



Guidelines for Researchers

Northern Plains Tribal Epidemiology Center • Aberdeen Area Tribal Chairmen's Health Board

Basic ethical principles must govern the conduct of biomedical and behavioral research involving human subjects. Federal regulations and committees provide oversight of the conduct of health research and assure that the ethical principals are upheld.

For research proposed in Northern Plain tribes and AI/AN communities, the Aberdeen Area Indian Health Service (IHS) Institutional Review Board (IRB) is responsible for reviewing all research protocols to assess the risks and benefits for the American Indian and Alaska Native (AI/AN) population and tribes involved in the research project. The IHS IRB has the responsibility to review all research activities that use IHS facilities, data, staff resources, or funding in the Aberdeen Area (Iowa, Nebraska, North Dakota, and South Dakota)

The IRB is required to review protocols using criteria set forth 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, degree of benefit, and the need for and quality of informed consent.

The Northern Plains Tribal Epidemiology Center (NPTEC) can provide technical assistance to 1) researchers in preparing research proposals for IRB and tribal review, and 2) tribes in reviewing research proposals presented to them.

NPTEC staff have experience with IRBs and in assessing the ethical conduct of health research in Indian Country. Our staff are currently serving or have served on IHS IRBs as chairs, members, and administrators. We are also familiar with the practicalities of conducting research, as staff have been involved at many levels of health research including principal investigator to projects. Please contact NPTEC if you would like assistance in preparing a protocol, in reviewing a proposed research study, or would like more information on how we may be of assistance.

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.

Adapted from the Portland Area IHS IRB *Guidelines for Researchers*.

Northern Plains Tribal Epidemiology Center

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Background: The Belmont Report



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 se-**

lection 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://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>, or you contact the Northern Plains Tribal Epidemiology Center at 605-721-1922.

Research in AI/AN Communities



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, as tribes are sovereign nations.

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



An assessment of a research proposal for human subjects protection 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. The following are documents necessary to conduct a thorough assessment of your research proposal, and may be required by the IHS IRB:

- ◆ 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 research 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.

The following sections describe the protocol and informed consent. See the Appendix for examples of several required materials.

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 should be addressed 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 *Nuremberg 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 com-

prehension 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, that 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 enti-

tled, 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 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?

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. You will find a sample resolution in the Appendix.

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. A sample service unit approval letter is included in the Appendix.

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.***

In addition to a detailed discussion of the components of the consent and assent forms and the administration process, you will need to include 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.).

Developing a Protocol



The quality of science is often improved when study objectives and methods are clearly thought through and described. A written protocol facilitates high quality science and is an invaluable tool to investigators as they develop and conduct studies.

Regardless of the scientific discipline in which the study is undertaken, the same scientific method is used. Further, while the scientific content will differ across studies, the general elements of the study protocol will be similar.

The Excellence in Science committee at the Centers for Disease Control and Prevention (CDC) has developed a general protocol checklist and companion guide to assist scientists in preparing protocols. The checklist is intended as an aid in suggesting a format for

writing protocols and in identifying issues that scientists should consider as they design the study.

The checklist was developed to have utility in conducting laboratory and basic science studies, epidemiologic studies, and behavioral and social science studies employing a variety of study designs. In using the checklist, investigators should select the items that apply to their types of studies. It is unlikely that any protocol would include every item on the checklist.

General Protocol Checklist

This checklist is intended as an aid in suggesting a format for writing protocols and in identifying issues that scientists should consider as they design a study or surveillance system. When using the checklist, investigators should select the items that apply to their specific

Section	Item	✓
PROJECT OVERVIEW	Title	
	Protocol summary	
	Investigators & roles/collaborators & roles/funding sources	
INTRODUCTION	Literature review/current state of knowledge about project topic	
	Justification for study	
	Intended/potential use of study findings	
	Study design/locations	
	Objectives	
	Hypotheses or questions	
	General approach	
PROCEDURES/METHODS DESIGN	How study design or surveillance system addresses hypotheses and meets objectives	
	Audience and stakeholder participation	
	Study time line	
PROCEDURES/METHODS STUDY POPULATION	Description and source of study population and catchment area	
	Case definitions	
	Participant inclusion criteria	
	Participant exclusion criteria	
	Justification of exclusion of any sub-segment of the population	
	Estimated number of participants	
	Sampling, including sample size and statistical power	
	Enrollment	
	Consent Process	WILL SEEK WAIVER
PROCEDURES/METHODS VARIABLES/INTERVENTIONS	Variables	
	Study instruments, including questionnaires, laboratory instruments and analytic tests (including abstract form, paper and electronic)	
	Training for all study personnel	

Section	Item	✓
PROCEDURES/METHODS DATA HANDLING AND ANALYSIS	Data analysis plan, including statistical methodology and planned tables and figures	
	Data collection	
	Information management and analysis software (abstracting software)	
	Data entry, editing and management, including handling data collection forms, different versions of data and data storage and disposition (including treatment data consolidation)	
	Quality control/assurance	
	Bias in data collection, measurement and analysis	
	Intermediate reviews and analyses (pilot test)	
	Limitations of study	
PROCEDURES/METHODS DISSEMINATION, NOTIFICA- TION, AND REPORTING OF RESULTS	Notifying participants of study findings	
	Anticipated products or inventions resulting from the study and their use	
	Disseminating results to public (including data publication guidelines and manuscript writing roles)	
REFERENCES	Literature searches	
APPENDIX MATERIALS	Data collection forms	
	Proposed tables and figures	
	Other relevant documents	

project. It is not expected that every item on the checklist is applicable to each protocol for a study or surveillance system.

PROJECT OVERVIEW

Title: Summarize the main idea under investigation. The title should be able to stand alone as an explanation of the study.

Protocol summary: Give a concise overview of the project. Describe the purpose of the study, including problem to be investigated and hypothesis(es) to be tested, the population, and the methods that will be used. Avoid the use of acronyms. Include the expected benefit of the study.

Investigators/collaborators/funding sources: Include the names and degrees of all investigators and their roles in the project. Note any conflict of interest for each investigator and acknowledge all funding sources.

INTRODUCTION

Literature review/current state of knowledge about project topic: Discuss relevant information about the subject of the project based on a review of the literature. In the Reference section, attach a bibliography of the sources used.

Justification for study: Explain the public health and scientific importance of the study. In the context of previous studies, describe the contribution this study will make.

Intended/potential use of study findings: Define the primary target audiences and discuss the expected applicability of study findings.

Study design/locations: Describe the study design and the locations where the study will be conducted.

Objectives: Clearly and concisely list the objectives that the project will address.

Hypotheses or questions: List the clear and focused question(s) that the study will answer. State the type of hypothesis(es) that will be explored or tested.

General approach: Describe whether the approach used will be descriptive, exploratory (hypothesis-generating), confirmatory (hypothesis testing), or developmental (focused on corrective action).

PROCEDURES/METHODS: DESIGN

How study design or surveillance system addresses hypotheses and meets objectives: Explain the appropriateness of the study design to the project and to the questions and objectives previously outlined. Distinguish between procedures that are experimental and those that involve routine care. Identify specific design attributes that characterize the study design (e.g., cross-sectional survey, case/control, cohort, focus group, chart review, etc.) or surveillance system (e.g., description of the system as active or passive, defining reported cases as individual versus aggregate and as laboratory confirmed or not).

Audience and stakeholder participation: Define the primary audiences for the project. Assess the major stakeholders and describe ways they can (and cannot) participate in the study. Explain the process by which those affected by the study can express their views, clarify their needs, and contribute to the project.

Study time line: Provide a calendar with estimated dates for implementing and completing key activities.

PROCEDURES/METHODS: STUDY POPULATION

Description and source of study population and catchment area: Demographically and in terms of

the specific public health conditions to be studied, define the population from which the participants, sample or surveillance subjects will be drawn and to what population inferences will be made.

Case definitions: Provide descriptions of illness, condition or health event which defines a study participant as having that condition.

Participant inclusion criteria: Describe conditions or characteristics applicable to the identification and selection of participants in the study and the conditions necessary for eligible persons to be included.

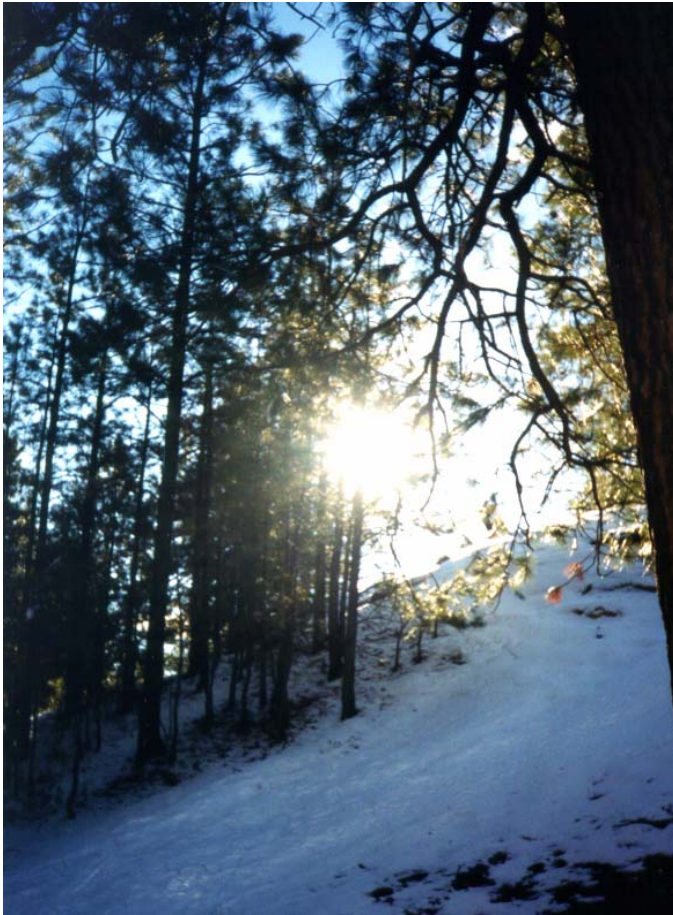
Participant exclusion criteria: Describe characteristics that would disqualify otherwise eligible participants from the project.

Justification of exclusion of any sub-segment of the population: If a sub-population as defined by gender, race/ethnicity, or age is excluded, provide reasons.

Estimated number of participants: State the estimated number of participants for the study. For a project establishing or using data from a surveillance system, this may include the expected number of reported cases per reporting period for epidemic and non-epidemic periods.

Sampling, including sample size and statistical power: Describe the sample (e.g., the sample will be one of convenience, a population-based representation or systematically chosen for some other purpose). State the sampling units and units of analysis. Estimate required sample sizes to answer questions and test statistical hypotheses (based on available information from pilot studies or previous reports). Include statistical power estimates. Explain the conditions under which sampling estimates would be revised. If group-level or aggregate information will be collected (e.g., from focus groups), explain how the groups will be comprised, or what procedures will be followed to create appropriate groups.

Enrollment: Describe the manner in which potential participants will be contacted, screened, and registered in the study. Describe procedures for tracking the number of persons who withdraw from the study. Explain the procedures for assigning participants to different groups. Include a discussion of how departures from the intended enrollment procedures will be handled and documented.



Consent Process: Describe procedures for informing participants about study and methods and for obtaining consent.

PROCEDURES/METHODS: VARIABLES/ INTERVENTIONS

Variables: List and briefly describe the categories, topics, or domains of information to be explored and variables to be collected. Address consistency of definition of variables for data collected from multiple sources. Traditionally, for outbreak investigations, “time,” “place” and “person” would be collected to construct the epidemiologic curve. Explain how the variables will be utilized and the process by which variables will be defined.

Study instruments, including questionnaires, laboratory instruments, and analytic tests: Describe strategies to elicit information, including specific techniques and study and laboratory instruments, and explain how they will be used. Describe the attributes of those strategies/ instruments as demonstrated in other studies, including appropriateness, validity and reliabil-

ity within the particular study populations, sensitivity and specificity of instruments, how well they yield reproducible results and whether any controversial methods are being used. Include a discussion of how changes to the study instruments will be handled and documented.

Training for all study personnel: Describe training, such as interviewer techniques, data collection and handling methods or informed consent, provided to study personnel. Address how inter-observer differences will be handled.

PROCEDURES/METHODS: DATA HANDLING AND ANALYSIS

Data analysis plan, including statistical methodology and planned tables and figures: Describe the sampling methods, information collection procedures, methods to maximize response rates, test procedures and relevant statistical quantities (e.g., variance, confidence intervals and power based on data from the study) in sufficient detail that the methods are reproducible. This includes calculation of relevant quantitative measures for tests and instruments, such as sensitivity and specificity. In outbreak investigations, it is common to employ an iterative process in the analysis (consisting of developing and testing hypotheses and planning and evaluating interventions) to identify the source of the outbreak and control it. For projects establishing or utilizing data from a surveillance system, this could include how and how often the surveillance system will be evaluated. Describe what tables and figures are planned to present study results.

Data collection: Describe data collection procedures, processes and documentation. For data emanating from a surveillance system, this would include frequency of reports.

Information management and analysis software: Provide the names of data entry, management and analysis software packages and computer programming languages to be used for the project.

Data entry, editing and management, including handling of data collection forms, different versions of data, and data storage and disposition: Describe the overall procedures for management of the data collected. Include in the description the process for entering and editing data. Describe how study

materials, including questionnaires, statistical analyses, unique reagents, annotated notebooks, computer programs and other computerized information, whether used for publication or not, will be maintained to allow ready, future access for analysis and review. Document operating procedures for managing and accessing different versions of data sets. State who the data belong to and any rights to and limitations to access for any primary and secondary data analyses and publications. Document procedures regarding confidentiality of the data, including how confidentiality will be preserved during transmission, use and storage of the data and the names of persons or positions responsible for technical and administrative stewardship responsibilities. Document what the final disposition of records, data, computer files, and specimens will be, including location for any relevant information to be stored.

Quality control/assurance: Describe the steps that will ensure no unintended consequences that could affect the quality of the data. Those steps might include methods to capture all reported data exactly as received, assuring logical consistency among all parts of a record and ensuring that manipulation or transformation of the data (e.g. from audio tape to transcribed text) produces no unintended changes, and verifying that statistical and arithmetic calculations are performed as proposed in the data analysis plan. For outbreak investigations, this would include verifying diagnosis and confirming the outbreak. Describe procedures for ongoing data quality monitoring to assure that information of appropriate depth, breadth, and specificity is collected and remains consistent within and among staff over time, and acceptable levels of such attributes as validity, reliability, reproducibility, sensitivity and specificity are achieved.

Bias in data collection, measurement and analysis: Describe the kinds of bias that may occur in collecting the data or in the measurement or analysis phases, and the steps that will be taken to avoid, minimize and compensate for the bias. Include factors in the study population or in study personnel that could bias results, as well as the steps that will be taken to assure valid self-reporting or recording of observations. Include any randomization and blinding procedures that will be used to eliminate/

minimize bias by investigators, other study staff or participants (e.g., in selection of participants, allocation to treatment groups, providing/receiving treatment).

Intermediate reviews and analyses: Describe the ways that progress will be tracked and the study will be evaluated prior to assessing final results.

Limitations of study: Explain factors that might reduce the applicability of study results. Discuss potential weak points or criticisms of the study, including alternative methods.

PROCEDURES/METHODS: DISSEMINATION, NOTIFICATION, AND REPORTING OF RESULTS

Notifying participants of study findings: Explain whether the participant will be offered the option of receiving overall study findings and the form they will take.

Anticipated products or inventions resulting from the study and their use: List any products, including inventions, derived from the study, and how those will be used.

Disseminating results to public: Define effective communication channels and best formats for presenting information that will be used to disseminate project results to specific target audiences.

REFERENCES

List bibliographic references used to create and delimit all aspects of the study.

APPENDIX MATERIALS

Data collection forms: Include any forms or documents used to collect data or from which data are abstracted. Examples of these are questionnaires, medical records and other abstraction forms.

Proposed Tables and figures: Provide table shells and examples of figures for presentation of data and study results.

Other relevant documents: Include any other relevant supplementary materials.



APPENDIX I. Sample Submission and Model Protocol

The following contain components of a sample submission. Note that the sample documents are not necessarily related to each other in content. Your protocol may require different or additional sections and documents. The components provided as samples are: 1) cover letter; 2) tribal resolution; 3) IHS service unit director letter of support; 4) IRB approval letter from collaboration institutions; 5) detailed research protocol; 6) informed consent; 7) questionnaire.

Sample Submission and Model Protocol

1. Cover Letter

On letterhead

March 28, 2002

Name, PhD, MPH, Chair
Indian Health Service Institutional Review Board
Address

Dear Dr. Name:

Enclosed please find the protocol and consent form for the study, "*Name of Study*." I have also enclosed a copy of the State University Institutional Review Board's approval, dated January 12, 2002, and the Tribal Council's approval, dated December 15, 2001.

We propose to conduct a population-based study of all tribal members age 60 and greater on the Tribe Reservation. Individuals participating in the project will receive both a comprehensive medical evaluation at the Tribal Health and Wellness Center and a safety and functional evaluation in their home performed by a tribal member. While providing researchers at State University data regarding the prevalence of dementia and other chronic disabilities, the study also offers valuable information to both individual tribal members and the Tribal community.

We have met with both staff and tribal members on the reservation on several occasions to discuss this project. We have received official approval of the project from both the Tribal Council and the Health and Welfare Committee.

We have scheduled a trip to the reservation on June 3, 2002, to begin this project. We would appreciate your informed review and approval of the enclosed material. If you have any questions or concerns, please contact me at (503) 555-5555, extension 555. I will serve as the contact person for this project. We look forward to your comments and approval.

Sincerely,

Jane Doe, MD, Principal Investigator

John Doe, RN, MN, Co-Principal Investigator

Sample Submission and Model Protocol

2. Tribal Resolution

On letterhead

WHEREAS, the Tribe is a federally recognized National pursuant to the Treaty of 1855 (12 Stat. 951); and

WHEREAS, the Tribal Council is the governing body of the Tribe, by authority delegated by Resolution ABCD-1234; and

WHEREAS, the Health, Employment, and Welfare Committee of the Tribal Council has been delegated the responsibility for providing the leadership, guidance, and oversight to all of the health, employment, and welfare programs and services; and

WHEREAS, nationwide statistical data has indicated that an increase in the number of elderly Native Americans has been observed in recent decades; and

WHEREAS, a National Indian Council on Aging study has shown that the life expectancy for Native Americans has increased by 19% since 1955; and

WHEREAS, the prevalence, causes, and risk factors for chronic disabilities including dementia in Native Americans are as yet completely unknown; and

WHEREAS, a study has been designed to determine the general health status and prevalence of major disabling conditions in elderly Native Americans, the functional status of elderly Native Americans, and the effectiveness of interventions that are currently used to maintain function; and

WHEREAS, the study was designed with input from tribal council members and health staff; and

WHEREAS, in implementing the study, the researchers will follow the protocol contained in the study design; and

WHEREAS, the researchers will work closely with tribal health staff to have a clear understanding of culturally sensitive issues and to ensure that the dignity of all people contacted is maintained; and

WHEREAS, the title of the study will be "*Name of Study*;" and

WHEREAS, permission from the Executive Board of the Tribal Council is sought by Dr. Jane Doe to implement the study; and

WHEREAS, there is to be no publication of the data collected in the study without the express permission of the Tribe.

NOW THEREFORE, BE IT RESOLVED, by the Executive Board of the Tribal Council, acting under authority delegated by Section IV-A of the Rules or Procedures, approved by the Tribal Council Resolution AAAB-0001, dated January 31, 1969, and meeting at the Governmental Headquarters of the Tribe, Anycity, Northwest State, that approval to initiate the study in question be signed.

BE IT FURTHER RESOLVED, that the Tribe does not waive, alter, or otherwise diminish their Sovereign Immunity whether expressed or implied by virtue of this contract, for any and all administrative or legal action, which may arise directly or indirectly from the same. Nor does the Tribe waive, alter, or otherwise diminish their rights, privileges, remedies, or services guaranteed by the Treaty of 1855.

DONE AND DATED on this 15th day of December, 2001, by the undersigned members of the Executive Board of the Tribal Council.

Name, Chairman
 Tribal Council

Name, Assistant Secretary
 Tribal Council

Name, Sergeant-At-Arms
 Tribal Council

Sample Submission and Model Protocol
3. IHS Service Unit Director Letter of Support

On letterhead

December 15, 2001

Jane Doe, MD
State University
PO Box 12
Anycity, Northwest State, 99999

Dear Dr. Doe:

This letter is to inform you that the Service Unit has reviewed and supports your research study titled, "*Name of Study.*" It is our understanding the project will begin on June 3, 2002. We are very interested in your efforts that may help improve our understanding of health in our elderly population.

If you have any questions or need further assistance, please contact me at (503) 555-5555.

Sincerely,

Jane or John Doe, Service Unit Director
Name of Service Unit
Anycity, Northwest State



Sample Submission and Model Protocol
4. IRB Approval Letter from Collaborating Institutions

On letterhead

STATE UNIVERSITY MEMORANDUM

Research Support Office

Eliot Hall, Room 426
(503) 555-5555, extension 555

Date: January 12, 2000
To: Jane Doe, MD
From: Jim Brown, MD, PhD, Chair, Institutional Review Board
Subject: Protocol #1234 "Aging and Health in Native Americans of the Tribe"

Protocol and Consent Form Approval

We have received your response to the IRB recommendations on 1/3/02.

