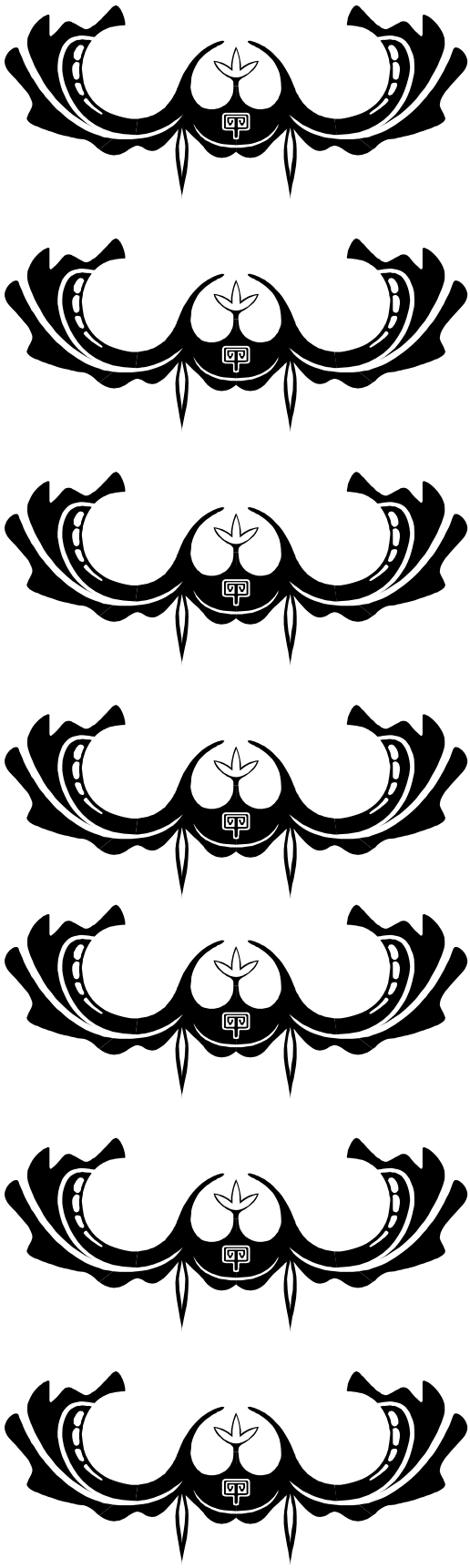

American Indian and Alaska Native

Genetics Research Policy Formulation Meeting

February 7 – 9, 2001

Summary Meeting Report

A meeting funded jointly by the
National Institute of General Medical Sciences
and
National Human Genome Research Institute

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American Indian and Alaska Native
Genetics Research Policy Formulation Meeting

February 7 – 9, 2001

Rio Rancho,
New Mexico

A Summary Meeting Report

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American Indian and Alaska Native
Genetics Research Policy Formulation Meeting

February 7 – 9, 2001

A Summary Meeting Report

Prepared by
Francine C. Romero, PhD, MPH, Principal Investigator

Introduction

The American Indian and Alaska Native (AI/AN) Genetics Research Policy Formulation Meeting was held in Rio Rancho, New Mexico from February 7 – 9, 2001. The National Institute of General Medical Sciences and National Human Genome Research Institute jointly funded the meeting. The formulation meeting was attended by Malcolm Bowekaty, Jay Butler, Mei-Ling Chang, Chester Clarke, Laura Commanda, Dena Davis, Thomas Drouhard, William Freeman, Connie Z. Garcia, Roger Gollub, Judith Greenberg, Debra Harry, Jeff Henderson, Marlene Jasperse, William Knowler, Jeff Long, Philip Lowenthal, Jean McEwen, Ben Muneta, Clifton Poodry, Terry J. M. Powell, Lisa Preston, Carolyn M. Robbins, Francine C. Romero, Brett L. Shelton, Paul Spicer, Lisa S. Sterling, and Michael E. Zwick. Participants were invited based largely on their interest and availability. They represent a group of concerned individuals interested in providing a public service.

The purpose of the meeting was to begin the process of creating procedures and documents that could be instructive to both tribal communities and researchers about the conduct of genetics research involving American Indian and Alaska Native people and their communities. The meeting was not organized as a summit of representative genetics research issues, but was intended to be an intense round-table work session with discussion of tribal concerns, tribal expectations, the process of research, existing genetic studies, research codes, and existing genetics policies. No formal presentations were given.

The summary report was written from meeting notes taken separately by Dena Davis, Rae Mae-Ling Chang, and Francine Romero. All meeting participants were given the opportunity to review and to make both editorial and content changes to the summary report. The readers of this document should not assume that all meeting participants agree with or support each idea discussed at the meeting or contained within this summary report. The views presented in this working document reflect the opinions of the meeting participants and should not be interpreted as the view of any tribe, institution, or government organization.

Two weeks before the meeting, participants were sent a binder of background resource materials. A listing of the resource materials is included in Appendix A. Resource materials that were distributed during the meeting are listed in Appendix B. Among the resource materials distributed prior to the meeting was "IHS Guidelines for implementing and complying with IHS Policy on specimens." The most current draft of this document is included in Appendix C.

Statement of Need

In recent decades, all humanity has witnessed unprecedented changes and advances in genetics research. The sequencing of the human genome, polymerase chain reaction, and automated sequencers are all examples of relatively recent developments that have changed the face of genetics research forever. Not surprisingly, the genetics technology does not necessarily run parallel to the policy surrounding specimen use and storage, human subjects protections, and ethical considerations, especially with regard to research with special populations.

Historically, the experience of American Indians and Alaska Natives (AI/AN) with research in general has contributed to their distrust of genetics research, particularly human migration studies. There are vast, often unrecognized, cultural differences between indigenous and western peoples. Furthermore, there is great cultural diversity among indigenous peoples. Failure to communicate or recognize these differences can result in faulty research, 'bad blood' between the researchers and tribal

communities, and distrust of research by native individuals and tribal communities.

This summary report encapsulates valuable contributions made by the meeting participants regarding genetics research and testifies to the ongoing efforts of individuals to make the field of genetics research accountable to native peoples.

Conference Planning Committee

There was no formal conference planning committee although Drs. Freeman and Poodry provided valuable guidance to Dr. Romero. The conference grant proposal was prepared and submitted by Dr. Francine C. Romero. Once funds were secured, all participants were invited to attend by Dr. Romero. Several criteria guided the invitation process: (1) for Native participants, knowledge of traditional and cultural concerns regarding research; (2) for researchers, experience and expertise in genetics; and (3) for agency representatives, interest and concern regarding genetics research. The size of the meeting was determined by both the structure of the meeting and funding.

