol, descriptions of studies in humans and animals, and drawings or photographs of the device.

Additional Information

- Describe how materials with potential radiation risk will be used (e.g., X-rays and radioisotopes).
- If you will use materials with potential radiation risk, describe the status of annual review by the Radiation Safety Committee. If the annual review has been approved, attach a copy of the approval.
- Describe the medical, academic, or other personal records that will be used.
- Describe the type of audio-visual recordings, tape recordings, or photographs that will be made.
- Explain if the Scientific Instrument Division will test all instruments. If not, describe the safety testing procedures.

Informed Consent

Informed consent is one of the primary ethical requirements underpinning research with human participants; it reflects the basic principle of *respect for people*. It is too often forgotten that informed consent is an ongoing process, not a piece of paper or discrete moment of time. Informed consent ensures that prospective participants will understand the nature of the research and can knowledgably and voluntarily decide whether or not to participate. This protects both the participant, whose autonomy is respected, and the investigator, who otherwise faces legal hazards.

The *Nuremburg Code*, developed by the International Military Tribunal that tried Nazi physicians for the "experiments" they performed on unconsenting inmates of concentration camps, was the first widely recognized document to deal explicitly with the issue of informed consent and experimentation on human participants. The first principle of the code states:

> The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject, there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

All subsequent codes and regulations, insofar as they pertain to competent, adult participants, follow these principles closely.

Federal regulations ***require*** that certain information must be provided to each participant:

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
- A description of any reasonably foreseeable risks or discomforts to the participants.

- A description of any benefits to the participant or to others, which may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the participant.
- A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained.
- For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- An explanation of whom to contact for answers to pertinent questions about the research and research participants' rights, and whom to contact in the event of a research-related injury to the participant.
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

The regulations further provide that the following additional information be provided to participants, where appropriate:

- A statement that the particular treatment or procedure may involve risks to the participant (or to the embryo or fetus, if the participant is or may become pregnant) that are currently unforeseeable.
- Anticipated circumstances under which the participant's participation may be terminated by the investigator without the participant's consent.
- Any additional costs to the participant that may result from participation in the research.
- The consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation by the participant. If your study offers compensation for participation, specify the effects of termination of participation on that compensation. (The compensation should be prorated to reflect the duration of participation rather than an "all or nothing" so that it appears fair and non-coercive).
- A statement that significant new findings developed during the course of the research that may relate to the participant's willingness to continue.
- The approximate number of participants involved in the study.

Investigators may seek consent only under circumstances that provide the prospective participant or his or her representative sufficient opportunity to consider whether or not to participate, and that minimize the possibility of coercion or undue influence. Furthermore, the information must be written in language that is understandable to the participant or representative. The consent process may not involve the use of exculpatory language through which the participant or representative is made to waive or appear to waive any of the participant's legal rights, or releases or appears to release the investigator, sponsor, institution, or agents from liability for negligence.

In your research protocol, you will need to explain the *process of administering consent*. The protocol should address the following questions:

- Is consent obtained in a reasonably quiet, unhurried setting?
- Is there a knowledgeable person present who can answer questions in a clear manner, using layman terms?
- Will this knowledgeable individual assess the participant's comprehension?

- Have you considered the availability of translators for those who may only speak their native language? Similarly, if you may be including participant who are illiterate, deaf, blind, etc., have you accommodated their needs?
- Do you plan to provide a copy of the consent form to each participant ?
- If children (under age 18) are involved in your study, do you have a parental consent form? If the study involves minimal risk, then consent of one parent is adequate; if it involves more than minimal risk, then you must obtain permission of both parents.
- If the child is old enough to make at least some decisions themselves (usually at least 5 or 6 years of age, but this is specific to their culture), have you set up a form and process for their assent?
- Who will explain the research to the potential participants? Should someone in addition to or other than the investigator be present?
- Should participants be reeducated and their consent required periodically?
- If a waiver of some or all of the consent requirements is requested, does the importance of the research justify such a waiver? Is more than minimal risk involved? Can the research design be modified to eliminate the need for deception or incomplete disclosure? Will participants be given more information after completing their participation? Would the information to be withheld be something prospective participants might reasonably want to know in making their decision about participation?

In addition to a detailed discussion of the components of the consent and assent forms and the administration process, you will need to include labeled copies of each form specifying its type (e.g., parental consent, child assent, regular consent), participant (e.g., community focus group members, adult vaccine recipients), and situation where it will be used (e.g., for pretest of screening instrument, administration of a provider questionnaire, etc.).