Your protocol and consent forms is approved for One Year effective 1/12/02.

The IRB protocol number and the date of this approval should be placed at the top right corner of the first page of the consent form.

Investigators must provide subjects with a copy of the consent form, keep a copy of the signed consent form with the research records, and place a signed copy in the patient's hospital and clinical medical record (if applicable).

If this project involves the use of an Investigational New Drug, a copy of the approved protocol must be forwarded to the Pharmacy and Therapeutics Committee (Pharmacy Services – Investigational Drugs, OP-16A).

If this is a cancer study, we will notify the Oregon Cancer Center (OCC) of the IRB approval. As the principal investigator, you are responsible for providing OCC with copies of the final approved protocol and consent form.

If other levels of review and approval are required, the project should not be started until all required approvals have been obtained. In addition, studies funded by external sources must be covered by an agreement signed by the sponsor and the State University. Principal investigators are not authorized to sign on behalf of the University.

Thank you



*Sample Submission and Model Protocol***5. Detailed Research Protocol***Permission granted for inclusion as model protocol from Francine Romero, PhD, MPH***2001 NORTHWEST TRIBAL BRFSS PROJECT
Wednesday, July 21, 2004****Northwest Portland Area Indian Health Board
527 SW Hall Street, Suite 300
Portland, OR 97201-5296
(503) 228-4185
FAX (503) 228-8182**

Principal Investigator: Francine C. Romero
Co-investigator: Kathleen McDavid (CDC)
Technical Assistance: Jay Friedman (CDC), Wyndy Amerson (CDC)

Funding Source

Centers for Disease Control and Prevention, U55/CCU016012-01

Introduction

In an effort to understand the types of health risk behaviors present among the tribal people of Portland Area (Oregon, Idaho, and Washington), the Northwest Portland Area Indian Health Board, through the Northwest Tribal Cancer Control Project, is conducting Behavior Risk Factor Surveillance System (BRFSS)-type surveys in six (6) tribal communities. The tribes have selected the modules and questions to be asked of their tribal members (~300 interviews per tribe, 150 males and 150 females over 18 years of age). Trained individuals from each of the respective local communities will conduct the face-to-face interviews.

Background

Cancer is the second leading cause of death among American Indians and Alaska Natives (AI/AN). Risk factors for developing cancer include age, genetics and environment. Because cancer is a chronic disease with a long latency period it tends to affect older people disproportionately. As life expectancy increases, so too does the proportion of AI/AN at risk for developing cancer. In an effort to augment existing risk factor information on AI/AN and provide population based estimates, we propose to conduct a Behavior Risk Factor Surveillance System (BRFSS)-type survey.

In 1984, the Centers for Disease Control and Prevention (CDC) established the Behavioral Risk Factor Surveillance System (BRFSS) for monitoring health risk behaviors. Since that time, all 50 states have conducted these surveys, as well as many tribes in the Northwest and elsewhere throughout the United States. It is estimated that twenty similar small-scale surveys, with between 300-500 respondents per survey, directed toward AI/AN groups have been carried out in different regions of the United States. The basic philosophy of the BRFSS is to collect data on health-related behaviors that would be useful for planning, initiating, monitoring, and evaluating health promotion and disease prevention programs.

Purpose

In order to increase tribal knowledge of current behaviors among American Indian men and women 18 years of age and older regarding cancer, we intend to conduct BRFSS surveys among members of six randomly selected tribes in the Northwest. The purpose of these surveys will be to assess the knowledge, attitudes, and behaviors of adult Northwest AI/AN males and females with regard to health risk behaviors. This survey will be conducted by the respective participating tribes in collaboration with the Northwest Tribal Cancer Control Project (NPAIHB) located at the Northwest Portland Area Indian Health Board (NPAIHB) in Portland, Oregon.

Methods

We will randomly select six tribes (two each in Idaho, Oregon, and Washington) to participate in these surveys. These tribes will be selected from all tribes in Portland Area with at least 1,000 tribal members. The six surveys will be conducted in relatively large communities instead of conducting fewer surveys in a larger number of communities. Because random samples of tribal members will be drawn, the results will be generalizable to each participating tribe. The results will also allow us to draw general inferences about American Indian adults throughout the three-state area.

We will send a letter to these selected tribes inviting their participation in these surveys. If a tribe declines to participate, we will go to the next randomly selected tribe on the list. A tribe's agreement to participate will comprise formal approval from the tribal health director, health board and tribal council to conduct the survey. The tribal letters of approval will be submitted to the Indian Health Service's and CDC's Institutional Review Board (IRB) upon receipt. In order to ensure a high level of acceptance of the survey and to thereby maximize participation rates, a significant effort will be expended in each participating tribal community to garner support for the survey, to alert the community to the purpose and timing of the survey, and to more generally raise community awareness of the issue of cancer. In order to accomplish this, NPAIHB and each of the participating tribes will hold public meetings and distribute a series of public announcements in the print, radio and television media, as well as through community organizations, to announce the upcoming survey; provide information on its purpose, methods, and timing; and provide a forum for exchange of ideas on the survey and encourage community participation.

The NPAIHB will provide financial support to each participating tribe to support the hire of a tribal project coordinator and tribal interviewers, including their training; local travel by survey staff; the compensation of respondents (\$10 per interview); and, the implementation of strategies that will promote participation in the survey. A local field coordinator may be hired in each participating tribal community to coordinate the survey activities including the interview schedule and staff. The tribes will have the option to utilize existing staff members as either local field coordinators or interviewers. The local coordinator will be available to answer questions from prospective survey respondents and the general public. The interview staff will be trained in conducting surveys and will be provided printed materials on cancer (e.g., American Cancer Society brochures and other resource materials) that can be distributed within the community. Dr. Howie Goldberg, Jay Friedman and Wyndy Amerson of the Centers for Disease Control and Prevention (CDC)/Division of Reproductive Health (DRH), have agreed to assist with interviewer training, data entry training, and data analyses through a cooperative agreement with the Indian Health Service at no cost to either the tribes or NPAIHB. Mr. Friedman has been an integral part of questionnaire and methodology development. Both Dr. Goldberg and Mr. Friedman have a strong record of successfully completing surveys in tribal communities, including those in Portland Area.

Within each tribe, we will select a simple random sample of up to 500 tribal community members 18 years of age and older from tribal enrollment lists and/or Indian Health Service or tribal health user population lists. The lists would contain a subset of the tribal population 18 years of age or older including the name, date of birth, address and telephone number. The lists will provide us with the most current and comprehensive tribal membership information, thereby enhancing the representativeness of the sample selected for the surveys. The survey seeks to complete between 300 to 400 interviews per community, to do this a random selection of 500 names will be used to take into account refusals, those who have moved, those who died, those temporarily away from the reservation, and loss to follow-up. The resulting sample size (up to 400 respondents in each tribe) will enable us to estimate parameters for the entire tribal community.

Each of the potential respondents will be contacted by the interviewers and invited to participate in the survey. Each respondent will sign an informed consent form prior to the interview. Appendix A contains a copy of the informed consent form. Each interview will require about thirty minutes to administer. Respondents will be compensated \$10 each for a completed interview in regard to their time and contribution. All interviews will be conducted face to face.

After the approval from the tribes and the appropriate IRBs, we will pretest the questionnaire to assure comprehension and flow and to identify any problems. Once these problems have been addressed, the questionnaire will be revised and finalized before implementation.

The questionnaire used in the conduct of these surveys has been constructed for the most part using standard, field-tested modules in common use in the BRFSS system and in small scale surveys among American Indian populations. Topics covered include general demographic and health status questions; disease-specific issues (e.g., diabetes, hypertension, cardiovascular, etc.); use of preventive and curative health care services; risk behaviors (e.g., tobacco use, alcohol use); and, risk-reduction activities (e.g., weight control, proper nutrition, etc.). Appendix B contains a copy of the questionnaire that will be used in these surveys.

The collected data will be entered at each tribal site. The final data set will be cleaned and edited by CDC/DRH then delivered to the NPAIHB staff for final editing, recoding, and statistical analysis. We will use basic descriptive statistics (e.g., frequency distri-

butions, means, etc.), bivariate statistics (e.g., contingency table analyses, t-tests of means, etc.), and multivariate modeling (e.g., logistic regression, ANOVA, etc.) to analyze the data, as appropriate. Each participating tribe will receive a copy of the final dataset. The software (SURVEY) for the data entry is in the public domain and will remain in the possession of tribes for use in any subsequent surveys.

NPaiHB will prepare a report summarizing the conduct of these surveys and the results of these analyses. We will distribute this report and present the results to each participating Tribal Council, Tribal Health Boards, Tribal Health Directors and their staff, as well as to all delegates of NPaiHB for use in stimulating discussion among health care providers and tribal communities and for guiding the development, targeting, and implementation of prevention programs. In addition, if results from these analyses add new and important information to the general knowledge about health risks and behaviors, NPaiHB will seek, with the participation and approval of all the participating tribes, to publish these results in a reputable, national medical or public health journal to aid other tribal efforts throughout the United States.

Protection of Privacy and Confidentiality

Each potential respondent will be first provided with an explanation of the purpose, general content, and time commitment involved in participating in the survey, and assurances of confidentiality. Each prospective respondent will be given the opportunity to ask any questions at the time of the interview, and will be provided with the name and telephone number of the local contact person who can answer questions before and after the interview is completed. Each potential respondent will be free to decline participation and/or refuse to answer any specific question without any loss of health care benefits or services.

No personally identifying information will be collected during the conduct of the interviews. Furthermore, once interviews are completed and the responses have been verified for completeness and internal consistency, all linkages to home address, telephone numbers and other locating information will be destroyed. Finally, no individual will be identified or identifiable in any report that is prepared based on the data collected as part of these surveys.

All data collected during the conduct of these surveys will be held in the strictest confidence at all times by both the field interview staff and NPaiHB staff. All datasets will be stored on secure, password-protected computers accessible only by authorized staff members (interviewers and site coordinators) of the respective tribes, NPaiHB (Epidemiologist) and CDC/DRH. All hard copy data will be stored in fire resistant, locked file cabinets.

Benefits and Risks

The risks to respondents are limited to the small risk of disclosure of personal information, which is unlikely given the steps that will be taken to protect respondents' privacy and confidentiality, as described above. The likely benefits to the individual respondents are minimal, however, the overall impact for the tribal community will be significant. In addition, the survey results will provide tribes and the NPaiHB with data on their adult members' knowledge, attitudes, and practices regarding cancer and other health-related issues to enhance health promotion and disease prevention programs.

Timeline for the Surveys

No contact with human subjects will be made prior to approvals by the IRBs. In the meantime, sample selection, community preparation, and the hiring of interview staff, will commence as soon as Tribal Councils give their approval and staff can be hired. It is anticipated that community preparation activities will begin shortly after January 2001, and that actual interviews will take place beginning in March-June 2001. A pre-test of the questionnaire will be done before the onset of data collection. The interviews should be completed within a 4-6 month period. Data preparation, analysis, and report-writing should take an additional 2-3 months to complete. Thus, final reports summarizing the results of these surveys should be available for distribution by the end of 2001.

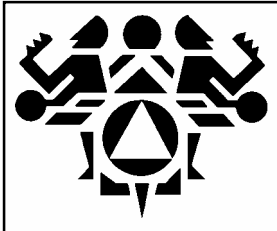
Additional Questions

If respondents have any basic questions regarding the survey, a local contact person will be available in each participating tribe. In addition or alternatively, these questions can be directed to the NPaiHB project staff, Dr. Francine Romero, Epidemiologist, at 1-877-664-0604 (toll free number). All information on contact names and numbers will be provided to respondents during the introductory segment of the interview.

For respondents who have specific questions related to cancer, local coordinators and NPaiHB project staff will answer basic questions, offer to send printed education and informational brochures to respondents, or refer them to the American Cancer Society (1-800-ACS-2345).

Questions regarding rights as a respondent of a research project can be addressed to Dr. Francine C. Romero, Chair, Portland Area Indian Health Service Institutional Review Board, at (503) 416-3286.

Sample Submission and Model Protocol
6. Informed Consent

APPENDIX A

Northwest Portland Area Indian Health Board
 527 SW Hall Street, Suite 300
 Portland, OR 97201
 (503) 416-3286
 FAX (503) 228-8182
fromero@npaihb.org

RESPONDENT INFORMED CONSENT FORM

Purpose and Benefits

The *Tribe's Name* and the Northwest Portland Area Indian Health Board are conducting a survey of current health behaviors with an emphasis on cancer. The purpose of these surveys will be to assess the knowledge, attitudes, and behaviors of adult *Tribe's name* with regard to the prevention of cancer and other health topics. Your participation will help us to identify health needs in our community and to enhance services and programs to improve the health of the *Tribe's name*.

Procedures

We will recruit about 500 adult tribal members 18 years of age and older to participate in the survey. The interview will take about 30 minutes to complete. The interview will include general demographics; health related questions pertaining to cancer, diabetes, hypertension, and, questions on health risk behaviors such as alcohol use, tobacco use, diet and nutrition.

Confidentiality

You will not be identified with the information you give because the survey is confidential. No one but the interviewer and field coordinator will know how you answered questions on the survey. The interviewer has signed a pledge to keep all information about you confidential. Your name will be torn off and a number assigned to the questionnaire. The linked list of names and numbers will be kept in a locked secure place until the questionnaire has been successfully entered into the computer. The identifying information will be destroyed immediately after the data have been entered into the computer and edits run. The questionnaires without your name on it will be destroyed after the data is analyzed. Only project staff will have access to study data. We will not use your name when we report results of the study. The information we collect from you will be combined with information from other Tribal members to help develop a profile of community health behaviors and attitudes.

Risks and Benefits

You may feel uncomfortable with some of the questions we ask on this survey. You can refuse to answer any question you are uncomfortable with or skip questions you do not want to answer. You can stop the interview at any time. The likely benefits to you are minimal, however, the overall impact for the tribal community will be significant.

Rights as a Volunteer

Your participation in the Health Behavior Survey is voluntary. If you decide not to take part or to stop the interview, you will not lose any services to which you are otherwise entitled.

The law requires that child and dependent abuse be reported. Suspected abusive situations will be referred to appropriate authorities in accordance with tribal law.

If you have any questions about this research project, you may call *the local field coordinator* at *phone number*. You may also call the Principal Investigator, Francine C. Romero, Northwest Portland Area Indian Health Board, at 1-877-664-0604 (toll free number).

If you have any questions about your rights as a respondent, you may call either Dr. Francine C. Romero, Chair, Portland Area Indian Health Service Institutional Review Board, at 1-877-664-0604, or Dr. Clark Marquart, Co-Chair, Portland Area Indian Health Service Institutional Review Board, at (503) 326-7272.

Respondent Agreement

The Health Behavior Survey has been explained to me. I voluntarily consent to participate. I have had an opportunity for my questions to be answered. I know that I may refuse to participate or to stop the interview at any time without any loss of health care benefits to which I am otherwise entitled. I understand that if I have questions about this study or my rights as a respondent, I may contact the local field coordinator or Francine Romero, Principal Investigator.

I understand that as compensation for my participation and completion of the survey I will receive \$10 for my time and contribution.

Respondent Signature

Date

Interviewer Signature

Date

Copies: Respondent Principal Investigator



Sample Submission and Model Protocol
7. Questionnaire

APPENDIX B

2001 Northwest Tribal BRFSS Project
Questionnaire

Questionnaire Intentionally Not Included in This Model Protocol



APPENDIX II. More on Informed Consent

For a checklist of required elements for consents forms, see Appendix IV, #13.

Model Volunteer Consent Documents in Indian Country - 4th Ed

William L. Freeman, MD, MPH, CIP
Human Protections Administrator, Northwest Indian College
July 27, 2004

Explanation

To help researchers write consent documents for their projects, I developed these 10 Model Volunteer Consent Documents while Chair of the Indian Health Service [IHS] National IRB. Several members of the IHS National and Area IRBs, and of Applied Research Ethics of North America [ARENA], helped develop this paper and the Documents.

The hypothetical situations for the Model Volunteer Documents include 7 research protocols typically seen in Indian Country, a protocol typical in tertiary-care (#5), and 2 EPI-AID protocols (#9, #10). The protocols, and thus the documents or sheets, range from complex (#1, #3, #5, #8) to simple (#4, #9). The specific hypothetical situations are:

- 1] a randomized, double-blind, placebo-controlled, Phase III clinical trial of an Investigational New Drug vaccine, i.e., with "greater than minimal" biomedical risk;
- 2] a screening by lab testing of a population for diabetes;
- 3] a survey about domestic violence, i.e., with "greater than minimal" social risk;
- 4] a simple questionnaire survey of users of a clinic for health services research;
- 5] a protocol to use and assess an experimental treatment for a life-threatening disease;
- 6] a "youth risk behavior survey" (YRBS);
- 7] community-based participatory research, using qualitative research methods, on the highly sensitive, emotionally-distressing, topic of miscarriage;
- 8] genetic research into a complex syndrome of colon and ovarian cancers, HNPCC; and
- 9,10] information sheets for investigations of simple (7) and complex (8) epidemics.

The last page (*see Appendix IV #13*) lists those elements in consent documents required by regulations 45 CFR 46 (marked by @), or needed by only some protocols (unmarked). The regulation's section for each element is cited. These Model Document are pre-HIPAA.

The 8 Model Consent Documents and 2 information sheets should be understandable by most people. The National Adult Literacy Survey (NALS), the results of which were released in early September, 1993, guided the way I wrote the documents [Kirsch IS, Jungeblut A, Jenkins L, Kolstad A. Adult literacy in America: a first look at the results of the National Adult Literacy Survey Washington, DC: National Center for Education Statistics, US Dept. Education. 1993]. Let me show how the NALS is relevant to consent documents.

In 1992, NALS tested a valid sample of 13,600 US adults for 3 types of applied literacy:

- o prose literacy, using new stories, articles about health, etc.;
- o document literacy, using payroll forms, transportation schedules, maps, etc.; and
- o quantitative literacy, asking them to balance a checkbook, complete order forms, etc.

The results for applied prose literacy were relevant to developing consent documents.

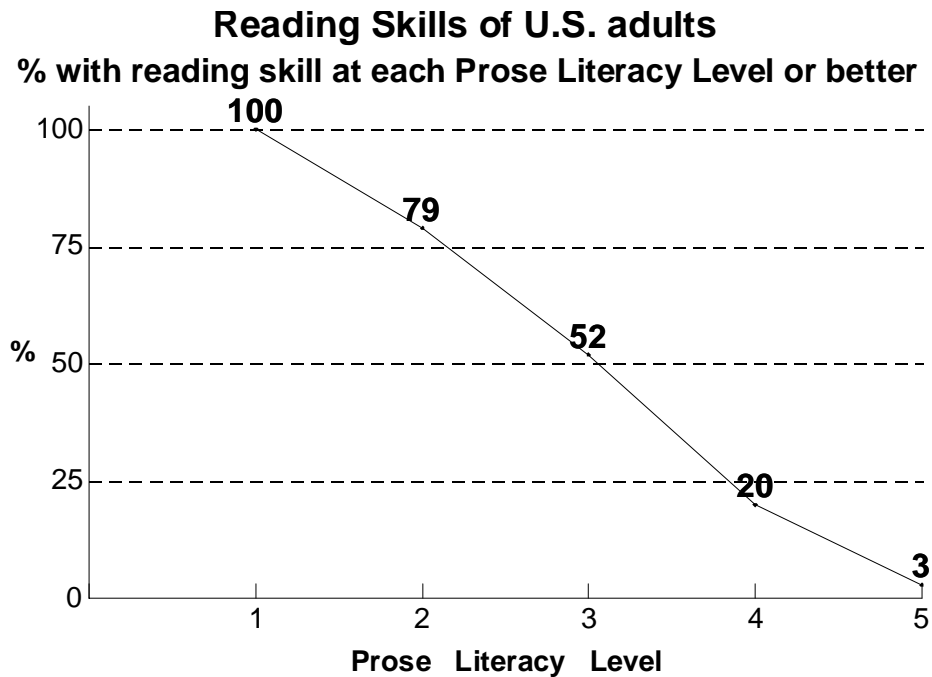
NALS divided the results into five Levels of prose literacy.

- 1 "read a relatively short text to locate a single piece of information" or unable to read;
- 2 "integrate two or more pieces of information to compare and contrast easily identifiable information," locate a single piece of information but the passage had several "distractors" ("plausible but incorrect pieces of information");
- 3 "make matches that require low-level inferences," "integrate information from dense or lengthy text that contains no organizational aids such as heading";

- 4 "integrate or synthesize information from complex or lengthy passages," "[c]onditional information is frequently present";
- 5 "search for information in dense text which contains a number of plausible distractors," must "use specialized background knowledge" to understand the text.

Levels 4 and 5 describe many consent documents we have all seen--and I have written!

How many US adults can understand Level 4 or 5 consent documents? See the graph below.



(Percentages calculated from data in the National Adult Literacy Survey.)

Apparently only 20% of US adults would understand the dense, complex, consent documents we are familiar with. How can consent documents be made understandable to more people?