Conference Moderators

Moderators led the four main sections of the meeting. The conference moderators included Drs. William Freeman, Jeffrey C. Long, Clifton Poodry, and Francine C. Romero. The moderators were chosen because of their knowledge of genetics and research and because of their ability to handle difficult questions, topics, and discussions.

Conference Site

The Best Western Inn at Rio Rancho in Rio Rancho, New Mexico, was chosen as the conference site because of its proximity to the conference organizer, Shipping, Receiving & Fulfillment Services (SRFS), and to the Rio Grande Pueblos.

Conference Agenda

February 7, 2001 – Setting the Research Agenda, the Tribal Perspective.
Moderator: Dr. Francine C. Romero

1:00 p.m. Welcome Prayer, Governor Malcolm Bowekaty (Zuni Pueblo)
1:15 p.m. Introductions, Overview of Meeting Objectives
2:00 p.m. Setting the Research Agenda, the Tribal Perspective
3:15 p.m. Break
3:30 p.m. Discussion of the Tribal Perspective
5:30 p.m. Adjourn for Day 1

February 8, 2001 – Setting the Research Agenda, the Researcher Perspective
Moderator: Dr. Jeffrey C. Long

8:00 a.m. Opening Prayer, Mr. Celestino Romero (Jemez Pueblo)
8:30 a.m. Setting the Research Agenda, the Researcher Perspective
10:00 a.m. Break
10:15 a.m. Discussion of the Researcher Perspective
1:00 p.m. Break

1:15 p.m. **Setting the Codes and Policy Agenda, the Review Boards Perspective**
Moderator: Dr. William L. Freeman

3:00 p.m. Break
3:15 p.m. Discussion of the Review Boards Perspective
5:30 p.m. Adjourn for Day 2

February 9, 2001 – Formulating the Policy: Education and Capacity Building
Moderator: Dr. Clifton Poodry

8:00 a.m. Opening Prayer, Mr. Frank Fragua (Jemez Pueblo)
8:30 a.m. Formulating the Policy: Education and Capacity Building
10:15 a.m. Break
10:30 a.m. Work Groups and Time Frames
1:00 p.m. Meeting Adjourns

Conference Results

The genetics research policy formulation meeting was conducted in four segments. The first segment concentrated on tribal concerns and tribal expectations. The second segment concentrated on the process of research and existing genetics studies. The third segment concentrated on existing research codes and genetics policies. The fourth segment concentrated on the synthesis of the ideas and needs presented at the conference. In this section each segment is presented separately.

During each segment, individuals representing each of the respective areas of tribal perspectives, researcher perspectives, or review board perspectives were provided with opportunity to express their concerns, ideas, or experiences regarding genetics research. There was an

ongoing question and answer session as each individual within a given segment spoke. After all the individuals within a segment had spoken, general discussion ensued for the remainder of time within each respective segment.

Although *all* meeting participants contributed to each segment of the meeting, each individual is not recognized for their comments in the summary report. The exclusion of individuals is in no way to infer that their individual contributions were not worth repeating or important. To the contrary, the contributions of each individual were extremely valuable. If more than one person expressed the same idea, their statement or idea was not repeated but was instead incorporated into the concepts summarized at the end of each segment (without reference to who said the particular statement).

In the following paragraphs, individual contributors are identified by name and affiliation with a narrative of their key ideas and points provided.

Segment One: Tribal Concerns and Expectations Regarding Genetics Research

Governor, Malcolm Bowekaty (Zuni Pueblo)

Governor of Zuni, Malcolm Bowekaty, delivered a comprehensive overview of the conduct of (genetics) research in tribal communities. Governor Bowekaty outlined for the group his tribal expectations of researchers, of the research process, and of his community's role in the research process. The expertise and review system currently present within Governor Bowekaty's community is a result of experience. Similar to other tribal communities, the Zuni are experiencing high rates of disease and limited resources. It is of utmost importance that any research conducted with the Zuni people be conducted respectfully and to the benefit of the tribal members.

Governor Bowekaty said a researcher should have respect for the Zuni people and must also earn the respect of the Zuni people. The Governor said the researcher should have the community learn about his/her background, training, interests, and family. A researcher should first approach the community by way of a letter of intent. The letter should summarize the research objectives, the value of the research, the research hypotheses, the benefits of the outcomes to the tribal people, the background on the research topic, and the outcomes of the previous work. The tribe expects copies of reprints and copies of relevant literature on the research question. A subcommittee within the tribe is formed to conduct an initial review. The subcommittee reviews how the outcomes will be measured, the analyses to be conducted, the benefits to the local community, any community capacity building activities, the requirements for the facilitation of the research (e.g., will a translator be necessary?), and the ethical considerations.

If the subcommittee review goes well, they will request a full proposal from the researcher. The full proposal includes samples of any survey instruments to be used. If the project does not involve the Indian Health Service (IHS), only the tribal health board will review the full proposal. If the project involves the IHS, the investigators must also submit their proposal to the National IHS Institutional Review Board (IRB) for review. In addition to the document, Governor Bowekaty said he requests a site visit by the researchers so that they can tour the local hospital and tribal museum. The researcher is informed of tribal taboos regarding bodily specimens. The site visit is seen as an indication of both the researcher and institution's commitment to the project. In return, the Governor stresses that the Zuni also expect to be able to have access to the sponsoring university, institute, or company for a site visit from the tribe.

In the full review process, the tribe will seek any necessary technical assistance for accurate interpretation of the protocol. The investigators will be asked if they are willing to provide insurance above and beyond what the IHS provides should injuries occur. The reviewers will pay particular attention to sample size, benefits, and interpretation. The instruments and tools are reviewed for their cultural appropriateness and sensitivity. If bodily specimens are to be collected, the review committee expects storage, access, and ownership issues to be clearly defined. The tribe owns the data and is co-author on any publications. The tribe reserves the right to review all manuscripts before publication.

Once approval is given to a particular research project, yearly status updates are required. The project is expected to work with existing tribal programs. The tribal program staff fulfills any translation needs. The ensuing results are evaluated on the basis of benefits to the tribe.

The tribal review process is a forum to answer community questions and to facilitate discussion. The underlying concern of the tribal leadership is the health of their community members. The

leadership is looking at the bigger picture of public health and is willing to work with researchers who want to work with them. Governor Bowekaty stressed that a researcher should not try to evade the tribal system.