Working with Tribes and IHS

All research involving AI/ANs must receive the approval of the appropriate tribal governments or organizations. To obtain this approval, you should involve all concerned groups as early as possible in the planning process. By incorporating their suggestions, reviews and approvals are more likely, with fewer changes required in the proposal.

If more than one tribe or tribal organization is involved, you must obtain approval from each. To facilitate the process of obtaining approval, you should submit a cover letter, research protocol, informed consent forms, other attachments, and a sample resolution. Please see our sample resolution.

If your research involves IHS, you will need to obtain approval for your project from the local IHS service unit. This will involve consideration and action by the medical staff, followed by a letter by the Service Unit Director or Health Program Director. Again, if more than one service unit is involved, you will need to get approval from each. Please see our sample service unit approval letter.

In some cases, a tribe or service unit may require that major changes be made to your protocol. If this happens, you may have to resubmit the revised proposal to all approving groups.

In addition to obtaining approval, you must report your results to the tribes and service units involved after the investigation has been completed and the data have been evaluated. The tribes and the service units should be the first to receive the results. The forum and the setting for the presentation can be determined by the appropriate tribal boards or councils. ***The results of your project must be approved by the tribes, service units, and IRBs before they are presented or published.***

Investigator Resources, a list of helpful resources

- Office for Human Research Protections: http://ohrp.osophs.ddhs.gov
- Headquarters-Albuquerque IHS IRB: http://www.ihs.gov/NonMedicalPrograms/Research/irb.html
- IHS Research Program: http://www.ihs.gov/Non MedicalPrograms/Research/index.html
- Portland Area IHS IRB: http://www.npaihb.org/epi/irb.html
- Portland Area IHS IRB Chair: fromero@npaihb.org
- Oregon Health and Sciences University IRB: http://www.ohsu.edu/ra/irb/index.html
- University of Washington Human Subjects Committee: http://depts.washington.edu/hsd
- University of Idaho Human Assurance Committee: http://www.uidaho.edu

Portland Area IHS IRB Review Process

Once the Principal Investigator (PI) has secured tribal and service unit approval, he or she must submit the complete proposal for Portland Area IHS IRB review. Once the IRB receives the proposal, a letter will be sent to confirm receipt of the proposal. This letter will also inform the PI if any essential components of the proposal are missing.

The Portland Area IHS IRB will submit the proposal to the National IHS IRB on the PI's behalf. The National IHS IRB will review the proposal concurrently. It is the PI's responsibility, however, to submit the proposal to other IRBs, such as a university, health maintenance organization (HMO), hospital, or other federal agency (e.g., CDC, NIH) IRBs, as necessary.

The IRB Chair will assign the proposal to a committee member who has the most experience and background in the area of study. This committee member will become the Primary Reviewer (PR). Using a detailed checklist, the PR will review the proposal per 45 CFR 46 requirements.

The PR provides the Chair and IRB committee members with a summary of his or her review. Each IRB committee member receives a copy of the submitted proposal and the PR's review two weeks prior to the next regularly scheduled IRB meeting.

During the IRB meeting, the committee has an opportunity to discuss the research proposal per 45 CRF 46 requirements. The Portland Area IHS IRB can vote to:

- Approve as is, or Approve with Recommendations
- Approve with Contingencies
- Defer
- Disapprove.

A letter with the decision is mailed to the PI. If the proposal is ***approved as is, or approved with recommendations***, the work may begin once the IRB receives final letters of approval from all IRBs. If any changes are made to any part of the protocol, the changes must first be approved by all the IRBs.

If the proposal is ***approved with contingencies***, the work may NOT begin until the PI has responded to the contingencies and has made appropriate changes to the proposal. The revised proposal must be submitted to the IRB for its review. The IRB members will review the PI's responses at the next regularly scheduled meeting and vote to either approve, approve with further contingencies, defer, or disapprove.

If the proposal is ***deferred***, the work may NOT begin until the PI has responded to IRB requirements. Most deferrals are missing key 45 CRF 46 requirements. The revised proposal must be submitted to the IRB for its review. The IRB members will review the PI's responses at the next regularly scheduled meeting and vote to either approve, approve with contingencies, defer, or disapprove.