One approach would reverse or omit those factors associated with **decreased** comprehension in the texts used by NALS. Those factors included the following.

Factors that DECREASE comprehension of prose material used by NALS

1.	Increased number of items or categories of information
2.	Decreased closeness of relationship of the text to the information being tested
3.	Increased length and density of the text
4.	Increased amount of background information needed by reader to understand the text, but not found in the text
5.	Increased number of distractors (information apparently similar to, but actually different from, the information being tested)
6.	Decreased amount of organizational aids in the format of the text.

To reverse the factors associated with fewer people understanding the NALS material, the Model Volunteer Consent Documents try to meet the following 6 criteria.

- 1. **Be brief, but have complete basic information** [factors 1, 2, 3].

The first factor cannot be eliminated entirely, because 45 CFR 46 requires more than a dozen items of information. However, omitting unnecessary or irrelevant items of information will help minimize factor 1, and help reverse factors 2 and 3.

Many potential volunteers do not read long consent documents or information sheets. The longer the document, the fewer the people who read it in its entirety, and the smaller the fraction of the document that is read by the rest. Thus, adding more information to be more comprehensive may result in less information actually transmitted.

The model documents include only the basic information needed by potential volunteers. We researchers have two tendencies: we tend to include too much scientific detail, and to minimize or omit less familiar required elements of 45 CFR 46. The models counter that bias; they do not try to answer every possible scientific question. For example, the first model, for the experimental vaccine, does not have information about how the vaccine was made. (That would be "basic information" only if it were controversial, e.g., made by tissues from aborted fetuses.) But the models do include all items required by the regulations. The model documents include only information closely related to the core information needed to be understood, analyzed, thought over, and remembered by potential volunteers.

"Non-basic information" can be given in a separate handout, perhaps in a Question-and-Answer format. We suggest including a list of questions at the beginning of the handout, to permit people to go directly to those questions they are most interested in.

2. Be less dense, with easy readability for most people [factors 3 and 4].

We all have encountered quite dense material that is difficult to read and understand. Readability measures one aspect of density. Several computer programs have 1 or more readability formulas, often expressed in school "grade" level. Most readability formulas are a linear relationship of: the average number of words per sentence, and the average number of syllables or letters per word. A consent document with "ninth grade readability" means that the relationship between words-per-sentence and syllables-per-word is similar to that in material read and understood by ninth graders.

The readability of Documents #1, #3, #5, and #8 is 8th grade, in spite of the topics' complexity. Readability of #6 and #9 is 6th grade; that for all others is 7th grade.

3. Be clear, and provide the background information needed [factor #4]. (Use familiar terms to explain unfamiliar terms. Organize in logical sequences.)

Words-per-sentence and syllables-per-word sometimes have little to do with understandability. Rare short words in short sentences may have a readability similar to lower grade texts, but be understood only by rare people. Beyond short words and short sentences, ways to improve readability include the following.

- Use **common** words in general.
- Use **active voice** rather than passive voice verbs ("We did" not "It was done").
 - Make clear the **links of logical sequences** and **of cause-and-effect**, even if that makes sentences longer ("We will do this, because that happened").

The models omit specialty terms and concepts not **essential** to be informed for making decisions, and define and explain each new term. They value understandability over scientific precision. (Writing that is scientifically precise but is understandable only by scientists in the field does not promote or yield informed consent by anyone else.)

People comprehend organized new material better than unorganized new material. Thus, organizing new material into succinct blocks, and putting the blocks in a logical clear sequence, helps maximize comprehension. Writers of consent documents should ask "What potential volunteer's questions are we trying to answer? What background information does s/he not have, but requires, to understand this project?"

4. Use only 1 meaning for important terms; eliminate "distractors" [factor #5].

"Distractors" include the same word with different meanings; the multiple meanings confuse people. Many consent documents have two distractors: "risk"; and "benefit."

"Risk" means the harms inherent in the research, and also sometimes the risk factors for the disease the research is dealing with. The Model Documents use "risk" only in the former sense: direct inherent possible risks of the research to people. "May get disease" or a similar phrase are used for risk factors.

"Benefits" means advantages inherent in the research, but also means advantages not to be foregone in the non-coercion disclaimer, and sometimes means payment given for participation. The Documents use "benefit" only in the first sense: direct inherent possible benefits of the research to people. "Care or services" are used in the non-coercion disclaimer, "reimbursement" or "payment" for participating.

5. **The format helps people comprehend and remember the information** [factor 6].

Format can help people comprehend and remember complex material. Research has shown that certain format elements help improve comprehension, including:

- **Headings;**
- indents;
- key words **bolded** or underlined;
- vertical lists (instead of run-on lists in long sentences);
- extra spacing between topics;
- short paragraphs, with only one major thought per paragraph;
- repetition (repeat important, difficult-to-understand, points);
- reasonable-size type (not small print to minimize pages);
- lower case, NOT UPPER CASE; and
- plenty of margins and empty space in general (not the daunting insurance policies with their wall-to-wall and top-to-bottom writing in small print).

These elements of format help the reader to:

- A] recognize the organization of the consent document;
- B] recognize, know, and remember the key points; and
- C] go back later to the document to retrieve important information, such as telephone number of the doctor to call if injury occurs.

6. **Serve as a script for the face-to-face discussions with the potential volunteers.** [This criterion is not related to the above factors suggested by the NALS.]

Face-to-face discussions between researchers and potential volunteers are the most important part of the process of informed consent. These Model Consent Documents are intended to be both the **written consent documents** and the **script for the verbal explanation** by the researchers. If the verbal explanation is almost the same as the written document, each will reinforce the other and avoid inconsistency. Thus, each Model Volunteer Consent Document is actually a **combined document-script**.

One benefit of this method is that the document-script with good readability--no more than 8th grade--helps researchers use simple language in their verbal explanation. Another benefit is that the same document-script can be used for potential volunteers who have difficulty reading, have low literacy, or need a translation--also increasing consistency of explanation among all volunteers. Investigators need develop only one document-script, not two, for people of all literacy levels to be potential volunteers. The document-script can also be used to videotape the explanation. The model document-scripts reinforce both the oral discussion and visual reading. For instance, the bolded headings are the key "take home" points of the information to be transmitted. The document-script approach should result in two editorial benefits.

- 1] **Bolded headings attract attention and are remembered.** By having key points as headings, the reader more likely will remember the key points. (Bolded headings that are just titles or questions attract attention but are not intended to be remembered.)
- 2] **The length is shorter.** There is little or no unnecessary verbiage.

Exemplary consent documents are not sufficient for informed consent.

Researchers and IRBs should go beyond the consent document in two ways.

First, the quality of the interpersonal communication in the process of consent--the two-way sharing of information by researcher and potential volunteer--is more important than the quality of written documents. The sharing should be two-way; researchers needs to impart information, as well as find out the level of understanding by potential volunteers and elicit questions they may have. IRBs

have not devised ways to assure high quality in the process of communication. One way may be that the researchers, the tribal government or personnel from the tribal health department, community health boards, and IRBs work out as partners consent processes that are culturally sensitive and respectful of each person and the tribe.

Second, because some research protocols are so distant from the background information possessed by most people, the amount of totally new information required to be in consent documents for those protocols may overwhelm even maximum clarity of writing. The model documents for the ribavirin trial (#5), and for the genetics study (#8), are examples. In such circumstances, 3 added steps may help.

- 1] Allow and encourage 24 hours or more for discussion and a decision. Simply having the person take the consent document home overnight can increase comprehension [Morrow G, Gootnick J, Schmale A. A simple technique for increasing cancer patients' knowledge of informed consent to treatment. Cancer 1978; 42:793-799].
- 2] What and how much people learn from written material varies by the amount of background information they have about the subject [Mosenthal PB, Kirsch IS. Learning from exposition: using knowledge modeling as a basis for assessing student's knowledge. J Reading 1992; 35:668-678]. A researcher could increase the background information of potential volunteers before they consider consent itself, by (for instance) presenting information in 2 stages, a day apart. The first stage would give basic information about the purpose and background; the second would answer questions and summarize the first day, then focus on procedures and the rest of consent. This approach is feasible if time is not critical--not the ribavirin protocol.
- 3] Educate people before they are asked to participate, by publicizing and discussing the protocol repeatedly in the media. One should use as many media channels as possible, e.g., radio, newspaper, TV, district or chapter house meetings, churches, etc. This approach is feasible when the community has high interest in the research.
- 4] For one-on-one discussions with potential volunteers, use media in addition to the printed page, e.g., videotapes, interactive computerized video discussions, etc.

In summary, consent documents should follow what is known about how to increase comprehension of written material. We should write consent documents that understandable by 70%-80% of the adult population. Even with more than 12 important items required by 45 CFR 46, consent documents at the NALS Level 2 are achievable for most protocols.

Hy'shqe siam! Thank you, respected people!

To the many people who have educated me on these issues:

Community members
 IRB members
 IRB staff people
 Researchers
 Participants
 Carolyn Robbins - wife.

To give suggestions or comments, or to ask questions, please call or write me at:

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Director of Tribal Community Health Programs; &
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MODEL VOLUNTEER CONSENT DOCUMENT #1

Background: a randomized, placebo-controlled, Phase III clinical trial of an Investigational New Drug vaccine. In all Model Documents, harms or risks are written as 'some people have gotten' [or similar wording]. Many people understand the typical wording of 'the vaccine may cause' or 'you may get' as being the future--what will happen to the person--not a statistical statement. The readability is 8th grade; the text is 1,258 words.

Goodvacc Vaccine Research Study.

We ask you to take part in research for a new vaccine for Severe disease.

The NoName Clinic, Topdrug Pharmaceutical Company, and Academia University are doing this study. The study has 2 purposes:

- 1] to see if Goodvacc vaccine prevents Severe disease; and
- 2] to see if the vaccine is safe.

Goodvacc is an experimental vaccine. 2,500 adults have received it without problems.

Goodvacc is an "Investigational New Drug," because it is still being studied. That is, it has not been licensed by the FDA (Food and Drug Administration) for general use. The FDA may use this study to decide if it should be licensed.

Goodvacc has been given to more than 2,500 adults. Almost all of them made antibodies to Severe disease. (The body makes antibodies to fight infections.) So far, no serious side-effects were seen in any of the people given the vaccine.

There is no other way to prevent Severe disease.

Severe disease is an infection that hits mostly elders. About one-third of elders with Severe disease die even though we give them the best medical treatment known. So we want to prevent the disease from hitting the elders, but there is no way known to prevent it now. If Goodvacc vaccine works, it would be the only way to prevent it.

We want to find out if this vaccine works, and to be sure it is safe.

This study will find out if Goodvacc, and the antibodies it produces, do prevent Severe disease. We also want to check for side-effects. We are testing Goodvacc vaccine here because many elders of NoName Rez get Severe disease, and more than one-third of them die from Severe disease.

There are several steps to this study.

We ask all patients age 60 or older, who come to NoName Clinic, if they want to take part in this study. We will check to see if there is a medical reason that they should not take part.

If you take part, we will give you a shot of either Goodvacc vaccine, or sterile water (a "placebo") that does not produce antibodies.

If you volunteer to take part, we will put you in one of 2 groups. Groups are assigned by chance or randomly, as by a flip of a coin. People in one group will get a shot of Goodvacc vaccine. People in the other group will get a shot of sterile water ("placebo"). You will not know which shot you get, the vaccine or the water. All shots are given by trained nurses.

Then we will draw one tube of blood three different times.

A skilled lab tech will draw one tube of blood (about two teaspoonfuls). We will draw the blood before the shot, in 1 month, and in 1 year. We use the blood tests to see if you already have, or make, antibodies to Severe disease. To draw the blood from you, we will ask you to come back to the NoName Clinic in 1 month and 1 year.

When you come back, a nurse will ask you a few questions to find out if you had any side-effects after the shot, and if you had Severe disease. The questions take about 10 minutes. The nurse will also check your medical chart at the Clinic to see if you had Severe disease.

We will give you \$10 for today's blood draw, and \$20 each for the second and third draw, to pay for time, gas, and other expenses.

Schedule:

Date	Type of visit	What will be done
Today	Clinic	health questions; blood draw; shot; \$10
1 month	appointment with us	health questions; blood draw; \$20
1 year	appointment with us	health questions; blood draw; \$20

The vaccine may have side-effects for some people.

So far, the side-effects of the 2,500 people given Goodvacc vaccine have been the following.

Local reactions at the shot:

redness or soreness or swelling.

General reactions:

fever for about 1 day.

Less than 4% (1 person in 25) of the people who received the vaccine had any of those reactions.

As with all blood draws, you may get a bruise where the blood was taken. It is very rare to get an infection at the site of the blood draw.

The vaccine may have risks that we do not know about.

Goodvacc may have a side-effect or reaction that we do not know about. A very few people who got other vaccines had rare severe reactions, or even death.

The vaccine may benefit some people who get it.

Some people who get the Goodvacc vaccine shot may be protected from Severe disease. We hope Goodvacc vaccine protects against the disease, because it protected animals in tests. However, we do not know for sure if it protects human beings from Severe disease. The purpose of this study is to find out if it does protect.

If you get the "placebo" shot, you will not get benefit now. But if this study shows that Goodvacc protects against Severe disease and is safe, we will offer to give you the vaccine immediately.

The NoName Rez may benefit from this study. If the vaccine protects elders from Severe disease, all NoName elders will be the first to be offered the vaccine, When we get the results of the study, we will report them to the Tribal Council first, before releasing the information to the general public.

We will guard your privacy.

We protect all information about you and your taking part in this study as much as we can. We have trained all staff not to tell anyone outside the study anything about people in the study. Medical records are held in a secure room. The FDA may examine our records of those who take part in the study. It is possible but unlikely that a court order may force us to reveal medical records to other people, as is true for all medical records.

In case of injury or reaction, call Dr. Ida H. Service at ___ - ___ - ____.

If you have an injury or reaction that may be caused by your shot or study procedures, please call Dr. Service immediately. Her telephone number is ___ - ___ - _____. You may use the NoName Clinic phone, or call collect, to make the call.



The NoName Clinic will provide medical care for any injuries or reactions caused by the Goodvacc vaccine or study procedures. The Topdrug Pharmaceutical Company will pay for needed medical care that Clinic does not provide.

If you have questions about the research, call Dr. Service at ___ - ___ - ____, or write her:

NoName Clinic, NoName Indian Nation

Happy Rez, XX 12345-6789

You may use an NoName Clinic phone for the call.

You have rights as a research volunteer.

Taking part in this study is voluntary. If you do not take part, you will have no penalty and lose no care or services by NoName Clinic or others. You may quit at any time, with no penalty or loss of any care or service for which you are qualified.

We may contact you later about taking part in other studies related to Goodvacc vaccine or Severe disease. You may choose to take part or not at that time. Your decision to take part or not in the future will not affect any care or services by the Clinic or others.

You may stop taking part in this study at any time. You will be reimbursed for each blood draw taken. We may end your participation in this study at any point if we feel it is in your best interests for your health. We will tell you any information we find that may affect how willing you are to continue in the study.

If you have a **complaint, grievance, or other concerns**, call or write Ed Ethics, NoName IRB, NoName Tribal Office, Noname Rez, XX 12345-9876, at

You may use a NoName Clinic phone for the call.

I consent to take part in The Goodvacc Vaccine Research Study.



MODEL VOLUNTEER CONSENT DOCUMENT #2

Background: This hypothetical protocol is for a community-based diabetes prevalence study. A team of health care workers and local tribal members wants to determine the prevalence of diabetes in the community. The ultimate purpose is to determine which geographic and demographic (age and gender) groups have the highest rates of undiagnosed diabetes, which will lead to screening and intervention focussed on those groups. High random serum glucose will identify community members needing more definitive workup and final diagnosis. The team obtained technical assistance for project design and sample size calculations. General Methods: The team will determine prevalence of diabetes in a stratified random sample of community members. The sampling will use a list of tribal members maintained by the tribal census office. This list will be sorted by sex and age. After a random selection of the first selectee, every nth name on the list will be selected as well. A field worker will visit the homes of all selected people and ask them to participate in the study. Anyone positive on a random serum glucose will be asked to go to clinic for definitive testing and diagnosis.

Is an "Informed Consent" document necessary? Is this truly "research"? Screening for diabetes is part of clinical care; a detailed process of informed consent is seldom done when screening for diabetes in clinical care. One may then ask, is this project really clinical care with community outreach, and not "research"? Although the project includes clinical care, it is also research due to its use of sampling and to the purpose of the project. Sampling will ensure that the prevalence rates found are valid for the entire community; but sampling is a method of research, not of clinical care. The primary purpose of the project is to determine the prevalence rates of undiagnosed diabetes, and how the rates vary by geography and demography. That primary purpose is research, although research results will be used to plan better clinical care, and participants diagnosed with diabetes will receive care.

Informed Consent by potential volunteers. Although finding undiagnosed diabetes will likely benefit people with that condition, making the diagnosis has potential harms; driver license and insurability may be adversely affected by a diagnosis of diabetes. The consent must describe all benefits and risks. The readability is 7th grade; the text is only 646 words.

Community Diabetes Research Project: Informed Consent for Volunteers.

We ask you to take part in research for the Community Diabetes Project.

The Tribal Health Program sponsors this research project. We want to find out how many people have diabetes but do not know it. We want to check 200 adults from all parts of the Rez. We picked the people randomly from the Tribal Census, like picking bingo numbers out of a drum.

Diabetes means that a person has too much sugar in the blood. Many people in this Tribe have diabetes. Although many people with diabetes are diagnosed in the Clinic, some people may not know they have it. If we know where most of those people live, we can set up stations to screen for diabetes in those Districts.

We want to check your height and weight, and do a blood test for sugar.

If you agree to take part, we will ask some questions about your health and how you are feeling. We then will check your height and weight, and get a drop of blood from you by a finger-stick. We will **test your blood for sugar right away, and tell you the results.** All this takes about 15 minutes of your time.

When we get back to the Clinic, we will put all the results in your chart, for the doctors to see.

If your test shows high blood sugar, we will ask you to go to the Clinic.

The test today does not diagnose diabetes. High blood sugar on the test today means just that you may have diabetes or tend to have it.

If the test today is high, we will make a Clinic appointment for you. **You can get the final tests to check for diabetes there.**

People and the community may benefit if you agree to take part.

People may benefit because they may learn if they have diabetes or not. If you have diabetes but do not know it, the Clinic can help you stay healthy. Our community may benefit because we will be able to plan for better health services.

We want you to know the risks for taking part, as well.

The finger-stick will sting for a couple of seconds. Some people may worry a lot if the test today is high. A high test today does not mean a person has diabetes for sure. The Clinic will do those tests. And for people who have diabetes, **the Clinic can help them return to good health.**

If you have diabetes, you may need to have the Clinic OK your Driver's License each year. Having diabetes may make it more difficult to get insurance. (Most insurance companies test for diabetes when people apply, anyway.)

We will keep all your information private.

All results go right to your Clinic chart for your doctor's use. After that, the Community Diabetes Project will remove all names. Because there are no names, no-one can know what your results are from the Project.

If you have questions about this Project, please call Mary Doeswell at ___ - ____.

You may use a District or Clinic phone for the call. You can also visit her at Tribal Headquarters.

If you have a **complaint, grievance, or other concern**, please call or visit **Ed Ethics** at ___ - ___ - ____ in the Tribal Office. You may use a Clinic phone for the call.

Taking part in this study is voluntary.

If you do not take part, you will have no penalty and will lose no care or services by Tribe, IHS, or others. You may quit at any time, with no penalty or loss of any care or services for which you are qualified.

We will give you a copy of this form.

.....
I consent to take part in the Community Diabetes Research Project.



MODEL VOLUNTEER CONSENT DOCUMENT #3

***Background:** This consent document is for a survey of adults of sensitive and risky information. The hypothetical research is about domestic violence. This research is in and by a hypothetical Family Crisis Center, serving battered women in a rural reservation community. It provides drop-in counseling services; shelter is provided by a network of "Safe Homes." The research is in two phases: [1] use the existing data of the initial care interview by the counselor; and [2] do follow-up interviews at 1 and 6 months. If the data in the first phase were anonymous, the phase could be exempt from IRB review by "using existing data anonymously." However, the researchers wanted to reinforce the self-empowerment of the women. Thus, they chose to ask for consent to use even that existing data. The benefits, risks, and management of risks for participating in the research for the potential volunteer are primarily similar to those for the woman going to the Center for help, and had been covered extensively in the discussion between counselor and woman.*

Most research about stigmatized, incurable, genetic, or sexual diseases, or illegal behavior such as substance abuse or prostitution, have some similar risks. Most protocols have greater than minimal social risk. An early planning step in "greater than minimal social risk" research is to outline fully all the potential harms. Risks in such research often include:

- 1] loss of confidentiality about the identity of the volunteers;*
- 2] loss of confidentiality about the information given by the volunteers;*
- 3] causing internal conflicts within volunteer-respondents, emotional reactions, or needs;*
- 4] causing external conflicts of social, stigmatizing, or physical damage against volunteers, e.g., assault by abusing partners or legal action by authorities, if study participation in the study became known;*
- 5] in some research, harming not only the volunteers in the research but also third-parties [e.g., in fetal alcohol syndrome research, the mothers of volunteers]; and*
- 6] harming ethnic and other communities or groups.*

The next step is to ensure that the protocol minimize those potential harms to volunteers and others. The researcher must try to ensure confidentiality; we suggest use anonymous data whenever possible. To minimize emotional risks triggered by the research itself, the interview time must include extended listening, ventilating, discussing, and referral to counseling services. (Cooperation of counseling services must be obtained before approving the research.) If the research concerns illegal behavior, e.g., a study of HIV and risk factors among prostitutes, the researcher may need to have the cooperation of local legal authorities. If there is a risk of triggering violence by abusing partners, the researcher must ensure that nothing given can identify a person as a volunteer. Harm to community may be minimized by researcher and community agreeing about publication, e.g., to identify the community or not.