The Governor and his tribal community recognize that the next phase of research involves genetics. Indeed, this 'new' approach had already been prophesized by the elders. The Governor recognizes the controversial issues stirred by genetics but also understands that controversial issues can be overcome. He takes very seriously his role of understanding the threats of genetic research while weighing the benefits. He states it is up to him and the tribal council to sift through the issues while giving the community an opportunity to speak. He underscored the power of the collective memory of people and explained how community norms are established.

Governor Bowekaty is looking at the future needs of his community and realizes that the optimal scenario includes his own people as the researchers.

Marla Jasperse (Navajo)

Ms. Jasperse has played an important role in the representation of American Indians at national meetings. Her experience with community-based projects has served as a guide in her discussions of community perceptions regarding genetic research. Ms. Jasperse has learned from elders that the threats of genetics are based on the compromising of the sacred. The elders stress that genetic research is not the same as other types of research because it deals with an individual's body parts. The bodily specimens that are currently used to extract deoxyribonucleic acid (DNA), e.g., blood, hair, and saliva, are very sacred to the Navajo. The respect for the body as a whole and the parts that come from the body have to be dealt with in the most respectful way possible. The elders are skeptical of genetic research because researchers have disrupted existing sacred arenas.

The Navajo Nation is one of the few tribes who have formed their own human subjects review committees. Ms. Jasperse states that the approval process must include an informed consent form that respects the Navajo perspective. The parameters for data collection, data storage, and data disposal must be acceptable. Ms. Jasperse states that the concept of anonymity does not ring true for the Navajo because anonymous samples do not disassociate from the individual. Indeed, among the Navajo, most illness is attributed to the result of the mishandling of body specimens separated from the body.

Ms. Jasperse believes that the community must be involved in the genetic research process. She is adamant that the project goals, objectives, and results be of benefit and be carried out as initially proposed.

Ms. Jasperse reiterates that we need to train our own people to become the researchers. We need to train our own people to both understand the issues involved with genetic research and to remember basic respect for people.

Rae Mei-Ling Chang (Kanaka Maoli)

Ms. Chang has worked closely with families experiencing hereditary disease and has experienced first-hand the promise and perils of genetics research. Because of her work with affected families, Ms. Chang has become knowledgeable in recent years about the laws and principles of ethics regarding genetics research. Although many of the individuals Ms. Chang works with are angry and disappointed, Ms. Chang continues to recognize the value of science and research.

Ms. Chang is an active member of the National IHS IRB. Her knowledge and experience with human subjects protection and principles of ethics will help families and individuals who have been injured by genetics research.

The *Kanaka Maoli* believe that every piece of an individual's body contains a life force, *Mana*, which flows through the universe. The disruption of *Mana* causes disease. The *Kanaka Maoli* believe an individual is more than the sum of their genes. To see the whole of the *Kanaka Maoli*, a researcher must look at the whole and understand how everything is related to everything else. The *Kanaka Maoli* want their culture and all else that is sacred to them to be understood within the context of their cosmology. If a researcher takes any aspect of their culture out of context, the researcher will get something artificial. Moreover, when a researcher fails to respect the *Kanaka Maoli* worldview, the researcher will cause disruption that may result in illness and injury to the *Kanaka Maoli*.

Terry Powell (Alaska Native)

Ms. Powell is a community member and co-chair of the Alaska Area IHS IRB. She and her fellow community members, although not formally schooled in scientific research methods,

thoroughly review and criticize research proposals, and are often able to recommend changes that will enhance the potential benefit to participants without reducing scientific merit.

Ms. Powell reminds researchers to do their homework when proposing to do research with a tribal community. The recommendation to do background research applies not only to the history and culture of the native group, but also to practical things. For example, Ms. Powell encourages any researcher who is interested in conducting research in Alaska to be cognizant of subsistence hunting and fishing. In Alaska, for example, there will be times of the year when data collection would be nearly impossible because an entire village will be out fishing.

As a rule of thumb, Ms. Powell also encourages researchers to remember the human element. She suggests researchers treat native participants the same way they would treat members of their own families if they were participating in a research project. Ms. Powell strongly advises researchers to ensure that participants are truly informed of the research protocol and to be mindful of translation needs. Be respectful and do not take advantage of people who may not know what they are voluntarily agreeing to participate in. Ms. Powell takes her responsibilities as an IRB member very seriously and will not hesitate to keep researchers in check.

Lisa Preston (Tohono O'odham)

Ms. Preston is an active community member of the National IHS IRB and serves as primary reviewer of informed consent forms for several genetics research protocols. Ms. Preston reiterates to researchers the need to respect people, traditions, cultures, and tribal governments. Ms. Preston briefly outlined the different review process that a researcher would need to go through at Tohono O'odham compared to the processes a researcher encounters at Zuni. Whereas at Zuni, a single tribal council made the decision on whether or not to agree to participate in a research project, the Tohono O'odham have 11 districts, each with a district council. Similar to Zuni, committees make recommendations to the legislative council. These recommendations, however, can be referred to the people who reside in three major localities. Not surprisingly, each of these bodies has different meeting schedules.

Ms. Preston also underlined a couple of key questions a genetics researcher will encounter when proposing a genetics research project to a native community. First, the researcher will be asked to explain why the genetics research is truly necessary within the context of the health and economic priorities of the Tohono O'odham. Second, the researcher will be asked to explain the use of body specimens because among the Tohono O'odham the use of body specimens is not acceptable.

Connie Garcia (Acoma Pueblo)

Ms. Garcia is personally touched by the world of clinical trials, genetic counselors, and genetic tests because she has a granddaughter with holoprosencephaly, a fatal genetic disorder. The challenges of having an affected granddaughter is compounded by the complexities of heredity, of feeling responsible for passing the genes that made her granddaughter sick. Ms. Garcia and her family were not prepared to deal with the issues of genetics, and they know the ramifications of her granddaughter's condition will affect a lot of people.

Ms. Garcia shares many words of wisdom with researchers: integrity, honor, acknowledgement, and understanding. Ms. Garcia stresses to researchers to be true to oneself. No matter what reason a researcher has for going into research or for choosing a particular field of research, he/she should always remember to do no harm. Ms. Garcia instructs researchers to honor native people. Although native people may walk a different path, we are all walking through this life together. Even if our belief systems are different and one person believes in heaven while another believes in the spirit world, our spirits exist. Do not harm the spirits.