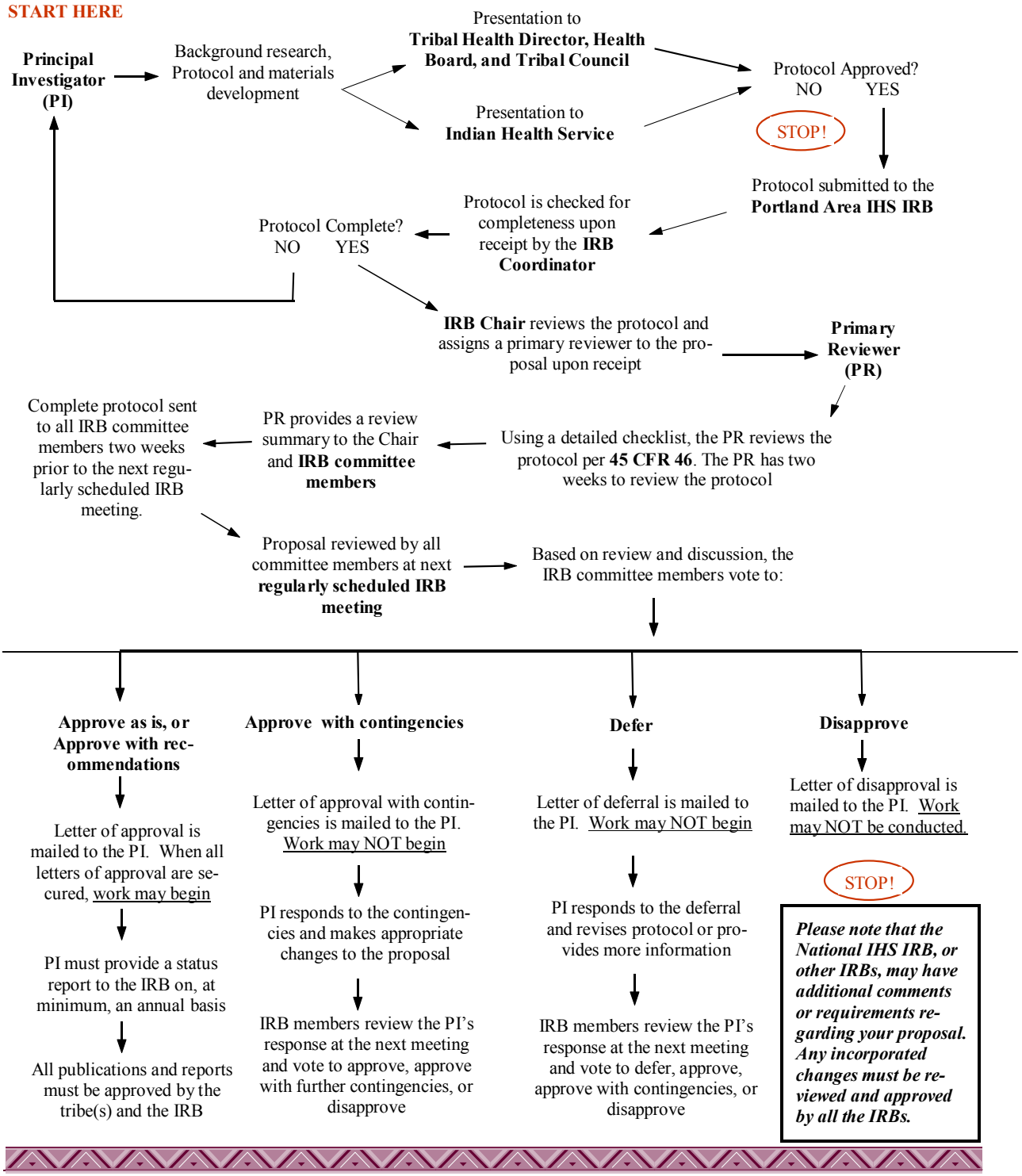
If the proposal is ***disapproved*** the work may not be conducted. Most disapprovals are missing essential 45 CRF 46 requirements.

Once the Portland Area IHS IRB approves a proposal, approvals will remain in effect for one year. At each anniversary of the initial approval, the PI must submit a research status report to the IRB. The annual reviews are in effect for the duration of the project. Should any changes to the protocol occur between reviews by the IRB, the PI should contact and notify the IRB Chair as soon as possible, especially in reference to adverse effects.

At the completion of the project the PI is required to submit a final report to the tribes and IHS service units involved with the project. The PI is also required to submit a copy of the final report to the IRB. The PI must obtain tribal, IHS service unit, and IRB approval before any public presentation or publication of the data occurs.

The Portland Area IHS IRB would like to thank Anthia Nickerson, BS; William L. Freeman, MD, MPH; and,Philip S. Deloria, JD, for writing key parts of the *Guidelines*. We also thank all the contributing researchers for samples of their work.

Flowchart of the Portland Area IHS IRB Review Process



Questions about the Portland Area IHS IRB may be directed to Francine C. Romero, PhD, MPH, Chair, (503) 416-3286, fromero@npaihb.org