Researchers should also maximize benefits to volunteers and community. For research on fetal alcohol syndrome, for instance, researchers should link to established, or help establish, real services of prevention and treatment.

Research involving emotionally-vulnerable subjects should avoid institutional pressure by caregivers. Many patients who are dependent on caregivers' help may feel that refusing to take part will lead to loss of the care they need, in spite of the written "non-coercion disclaimer" in consent documents. One way to avoid the problem is to emphasize repeatedly the freedom to refuse. Another is to have at least the consent, and sometimes the research as well, done by people other than the caregivers. (In this hypothetical project, the researchers did not want to introduce a stranger into the relationship, due to extreme vulnerability of victims of domestic battering; thus, they felt that the counselors should be the people to solicit consent and do the follow-up research. But both the counselors doing the verbal explanation and the document repeatedly emphasized the freedom to choose.) In an actual project similar to this hypothetical research, several women did refuse to take part, indicating true freedom.

Please note the Certificate of Confidentiality. The survey included legally sensitive answers about the subject and third-parties, and it retained identifiers for the longitudinal survey. The researchers thus got a Certificate. The explanation about the Certificate should be short and understandable, not long and not in legalese.

The readability of this Document is 8th grade, and the text is only 1,031 words. Yet it meets all requirements for consent documents for research that is greater than minimal social risk.

Volunteer Consent to a Study about Domestic Violence.

The NoName Family Crisis Center asks you to take part in research about violence in families on the NoName Res.

The study will help us understand the type and severity of violence that occurs in NoName homes. The Crisis Center will use the study to plan better programs to prevent domestic violence, and to treat the family victims of violence including children.

We are asking to interview all women seen by the Center. **Please understand that you will always get care by the Family Crisis Center whether or not you agree to take part!**

If you agree to take part, your counselor will put some of your story into the study. Neither you nor anyone will be named or identified.

You told the counselor your history already. If you agree, she will use the facts of your history for the study. She may ask a few more questions, to complete your history. A Clinic doctor will also review your chart for injuries you had that may be related to problems with your partner.

She will also want to talk with you in 1 month and 6 months.

She will ask you how you are doing. You can tell her then what you thought about the Crisis Center, and what should be done to help you and other women, families, and children.

She knows that your partner may be angry if he found out you talked with us. So, she will ask you what is the best way to contact you to set up a time to talk. **She will contact you only by the way you want.** The Family Crisis Center is a safe place to come and talk.

The benefits to you taking part are seeing your counselor on a scheduled basis.

She will help you think through your situation, like she did today. You both can discuss your needs then. She may suggest programs or people that can help you then.

If you take part, however, the main benefit is to the community.

The Crisis Center will use the results of the survey to improve programs to help families, women, children, and partners in need. You and your family are not alone! More than 1 out of every 5 NoName families have suffered violence.

Some people have felt discomfort by taking part.

You and the counselor have already talked about things full of emotion for you. In her talk with you in 1 and 6 months, she will listen and spend as much time with you as you want. Most women feel better after talking like that.

The Family Crisis Center has tried to prevent any risk to you.

No-one in the Center tells anyone who has come here to talk or for help. If your partner finds out from others that you were here and asks you what you did, you can say we gave you help about "**women's issues.**" They included child care and transportation to Clinic.

We give everyone a list of services and people to call for help about violence in the home. To avoid making any woman's partner angry, that list contains other numbers and programs as well. In fact, it is a list of every social program in the NoName community. There is no sign that the list is related to violence in the home.

You do not have to sign a volunteer consent form to take part. You can agree to take part just by telling us, if you want. You can take a copy of this volunteer consent form with you, but we suggest you do not, to avoid triggering violence by your partner.

The Family Crisis Center tries to make sure no-one else can know what you say.

Your name is not on the study form with your answers. Only a special code number is there. Your counselor will keep your code number and name locked up with the Center's records.

For even more protection, the Crisis Center also has a Certificate of Confidentiality from the federal government. It was made to protect all information from disclosure, even that ordered by a court, without your written consent. That is, it was made to keep the information private, like your medical record.

No reports about the survey will contain your name or the name anyone in the study.

If you tell the counselor that someone, you or your children, is in danger of great physical harm, she will tell the Clinic to provide protection. The same thing would happen if you gave the same information to a doctor, nurse, or counselor in the NoName Clinic.

Taking part is voluntary.

If you do not take part, you will lose no care or services from the Family Crisis Center, Clinic, or anyone else. The Crisis Center will continue to give you help. You may refuse to answer any question, but we hope you answer as many questions as you can. You may also refuse to take part in the interviews at 1 month and 6 months from now, but we hope you will take part then.

If you have **questions about this study**, please contact **Mary Doeswell**, phone ____-____, or in her office at the Center.

If you have a **complaint, grievance, or other concerns**, please contact **Jane Goodlawyer**. She is a staff attorney for the Noname Legal Defense Office (NLDO). She is also a member of the NoName Institutional Review Board (IRB). Call her at ____-____ or visit her at NLDO. You may use a Clinic phone to make the calls.

Thank you for helping build a better NoName community for all families.

We will report the results of this study at the NoName Nation's Annual Meeting, in May 1994. A summary will be available at the Center shortly before the meeting. You can also discuss the results with any Center counselor.

.....

I agree to take part in the NoName Family Crisis Center study about violence in the home. I may refuse to answer any question I want. I have received a list of helping programs and people, and their telephone numbers.

MODEL VOLUNTEER CONSENT DOCUMENT #4

***Background:** This anonymous survey, done by giving the written questionnaire to every adult seeking care in the Clinic during a 2 month period, asks for no sensitive information. The research is no more than minimal risk, is a survey of adults, and does not involve vulnerable subjects; thus, it meets the conditions for waiver of signed consent and for being exempt from IRB review. Nonetheless, the consent process should minimize institutional pressure to participate possibly found in tribal or IHS settings. This document assures potential volunteers that their IHS and tribal services are unrelated to their choice to take part. The readability of this Volunteer Consent Document is 7th grade; the text is 292 words.*

NoName Health Service Research Study.

The NoName Indian Health Board asks you to take part in research about what services Clinic patients need.

We will use the results of the study to plan for better services for all of us. The Health Board wants to know what things are done well, what things need to be improved, and what new services are needed.

We ask all adult patients seen by the Clinic, and parents of children, to fill out the form. We know of no risks to you to taking part, because the survey is anonymous. That is, no-one can know who filled out a form, because no names are on it. It takes about 10 minutes to finish.

The NoName Tribe may benefit if most patients answer the survey and give their ideas!

Taking part is voluntary.

If you do not answer the survey, you will have no penalty and will lose no care or services by the Clinic or others. You may leave any question blank, but we ask you to answer as many questions as you can.

If you have **questions about the survey**, please contact **Mary Doeswell**, phone ___ - ___ or at the NoName Tribal Office. If you have a **complaint, grievance, or other concerns**, please contact **Ed Ethics**, Chair, NoName IRB. Call him at ___ - ___ or visit him at the Tribal Office. You may use a Clinic phone to make the calls.

Please leave the survey form in the boxes by pharmacy, lab, or medical records.

Please take this cover sheet of explanation with you. Medical records and Mary Doeswell also have copies of the cover sheet and survey.

Thank you for helping build a healthier world.

We will report the results of this survey at the Nation's Annual Meeting, May 2. Please attend!



MODEL VOLUNTEER CONSENT DOCUMENT #5

Other collaborators for this generic consent document were: Drs. Louisa Chapman [CDC], Greg Mertz [UNM], and Ray Reid [Navajo physician-researcher with Johns Hopkins U]. The readability of this Document is 8th grade, in spite of the complexity; the text is 1,161 words.

Ribavirin Treatment of Hantavirus Illness Acquired in the United States.**We offer ribavirin as a treatment for the "Mystery Illness."**

"Mystery Illness" is an infection caused by a type of **hantavirus**. The illness is now called "**Hantavirus Illness**." This **hantavirus** is a tiny germ, a virus. It comes from a mouse. Some people infected with **hantavirus** get sick but get well. Since May, more than half of people sick with **hantavirus illness** have died.

There are different types of **hantaviruses**. We are not sure of a way to treat the type here. But **ribavirin** may be a treatment. A study suggested that **ribavirin** may help cure illness caused by a related **hantavirus**.

The use of ribavirin to treat hantavirus illness is experimental.

There is no medicine now to treat this type of **hantavirus illness**. **Ribavirin** is a medicine used in the U.S. When given by breathing it in, it helps cure a severe viral lung infection in children. But we do not know if **ribavirin** can treat the **hantavirus illness**. We feel **ribavirin** may be able to treat your illness. Because **ribavirin** is experimental for **hantavirus**, it can be used only in research.

The purpose of the research is to see if ribavirin can treat the hantavirus illness.

We also will check the side-effects and safety of **ribavirin**.

Dr. Infection Doctor, School of Medicine, is in charge of the study.

Doctors in the hospital can use **ribavirin** under the research plan by Dr. Doctor.

For the treatment, we will give ribavirin injections by vein for 10 days.

We will give it every 6 hours for 4 days, then every 8 hours for 6 more days. We will give the first dose right away. We will give bigger doses the next 4 days, and smaller doses the last 6 days. Those are the same doses used for many years to treat other viruses.

We will get lab tests every day.

Before we give the first dose, we will get some urine to test for **hantavirus** and check kidneys. We will get 3 tubes of blood to check blood, liver, and kidneys. We will ask women if they are pregnant. We will do a urine or blood test for pregnancy, as a check.

While a person gets **ribavirin**, we will get 3 tubes of blood each day to check blood count, liver, and kidneys. We will get 1 tube of blood a month from now, as a final check.

We want to learn how to better diagnose and treat the **hantavirus illness**. We will save some blood and urine samples to do that research.

There are possible risks with ribavirin. Only people with hantavirus illness should get it.

We think you are infected with **hantavirus**. But if we find out by our tests that you do not have **hantavirus illness**, we will stop the medicine. If the **ribavirin** causes damage to any person, we will stop the medicine.

We cannot give ribavirin to women who are pregnant.

When tested in pregnant animals, **ribavirin** caused severe birth defects or death of the unborn animals. Thus, if given to a pregnant woman, **ribavirin** may cause severe birth defects, or the unborn baby may die. So, **we will not give ribavirin to pregnant women.** That is why we test women for pregnancy, and ask about the history of last menstrual period.

Women who receive ribavirin must not become pregnant for 3 months.

The medicine can stay in the body for 3 months. Because it can harm an unborn baby, women should not get pregnant for 3 months after finishing it. **All women must not get pregnant for 3 months.**

Ribavirin may cause minor changes in the blood.

Most people treated with **ribavirin** elsewhere got a mild anemia, or low blood count. The low blood count did not cause permanent damage. After the 10 day treatment, the blood count returned to normal.

Also, about 1 of every 50 people who received **ribavirin** had slightly higher bilirubin in the blood. Bilirubin can cause some people's skin to look yellow. The bilirubin returned to normal after finishing the medicine.

Less than 1 of every 250 people had a small increase in uric acid for a while. It returned to normal.

Ribavirin may have other risks we do not know about.

It may have a rare side-effect or reaction not known now. Any medicine can, very rarely, cause death from an allergic reaction.

Ribavirin may have benefits, too. We hope it will help people with hantavirus.

There is now no other medicine for **hantavirus illness**. We hope **ribavirin** will treat this **hantavirus**, because a study suggested that it may help cure illness by a related virus.

If you decide not to take ribavirin, we will give you the best standard treatment we can.

We will give all people the best care we can, whether they take **ribavirin** or not.

We will guard everyone's privacy.

We will keep information about every person private to the best of our ability. We will not use any name outside this study. The U.S. Centers for Disease Control and Prevention, and the U.S. Food and Drug Administration, may check medical records. A court could order us to show medical records to other people, but that is not likely.

All reports to the Tribe, community, other doctors, and medical journals will not have any person's name.

If you later have questions about the study, call Dr. Doctor at () ___-___.

Call Dr. Doctor in at ___-___ between [times]. All other hours, call () ___-___ and ask for **Dr. Oncall**.

If anyone gets an **injury or reaction** that may be caused by **ribavirin** or procedures, please call Dr. Doctor at ___-___ right away. The Hospital will give everyone all the care that is needed.

The ribavirin is given free.

There is no charge for the medicine.

We will provide care for any adverse affects of ribavirin.

There is no program to pay people if they have an adverse affect.

Research volunteers have certain rights.

Taking part in this study is voluntary. If you do not take part, you will have no penalty and lose no care or services. You may quit at any time, with no penalty or loss of care or services for which you are qualified.

You may stop taking ribavirin at any time. We may stop it if we feel stopping is best for a person's health. We will tell every person taking part all information we find that may affect their willingness to keep getting the medicine.

We may contact people later about taking part in a follow-up study related to **ribavirin** or the **hantavirus illness**. Everyone can choose to take part or not at that time.

For answers to your questions about a complaint, grievance, or other concerns, call the University Institutional Review Board (IRB) at (____) ____-____.

.....
I agree to take part in the research Ribavirin Treatment of Hantavirus Illness.



MODEL PARENTAL PERMISSION DOCUMENT #6 (Youth Risk Behavior Survey)

***Background:** Many states, Tribes, and school districts want to measure or monitor the levels of risky behaviors of the adolescents in middle and high schools by a Youth Risk Behavior Survey (YRBS). The Centers for Disease Control and Prevention (CDC) have a version of YRBS; the University of Minnesota has another. Most YRBSs ask about risky behaviors such as sex (both protected and unprotected), drug and alcohol use, violence (both receiving and giving), and emotional health (such as desires to commit suicide). The purpose of the YRBS is that the school district, Tribe, or state use the information to do appropriate interventions for problems identified, if any. (The data from the YRBS usually must activate the citizens of the district, Tribe, or state to demand interventions for major changes to occur.)*

Many states in the past have conducted their YRBS without IRB review or even Tribal review. Most school districts have reviewed the YRBS and usually had the option of not participating (i.e., disapproving the YRBS in their district). Most YRBSs are done by "passive consent," in which if the parents do not send back to the school a signed document refusing to let their adolescent child take part, the YRBS "assumes" that the parent has given permission.

I consider YRBSs to be research, because the YRBS is a "systematic investigation ... designed to develop or contribute to generalizable knowledge" [45 CFR § 46.102(d)] about, in this case, the behaviors of students in the district, Tribe, or state. Usually the protocol of YRBS should ensure anonymity of the individual adolescent. According to Subpart D (research with children) of the DHHS regulations 45 CFR 46 about ethical research, the exemption from IRB review, of survey research that is conducted anonymously, does not apply to research involving children. (The Department of Education has proposed almost identical regulations for itself.) Therefore, the YRBS must be reviewed and approved by the local IRB[s].

"Passive consent" does not meet the definition or standards of informed consent (for YRBS, informed parental permission). IRBs can waive some or all elements of informed permission [45 CFR § 46.116(d)] if 4 conditions are met: 1] the YRBS is no more than minimal risk to the children; 2] the waiver will not adversely affect the rights and welfare of the parents or children; 3] the YRBS could not practicably be done without the waiver; and 4] the children-parents will get pertinent information after the YRBS is done. For a YRBS to be done using "passive permission," the IRB must find that the survey meets those 4 conditions. (Rigorous anonymity, and preventing stigmatization of students who do not take part can meet "1]." Reporting results to the school district in public can meet "4]." The IRB must use its judgment for "2]" and "3]." I outlined possible procedures for doing the YRBS in a separate paper, for an IRB to waive full parental permission. The paper, a presentation to an Applied Research Ethics National Association [ARENA] meeting in 1992, is available from me.

This Model Document #6 assumes full permission. The document can easily be adapted to serve as "passive permission" if the local IRB[s] approve the waiver of permission. The assent document for students can be adapted from the permission document. To fully ensure anonymity, the assent document should be an information sheet, neither signed nor collected. As with the permission document, it should have the name and telephone number of counselors for students. To ensure a good response rate with "active permission," the school will probably have to send it out three times, perhaps by both mail and as a take-home by the students, and with multiple announcements in multiple media and settings. To ensure that "passive permission" in fact reaches every parent, the school should also do three distributions with multiple announcements. Those activities will also help establish a receptive framework in the community for the results.

The readability of this Parental Permission Document is 6th grade; the text is 592 words.

The NoName School's Youth Risk Behavior Survey.

The NoName Tribe and School District ask that you give permission for your child to take the Youth Risk Behavior Survey.

This research survey asks students in grades six to twelve about risky behaviors they may do. The survey ask about the following.

- Drug and alcohol use, if any -- what drugs, how often.
- Auto passenger and driving habits -- seat belt use, driving while intoxicated.
- Sex, if any -- how often, protection used.
- Violence, if any.
- Feeling down, thoughts of suicide.

The purpose is to try to prevent unhealthy behaviors among our kids.

We will use the results of the survey to see if many students have problems with these. The Tribe and School will let you know the results. We may need to improve programs of prevention, or develop new ones.

You can look at the survey, if you want, to see what the questions are.

Copies of the survey are in the school, in the front office.

The survey will have no name of any student. It will take steps to make sure the survey is anonymous.

The survey will be handed out in each class on Friday morning, May 1. Each student will be free to take or not take the survey. Each student can not answer any or all questions. A booklet about Tribal history will also be given out in the same envelope.

The survey takes less than one hour to finish. At the end of the hour, each student will seal the survey in a blank envelopes, and put them in a large box. The school will send all sealed surveys to the Area Indian Health Board for analysis.

If you do not let your child do the survey, he or she will receive a survey with no questions and the history booklet. He or she will hand in the blank sealed survey, like the other students.

The survey has little risk for your child.

The steps will prevent anyone from knowing which survey was handed in by any student. The survey may make some students want to talk to a student adviser about their behaviors or concerns. Students can talk with **Mary Leader** or **Al Mentor** at the school, phone ___-____.

Each student will not directly benefit by doing the survey.

However, the NoName Tribe and School may benefit from finding out what problems our kids are having. That may lead to helping our kids be more healthy.

Taking part is voluntary.

If you do not give permission, you and your child will have no penalty. If you give permission, your child may leave blank any or all questions. You and your child will lose no care or services by the school or anyone else.

If you have **questions about the survey**, please contact **Mary Leader**, phone ___-____, at the School.

If you have a **complaint, grievance, or other concerns**, please contact **Ed Ethics**, Chair, NoName IRB. Call him at ___-____ or visit him at the NoName Tribal Office. You may use a school phone to make the calls.

Please sign this permission form, if you agree. Then send it with your child to the school.

You may also mail the form in the attached envelope. Please keep the copy of this sheet.

Thank you for helping our kids keep healthy.

We will report the results of this survey at the first PTA meeting next fall, and in the NoName Newspaper.

.....
I agree to let my child, _____, take the Youth Risk Behavior Survey, if he or she wants to. I can read the survey form at the school, if I want.



MODEL VOLUNTEER CONSENT DOCUMENT #7 ("CBPR," Qualitative)

***Background:** Some researchers think that qualitative research cannot harm anyone. That is not correct. In this research of feelings experienced by women who had a miscarriage, major harms were possible. In psychologically-sensitive research, minimizing harms depends in part on the interpersonal skills of the researcher. The consent document also has a role; for instance, the lay word "miscarriage" is used, instead of the medical terms "spontaneous abortion" or "early fetal death" that would be harsh and severe to the women being asked.*

Some medically-oriented IRBs feel unsure about how they can judge the possible scientific benefit of qualitative research. One article in particular ["Assessing quality in qualitative research" BMJ 2000; 320:50-52, <http://www.bmj.com/cgi/content/full/320/7226/50>] can help IRBs understand and recognize good qualitative research with the potential for scientific benefit. The article also has a set of good references.

This research is also community-based participatory research (CBPR). Some IRBs have little experience with CBPR. Two articles can help IRBs understand and review CBPR protocols: ["Participatory research maximises community and lay involvement" BMJ 1999; 319:774-778 <http://www.bmj.com/cgi/content/full/319/7212/774> (the references are a good set of sources to understand CBPR, and it describes a Community Advisory Board)]; and ["Using qualitative methods in health related action research" BMJ 2000; 320:178-181 <http://www.bmj.com/cgi/content/full/320/7228/178>]. I have a larger reference list on qualitative research for IRBs; if you want it, please send me an e-mail to request it.

This is a modification of the consent document for an actual research project, by Kristen M. Swanson, RN, PhD, FAAN; Professor and Chair, Dept. of Family and Child Nursing; University of Washington, Box 357262; Seattle, WA 98195; 206-543-8228, fax - 543-6656. The readability of this Volunteer Consent Document is 7th grade; the text is 1,109 words.

Feelings about Miscarriage in the NoName Tribe.