Ms. Garcia instructs researchers to acknowledge honesty. If the researcher needs body specimens, be honest about the need for specimens. Do not couch genetic research as anything other than what it is. The tribe, in turn, will be honest in responding with what they are willing to do or not do. Lastly, Ms. Garcia stresses to researchers the need to understand. She acknowledges that it is equally important to understand as to be understood. Ms. Garcia is anxious to share her experiences so that those whom she teaches will go on and teach others. In sharing these words of wisdom, Ms. Garcia is paying tribute and staying true to the teachings of her grandmother.

Ben Muneta (Navajo)

Dr. Muneta stressed the importance of educating scientists on culture and tradition. Specifically, Dr. Muneta expressed concern about researchers not always having respect for those that are

deceased. In most native cultures there is reverence for the deceased, and it is sacrilegious to conduct research on the deceased. Dr. Muneta asked researchers to be responsible to people and to be fair in the work they are doing. For example, it is not acceptable to obviate tribal relationships with skeletal remains so that studies can be conducted.

Debra Harry

Ms. Harry underlined the importance of communicating with tribal councils and ensuring that tribes have been consulted and are well informed about the proposed genetics project. Ms. Harry expressed concern about the validity of genetic research in the face of unmet social and medical conditions challenging tribal communities. Ms. Harry also questioned the premise for conducting genetics research on behavioral conditions (for example, alcoholism) or on physical conditions caused by certain behaviors (for example, diabetes resulting from poor diet and heart disease resulting from tobacco use).

Ms. Harry was concerned about who takes responsibility to protect the rights of community members, who gives authorization for research to be conducted, and who has ultimate responsibility to monitor the harms that can result from genetics research. There currently is no line of accountability or liability when genetic research harms groups. There needs to be multiple layers of protection at the tribal, institutional, and federal level, including funding agencies. Ultimately, tribes themselves have the right to control every aspect of genetic research.

Clifton Poodry (Seneca)

Dr. Poodry is a key player in the world of genetics research in native peoples because he is native and a geneticist by training. Dr. Poodry serves as a role model and is a strong proponent of genetics education for native peoples. Dr. Poodry reiterated the diversity among tribes in terms of economic status, empowerment status, government structures, and perceptions of what may be harmful and/or risky in participating in genetic research. The tribe is the ultimate authoritative basis for deciding whether the tribe says yes or no to research. The Seneca are matrilineal, and the clan mothers determine how both tribal politics and any proposed research will play out. If the tribe says no to research, the answer is no.

However, Dr. Poodry pointed out that tribes do have conditions they would like to have studied. For example, Dr. Poodry's tribe may be open to having their prevalence of arthritis studied further. If a researcher is truly interested in benefits to the community, part of the homework could involve finding out the concerns and priorities for that tribal community.

Jeffrey Henderson (Lakota, Cheyenne River Sioux)

Dr. Henderson is very familiar with both the clinical care needs and research needs of native peoples. Dr. Henderson is currently co-investigator for the Strong Heart Study – Dakota Center, funded by the National Heart, Lung, and Blood Institute of NIH. Similar to the Zuni and Navajo, the Cheyenne River Sioux have been extensively exposed to research and have a formal review and approval process for research. A key question for the Cheyenne River Sioux tribe is "How will this research project affect our tribal sovereignty?" A researcher first must first present his/her study to the health committee. The health committee reviews the proposal and, if favorable, makes a recommendation and writes a resolution in support of the project to the tribal council. The researcher then presents his/her study to the full tribal council simultaneously with a review of the proposal by the tribe's legal department to ensure that the tribe's legal interests are well represented.

Dr. Henderson advises researchers that there have been instances when the tribal council has not approved research projects for a variety of reasons. The tribe will weigh heavily the value of the research to the community and the benefits to individuals and families.

Brett Lee Shelton

Mr. Shelton stated that he was not representing any tribe, but rather was speaking from his own experience. He drew a parallel between genetics research and the collection of native artifacts. Similar to how some tribes purposefully sold artifacts to collectors and museums, he adds that there will be tribes who willingly participate in genetic research and others who will be adamantly opposed to it. Mr. Shelton says tribes may not always be totally informed, however, about the potential pitfalls of research such as immortalization of cells and the circulation of samples among colleagues. The immortalization of cells and sharing of samples will make the repatriation of body specimens difficult.

Mr. Shelton highlights the need for education of native community people regarding the dangers and realistic benefits of participating in genetics research. He cautions about various levels of dangers to groups, including stigmatization of a community, of individual families, or of native peoples in general.

Carolyn Robbins (Aleut)

Ms. Robbins stated that tribal diversity needs to be underlined and that researchers should not assume that the priorities of the tribe are similar to their own. When a researcher gets to the community level, the researcher will find many things have already been thought through. Ms. Robbins is a strong proponent of participatory research and knows tribes will come up with ways to answer questions they may have about things not so well understood, as in the case of genetics research.

Summary Segment One

The perspectives represented in the round table discussions underline the dangers of generalization and emphasize the need for greater responsibility by the research community and funding agencies.

- Researchers should never assume that the tribal concerns, customs, and expectations will be the same from one tribe to another.
- Researchers should never assume that the tribal concerns, customs, and expectations of a given tribe at one point in time are the same as at another point in time.
- Researchers should never assume that tribal concerns, customs, and expectations would not be directly affected by the results of the research, irrespective of the findings.
- Researchers should never assume that tribal concerns and expectations are similar to their own, especially with respect to the use of body specimens.
- Researchers and institutions have not taken full steps to minimize and repair the disruption of genetics research on individuals, family, and community.
- Individual researchers and institutions need to consider their agreements with the tribes as contracts, and they must honor, comply with, and fulfill what was agreed with the tribe.
- Researchers need to recognize the expertise of tribal health boards and the IHS IRBs. Investigators often think of IRBs as another hurdle to get over rather than as a resource.
- Institutions need to take responsibility for the unethical behavior of their students and faculty.
- Funding agencies need to be responsive to the needs of non-traditional grantees.

The roundtable also discussed the various responsibilities tribes need to assume if they are participating in genetics research.

- Tribes need to develop an agenda of what they would like to have studied and have researchers and funding agencies be responsive to that agenda.
- Tribes need to take responsibility in enforcing contracts and developing minimum damage breech clauses.
- Tribes need to form partnerships with both the researcher and funding agency, i.e., a three-way triangle.
- Tribes need to require legally binding contracts with universities.
- Tribes need to demand community capacity building with each proposed research project.
- Tribes need to follow up on the status of projects, the behavior of researchers, and the status of body specimens.
- Tribes need to encourage educational attainment among their tribal members.

Segment Two: Researcher Perspectives Regarding Genetics Research

Jeffrey C. Long (National Institute on Alcohol Abuse and Alcoholism)

Dr. Long identified the process of research for the participants. Understanding the process is very important if we are to resolve barriers to improvement. Dr. Long stressed that in research, although there may be a list of steps involved, getting through the steps is not equivalent to simply walking up a staircase. The steps of research are interactive, and many steps in the process can run in parallel. All the steps in the research process must be undertaken to complete the task, however.

The first step of the research process begins with the identification of a topic. There are several ways to identify a research topic. For example, a physician may see a medical condition and want to sort out the disease process. Similarly, the identification of a research topic could be set by a

larger national agenda, e.g., the NIH research initiatives focused on diseases or cluster of diseases. Finally, a research topic could be identified by self-interest in a particular field.

Each of these examples is a legitimate starting point. The next step is figuring out the best way to pursue the question. In many cases of genetic research, the question would be best answered by collecting a sample for study that will resolve the issues and allow for the topic of interest to advance our knowledge. The sample will depend on the question and can include human subjects, animal models, computer simulations, organisms, etc. A question can include multiple sampling schemes.

Funding is necessary to conduct the research. Dr. Long is a government researcher, and his program has a budget, but other individuals may have to write proposals and submit the proposals to funding agencies. Grant proposals are reviewed for scientific merit with a section on human subjects protection if the study includes people. Although reviews may not be perfect, Dr. Long states there has been a recent acceleration of research protections.

Before a researcher submits his/her study for funding, the researcher must have a complete plan of what he proposes to study. The plan must include the goal, a hypothesis, the details of the plan for data collection, the types of data that will be used, the methods of data analysis, and the decision making process. The completed plan must go before the IRB, sometimes several IRBs. Sometimes the different IRBs may not totally agree with each other on their review of the research plan. Often this type of review requires revisions to the research plan by the researcher. The proposal can go through many revisions to meet everyone's requirements. There is a lot of interaction that goes on between the tribe, researcher and funding agency.

The researcher should justify why the proposed research questions are important to ask. In Dr. Long's experience of conducting genetics research studies among American Indian populations, the tribal council and the health committees have reviewed the proposals. In addition, the tribes have formed focus groups to review his grant proposals. The research proposals were evaluated in light of the cultural norms. Dr. Long has experienced first hand the variation in tribal approval processes.

The data collection step can include either primary data or secondary data collection. Primary data is information that comes directly from a person and can include a blood sample, cheek swab, etc. The body specimens require laboratory analyses. Data gathered from already existing reports, from other researchers, or other sources are called secondary data. All data that are collected must be entered into a database and validated. Validation is a very important step and occurs at different times during the research process.

One step where vulnerabilities exist is the data storage step because the confidentiality of individuals or a community might be compromised.

The next step is the analysis. The analysis step includes applying statistical methods to describe the data and to see if there is something in the results that was not anticipated. The results from the analysis of the data are reported to the tribe, the IRB, and the scientific community. By law, the project will be subject to annual IRB review if the project extends beyond one year. All reports to the tribe should correspond with the agreements made between the researcher and the tribe at earlier stages of the research.

The final steps in a research project include the completion and closing of a project. An important question for tribes and researchers to consider is how the samples will be stored or disposed of. In the long history of research, these are two areas that have received less attention.

Dr. Long asked all individuals involved with a research project to ask, "How do researchers perceive risks?" There are risks to individuals, risks to communities, and risks associated with different research goals. We hope from genetics will come underlying mechanisms to develop treatment strategies for human disease. By identifying risks, we can work toward prevention of disease, but in identifying higher risk individuals we cause harm by stereotyping others with similar characteristics. In addition, because a study is done, there is often a perception that the incidence of the disease is high. For all reviewers of research protocols and research personnel, the risks should be identified and particular attention paid to how those risks will be treated. What are the risks that are identified by researchers? The risks to individuals (e.g., loss of insurance, discrimination by others) are noted on the consent form, and risks to families are also identified. In talking with tribes and negotiating memoranda of agreement, there is a more established approach to individual risks than in itemizing the risks to communities. Dr. Long states that pedigrees

should not be published if individuals can be identified.

Dr. Long also mentioned that research has traditionally been an academic pursuit. The combining of academic science with business is new. There would be clear conflicts of interest for researchers who have vested interests in biotech companies, pharmaceutical companies, etc. These interests would need to be stated very explicitly by researchers.

Clifton Poodry (National Institute of General Medical Sciences)

Dr. Poodry warns both researchers and tribes that things do not always fall into place when proposing a research project. The research project may not work because: (1) the timing is not right for asking a particular question, (2) the tools necessary to answer the question are not available, or (3) the funding agency or the population of study deems the question unimportant or unnecessary. Dr. Poodry recommends to researchers that equal investments be made in thinking of the question and in getting buy-in from the population of study. A true measure of a strong research proposal is the ability of a researcher to follow through when things do not work as expected.

Judith Greenberg (National Institute of General Medical Sciences)

Dr. Greenberg stated that the objective of basic research such as cell biology and genetics is to understand the underlying mechanisms of how cells work and how cells are regulated. Basic research follows circuitous paths that intersect with other research paths in unexpected ways. The research process is long and almost infinite because by the time you answer one question, the researcher will have many other questions that are raised. The goal of basic research is to understand the underlying cellular mechanisms in order to eventually prevent disease. Many basic scientists do not go into research thinking they want to find a cure, but rather because they are curious to understand why things are.

Dr. Greenberg is the project officer of the NIGMS Human Genetic Cell Repository at the Coriell Institute for Medical Research. She explained that researchers send samples from participating individuals to the repository. For samples related to genetic disorders, clinical information is kept on the samples. However, no information that would identify the individual is kept. The repository requires that the informed consent forms signed by sample donors make clear that their sample will be included in the repository.

Dr. Greenberg stated that the NIH is developing data sharing policies that incorporate confidentiality and privacy.

On September 25-26, 2000, NIGMS sponsored the "First Community Consultation on the Responsible Collection and Use of Samples for Genetic Research." The recommendations, issues, and concerns can be found at http://www.nigms.nih.gov/news/reports/community_consultation.html.

The Policy for the Responsible Collection, Storage, and Research Use of Samples from Identified Populations for the NIGMS Human Genetic Cell Repository can be found at http://locus.umdnj.edu/nigms/comm/submit/collpolicy.html.