I am First Lastname, a researcher and a nurse.

I have worked for many years with people who have had miscarriages.

I am asking you to take part in a research project.

I would like you to talk with me and share your story about miscarriage and healing. I want to learn what miscarriage and healing has been like for the NoName people.

I have two purposes with this project.

- 1] I want to help the NoName people. In my work as a nurse, I have found that people who miscarried often feel better after talking about it.
- 2] I also want to teach nurses and others how one community dealt with many pregnancy losses. They may then be better able to care for women and families with miscarriage.

This is both a research and a healing project.

It is different from most research, because one purpose is to help the NoName people deal gently and respectfully with the miscarriage of their children.

It is different, also, because tribal members help plan the project. This project will try to help tribal members themselves address the pregnancy losses with respect. The Tribe and I hope to learn together how best to deal with these experiences.

I would like to ask you a few questions and listen to you.

If you agree to take part, we will set up a time to talk. I can meet with you alone, or in a small group.

I will keep a personal journal about this project. I will write down what I learn each day. I will also summarize talks that are shared with me. I will not show my journal to anyone from the community.

I will come to the NoName Tribe once or twice a month for several months. I will stay two days each time. If you want to talk with me when I come, please call me at ___-___-____. You can use the Clinic phone to do so. Or, you can ask Clinic Person to call me. Or, you can e-mail me at ____.

If you agree to take part, I may ask you later for reactions to what I think I have learned. That is, I will want to check with you, to make sure I have it 'right.'

You, the Tribe, and others may benefit by this project.

Some people may feel better after talking with me about their experience. I have helped people for many years to care for themselves, their feelings, their memories, and those they love after a miscarriage.

The Tribe and Health Program may learn good ways to deal with pregnancy loss. The Tribe has named a Community Advisory Board to help plan the project. The Board will help increase the benefits of the project to the Tribe.

The Tribe's experience may teach nurses and others how pregnancy loss affects people, families, and communities, and how to care for them.

I want you to know about possible harms, as well.

Taking part may bring up hard feelings in some people who talk about their miscarriages. To help deal with that, I will give you a list of local counselors who can help. If I think you need help, I will refer you for counseling.

Some people may want to talk more about the miscarriages after I leave. They may feel lonely. To help prevent that, I will let you know about other women in the Tribe who would like to listen and share experiences.

If you take part, other people in this small a community may wonder what you are up to. To help prevent that, I and others will inform the Tribe about the project.

Some research has harmed communities. To prevent that, the Community Advisory Board has helped plan this project. That Board will review all articles and presentations before I make them. The Tribal government has approved this project.

You can get help, if you want it, without taking part in this project.

If you do not take part in this project, you still can get counseling from the Health Program if you want. I will not be the person you will talk to, however.

I will try to keep all information confidential.

I will keep all material in a locked file cabinet in the School of Nursing.

I will not give or tell your name to anyone. No names or identifiers will be in any article or presentation. Even so, some people who know you may think they recognize you, when I describe some things that happened to people. To help prevent that, I will try to disguise those reports. Review by the Community Advisory Board may help prevent that, as well.

If you have any questions about this project, please call me at

You can use a Clinic phone to call me. You can also ask questions to Clinic Person.

Please ask me now any questions you have about this project. After all your questions are answered, you can decide if you want to talk with me or not.

If you have a concern or grievance about this project, please call IRB Person at

She is at the School of Nursing. She answers complaints by people in research. She is not part of this project. You can use a Clinic phone to call her.

You can also talk to a member of the Community Advisory Board. Clinic Person can give you their names.

If you think you have been injured or hurt by this project, please call IRB Person at

Being in this project is up to you.

If you do not wish to be in this project, it is perfectly ok. If you do not take part, you will not lose any rights to health care or any other benefits that you already have.

If you start to take part in this project, you can change your mind later on. You can stop being in the project at any time. If you want, you can also ask me to delete all your stories and facts from the project. If you do so, you will not lose any rights to health care or other benefits.

When you and I sign this form, we agree to treat each other with respect.

I promise to honor what you have shared with me. I promise to treat your personal story with the dignity that you and your memories deserve. I promise to write about your experience so that your identity is hidden.

I will give you a copy of this form.

I agree to take part in your research into feelings about miscarriage.

MODEL VOLUNTEER CONSENT DOCUMENT #8 (Genetic Research)

***Background:** Genetic research is sensitive for many Native American people and tribes. Consent documents should include potential harms to individuals and to tribes--the most frequent being psychosocial. Potential harms or risks are written as events that 'some people have gotten-felt-(etc.).' In this research project, and in many similar research projects, the volunteers, tribes, and IRBs have control over future uses of saved specimens not specified in the protocol. This Document was modified from one for an actual research project, by Henry T. Lynch, MD; Creighton University School of Medicine. This Consent Document is about a quite complex topic, and must cover much information. Even so, its readability is 8th grade; its text is 3,448 words, almost 3 times longer than the next longest Model Document.*

Genetic research about cancer in families: Hereditary Nonpolyposis Colorectal Cancer.

We ask you to take part in research about genes that lead to the Hereditary Nonpolyposis Colorectal Cancer (HNPCC) disease.

We are asking many people in the NoName Nation to take part. All people asked have a type of cancer, or have HNPCC cancers in their family. To take part in the study is wholly voluntary.

Dr. Longtime Researcher, of the Cancer Research Center, heads the study.

Many people with HNPCC have come down with cancer of the colon (large bowel), rectum, womb, ovaries, or other cancers.

"Colorectal cancer" is of the colon and rectum. It is a common cancer in humans.

HNPCC colorectal cancer runs in families. That means colorectal cancer in at least two generations in a family, in several family members, and at younger ages than usual.

Some HNPCC family members have come down with other cancers, such as of the womb, ovary, or stomach.

Some people with a HNPCC gene get one of those cancers.

A change from the usual in one of four genes seems to cause HNPCC. We call that an "HNPCC gene."

In HNPCC families, the HNPCC gene is passed down from parent to child.

An HNPCC gene can be found by a genetic test of blood or other tissues. "Genetic test" is also called a "DNA test."

One purpose of this study is to see who has an HNPCC gene. Another purpose is to see what kind of HNPCC genes are present in NoName families with HNPCC.

The study will draw blood from people who take part. We then will do a genetic test to see if an HNPCC gene is present.

If we have already found a specific HNPCC gene in other members of the person's family, we will test the blood for only that gene.

This study has several steps.

First, we will discuss with you the pros and cons of getting tested. That step is part of asking for your consent for this study.

Then we let you take time to decide. Some people want to go home and talk with their family before deciding. Some people decide to take part, while other people decide not to.

Then, if you want to take part, we will take a medical history in the NoName Clinic. We will also do a "family tree" of your relations. This may take up to one hour.

Then we will draw about 14 teaspoons (seven tubes) of blood, by a usual blood draw. If you are having surgery, the surgeon may use a small piece of the tissue removed for the test, instead of blood.

Then a certified genetics lab will make a sample called a "living cell line" from the blood draw or tissue. In a living cell line, the cells grow for ever in the lab. We get the DNA we need to test from these living cell lines. That way, we do not have to ask people over and over to do another blood draw. We will store the sample.

Then the certified lab will test the DNA for HNPCC genes. Due to the time needed to run the tests, we can not say when we can give you your test results.

When your results are ready, we will contact you for a meeting to give them to you. You can bring other family members or friends with you if you want.

In that meeting, we will first describe again what the HNPCC is. We will discuss what are the options to prevent HNPCC and other cancers.

Then we will discuss the pros and cons of receiving the test results. Some people decide to get the results, while other people decide not to get the results. If you want to get your results, we will ask your consent to do so. We will also ask you to sign a second consent form.

Then we will give you a copy of your genetic test results. We will also explain the meaning of those results.

We may want to contact people in the study later, for new requests. We may ask to do other tests on the stored sample or to update the medical history. We will do so only if the person agrees. We ask people who take part to tell us if they move.

We also discuss the study and HNPCC with families.

Family members may also discuss the study with us. We will explain the pros and cons to the family of the test. We will also explain what the test means. We will not give the results of your test to any family member without your permission.

Twice a year we invite HNPCC patients and family members to meet with us. We explain HNPCC. We talk about the findings of the study, and what we and other researchers have learned about HNPCC. And we discuss how to prevent cancer. We do not mention any person or family by name.

We discuss the study and HNPCC with the NoName Nation, too.

We discussed this study with the Tribal Council. The Council approved this study. We update the Council about the study once a year.

We also discussed this program with the NoName Health Department. We update it every year, as well.

We want to answer all your questions.

Many people think of new questions later. So you or your family may call to talk with us in the future. We will also give you a list of local genetic counselors, if you or your family want to talk with someone else.

It is important to know before getting tested what the results will mean.

It is very unlikely that the results of this genetic test will be in error.

A positive genetic test, that the person has an HNPCC gene, means these points.

- 1] Out of 20 people with an HNPCC gene, about 16 to 18 may get colorectal cancer. About three to four of them may get other cancers, too, of the womb, stomach, ovary, and others.

- 2] Some people may get emotional distress if they learn they are more likely to get cancer, due to having an HNPCC gene. Some people get spiritually troubled.
- 3] If you take part, we will discuss with you the meaning of your results. We will also recommend cancer screening, and give choices for cancer prevention and management. We will give you a written summary.

A negative test means these points.

- 1] People with no HNPCC gene do not have an increased risk to get colorectal cancer. They have the same risk to get colorectal cancer as everyone else. About one out of 20 people with no HNPCC gene may get colorectal cancer. We advise that all people follow the advice of the American Cancer Society to prevent cancer. We will give you a written summary.
- 2] People with no HNPCC gene can not give their children any HNPCC gene.
- 3] Some people may get emotional distress or spiritually troubled if they learn they are different from family members with an HNPCC gene, who are more likely to get cancer.

The meaning of results is limited, however.

Some people with an HNPCC gene have never developed cancer. Having an HNPCC gene does not mean that the person will surely get cancer.

Some people with no HNPCC gene have developed colorectal or other cancer. They still have the risk of the general population for all cancers. We recommend that people with no HNPCC gene follow the advice of the American Cancer Society advice about cancer screening.

A few people have test results that we can not interpret. We will discuss such results with each person. We then may ask for another blood test.

We may not know some future consequences of genetic testing.

We plan store your "living cell line" permanently, at the Cancer Research Center.

The Center, however, may dispose of your sample after 15 years. The Center will handle your sample carefully, but there is a small chance of accidental loss or destruction. All samples will be disposed with respect.

We may do more research, but only about HNPCC.

If we do not find a specific HNPCC gene in your family, in the future we may test for other genes that may become known.

We may send DNA from your sample to other researchers. The sample will have only a code number, no name. They will only test for changes in the HNPCC genes under study. When they are finished testing, the sample will be disposed or returned to the Center. All disposed samples will be treated with respect.

Only researchers at Center who are doing the present study can access the stored samples. The Center will do no tests on the stored samples other than the tests noted in this consent, unless it first obtains another specific consent.

No sample from this study will be used for any other research or purpose, unless both the NoName Nation and the person consent. The NoName Nation's Institutional Review Board (IRB), and the Center's IRB, oversee this study. They must also approve that use.

We try to keep private every person's medical history, testing, and results.

We also try to keep private who took part in this study.

We store all data only with code numbers, no names. The labs keep the samples only with code numbers. We keep the list of each person's code number and name only in a separate, locked, file.

We store all data and samples at the Center. Only researchers in this study can access the data and samples.

All publications or talks about this study will not identify any person, family, or Tribe. They all will be reviewed and approved by the Tribe, to make sure that the Tribe can not be known.

We try very hard to keep private all data about each person. Our records, however, could be subpoenaed by a court of law. To prevent a release of our records, the Center has a Certificate of Confidentiality. We got it from the federal government, Department of Health and Human Services. (The Certificate is not an endorsement of this study by the Department.) It protects us from giving anyone's name to any Federal, State, or local court. It also protects us in all civil, criminal, administrative, legislative, or other actions. It lets us keep private all data in this study. It gives permanent protection. The protection continues even after death of a person. If you want a copy of the Certificate, please ask us for one.

The Certificate does not protect data from this study that is in a medical record by a health care provider. It does not protect information voluntarily given out by you or the researchers.

Certain audits, reviews, or program evaluations may look at the data. The Food and Drug Administration, and the National Institutes of Health, can review records of people in this study. The NoName Nation's and Center's IRBs can review records of people, if needed for their oversight. All people doing such reviews are required to not reveal any person's name.

If you want, we will give the results of your genetic test to your personal doctor. You must first ask us to do so.

Please be aware that once your doctor has your results, we can not protect your privacy as fully. Our Certificate does not cover your doctor. If the doctor records your results in your chart, other health care people, and health or life insurance carriers, may learn your genetic status. They may also learn your status if your doctor screens or does preventive treatments for HNPCC.

Some people want their personal doctor to know their test results, but to keep those results from others. If so, please ask your doctor not to record in your medical record your test results or that you had a genetic test done.

There may be some potential direct benefits for some people, if they take part.

We will give each person advice about how to prevent cancer, based on their gene status.

Some people get relief from the uncertainty about their gene status, no matter what their result.

People with a negative test will not need to see the doctor to prevent cancer more often than recommended for the general population.

But some people who take part may get no personal benefit from the study.

There may be some potential benefits for families.

People in your family may learn important information about their risk for HNPCC, based on your results. They then may seek genetic counseling, tests, or advice for cancer prevention. It is your choice whether to tell them about your results. You can ask us to tell your family members about your results, if they want to hear about them. (To do so, you must give written consent to give them your results.)

Members in some families come closer to each other.

There may be some potential benefits for other people.

We hope to learn more about HNPCC, to better help all people and families with this condition.

There may be some potential physical harms for some people if they take part.

The physical risks of having blood drawn are small. Some people have had local discomfort or bruising at the blood draw site. Rarely has anyone had a clot, an infection, or pain.

There are some potential personal, familial, social, and tribal harms, too.**Some people have suffered personal harms.**

Some people with a positive test have felt distressed due to anxiety, worry, or depression. Some people have gotten spiritually troubled.

Some people with a negative test have developed feelings of guilt because they are more fortunate than others in their family.

Please consider carefully your own possible reactions to positive and negative results before agreeing to this genetic test.

If any of that happens to you, please let us know. We have counselors who can help people handle those problems.

Some people have suffered harms in their family.

A few people with a positive test have been shunned by some family members who hear about the results. It is your choice whether to tell your family about your results. You also can ask us to tell family members about your results, if they want to hear about them.

The genetic test may reveal that family relationships are different than had been assumed. For instance, a genetic test may show that a parent could not be a biologic parent of a son or daughter. This information may disrupt the person or family. Our policy is not to tell anyone of those results, however.

Some people who learn about their genetic status change their ties with family members. Before deciding to get tested, many people find it helpful to discuss possible testing with their family. That discussion could be with parents, sisters, brothers, spouse, and children. The discussion could include the meaning for the family of positive and negative test results.

If any of that happens to you, please let us know. We have counselors who can help families handle those problems.

Some people have suffered harms from their friends or society.

A few people with a positive test have been shunned by friends. It is your choice whether to tell other people about your results. If you tell your results to even just one person, the results often get passed on to other people.

Loss of secrecy about a positive test may cause bad things to some people. Some people have been hurt or stigmatized by others. Some have been discriminated against in hiring, job retention, or promotion. Some have been refused insurance.

If any of that happens to you, please let us know. We have counselors who can help people handle those problems, and fight discrimination.

A few tribes have suffered disruption, as well.

Many tribes are worried that other studies may use the stored samples without the tribe's permission.

We have promised the Tribe, and promise you, that NO study will ever be done on the samples we collect without the Tribe's permission.

A few tribes have been hurt by society because they have a "genetic problem." A few tribal members have felt badly about their tribes because some families have a genetic disease.

If any of that happens, please let us know. We will help the Tribe handle those problems, and fight discrimination.

A few tribal people have felt that genetics is simply not a good thing to do or learn about, or that it is against tradition.

We will discuss those concerns with anyone.

Some people may experience benefits or harms in the future we do not know about now.

We will let you know if we learn about new potential benefits or harms.

You have an alternative to being in this study.

You can choose not to be tested, or not to receive your test results. If you do, we will still discuss how to screen for and prevent cancer, based on what we know from your family tree.

You are also invited to the meeting of HNPCC patients and families we hold twice a year.

People will not have any money costs from the study.

No-one is billed for the sample, testing, or counseling. We can not pay for genetic counselors outside the study. The NoName Clinic will do all recommended steps to screen for and prevent cancer for people eligible for care there.

The study will not give a money payment to people to take part.

You can see all your personal data from the genetic tests done in this study.

You may not see the results of tests of other family members, however, unless we receive their permission.

You can refuse to take part, without penalty to you.

All people who do not take part will not lose Clinic care, or other care for which they qualify.

You can also change your mind after you start in the study, without penalty to you.

You can refuse any more genetic testing.

You can quit the study.

You can have us destroy your stored sample. You can have us remove unused medical data about you from our records. We will keep the data we have used before to your decision to quit or have sample destroyed.

If people who take part pass on, their guardian or next of kin control the samples.

They can let us keep the stored samples, to continue the tests. Or they can ask us to destroy the samples. Or they can request that we send the samples to the NoName Clinic Hospital, to be disposed there.

The NoName Clinic will give medical care for any injuries due to the study.

The care will be at no expense to the person injured.

The study does not compensate for injuries from taking part in this study. The study does not give payment for lost wages or other losses due to those injuries.

If you have any question about the research, please call us.

You can call Dr. Longtime Researcher, at ___-___-___. You can use the Clinic phone, or call collect.

You can also call Dr. Local Doctor at the Clinic, ___-___-___.

If you think you have been injured by the study, please call Dr. Local Doctor.

Please call right away. Her telephone number is ___-___-___. It is answered 24 hours a day.

If you are not satisfied with this study, please call an IRB.

If you have a grievance or complaint, please call an IRB. The NoName Nation and Center IRBs oversee this study. Their telephone numbers are as follows.

You can use the Clinic phone, or call collect.

We will give you a copy of this consent.

.....

IN SUMMARY:

We ask you to take part in genetic research. It is a blood test for a cancer gene. It will find out if you have a HNPCC gene, for colon cancer.

Some people may benefit from the testing. The tests help doctors know best ways to prevent these cancers. Some families may benefit, too.

Some people with positive test results have been distressed or troubled. Some people with negative results have felt guilty that they do not have the HNPCC gene. Some families disrupted by the results. The study has staff to help people and families deal with those problems.

You can refuse to take part with no penalty, or loss of NoName Clinic care or other care for which you qualify. You can also change my mind later, and quit the study.

The study may store my "living cell line" sample permanently, even after my own death.

The Cancer Research Center may contact me in the future to ask for my consent to use my stored sample or medical data.

We want to answer all questions to my satisfaction. You can ask any question in the future. Do you have any more questions now?

.....

I volunteer for this research about the HNPCC gene and colon cancer.



MODEL INFORMATION SHEETS #9 and #10

These two Model Information Sheets are for public health investigations, the first of a simple outbreak, the second of a life-threatening epidemic. The investigations are public health care not "research." Both investigations have a survey and a blood draw. Similar information sheets can be used in program evaluation: studies by a program to evaluate itself.

Because initial public health investigations and program evaluations are not research:

- *compliance with 45 CFR 46, including review by an IRB, is not required;*
- *the word "research" should not be used in the information sheet; and*
- *a signature need not be required.*

That latter point is important because simply requiring a signature reduces the participation rate by about 15% among people already fully informed who agree to participate before being asked to sign a consent document (Singer E. Am Soc Review 1978; 43:144-162).

Information sheets for public health studies or for program evaluation have 7 elements:

- [1] *purposes of the study;*
- [2] *procedures;*
- [3] *potential benefits to the community and individual;*
- [4] *potential risks or harms;*
- [5] *confidentiality;*
- [6] *reporting results; and*
- [7] *whom to call with questions.*

The first Model Information Sheet is for a simple outbreak such as gastroenteritis; it does not involve unusual or strong concerns by potential volunteers. The sheet gives "basic" information. The other investigation is of a new severe disease. It involves all possible strong concerns of volunteers, i.e., asking about sensitive information [e.g., sexual behavior, drug use or other illicit behavior, sexual orientation, etc.], testing blood for stigmatizing diseases, and doing the study in the workplace with the concern of possible affect on employment. Because the sheet addresses almost all possible major concerns, it gives "maximal" information. Some EPI-AID investigations involve concerns more than "basic" but less than "maximal." [For instance, a study might involve only non-sensitive questions, but be done in the workplace.] The relevant sentence(s) in the "maximal" sheet--in the example cited, about employment--can be added to the "basic" model sheet.

Information sheets with these 7 elements help both to inform potential volunteers and to increase the rate of participation. Many Indian communities have a high prevalence of mistrust of studies; people remember and perceive studies as "taking away information" from the community without anything of value being returned. Reporting the results to the Tribal Government and the affected districts of the reservation, and telling potential volunteers about that reporting, may thus help increase participation. Because reporting is important to people in non-Indian communities as well, it should be included in most or all sheets, referring to the local government. The sheets have a 7th grade readability level or less. Making information understandable helps engender a feeling of reciprocity between the investigator and potential volunteer. Including the name and telephone number of people to call with questions also increases that feeling. The increased feeling of reciprocity, of being respected and sharing the endeavor, helps increase the participation rate.