Jeff Henderson (Black Hills Center for American Indian Health)

Dr. Henderson received training as a clinician within the IHS. Initially, Dr. Henderson had no real thoughts about going into research. While looking at the disease status of AI/AN, he became interested in utilizing the primary health care model for looking at public health. Dr. Henderson completed his Master of Public Health training and joined the Strong Heart Study (SHS) in Rapid City, South Dakota. He received a young investigator award and became a co-investigator of the SHS. Dr. Henderson is only the second American Indian to be a member of the Steering Committee of the SHS, which is a multi-site, longitudinal study looking at risk factors for heart disease among American Indians.

Dr. Henderson says that nearly all SHS field staff and coordinators are tribal members. Eight student SHS staff members have gone on to pursue health careers, and three of them are presently completing medical residencies. Dr. Henderson is pleased to see that there is an increasing number of AI/AN study investigators. Although the change has been gradual, Dr. Henderson looks forward to the time when tribes and their members will drive the research agenda.

Dr. Henderson's research interests are presently focused on polypharmacy, quality of life issues, cancer, and thyroid disease.

Michael Zwick (Johns Hopkins University School of Medicine)

Dr. Zwick answered the question, "Why would a researcher be interested in studying AI/ANs?" Scientists are interested in genetic variations, and certain genetic variations may be easier to identify in isolated populations. Isolated groups may have unique genealogies of genetic variants, which makes it possible to identify those variants with underlying Mendelian traits. In the past, even in the absence of good genetic maps, it nevertheless has been possible to map many genetic variants of large effect with underlying Mendelian traits in isolated groups (i.e., human linkage studies that focus on families). Why is this? Because we expect to find a relatively small number of variants in a single gene that lead to a specific disorder. Furthermore, the variants will exhibit extensive linkage disequilibrium, thus making it easier to map the causative variant. This makes the problem much simpler for geneticists. This is the value to geneticists of any isolated group of humans.

Dr. Zwick strongly cautioned that geneticists interested in genetic variations should not be confused with or generalized as geneticists interested in human migration or human evolution studies.

Thomas Drouhard (Indian Health Service)

Dr. Drouhard is a surgeon who observed high frequencies of colon cancer among his patient population. He contacted a well-known cancer geneticist, Dr. Henry Lynch. Together, Drs. Drouhard and Lynch were able to identify the disease (which became known as the Lynch II Syndrome) and reduce by half the size of the population group that are identified as at-risk to develop the disease. Drs. Drouhard and Lynch have been extremely sensitive to cultural, familial, and community situations and have worked with the tribal entities to ensure respectful research. Dr. Drouhard's work among his patient population is an example of a genetic study that has had immediate benefits to the tribal community and individual families.

Dr. Drouhard is now busy studying the high prevalence of ovarian cancer among a patient population.

William Knowler (National Institute of Diabetes, Digestive and Kidney Diseases)

Dr. Knowler has long been interested in Type II diabetes complications and practical applications. Much of Dr. Knowler's research has focused on kidney failure. Type II diabetes is a complex disease and does not have a single cause. Type II diabetes is caused by many factors including socioeconomic factors, lifestyle factors, and inherited factors. Dr. Knowler does not believe that genetics will identify a single cause because our genes are only a part of the big picture. Dr. Knowler is hoping his research will help identify the individuals with the biggest diabetes disease risk so that efforts can be concentrated to help them. Dr. Knowler is also hoping his research will help us understand the metabolic basis of Type II diabetes. He is hoping his research will help identify better ways to treat Type II diabetes. Dr. Knowler says it is through understanding the cause that we can hope to better treat the disease.

William Freeman (Indian Health Service)

Dr. Freeman asked the question, "What is the benefit of genetic research?" Dr. Freeman would like communities to hear the reasoning behind the genetic study of conditions and diseases such as alcoholism or diabetes, which are caused by environmental, biological, and genetic factors. The rationale should explain that even after a gene is found, it takes years and years before possible treatments are developed, i.e., the rationale should neither overpromise nor minimize the potential value of the research.

Should the work be done in AI/ANs knowing that there is not an immediate benefit? It is possible to answer "yes." Should the formative work be done elsewhere? For example, Dr. Freeman wonders how many people who join a Phase I cancer clinical trial enter the study thinking they are getting a cure. In reality, the Phase I cancer clinical trials are designed to study the dosage of therapeutic medications. Some participants are not given enough of a dosage to treat their cancer, and all are not given the medication long enough to treat their cancer. Therefore, they have a misconception about the therapy. The statements given to participants are not necessarily wrong; they just do not explain succinctly that patients will not necessarily benefit.

Dr. Freeman says there exists a similar problem with a community's therapeutic misconception. A community may see a problem within their community and want a cure so badly that they see the research as the cure. Researchers should not permit a community with wishes for a cure to assume that their decision to participate in a research project will soon cure or prevent the condition. Rather, the community should understand that the research is likely only to contribute a part of the process of developing a cure.

Summary Segment Two

- Research is intended to find out things we do not know.
- Researchers need to be honest with individuals and communities about the actual vs. potential benefits of a research project. There should be initial true and complete disclosure of the risks and benefits of the proposed research. Researchers must disclose all possible conflicts of interest.
- Researchers need to negotiate with the tribal communities.
- The informed consent made with individuals and communities must include ongoing communication. Each time the question changes, there should be feedback to the individuals and the communities involved to keep them informed and to renegotiate as necessary.
- Researchers need to explain the state of the art for their particular area of research, including the technology, and explain the eventual benefits the researchers expect of their research for tribal communities and individuals. The potential need of keeping samples for these eventual projects needs to be part of the initial discussion and negotiation.
- Researchers need to identify problems as soon as possible.
- Researchers need to know that tribes are looking at control issues for samples and want to be at the table when these issues are being discussed.
- Researchers should actively develop community research capacity and capability.
- Researchers must always have respect for data and samples.
- Researchers should not permit a community with wishes for a cure to assume that their decision to participate in a research project will soon cure or prevent the condition. Rather, the community should understand that the research is likely only to contribute part of the cure.

Segment Three: Review Board's Perspectives Regarding Genetics Research

Indian Health Service National Institutional Review Board: William Freeman

Dr. Freeman briefly explained the purpose of the IHS IRB. Like other IRBs, the National IHS IRB helps ensure that all research in AI/AN communities observes basic ethical principles that underlie acceptable conduct of research involving human participants. The IHS IRB is unique, however, in its formal requirement for tribal consent on behalf of communities in addition to individual consent to participate in research.

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 as well as 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.

All research that is reviewed by the National IRB must also receive tribal approval. The goals, objectives, and methods must be clearly stated in the research proposal. The benefits and risks of the research to the individuals and tribes must also be clearly stated. The IRB pays particular attention to the disposition of data and specimens. The involvement by the community must be stated. The funding, budgets, consent process, and consent document are also reviewed. After initial review, all modifications to the research

proposal must go to the IRB. All future uses of the specimens must be clearly stated within the consent form. The IHS IRB does not condone blanket approvals for future uses of body specimens, because with blanket approvals the person is not told and cannot know either the potential harms or the potential benefits of the specific future research, and thus, the consent is not "informed." The IRB encourages pre- and post-test genetic counseling to minimize risks and harms. The storage of all data must be secure and respectful. The disposal of samples must also be done respectfully and safely (specimens may pose biohazards).

The National IRB understands policies are not set in concrete because situations change. The review of research protocols is a task continuing over time. The most recent IHS Genetic Research policy is included in Appendix B.

Navajo Nation: Marla Jasperse and Thomas Drouhard

Marla Jasperse (University of New Mexico)

From the 1960s to the 1990s, the IRB was under the Navajo Area IHS. The members on the IRB were IHS personnel, and Ms. Beverly Pigman recognized the need for more community representation. A research code was drawn for the Navajo Nation with the assistance of the UNM Law School. The research codes were reviewed and approved by the Navajo Nation Tribal Council and by the Navajo people. Although independent, the Navajo Nation IRB continues to work closely with the National IHS IRB. The Navajo Nation IRB shares its Multiple Project Assurance (MPA) with the National IHS IRB.

The research process on Navajo includes buy-in and feedback from the communities to be included in the research project. The community needs to benefit from the outcomes of the research, and the community needs to have their members participate in the research as more than subjects. The researchers are expected to sponsor training sessions for the local community people. Researchers are also expected to participate in the annual community based research conference. The conference is a forum for researchers to return and present their study to the community. The studies are translated for the Navajo people so that they can understand the implications of the research. The Navajo elders have found the translation of study results particularly interesting and educational.

Ms. Jasperse recommends that all researchers work with the local people. The local people will guide the researcher. Researchers should not assume that something seen at the national or regional levels has not also been recognized at the local level. Chances are, the local community has already come up with a way to deal with the problem. Obstacles should not be seen as barriers but as learning blocks. In research, a researcher learns about himself/herself first.

Thomas Drouhard (Indian Health Service)

Dr. Drouhard explained his experiences of having his genetics protocol reviewed by the Navajo Nation and the IRBs. Dr. Drouhard had his protocol reviewed by the local health board, the IHS, and the local community governing boards. The protocol included family history of affected patients and controls. Biopsies were taken to look for a particular gene. In 1993, the mutated gene was discovered. During group sessions the basic principles are discussed and individual results are given privately.

Dr. Drouhard reports back to the local community on an annual basis. The Navajo Nation IRB requires a quarterly report of the project. All publications are to be reviewed by the Navajo Nation. Anonymity is stressed strongly by all individuals involved with Dr. Drouhard's study.

Dr. Drouhard relayed his frustrations in dealing with the many layers of approval processes required, but stated that he learned to respect and appreciate the importance of tribal and IRB review.

Alaska: Terry Powell and Jay Butler

Terry Powell (Alaska Area Institutional Review Board)

Tribes and tribal consortiums control the Alaska Area Institutional Review Board. There are nine members on the board, and Ms. Powell shared with the group their minimum requirements. A researcher should submit to the Alaska Area IRB a one-page summary of his/her research project that will be understandable to a layperson. The researcher should send 11 copies of their protocol and 11 copies of his/her curriculum vitae. The protocol needs to be sent to the IRB three weeks before the next scheduled meeting. Researchers should not be surprised if their protocols do not make it through the review process during the first submission. The whole review process takes about 90 days to complete. The IRB asks for periodic updates and does not approve of

specimen sharing. The IRB requests specific lists of what the samples will be used for.

Although the review process sounds difficult, Ms. Powell says most research is completed in a timely fashion.

Jay Butler (Centers for Disease Control and Prevention)

In 1948, the Arctic Health Research Center was established by the Public Health Service as part of the new Alaska Native Medical Center in Anchorage. Since 1973, the program, now known as the Arctic Investigations Program (AIP), has been part of the Centers for Disease Control and Prevention. Today, AIP includes CDC staff, direct tribal hire personnel, IHS personnel detailed to the Alaska Native Tribal Health Consortium, and visiting scientists. The goal of the laboratory is the prevention of infectious disease morbidity and mortality in the Arctic with a special emphasis on disease of high incidence and concern among indigenous peoples. The diversity of Alaska dictates that researchers approach communities for each project. Dr. Butler says going out into the community motivates the scientists at AIP. All their projects must go through the Alaska Area IRB, the National IHS IRB, and the CDC review processes. Sometimes the reviews can be contradictory, and this can be frustrating. Dr. Butler thinks the community involvement on IRBs is really good.

Dr. Butler says that when his staff members conduct research in tribal communities the same project team stays with the project until completion. Dr. Butler says there needs to be accountability back to the community from the researchers. People remember. This is not unique to Native communities--Dr. Butler said he once worked in a non-Native community in rural Wisconsin where the people still remembered a project from years earlier, and the community had still not been given the results by the researchers.

Indigenous People's Council on Biocolonialism: Debra Harry and Brett Shelton

Debra Harry

Ms. Harry described a proposal by the Indigenous People's Council on Biocolonialism titled "Indigenous Research Protection Act." The Indigenous Research Protection Act allows for different levels of review and provides a framework so that tribes can protect their interests. Existing tribal models were used as background for the Indigenous Research Protection Act. The Indigenous Research Protection Act is meant to be dynamic because science is dynamic. Tribes can freely adapt and adopt changes to reflect their needs.

Brett Lee Shelton

Mr. Shelton stated the Indigenous Research Protection Act covers all types of research with sections specific to contracts and agreement assurances. The Indigenous Research Protection Act provides guiding principles, respectful ways to conduct research, fees for administration, costs associated with going through these processes, equity, and establishment of participatory research partnerships. The goal is to shift the paradigm of research so that tribes are in control of research concerning them. A few tribes are considering adopting the Indigenous Research Protection Act.