Giving complete information in a succinct manner may not hinder, but rather may aid, fuller participation. People who refuse to take part because they have not received sufficient information in an understandable way or to answer their concerns, are lost to the study.

MODEL INFORMATION SHEET, #9 ("BASIC")

The readability of this "basic" Information Sheet is 6th grade. The text is only 188 words and 1/3 a page, yet it has all 7 key elements to be informed.

The study of a Mystery outbreak.

The Centers for Disease Control ask you to help find the cause of a Mystery outbreak.

An outbreak of Mystery struck 50 people of the NoName Rez last week. We are doing this study to find the cause. We ask all people affected to answer some questions, and let us draw blood. The questions will take about 20 minutes. They ask what you did just before you got sick. We will also draw a tube of blood, to test for possible Known disease.

The study may tell us the cause of the Mystery outbreak and how to prevent it.

Only CDC will see the answers and blood test results. The blood draw may sting for a second. We know of no other risks to you by taking part. We will tell the NoName community what we find out.

Taking part is voluntary.

If you have questions about the study, please ask them now. You may ask questions later by calling **Dr. Clara D. Clark** in Atlanta, at ___-___-____, or locally **Dr. Ida H. Service**, at ___-____. You may use a Clinic phone to make the calls.

Thank you for helping.



MODEL INFORMATION SHEET #10 ("MAXIMAL")

This epidemiologic study touches serious concerns of potential volunteers, yet the Information Sheet's readability is 7th grade, and its text only 380 words. It has all 7 information elements for a public health response to an epidemic, and answers those serious concerns.

The Search for the Cause of the Mystery Disease

We ask for your help. We are the NoName Tribal Government, Council of Elders, NoName Service Unit, and Centers for Disease Control. We are fighting the Mystery Disease. We need you to take part in a study to find the cause of the Mystery Disease.

The Mystery Disease struck 25 people of the NoName Rez in the past month. We do not know the cause. This study will try to find out the cause. From that, we hope to prevent it from striking more people.

We ask all adults living in NoName Rez to answer some questions and let us draw blood. The questions will take about 20 minutes. They ask what you did in the past month. We hope you will answer all questions. A trained person will draw 2 tubes of blood in your home, just like in the Clinic. We will test the blood for infections you had in the past. We may use your blood later to do other tests about the Mystery Disease. We also may want to ask you a few other questions later.

This study may help the NoName community, your family, and you.

Everyone's answers, and their blood tests, may tell us what causes the Mystery Disease. We will tell the community what we find out, and how to prevent the disease. We will let you know if we find out anything about your health from your tests.

Only CDC will see the answers and blood test results. Your employer will not see your answers or test results. Taking part or not will not affect your employment.

Your answers and tests are protected like a medical record. They are private, under the federal government's Privacy Act. CDC has studied more than 100,000 people in several thousand outbreaks in the past 40 years. It has maintained the privacy of all those people.

The blood draw may sting for a second. We know of no direct harms to you by taking part.

Taking part is voluntary.

If you have questions about the study, please ask them now. You may ask questions later by calling **Dr. Clara D. Clark** in Atlanta, at ___-___-____, or **Dr. Ida H. Service** locally, at ___-____. You may use a Clinic phone to make the calls.

Thank you for helping the NoName Rez get well again.

APPENDIX III. General IHS IRB Review Process

Not all IHS IRBs follow the same review process.

Once the Principal Investigator (PI) has secured tribal and service unit approval, he or she must submit the complete proposal for IHS IRB review.

The 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 may 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). The PR is responsible for conducting a thorough assessment of the protocol based on 45 CFR 46 requirements.

During the IRB meeting, the committee has an opportunity to discuss the research proposal per 45 CFR 46 requirements. The 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 CFR 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 CFR 46 requirements.

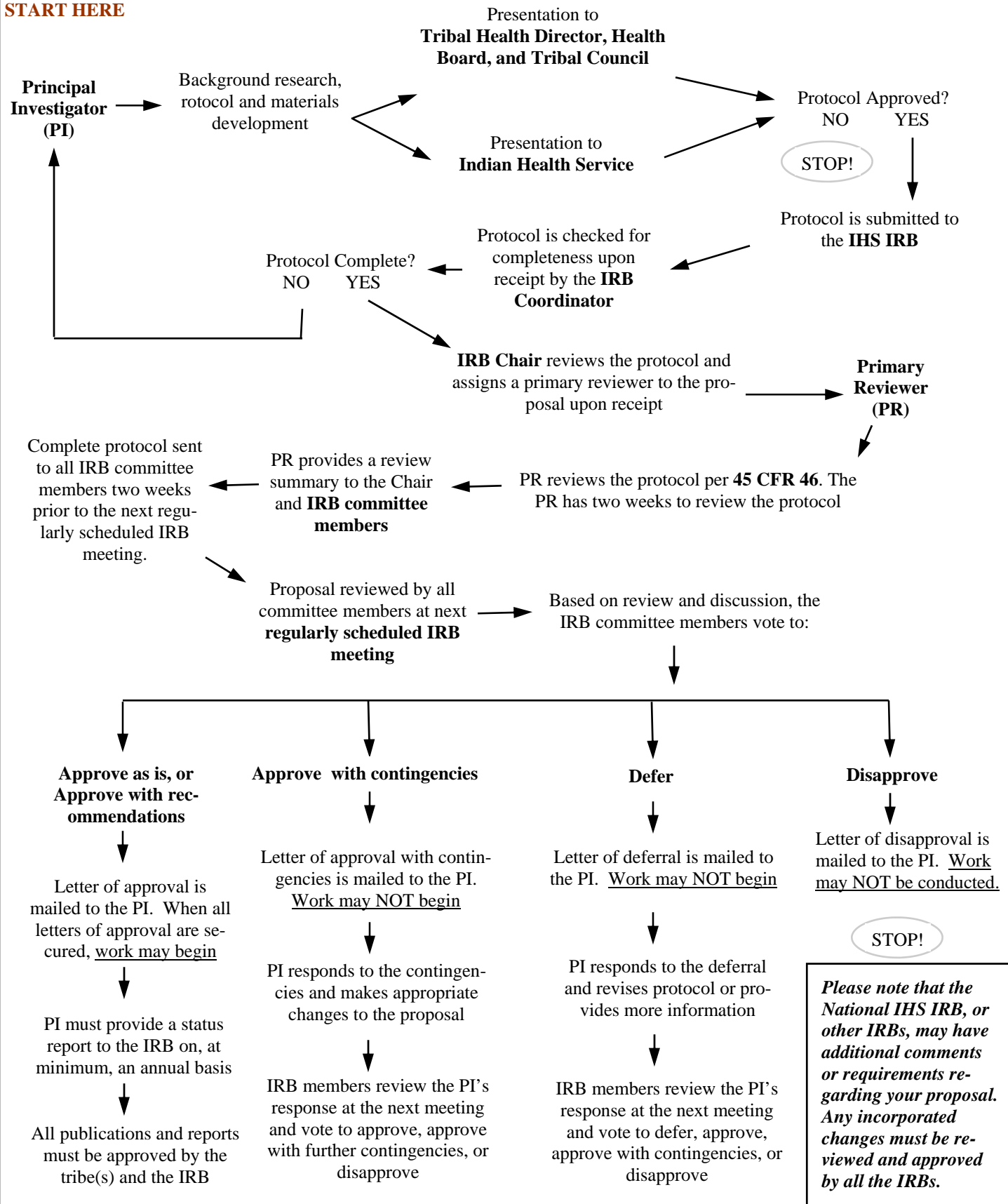
Once the IHS IRB approves a proposal, approvals will remain in effect for one year. At each anniversary of the initial approval, the PI must submit a research status report to the IRB. The annual reviews are in effect for the duration of the project. Should any changes to the protocol occur between reviews 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.

You may reach the Aberdeen Area IHS IRB at 866-311-5794.

General IHS IRB Review Process Flowchart

START HERE



Please note that the National IHS IRB, or other IRBs, may have additional comments or requirements regarding your proposal. Any incorporated changes must be re-viewed and approved by all the IRBs.

APPENDIX IV. 45 CFR 46 IHS IRB Checklist

This checklist is used by the PR to assess protocols.

IHS Institutional Review Board (IRB) Checklist (12/01/01)

P.I.: _____ **Institution:** _____

Title: _____

Primary Reviewer: _____ **Date:** ___/___/___

6 Basic Steps of IRB Review:

1. **Understand the research as written.**
 - A. **Science & methods:** type of research, scientific merit, risks & benefits.
 - B. **Study population:** definition, inclusion-exclusion, rationale, risks/benefits distribution.
 - C. **Influencing factors & contexts:** confidentiality & security, coercions on research team [e.g., type of compensation], conflicts of interest, Tribal/community involvement.
 - D. **Consent process:** capacity to consent, feasibility, compensation/coercion, waivers.
2. **Obtain additional information:** resolve contradictions, needed information not present.
3. **Minimize potential harms:** biological, medical, psychological, social, and cultural harms to individual, family, and community.
4. **Maximize potential benefits:** to individual, family, community, and society [knowledge].
5. **Ensure justice:** Is the intended population appropriate? Does it receive maximum benefits?
6. **Ensure that the consent process fully informs & freely consents potential participants.**

Summary [fill out after completing review]:
The check for the 'IRB-critical' answer is always in the far right column.

General:	<u>No</u>	<u>n/a</u>	<u>Yes</u>
1. Does the research involve <u>special concerns</u> ?	___	___	___
2. Should the research be <u>exempt</u> from IRB review?	___	___	___
3. Does the research qualify for <u>expedited review</u> ?	___	___	___
Context:	<u>Yes</u>	<u>n/a</u>	<u>No</u>
4. Are <u>anonymity, security, confidentiality, and privacy</u> maintained?	___	___	___
5. If research with <u>children</u> and <u>> minimal risk</u> , does it meet regulations?	___	___	___
6. Does the research meet requirements and recommendations for <u>trials</u> ?	___	___	___
7. Are all appropriate <u>documents from other IRB(s)</u> included?	___	___	___
8. Will the research <u>comply with best practices and government policies</u> ?	___	___	___
Risks, Benefits, and Justice:	___	___	___
9. Does <u>scientific merit outweigh risk</u> ? For individuals, communities, and families, are <u>risks minimized</u> , <u>benefits maximized</u> , and <u>justice ensured</u> ?	___	___	___
Informed Consent:	<u>No</u>	<u>n/a</u>	<u>Yes</u>
10. Should the IRB <u>waive all, or some elements of</u> , informed consent?	___	___	___
11. Should the IRB <u>waive requirements to document</u> informed consent?	___	___	___
12. Are procedures adequate to <u>negotiate and administer full consent</u> ?	___	___	___
13. Are all <u>necessary elements of informed consent</u> included?	___	___	___
Additional IRB Decisions:	___	<u>No</u>	<u>Yes</u>
14A. Should the IRB seek reports of compliance from other than the PI?	___	___	___
14B. Should it review the research sooner than annually, or monitor the process?	___	___	___
14C. Is the research <u>more than minimal risk</u> ? (<i>needed for 'Annual' Reviews</i>)	___	___	___

1.	Does the research involve <u>special concerns</u>?	<u>Present</u>
A.	Vulnerable potential research volunteers with <u>special</u> protections:	
	1) Children [Read Subpart D if research is more than minimal risk]	_____
	<i>Both assent of child and permission of parents required. Observational research (if researcher is a participant), surveys, and interviews are not exempt from IRB review. Research with more than minimal risk but no direct benefit to the child is restricted.</i>	
	2) Fetuses (and pregnant women) [Read Subpart B!]	_____
	<i>(Pregnant women are <u>not</u> 'vulnerable.')</i> Research is severely restricted. The IRB must assure appropriate process to select, inform, and obtain consent of volunteers; the father's consent is usually required.	
	3) Prisoners [Read Subpart C!, & 28 CFR 512 for Fed. Bureau of Prisons]	_____
	<i>Research severely restricted; OHRP must review if > minimal risk; IRB must have a prisoner or prisoner-representative.</i>	
	4) People with mental impairment [no special regulations]	_____
	<i>Because informed consent is problematic and the people vulnerable even if ambulatory, this type of research should be limited.</i>	
B.	The research presents more than "minimal risks."	_____
	<i>"Risk" means both the magnitude of harms, and the probability of incurring them. "Minimal risks" means risks a person ordinarily encounters in daily life and in routine medical, dental, or psychological exams. For research with more than minimal risk, the IRB should ensure that the research's <u>benefits are maximized</u> and <u>risks minimized</u>, and <u>compare its scientific merit with its risk</u>. "C" through "H" below are usually more than minimal risk.</i>	
C.	Genetic research (and some research using blood and other body tissues).	_____
	<i>Risks include: family and community disruption, self-stigmatization, external stigmatization, survivor guilt, loss of insurance, discovered misattributed paternity, etc. See the IHS policy on specimens.</i>	
D.	Sensitive information that could affect insurability, compensation, litigation.	_____
	<i>E.G., child abuse, violence, some infectious diseases, drug abuse. Research records are not medical records, and can be subpoenaed; they may be protected by a <u>Certificate of Confidentiality</u>.</i>	
E.	Screening for, or diagnosis of, diseases with significant potential for loss of insurance or other services, stigmatization, or self-stigmatization.	_____
	<i>E.G., screen for carrier of an incurable genetic disease, HIV.</i>	
F.	Radiation (may require approval by a Radiation Safety Committee; not permitted in studies of healthy children with no benefit to them).	_____
G.	Possible coercion, on potential participant or on researcher, to entice consent.	_____
	<i>E.G., high incentives to participants, unequal relationship [employer-employee], capitation payments to researchers to enroll people.</i>	
H.	Deception: <u>major</u> (e.g., mislead volunteers about their health status, the researchers, or research purpose); <u>minor</u> (e.g., incompletely disclose a research purpose to avoid biasing the results).	_____
2.	Should the research be <u>exempt</u> from IRB review? [45 CFR 46.101(b)]	<u>Present</u>
	<i>Research is exemptible when <u>all</u> research methods are <u>only</u> one or more of the following methods. If the research uses a method that is not one of the 5 categories below, the research is not exemptible from IRB review.</i>	
[.101(b)(4)]	A. Use only <u>existing</u> data, documents, records, or specimens properly obtained.	_____
	<i>The research must also comply with <u>one</u> of the following:</i>	
	<i><u>either</u> that</i>	
	1) "the information is recorded by the investigator [so that] subjects cannot be identified" in the research data directly or statistically, and no-one can trace back from research data to identify a participant;	()
	<i><u>or</u> that</i>	
	2) the sources are publicly available.	()



[.101(b)(5)] B. Research or demonstration service/care programs, e.g., health care delivery. _____

The research must also comply with all of the following:

that

1) the research/demonstration is directly conducted or approved by the head of a US Govt. department or agency, e.g., Director of the IHS; _____ ()

and that

2) it concerns only issues under usual administrative control (48 Fed Reg 9268-9), e.g., regulations, eligibility, services, or delivery systems; _____ ()

and that

3) its research/evaluation methods are also exempt from IRB review. _____ ()

[.101(b)(2)] C. For research not involving vulnerable people [prisoner, fetus, pregnancy, children, or mentally impaired]: observe public behavior (including participatory observation), or do interviews or surveys or educational tests: _____

The research must also comply with one of the following:

either that

1) the participants cannot be identified, directly or statistically; _____ ()

or that

2) the responses/observations could not harm participants if made public; _____ ()

or that

[.101(b)(3)] 3) federal statute(s) completely protect all participants' confidentiality; _____ ()

or that

4) all respondents are elected, appointed, or candidates for public officials. _____ ()

[.101(b)(1)] D. In educational settings, research or evaluate normal educational practices. _____

[.101(b)(6)] E. For research not involving vulnerable volunteers [see "C." above], do food research to evaluate quality, taste, or consumer acceptance.

The research must also comply with one of the following:

Present

either that

1) the food has no additives; _____ ()

or that

2) the food is certified safe by the USDA, FDA, or EPA. _____ ()

Yes n/a No

If not exempt now, can the research be made exempt by minor changes? _____

(If so, see if the PI will make those changes.)

For the IHS IRB to consider it Exempt, that is not to review it, the research must also meet all 4 criteria, below:

A) It is in fact less than minimal risk to individuals, families, and communities; _____

and that

B) if potentially exempt because participants cannot be identified, the research indeed protects anonymity

[see 4.A.]; _____

and that

C) if volunteers give information about others, inadvertent disclosure presents no more than minimal risk to those others; _____

and that

D) if done in an IHS facility, info sheet has the IHS disclaimer [13T] _____



3. Does the research qualify for expedited review, not by the full IRB? [46.110] Present

Expedited review is by one IRB member and the Chair. It can be done only if all the research is only one or more of the following and "exempt" categories.

The IRB review:

either is of

(per FDA) A. emergency use of an IND therapy for non-research care to a patient; _____

or it is of

B. minor changes in previously approved research within the approved period;

or it is an

C. 'Annual' Continuing Review, and the research meets *one of the following* _____

- *either* had received expedited review initially & *has had no adverse events* ()
- *or* was found by full IRB to be not > minimal risk & *has had no adverse events* ()
- *or* finished enrollment, & completed all interventions, & has only long-term f/u ()
- *or* has not yet enrolled any person, and has found no new risks for the research ()
- *or* is doing only data analysis ()

or it is of

D. new research that is not more than minimal risk, with all methods one or more of the following. *All methods must be one of the categories below, or an exemptible category -- otherwise the research is not expeditable.* _____

- existing data, documents, records, specimens originally for nonresearch purposes ()
If from IHS records or specimens, Privacy Act may apply: see 8.C.
- non-exempt research on individual/group behavior or characteristics by surveys, interviews, focus groups, oral histories, program evaluations, human factors evaluation, or studies of quality assurance methods ()
- collect data of adult/child by noninvasive clinical procedure, e.g., weight, hearing ()
- collect data by clinical non-radiation devices (MRI, EKG, EEG, ultrasound, doppler, echocardiogram, infrared, thermogram, measure natural radiation) ()
- moderate testing of/by exercise, muscle strength, flexibility, or body composition ()
- research on drugs or devices not needing IND drug or IDE device application ()
- venipuncture/fingerstick blood <=2x/wk: healthy non-pregnant adult >109 lbs (<=550 ml / 8 wks); healthy adult <110 lbs or child (<=3 ml/kg or 50 ml) ()
- noninvasively collect hair, nail clippings, deciduous or permanent teeth, gingival dental plaque/calculus, sweat, saliva, amniotic fluid, sputum, placenta, skin-mucosal-buccal cells *[But are there cultural harms in this research?]* ()
- collect data from voice, video, digital, or image recordings made for research ()

Yes n/a No

If not expeditable now, can it be made expeditable by minor changes?

(If so, see if the PI will make those changes.)

NOTE: expedited research must meet all IRB requirements, i.e., fill out checklist.

4.	Are <u>anonymity, security, confidentiality, and privacy</u> maintained?	Yes	n/a	No
A.	If 'anonymous,' are all data <u>in fact</u> anonymous, e.g., no birthdates?	___	___	___
B.	Are all computer & non-computer data held in a secure manner?	___	___	___
C.	If 'confidential,' are confidentiality measures adequate?	___	___	___
D.	If sensitive identifiable data, is there a <u>Certificate of Confidentiality</u> ?	___	___	___
E.	Do the procedures protect against the risks sufficiently?	___	___	___
5.	If the research involves <u>children</u> (age <18) and is <u>greater than minimal risk</u>, does it meet the regulations? [46.405-408]	Yes	n/a	No
[.405]	A. Does the research <u>present the prospect of direct benefit to child</u> ? <i>If yes: IHS IRB may approve. If no, go to "B."</i>	___	___	___
[.406]	B. Is it <u>both only a minor increase</u> over minimal risk, and will it give <u>vitaly important knowledge about child's disorder</u> ? <i>If yes: IHS IRB approval; both parents must permit. If no, go to "C."</i>	___	___	___
[.407]	C. Does it present opportunity to understand, alleviate, or prevent a <u>serious problem affecting children</u> ? <i>If A and B are "no" but C is "yes," send protocol to OHRP for review. If A, B, & C are "no," it is not approvable.</i>	___	___	___
6.	Does research meet requirements and recommendations for <u>trials</u>?	Yes	n/a	No
[.111(a)(6)]	A.A monitoring committee for safety (Phase II) or for data & safety (Phase III), especially for double-masked ('blind') trials?	___	___	___
	B.If a <u>controlled</u> trial, will all eligible volunteers be offered the proven effective treatment? [see 9.E.(2)]	___	___	___
7.	Are all appropriate <u>documents from other IRB(s)</u> included?	Yes	n/a	No
	Is an entity with an IRB (e.g., state, university, CDC, NIH) involved? <i>If "yes," does the research have <u>both</u></i>	___	___	___
A.	Form 596 or letter with MPA #, effective date, and conditions? <u>and</u>	___	___	___
B.	Is the approval still valid, <i>i.e.</i> , <u>effective date < 1 year old</u> ?	___	___	___
8.	Will the research <u>comply with best practices & government policies</u>?	Yes	n/a	No
A.	Does it minimize harms and maximize benefits to the tribe(s) by Participatory Research (PR) [see <u>BMJ 1999; 319:774-778</u>]? <i>Whether or not PR, does the research plan to:</i>	___	___	___
1]	work with communities <u>to identify & minimize harms</u> ; and	(___	___	___
2]	<u>report timely results</u> to the tribe(s), and to IHS; and	(___	___	___
3]	have the tribe(s)--& IHS if relevant--review all publications?	(___	___	___
B.	Will OMB or the tribe(s) approve the questionnaire(s), if indicated?	___	___	___

- C. Will the researchers comply with the Privacy Act? *It applies to non-federal-government research that wants confidential identifiable data from government records [e.g., medical] without consent of the person. DHHS or IHS must:*
- a) *determine that the use or disclosure does not violate law or policy;*
 - b) *determine that the research 1) could not be accomplished without providing records with individual identifiers; & 2) warrants the risk to privacy;*
 - c) *require the receiving researchers to*
 - 1) *have reasonable administrative, technical, & physical security of all data,*
 - 2) *remove or destroy individual identifiers at the earliest possible time, and*
 - 3) *make no non-emergency use/disclosure of data without prior approval; and*
 - d) *obtain a written statement by the researchers that they will abide by a-c) above.*
- 1) If the Privacy Act applies, have the researchers complied with the Privacy Act? ___ ___ ___

9. **Does scientific merit outweigh risk? Are risks minimized, benefits maximized, and justice ensured to individuals, families, communities?** [46.111(a)] No n/a Yes

A. Is the research more than minimal risk? ___ ___ ___
*Phase I, II, or III trials of INDs-IDEs are 'indeterminate risk,' i.e., more than minimal risk [$>MR$].
 Due to workload, this IRB usually only assesses risks, benefits, and science methods in $>MR$ research.*

[.111(a)(2)] B. *If $>MR$, do its scientific methods and merit outweigh its risks?* Yes n/a No
___ ___ ___

Does the research have the scientific methods that are essential for good quantitative and qualitative research?

- 1) For **quantitative** research, e.g.,:
 - (a) validated measures, ___ ___ ___
 - (b) adequate sample size, ___ ___ ___
 - (c) pretest, ___ ___ ___
 - (d) controls, ___ ___ ___
 - (e) other [_____]. ___ ___ ___
- 2) For **qualitative** research [see: BMJ 2000; 320(1):50-52], e.g.,:
 - (a) respondent validation, ___ ___ ___
 - (b) negative cases, ___ ___ ___
 - (c) triangulation, ___ ___ ___
 - (d) good methods to collect & analyze data, ___ ___ ___
 - (e) fair dealing, ___ ___ ___
 - (f) reflexivity, ___ ___ ___
 - (g) other [_____]. ___ ___ ___

If not, what should be changed? _____

_____?

[.111(a)(1)] C. *If $>MR$, are potential harms minimized to individuals, families, and communities? [E.G., provide follow-up counseling to families and individuals. See 8.A. to minimize community harms.]* ___ ___ ___

If not, what should be changed? _____

[.111(a)(2)] D. *If $>MR$, are potential benefits maximized to individuals, families, & communities? [E.G., newsletters to participants with the status of the research and meaning to individuals, families, and community of the results. See 8.A. to maximize community benefits.]* ___ ___ ___

If not, what should be changed? _____



- [.111(a)(3)] E. Is justice ensured to individuals, families, and communities? i.e.,:
- 1) The study population is suitable for research ___ ___ ___
 - 2) In RCTs, offer the treatment proven effective to individuals, families, and communities in the RCT ___ ___ ___
 - 3) Other [_____] ___ ___ ___
- If not, what should be changed? _____

10. Should the IRB waive the requirement to obtain informed consent, or some required elements of informed consent? [46.116(c) or (d)] Present

A project can qualify for waiver of requirements to give all essential elements of informed consent, if it meets both conditions A) and B), below.

Both that

- A) The research could not "practicably" [=feasibly] be done without the waiver. ___

and

- B) The research is either 1) or 2), below: ___

Either it is

- [.116(c)] 1) a research or demonstration project (___)

both that

- (a) is directed or approved by state, local, or tribal governments, [___]

and that

- (b) concerns only administrative/regulatory issues in service programs; [___]

or it is

- [.116(d)] 2) a type of research (e.g., an activity for which consent is usually not obtained, or research that involves deception of the volunteer and thus cannot seek fully informed consent initially) (___)

(___)

meeting all of the following, that

- (a) involves no more than minimal risk, [___]

and that

- (b) will give volunteers pertinent information at the end if appropriate, [___]

and that

- (c) the waiver will not adversely affect volunteers' rights or welfare. [___]

NOTE: If the research obtains IHS records or specimens, and if the IRB waives consent, the Privacy Act may apply: see 8.C. Yes No

- C. If the research qualifies for waiver of informed consent, ***should the IRB still require the research to obtain full informed consent?*** ___ ___

11. Should the IRB waive requirements to document informed consent? [46.117(c)] Present

A project can qualify for waiver of written documentation that informed consent was obtained, if it meets either condition A) or condition B), below:

either that

- [.117(c)(1)] A. the existence of signed informed consent forms itself would place the volunteer at major risk (e.g., potential loss of confidentiality or anonymity of people interviewed about extremely sensitive behavior); ___

or that



[.117(c)(2)]	B. the research <i>both</i>	_____
	1) _____ presents only minimal risk,	()
	<i>and</i>	
	2) _____ involves no procedures which normally require written consent.	()
	C. If the research qualifies for waiver of documenting informed consent, should the project still require the research to	<u>Yes</u> <u>No</u>
	<i>either to</i>	
	1) _____ document fully informed consent,	_____
	<i>or to</i>	
[.117(c)]	2) _____ offer each volunteer a written fact sheet?	_____

12. Are procedures adequate to negotiate and administer full consent? No n/a Yes

A.	May <u>researcher compensation</u> [e.g., capitation payments] or other factors influence them to try too strongly to enroll participants?	_____	_____	_____
B.	May the method or amount of <u>participant compensation</u> or other factors unduly influence or coerce them to 'consent'?	_____	_____	_____
C.	Does the project adequately describe the <u>all processes of consent</u> :	<u>Yes</u>	<u>n/a</u>	<u>No</u>
	<i>Both that</i>			
	1) _____ inform prospective volunteers (e.g., <i>skilled negotiating, unhurried time, setting facilitates information transfer</i>);	_____	_____	_____
	<i>and that</i>			
	2) _____ offer time for prospective volunteer to discuss with family;	_____	_____	_____
	<i>and that</i>			
	3) _____ assess prospective volunteers' comprehension;	_____	_____	_____
	<i>and that</i>			
	4) _____ document the consent process.	_____	_____	_____
D.	Does the research have <u>all relevant consent documents</u> , including:			
	1) consent,	_____	_____	_____
	2) assent script,	_____	_____	_____
	3) parental permission,	_____	_____	_____
	4) telephone script,	_____	_____	_____
	5) soliciting advertisement,	_____	_____	_____
	6) introduction/approach letter, and	_____	_____	_____
	7) other [_____]?	_____	_____	_____
@ [.117(a)]	E. Give an <u>information copy</u> of the consent document to all volunteers.	_____	_____	_____
@ [.408(b)]	F. For children age 0-17, a form and process of <u>parental permission</u> .	_____	_____	_____
@ [.408(a)]	1) For minors old enough, a process of their <u>assent</u> .	_____	_____	_____

13. Are all necessary elements of informed consent included?

	<i>[Explanation of item]</i>			
	@ = <u>Items required by regulation [45 CFR 46.116(a)/(b)]</u>	<u>Yes</u>	<u>n/a</u>	<u>No</u>
@ [(a)(1)]	A. A clear statement that the study is " <u>research</u> " <i>[The word "research" should be early in document & not hidden]</i>	_____	_____	_____
@ [(a)(1)]	B. <u>All</u> the research <u>purposes</u> [i.e., <u>research objectives</u>] clearly stated <i>[Check the document's list of purposes against the protocol's list]</i>	_____	_____	_____



[(b)(6)]	C. How and why prospective volunteers are <u>selected</u>	___	___	___
@ [(a)(1)]	D. Expected <u>duration</u> of the volunteer's involvement <i>[Necessary if the duration is long, or is not obvious]</i>	___	___	___
@ [(a)(1)]	E. <u>Procedure(s) or treatment(s)</u> to be done	___	___	___
@ [(a)(3)]	F. Reasonably expected <u>benefits</u> to volunteer and others <i>[Do not overpromise-->thus, "<u>possible</u> benefits," "benefits <u>may</u> ..."; state if no benefits to individual; "possible benefits to tribe ..." is permissible; compensation is not in benefits but is separate--see OHRP]</i>	___	___	___
@ [(a)(2)]	G. Reasonably foreseeable <u>discomfort & risks</u> --including all in protocol <i>[Check the document's list against the protocol's list]</i>	___	___	___
[(b)(1)]	H. Especially for experiments, a statement that the treatment(s) or procedure(s) "may involve risks that are currently unforeseeable" <i>[Applicable most often in clinical trials of drugs or procedures]</i>	___	___	___
@ [(a)(1)]	I. Which procedures-treatments are <u>experimental</u> --say "experimental" <i>[Applicable only to experimental research, not observational]</i>	___	___	___
@ [(a)(4)]	J. The <u>alternatives</u> to the research's diagnostic method or treatment <i>[Applicable primarily to research of diagnosis or treatment. A boilerplate "the alternative not to take part" is seldom sufficient; rather, what are the <u>real</u> alternatives (e.g., routine care)?]</i>	___	___	___
[(b)(4)]	K. Procedure for the <u>orderly termination</u> of a volunteer's participation <i>[K, K1, and K2 are applicable primarily to clinical trials, sometimes to compensation--if early termination will decrease compensation]</i>	___	___	___
[(b)(4)]	1) Consequences of a volunteer's <u>withdrawal</u> from the research	___	___	___
[(b)(2)]	2) When may the researcher <u>terminate</u> a volunteer's participation without the volunteer's consent	___	___	___
[(b)(5)]	L. Plans to <u>inform</u> volunteers of <u>significant research findings</u> during or after the study relevant to their continued participation or treatment <i>[Applicable primarily either to clinical trials, or to "deception" research in which debriefing at the end is a standard procedure]</i>	___	___	___
@ [(a)(6)]	M. If > minimal risk: " <u>In case of injury or severe adverse affect...</u> " <i>[Per regulations, M is applicable only to greater-than-minimal-risk research. A not-greater-than-minimal-risk-research protocol may want to include M, M1, M2, or M3--or IRB may want them included]</i>	___	___	___
@	1) will <u>medical care for adverse affects</u> be given? who? where?	___	___	___
@	2) is <u>compensation for adverse affects</u> available? how?	___	___	___
@ [(a)(6)&(7)]	3) <u>whom</u> should a volunteer contact with injury or adverse affect?	___	___	___
@ [(a)(7)]	N. Who will answer <u>questions about the research itself</u> ? <i>[Usually the PI, with telephone #-collect call if long distance]</i>	___	___	___
@ [(a)(5)]	O. How <u>confidentiality</u> (___) or <u>anonymity</u> (___) are maintained	___	___	___

- @ [(a)(7)] P. Who will answer other concerns, complaints, or grievances? ___ ___ ___
[Regulations call this "subject rights"; usually the IRB, with telephone #-collect call if long distance]

- [(b)(3)] Q. Financial factors (extra costs of, or compensation for, participation) ___ ___ ___

- [(109)(b)] R. Other elements a reasonable person would want to know ___ ___ ___

- S. If a Certificate of Confidentiality, an appropriate description ___ ___ ___
 E.G., "**We have a Certificate of Confidentiality from IHS.** The Certificate means that no-one can make us give information about you to anyone outside the study without your consent, not even police or courts. We will not share anything you give us with anyone, except in one case. If you tell us that you or someone may be in danger of great harm, or of physical or sexual abuse, we will report it. The Certificate does not mean that the Department of Health and Human Services or IHS endorse this research." *This is 10th grade readability.*

- @ [(a)(8)] T. Non-coercion disclaimer. ___ ___ ___
 E.G., "Taking part is voluntary. You may refuse to take part without any penalty or loss of care or services by IHS or others. You may quit at any time, without penalty or loss of care or services for which you are qualified." *[This is sample wording; if IHS is not involved, omit 'by IHS or others']*

14. Additional IRB decisions: *[46.103(b)(4)(ii), 46.111(a)(6)]* No Yes

- [(103)(b)(4)] A. Should IRB seek compliance reports from sources other than the PI? ___ ___
 If "Yes," reason(s): _____

- B. Should the IRB:
 - [(103)(b)(4)] 1) get reports from or review the research sooner than annually, or ___ ___
 - [(111)(a)(6)] 2) monitor the research or consent procedures? ___ ___
 If "Yes," reason(s): _____

- C. Is the research > minimal risk? *(This is necessary for 'Annual' Reviews.)* ___ ___



APPENDIX V. Role of Tribal Governments in Regulating Research from the Model Research Code

THE ROLE OF TRIBAL GOVERNMENT IN REGULATING RESEARCH

Philip S. Deloria

The regulation of research by government raises sensitive issues. Society places strong value on academic freedom. Research, it is felt, leads to future scientific and technological developments which benefit society as a whole. Government regulation causes concern about the prospect of political or bureaucratic interference with the purely scientific considerations that should govern research policy. But recent revelations of abuses of human rights by researchers have made us realize that science has no more right to be free of accountability than any other social institution. So the federal government, through its power to place conditions on the use of federal funds, has acted to ensure the protection of the rights of human subjects of research by requiring the establishment of Institutional Review Boards to review proposed federally funded, conducted, or sponsored research, including research involving Indian people and communities.

Regulation of research in an Indian context raises additional issues. Size makes a difference. A society of 250 million people can regulate research wholesale, but regulation of research affecting Indian communities is much more direct and personal. It is difficult to relate particular actions to general guiding principles because of the relatively small number of communities and individuals affected. Other questions arise. Is there a special need for protection of Indian individuals and communities because of unique aspects of Indian culture, because people fear the consequences of declining to participate in federally-sponsored research when the IHS is central to the Indian health system; because depressed economic conditions in Indian communities render some Indian people relatively powerless? Does the federal government's trust responsibility (in the larger sense) entail a special obligation to protect Indian people and communities that it might not have with respect to the larger society? And, should the federal government assume the full obligation of regulation or is there a necessary role for tribal governments? Is the special obligation of the federal government, if any, the result of the trust responsibility or simply because the federal government is presumed to have the expertise or the resources to hire the expertise?

Federal regulation in the interest of Indian people is not totally effective. The federal government has a fundamental obligation to support research in the public interest and to support academic freedom. This obligation sometimes may conflict with the special duties to Indian people, and history has shown that the Indian people often are dissatisfied with the result of the balancing process when the federal government balances its duty to Indians with its duty to the general public interest. Despite its many years of experience with Indian people, the federal government cannot be presumed to know the needs of each Indian community and the values they wish to protect in a research situation, and it is unlikely ever to exercise its powers to regulate research broadly enough to reach privately sponsored research, which can also be a source of great annoyance to tribes. Tribes can and should act to ensure that the IRBs function as effectively as possible and reflect their needs and interests. But the fundamental responsibility to articulate the interest of Indian communities lies in these communities themselves, acting through their tribal councils and other bodies, to articulate the conditions in which research will be permitted.

Do Indian tribes have the power to protect their communities and their citizens by regulating research? Under general principles of federal Indian law, the initial inquiry is not whether tribes have a power but whether they have lost it. They have all the powers of internal self-government except those which have been surrendered by treaty or agreement, limited by federal law, or are inconsistent with tribal status as domestic dependent nations. There is no federal law expressly limiting tribal regulation of research. The "inconsistent with tribal status" test should not present a barrier. The Indian Civil Rights Act has language similar to the U.S. Constitution's First Amendment, and it not a general barrier to tribal regulation of research.

Assuming no barrier in federal law, the next step is to determine whether a particular tribal government has been given the power by its people to regulate research. If the tribe has a written constitution, it should be examined for language in the "Powers" section. Most tribes have provisions to promote the general welfare of the tribe, to maintain peace and order, or to protect individual and tribal rights, any of which could be interpreted to include the power to regulate research. Many tribes also have the power to require licenses or impose taxes and fees on those doing business on the reservation. And finally, one of the fundamental tribal governmental rights that has always been recognized in federal law has been the right to exclude outsiders from the tribe's territory. Implicit in the power of removal is the power to determine the conditions in which outsiders will be allowed to enter the reservation and remain.

The removal power must be exercised according to an ordinance that accords due process of law to those affected and that spells out the conditions in which non-members are allowed on the reservation.

Most tribes have power to regulate research on the reservation, especially research involving the Indian people themselves. Tribes must address various underlying policy considerations in deciding how to exercise this power. What specific rights of the people require protection? What is the tribe's obligation to participate in research for the good of humanity, and how will this obligation be balanced against the interests of the Indian people? What constitutes informed consent to participate in research? How can tribal powers be enforced other than in the decision to let researchers into the community in the first place? Are economic and employment considerations relevant? Can the tribe hope to realize economic benefit from research? Will strict regulations deprive the people of the opportunity to participate in research which may benefit them? Must research show an immediate benefit? Do tribal members have an individual right to participate in research despite tribal opposition? Does the tribe have access to technical assistance to enable it to make informed decisions regarding particular research proposals?

These questions must be addressed as tribes develop a regulatory scheme which makes researchers appropriately accountable to the Indian community. Tribes should review their procedures periodically and adjust them as circumstances warrant. But, despite the skepticism of some academics about the appropriateness of tribal involvement in this area, it seems fundamental that Indian tribal governments have both the power and the duty to address this important area on their own in addition to the steps they take to ensure the effectiveness of federal regulatory efforts.



APPENDIX VI. Protection of Potential Individual Volunteers and Tribal Communities

THE PROTECTION OF POTENTIAL INDIVIDUAL VOLUNTEERS AND TRIBAL COMMUNITIES IN RESEARCH INVOLVING THE INDIAN HEALTH SERVICE (IHS)

William L. Freeman, MD, MPH

U.S. Congressional law is the basis for federal health services to American Indian and Alaska Native (AI/AN) people. The Indian Health Service (IHS) of the Public Health Service has primary responsibility for those services. The IHS goal is to raise the health status of AI/ANs to the highest possible level. Its mission is to ensure equity, availability, and accessibility of a high quality comprehensive health care system. Its mission also is to maximize the involvement of AI/ANs in defining their health needs, setting health priorities for their local areas, and managing and controlling health programs. Tribes can and do manage the programs in their communities under Public Law 93-638, Indian Self-Determination Act of 1975. Tribes also can and do take over their entire federally-funded health programs under the process of Self-Governance.

IHS has 12 Area (regional) offices. IHS provides and supports a broad set of preventive, curative, rehabilitative, and environmental services. As of October 1998, Tribes operated 85 local administrative "Service Units," 12 hospitals, 155 health centers, 3 school health centers, 76 health stations, and 160 Alaska village clinics. IHS operated 66 Service Units, 37 hospitals, 59 health centers, 4 school health centers, and 44 health stations. More than 1 million members of AI/AN tribes received services in those facilities in 1998.

Much research is done in AI/AN communities by outsiders such as universities, by Tribes and IHS Service Units, and by the IHS Research Program. Institutional Review Boards (IRBs) help ensure that all research observes three principles of ethics: (1) respect for persons; (2) beneficence (to do no harm, and to maximize benefit); and, (3) Justice. IRBs look closely at the negotiation between researcher and each potential volunteer, called the "informed consent process." Due to concern about Tribal sovereignty and self-determination, the IHS IRBs look both at the negotiation between researcher and *each potential volunteer*, and also that between researcher and *the tribal community*. That is, IHS IRBs help ensure that all research observes the same principles – respect for persons, beneficence, and justice – applied to the AI/AN communities.

The following table shows how those three ethical principles in research apply to individual volunteers and to AI/AN tribal communities.



Ethical Principles	Individual Person	Tribal Community
Respect for Person and Respect for Tribal Community	People are autonomous; researchers must give them required information and obtain their fully informed consent The research does only what the person consents to. For instance, people are not identified in results without their explicit consent; they can refuse or withdraw their participation without pressure Special people have special concerns. For instance, IRBs should include members with expertise about such concerns.	Tribal communities are autonomous; researchers must give them required information and obtain their fully informed consent The research does only what the Tribe consents to. For instance, Tribal communities are not identified in results without their explicit consent; they can refuse or withdraw their participation without pressure Tribal communities have special concerns. For instance, IRBs should include Tribal members with expertise about community concerns.
Beneficence	Maximize benefits to individual volunteers. For instance, report their findings to them. Minimize risks to individuals. For instance, protect their privacy to avoid being stigmatized	Maximize benefits to tribal communities. For instance, report research results to them; researchers and Tribes plan research together. Minimize risks to tribal communities. For instance, protect their privacy to avoid being stigmatized
Justice	People with less power should not be asked to undergo risky research that is of little benefit to them People with less power should be included in potentially beneficial research	Tribal communities should not be asked to permit risky research that is of little benefit to their members or themselves Tribal communities should be included in potentially beneficial research

IHS has 12 IRBs, one for each Area and a Headquarters IHS IRB that also covers the Albuquerque Area. The Navajo Nation has its own IRB, whose members the IHS also appointed to its Navajo Area IRB.

The IHS IRBs use the ideas outlined in the table to ensure protection not only of the individual volunteers in research, but also of the tribal communities in which the research takes place. The IHS is committed to the self-determination and cultural integrity of AI/AN communities. Three IHS policies reflect that commitment:

- By Federal regulations 45 CFR 46, every IRB must have at least one member whose primary interest is “non-scientific.” In the IHS IRBs, the “non-scientific” members must be enrolled members of tribal communities. In most IHS Area IRBs, the proportion of members who are AI/AN is close to or exceeds 50%.
- All research and resulting publications must be approved by the governments of the tribal communities involved in the research
- IHS IRBs encourage researchers to give, and tribes ask for, a required set of elements of information (similar to the required set of elements in 45 CFR 46 for individual volunteers’ consent), to ensure that the tribes’ consent is truly informed.



APPENDIX VII. Genetic Research: Possible Harms and Benefits

WHAT ARE THE POSSIBLE HARMS IN GENETIC RESEARCH?

February 8, 2002

William L. Freeman, MD, MPH

Francine C. Romero, PhD, MPH

Terminology: "Possible harms" is the mirror image of "possible benefits";
"risks" = 'possible harms' times 'probability that harms will occur'

Hypothetical research project with its background information. Recent research proved that screening populations for early schizophrenia (with subsequent early diagnosis and treatment) led to better outcomes for people with schizophrenia. Other research narrowed the probable gene[s] causing schizophrenia to three different loci. One research result showed that PCB exposure among siblings of schizophrenic people was associated with a higher risk to develop schizophrenia, i.e., there was an environment-gene interaction. One other research result showed that being more traditional in Native culture, and having a higher percentage of Native ancestry, was associated with lower risk to develop schizophrenia. The research project involves a large Indian reservation with a rate of schizophrenia apparently several-fold higher than in any other reservation or in the general population. It is isolated, but has nearby a toxic waste dump with PCB. The research hypotheses are that:

- 1 the prevalence rate of schizophrenia (as found by careful mental health screening of the population) is indeed higher;
- 2 personal PCB exposure is associated with development of schizophrenia;
- 3 the prevalence of schizophrenia-associated variants of at least one of the three suspected genes differ from the prevalence in the general Canadian population;
- 4 that, within the reservation, people scoring as more traditional on a traditionality questionnaire have lower rates of schizophrenia than those scoring less traditional; and
- 5 that, within the reservation, people with a higher percentage of Native ancestry have lower rates of schizophrenia than those with a lower percentage.

Research methods include: qualitative ethnography; pedigree mapping (to estimate degree of Native ancestry); a quantitative survey of traditional beliefs; mental health screening questionnaires (to diagnose untreated schizophrenia, and to assess possible confounding factors [e.g., alcoholism]); and blood draws for PCB, other environmental toxins, variants of the three suspected schizophrenia genes, and genetic markers of Native ancestry. Specimens will be stored for future genetic and environment tests not yet developed.

In complex genetic research, such as the protocol above or similar protocols, what are:

- A Possible harms to individuals?
- B Possible harms to families?
- C Possible harms to special or vulnerable populations --
 - o minority, non-western, or discriminated-against communities (e.g., American Indian or Alaska Native, Canadian First Nations or Inuit, Amish, African American, Hispanic or Latino, people with HIV/AIDS, etc. groups), or
 - o disease-defined groups (e.g., families with pseudoxanthoma elasticum [PXE])?

Please list what you think are the possible harms, before you go further.

.....
Listed next are actual harms that have in fact occurred with one or more protocols.

Possible harms to individuals?

- o insurability
- o job discrimination
- o misattributed paternity
- o false positive--or false negative--diagnosis of individual or results
- o altered feelings of self
 - "survivor guilt" if test negative
 - "fear-of-future" if test positive

- o external stigmatization
 - "other's image"
- o internal self-stigmatization
 - "self-image" of physical self
 - e.g., diagnosis of epilepsy
 - "self-genetic-determinism"
 - e.g., "it is inevitable that"
- o "dignitary harms" -- insult to a person's respect and control
 - giving your specimen away or putting it in a repository, without your approval
 - e.g., Nuu-chah-nulth

Our impression: the most frequent and most severe potential harm to individuals is ...
"psychological disruption"

Possible harms to *families*?

- o insurability
- o job discrimination [via insurance]
- o misattributed paternity
- o misattributed non-relationship
 - adoption with later marriage of people who turn out to be close kin
- o false positive--or false negative--diagnosis of a family member or results
- o external stigmatization of members
- o internal self-stigmatization of members
- o external genetic determinism
 - "You are doomed"
- o internal self-genetic-determinism
 - "Our family is doomed"
- o altered family dynamics, e.g., cystic fibrosis
 - distancing carrier sibs/members
- o "dignitary harms" -- insult to a family's respect and control
 - a researcher passes around one's specimen, or puts them in a repository, without permission
- o when the family recruits participants, altered family dynamics
 - intra-family coercion
 - intra-family discord
 - raise expectations that are not met--mobilize the family to get more benefit from the research than the research and researcher can give

Our impression: the most frequent and most severe potential harm to families is ...
"family disruption"

Possible harms to *communities*, by original project & subsequent research with specimens?

- o false positive--or false negative--diagnoses or results
 - cultural misdiagnosis: historical characterizations of traditional spiritual healers as 'schizophrenic'
 - cultural misdiagnosis: using a recent mental health survey of a poor non-western people, researchers overdiagnosed hallucinations due to the ways the people described their physical symptoms
 - gender misdiagnosis: historical characterizations of women and "hysteria"
 - ethnic misdiagnosis: research on "IQ" and "race"
- o external genetic determinism / stigmatization of group
 - "Ashkenazi Jews are prone to cancer [schizophrenia, ..., etc.]"
 - "American Indians and 'the gene for alcoholism' [diabetes, ..., etc.]"
- o internal self-genetic-determinism / self-stigmatization of group
 - "We Jews are defective because our genes make us prone to cancer"
 - "We American Indians are defective because our genes make us prone to alcoholism"

- o other external, & internal self-stigmatization
 - "[You] / [We] are unhealthy, sick."
 - external stigmatization, e.g., "[All] Indian adolescents have high suicide rates" (based on a studies of a small number of communities)
 - internal self-stigmatization, e.g., "Our Indian adolescents have high suicide rates" (believed by communities that actually have low rates, based on those studies)
- o other genetic determinism, e.g., in/by public policy
 - determining group membership by genes [a proposed Vermont state law; a tribe removed from its membership rolls people lacking the "Indian markers"]
- o job discrimination against members
 - @ - job discrimination by following public stereotypes about a community due to reports from research--for instance, research on glue sniffing among Canadian First Nations youth, studies comparing IQ of African Americans with white Americans
 - NOTE: not yet seen due to a genetic study
- o promoting/permitting other discrimination/stigmatization by some people in the surrounding society
 - linking the tribe to socially undesirable situations [e.g., investigation of hantavirus or of an outbreak of congenital syphilis]
- o violation or disruption of the tribe's values
 - private knowledge made public in the anthropology study
- o exacerbation of intra-community stresses or conflicts
 - e.g., comparing "traditional" vs. "non-traditional" (or "acculturated" or "assimilated") as risk factors for health or for behavior-linked conditions
- o results alter community, e.g., a community's religious understanding of "Who we are."
- o dashed expectations--starting services that later are discontinued due to lack of funding
- o dash trusted relationship--the researcher whom the tribe trusts leaves for a promotion at a distant university [the tribe's experience may be like an unwanted divorce]
- @o decreased political or social status in dominant society
 - "Indians are immigrants just like us" [from an editorial]
 - report the accuracy of tribal membership rolls by comparing the percent of Indian ancestry in detailed genealogies with that given in the rolls for each person
- o "dignitary harms" -- insult to a community's respect and control
 - recruiting urban-residing members of a Tribe to obtain specimens from that Tribe without Tribal permission (violating or disregarding a community's decision)
 - a research has a public affair with a married person in the community (egregiously violating community norms and disrupting a family)
- o weariness toward all research
- o distrust toward all genetics and all genetic research

Our impression: the most frequent and most severe potential harm to communities is ...

"community disruption"

(NOTE: the disruption is usually at the stage of:

- o publication and release of the research results; or
- o secondary use of existing specimens)

@ The only harms that communities have actually experienced that might meet the description of harms that IRBs should not consider, in 45 CFR 46.111(a)(2):

The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

All other harms to communities listed here occurred shortly after the research short-term (and thus were not "long-range effects"), were not due to "applying knowledge gained," and did not concern "public policy."

How many people know all those possible harms, that have actually occurred to individuals, families, and communities?

In our experience: Most researchers, Institutional Review Boards (IRBs) or Research Ethics Boards (REBs), and ethicists -- including both of us -- have not known

- A* some harms to individuals, and
- B* some harms to families, and
- C* many harms to specific "vulnerable" or non-"mainstream" ethnic communities, ...

unless and until they listen to and discuss possible harms with individuals, families, and communities already affected or to be involved.

How many people know how to minimize all those possible harms to individuals, families, and communities?

In our experience: Most researchers, IRBs or REBs, and ethicists--including both of us--do not know some useful ways to minimize harms to individuals, families, and communities ...

unless and until we-and-they listen to and discuss possible solutions with individuals, families, and communities already affected or to be involved.



WHAT ARE THE POSSIBLE BENEFITS IN GENETIC RESEARCH?

February 8, 2002

William L. Freeman, MD, MPH
Francine C. Romero, PhD, MPH

Terminology: "Possible benefits" is the mirror image of "possible harms";
[no word] = 'possible benefits' times 'probability that benefits will occur'

Hypothetical research project with its background information. Recent research proved that screening populations for early schizophrenia (with subsequent early diagnosis and treatment) led to better outcomes for people with schizophrenia. Other research narrowed the probable gene[s] causing schizophrenia to three different loci. One research result showed that PCB exposure among siblings of schizophrenic people was associated with a higher risk to develop schizophrenia, i.e., there was an environment-gene interaction. One other research result showed that being more traditional in Native culture, and having a higher percentage of Native ancestry, was associated with lower risk to develop schizophrenia. The research project involves a large Indian reservation with a rate of schizophrenia apparently several-fold higher than in any other reservation or in the general population. It is isolated, but has nearby a toxic waste dump with PCB. The research hypotheses are that:

- 1 the prevalence rate of schizophrenia (as found by careful mental health screening of the population) is indeed higher;
- 2 personal PCB exposure is associated with development of schizophrenia;
- 3 the prevalence of schizophrenia-associated variants of at least one of the three suspected genes differ from the prevalence in the general Canadian population;
- 4 that, within the reservation, people scoring as more traditional on a traditionality questionnaire have lower rates of schizophrenia than those scoring less traditional; and
- 5 that, within the reservation, people with a higher percentage of Native ancestry have lower rates of schizophrenia than those with a lower percentage.

Research methods include: qualitative ethnography; pedigree mapping (to estimate degree of Native ancestry); a quantitative survey of traditional beliefs; mental health screening questionnaires (to diagnose untreated schizophrenia, and to assess possible confounding factors [e.g., alcoholism]); and blood draws for PCB, other environmental toxins, variants of the three suspected schizophrenia genes, and genetic markers of Native ancestry. Specimens will be stored for future genetic and environment tests not yet developed.

In complex genetic research, such as the protocol above or similar protocols, what are:

- A Possible benefits to individuals?
- B Possible benefits to families?
- C Possible benefits to special or vulnerable populations --
 - o minority, non-western, or discriminated-against communities (e.g., American Indian or Alaska Native, Canadian First Nations or Inuit, Amish, African American, Hispanic or Latino, people with HIV/AIDS, etc. groups), or
 - o disease-defined groups (e.g., families with pseudoxanthoma elasticum [PXE])?

Please list what you think are the possible benefits, before you go further.

.....

Listed below are **actual** benefits that have in fact occurred with 1 or more protocols.

Key to numbers:

- 1 = "Possible benefit" usually expressed by researchers and bioethicists
= often appreciated as well by people affected by genetic-related disease
- 2-5 = benefit from the viewpoint of the individual, family, or community
- 2 = a theoretic benefit, but apparently not observed or documented yet
= "Tentatively possible benefit"
- 3 = has been observed in genetic and other advocacy groups, not yet fully in tribes or in other Native or ethnic groups
= "Possible benefit" seen in advocacy responses to the genetic disease or research
- 4 = has been observed in tribes, or in other Native or ethnic groups
= "Possible benefit" seen in tribal responses to the genetic disease or research
- 5 = has been observed both in genetic and other advocacy groups and in tribes and in other Native or ethnic groups
= "Possible benefit" seen in advocacy group and tribal responses to the genetic disease or research

Key "3" has been seen in the experience of advocacy groups, primarily in community-based, community-driven, participatory research. They include: the Genetic Alliance and its member organizations, PXE, National Action Plan for Breast Cancer, National Breast Care Coalition.

Possible benefits to individuals?

- 1 learn one does not have a disease-inducing genetic variant
 - reduce anxiety and uncertainty
- 1 Primary Prevention (identify antecedent factors causing disease, when factors are still modifiable and disease preventable -- "predisposition genetic testing")
- 1 Secondary Prevention by early diagnosis (identify early asymptomatic disease, when it is still modifiable and complications preventable -- "presymptomatic genetic testing")
- 1 Tertiary Prevention by correct diagnosis of symptomatic genetic disease
- 1 in randomized clinical trials (RCTs), get an effective intervention
 - ***benefit primarily if intervention is effective!***
 - for control, get effective intervention at end of RCT
- 1 (INDIRECT) contribute to knowledge to help:
 - the future family,
 - the future community,
 - the future self [possible, but less likely]
- 1 (INDIRECT) contribute to knowledge in general
- 2 external respect?
 - "other's image"?
- 3 internal self-respect, "self-esteem"
 - pride of resiliency
 - reinforce pride of individual's membership in the resilient group
- 3 the family or group can help foster "return-to-health" changes by the individual

Most possible near-term benefits: **individual resiliency = the individual's ... positive response to the adversity of disease or of stigmatization ('bend and bounce back; do not break')--"physical-psychological individual health and self-mastery"**

Possible benefits to families?

- 1 learn the family does not have a disease-inducing genetic variant
 - reduce anxiety and uncertainty
- 1 Primary Prevention of some familial genetic diseases
- 1 Secondary Prevention of some familial genetic diseases
- 1 Tertiary Prevention of some familial genetic diseases
- 1 in RCTs, get an effective intervention for some familial diseases
 - ***benefit primarily if intervention is effective!***
- 1 (INDIRECT) contribute to knowledge to help:
 - future family,
 - future community
- 1 (INDIRECT) contribute to knowledge in general
- 3 external respect of the family
 - "other's image" of the family
- 3 overcoming external genetic determinism
 - resiliency of family--"In spite of your genetics,..."
- 3 overcoming internal self-genetic-determinism
 - resiliency of family--"In spite of our genetics,..."
- 3 improved family dynamics
 - family members closer in mutual support
- 3 when the family recruits participants, improved family dynamics
 - promote intra-family cohesion and cooperation
 - mobilize the family to realize potential benefits from the research
 - protect the family from potential harms from the research?
- 3 internal self-respect, "self-esteem" of the family
 - reinforce pride for in the resilient family
 - reinforce pride of family's membership in the resilient group

Most possible near-term benefits: **family resiliency = the family's ... positive response to the adversity of disease or of stigmatization--"physical-psychological family health and self-mastery"**

Possible benefits to communities, by original project & subsequent research with specimens?

- 1 Primary Prevention of some community genetic diseases
- 1 Secondary Prevention of some community genetic diseases
- 1 Tertiary Prevention of some community genetic diseases
- 1 in RCTs, get an effective intervention for some community-specific diseases
- **benefit primarily if intervention is effective!**
- 1 (INDIRECT) contribute to knowledge to help the future community
- 1 (INDIRECT) contribute to knowledge in general
- 3 external respect of the community
- "other's image" of the community
- 3 overcoming external genetic determinism
- resiliency of community--"In spite of (or--'In response to') genetics,..."
- i.e., the response of activism to the threat of the disease or research
- 3 overcoming internal self-genetic-determinism
- resiliency of community--"In spite of (response to) genetics,..."
- i.e., the response of activism to the threat of the disease or research
- 3 improved community dynamics
- community and advocacy group members become closer in mutual support
- people affected in isolation become an advocacy community
- 3 when the community recruits participants, improved community dynamics
- promote intra-community cohesion and cooperation
- protect the community from potential harms from the research
- mobilize the community to realize potential benefits from the research
- 3 the community's values are incorporate in the research itself
- teenagers' want researchers to report to parents or authorities when they are in danger
- 3 actively fight genetic racism, genetic stigmatization, genetic discrimination
- 3 "buy-in" by the community
- help set the research agenda, obtain funding, promote researcher cooperation
- help recruit participants
- 3 increased efficiency and relevance of research to fighting the genetic disease
- 3 "dignitary benefits"--reinforce a community's respect and control
- 3 internal self-respect, "self-esteem" of the community
- reinforce pride in the resilient community
- 4 results reinforce the community's understanding of "Who we are"
- e.g., genetic descendancy matches community's history
- **Only if research results match what are hoped for!**
- 4 added information for the community about "all their relations"
- e.g., pride of meeting related tribes several thousand miles away
- 3,5 research team establish clinics, or provide increased care, or help establish intervention programs (for the specific conditions studied, or for general care)
- 3,5 use genetic epidemiology results for health planning and for advocacy for resources
- 3,?5 increased positive attitudes toward genetics and genetic research
- for most tribes, however, positive attitudes toward one researcher and research project seldom replace general distrust or generalize to other researchers or to future research; rather, trust must be earned by each researcher and project

Most possible near-term benefits: **community resiliency = the community's ... positive response to the adversity of disease or of stigmatization--"physical-psychological community health and self-mastery"**

How many people know all those possible benefits, that have actually occurred to individuals, families, and communities?

In our experience: Most researchers, Institutional Review Boards (IRBs) or Research Ethics Boards (REBs), and ethicists -- including both of us -- may not know

- A* some possible benefits to individuals, and
- B* some possible benefits to families, and
- C* many possible benefits to specific "vulnerable" or non-"mainstream" ethnic communities, or to genetic advocacy groups/communities,

unless and until we-and-they listen for possible benefits with individuals, families, and communities already affected or to be involved, and gently ask about them.

How many people know how to maximize all those possible benefits to individuals, families, and communities?

In our experience: Most researchers, IRBs or REBs, and ethicists -- including both of us -- may not know some useful ways to maximize benefits to individuals, families, and communities ...

unless and until we-and-they listen for possible ways with individuals, families, and communities already affected or to be involved to, and gently ask about the ways.

Note 1: The implications of "possible benefits" are different than those for "possible harms" for 2 reasons: the priority for avoiding harms; and how benefits to the group are achieved.

The priority for harms before benefits. For many reasons, especially the history of bad outcomes from their interactions with the US society and government, many tribes have an underlying distrust toward research. That is, many tribes are often more concerned about minimizing possible harms than about maximizing possible benefits. Focussing on potential benefits first, therefore, may be less credible for many tribes than focussing on:

- 1 first, assuring little or no harm to them; and
- 2 second, promoting their cultural and physical survival.

Achieving the near-term group benefits through the community's resiliency. Most possible benefits from genetic research are in the long term (i.e., distant future), or are indirect (i.e., contribute to knowledge). The few possible near-term benefits, in current time, primarily pertain to group resiliency--that is, how the group responds to adversity. Note that "adversity" is not something the community has voluntarily chosen for itself, and usually is not desirable. Rather, the adversity is usually either a disease, or stigmatization. Because the potential benefits by the resiliency of the community are not inherent in the research, we recommend that researchers should not initiate discussion about those potential benefits; researchers, rather, should respond to community-initiated discussion, and should offer to assist the community to promote and develop its own resiliency.

Note 2: Few, if any, tribes have experienced benefits of genetic research similar in quality and quantity to those experienced by advocacy groups. The most important characteristic that would promote those benefits to tribes or groups (and thus to family and individual members of the tribes or groups) is that the research be community-based, community-driven, participatory research. The immediate task on the ethical and research agendas is to convert type key "3" (potential benefits) to key "5" (actualized benefits) for tribes.

Additional Resources

Following are additional resources pertaining to IRBs and ethical issues in health research:

Office for Human Research Protections: <http://www.hhs.gov/ohrp/>

Belmont Report: <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>,

IHS IRB

- ◆ Headquarters-Albuquerque IHS IRB: <http://www.ihs.gov/MedicalPrograms/Research/areairb.cfm>
- ◆ IHS Research Program: <http://www.ihs.gov/NonMedicalPrograms/Research/index.html>
- ◆ Aberdeen Area IHS IRB: Elaine Miller, MD, Chair, 605-226-7341.

University IRBs:

- ◆ University of Nebraska Medical Center IRB: <http://www.unmc.edu/irb/>
- ◆ University of Iowa IRB: http://research.uiowa.edu/hso/index.php?get=irb_overview
- ◆ University of North Dakota IRB: <http://www.und.nodak.edu/dept/orpd/regucomm/irb/Default.htm>
- ◆ University of South Dakota Office of Research Compliance: <http://www.usd.edu/oorsch/compliance/compliance.cfm>



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