National Institutes of Health: Judith Greenberg and Jean McEwen

Judith Greenberg (National Institute of General Medical Sciences)

Samples submitted to the NIGMS Human Genetic Cell Repository undergo several levels of review. For samples from identified groups, the community must be consulted. They must also, of course, be approved by the submitting researcher's IRB. If a decision is made to accept a collection of samples from a group, a community advisory group (CAG) will be constituted that will serve as the liaison between the community and the Repository. If a community no longer wishes to participate, or has other concerns, it can make its views known by means of the CAG. This CAG would also be expected to inform the community when research results are made available. At present there are no samples identified as Native American in the repository.

Jean McEwen (National Human Genome Research Institute)

When we talk about genetic research, the hardest issues often arise out of the fact that this kind of research more and more involves common, complex diseases with environmental components. Also, these diseases are often present in the larger population, not just in the population under study, so if and when any benefits come from the study, they may go

primarily to the larger population and not to the actual population that was involved in the research. These issues, although difficult, are ones that review committees need to consider.

Dr. McEwen also said that studies of common, complex diseases need to look at the gene-environment interaction more closely. There is a responsibility on the part of the researcher to make sure information they convey to the mass media does not portray complex disorders as being genetically predetermined but that they also acknowledge the possible relevance of environmental components.

National Indian Health Service Institutional Review Board: Roger Gollub, Lisa Preston, Connie Garcia, Malcolm Bowekaty

Roger Gollub (Indian Health Service)

Dr. Gollub shared with the group how the discussion has helped him to become a better IRB member. From the discussion he has learned to encourage researchers to:

1. Initiate true and complete disclosure from the onset;
2. Negotiate with the community under investigation;
3. Keep ongoing communication open;
4. Identify problems early on;
5. Encourage community control of specimens;
6. Develop the research capability of the community; and,
7. Optimize benefits to the participants and communities.

Lisa Preston (Indian Health Service)

Ms. Preston stressed to researchers that the informed consent form should reflect the true nature of the research project. The informed consent should be written in readily understandable language without a lot of technical jargon or acronyms. In her experience, Ms. Preston has not seen as much detail on informed consent forms as there might be. Ms. Preston said there are many issues confronting her tribe, the least of which involves genetics research, but she understands the importance of forming the policy. Ms. Preston is glad these policies are being formulated because they will be in place for her tribe and other tribes for future use.

Connie Garcia (Albuquerque Area Indian Health Board)

Ms. Garcia is looking to the Zuni and hopes to learn from them. Ms. Garcia said many tribes are afraid of research because their communities will potentially be stigmatized, but the Zuni have demonstrated that tribes can be in the driver's seat. Ms. Garcia hopes that tribes will utilize the expertise of their tribal members who have obtained higher education and recognize the value of what other tribes, such as the Zuni, have accomplished. Although Ms. Garcia recognizes that the challenges of research include tribal history, researcher accountability, and differing research priorities between the tribes and researchers, nevertheless, she is grateful to be an agent in the process of formulating a positive genetics policy.

Malcolm Bowekaty (Zuni Pueblo)

Governor Bowekaty said disseminating information, such as review board policies, is difficult to accomplish in Indian Country because of the diversity of tribes. The national and regional Indian organizations are not always reliable or representative of their tribal constituencies. For his community, utilizing the full capacity of their tribal sovereignty status and becoming self-reliant have been the keys to his tribe's success. His tribe has maintained their traditions and religion, and this allows for the consistency that he and his people rely on.

The Zuni tribal government has made improving the quality of life for all their tribal members their ultimate goal. The operationalization of their vision has made the tasks of the Governor and his staff much easier. The Zuni do not believe accountability is a bargaining chip. All research issues must be personalized and up front.

Summary Segment Three

- IRBs help ensure that all research in AI/AN communities observes basic ethical principles that underlie acceptable conduct of research involving human participants.
- Respect for people, beneficence, and justice are the three quintessential requirements for the ethical conduct of research involving humans.
    - 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.

- The principle of justice requires that participants be fairly selected.
- These three principles apply to individual participants as well as to the tribal communities of the participants.

- All research that is reviewed by the National IRB must also receive tribal approval.
- Lay versions of protocols and manuscripts should accompany all submissions.
- All uses of specimens must be clearly stated within the consent form. The IRB does not condone blanket approvals for future uses of body specimens.
- The IRB encourages pre- and post-test genetic counseling to minimize risk and harm.
- Sample and data storage, and sample disposal, are areas in which the respect for tribal wishes are very important.
- Studies should be designed to look at both genetics and environment.
- The general public needs to be aware that complex diseases have strong environmental components.

Segment Four: Developing Documents Contributing to a Genetic Research Policy - Education and Capacity Building

Science exists for people so that we can have a healthier world. The meeting participants all recognized the importance for tribes and researchers to work on the issues surrounding genetics together. It is important not to set a dichotomy between what researchers might want and what the communities might want. We must ensure that research is done in partnership. Even people with the best intentions still have to be accountable for showing respect for people.

The meeting participants decided to complete several tasks within the next several months. The tasks include: (1) a presentation at the University of Colorado genetics meeting; (2) the completion of a summary meeting report to NIH; (3) the publication of a summary meeting report; (4) the development of four primers – for tribes, researchers, Institutional Review Boards, and funding agencies; (5) the organization of a tribal leaders genetics summit; (6) the posting of workgroup notes on NIGMS and NHGRI websites; (7) the organization of regional ELSI grant writing workshops; (8) a follow-up genetics research formulation meeting; and (9) the development of primers – for University students and faculty, and for native students and communities. The tasks all maintain the goal of forming genetics research policy.

The genetics research policy formulation workgroup intends for the initiatives and documents to:

(1) Ensure that AI/AN Tribes and individuals involved in existing genetic research are fully informed and have given consent.
(2) Ensure that AI/AN Tribes and individuals included in publications are fully aware of their inclusion and have given consent.
(3) Ensure that AI/AN Tribes and individuals understand all that is involved in the research protocol, including implications, data storage, specimen use and access, rights of participants, etc.
(4) Ensure that researchers understand the cultural issues and sensitivities involved with conducting genetics research among AI/AN populations.
(5) Ensure that there is mutual benefit to both the AI/AN Tribe, the individual participating in the research, and the researchers (for example, opportunities for tribal youth to learn data collection, laboratory techniques, data analyses, etc).
(6) Ensure that all risks to individuals and communities are clearly understood and the terms of the research are negotiated between the researcher and the tribes.

Summary Segment Four: Next Steps

Each of the tasks is described in the following narrative and includes the names of meeting participants who volunteered to assist with the completion of each task.

I. Disseminate information about the Genetic Policy Formulation Meeting at the University of Colorado genetics meeting, Aspen, Colorado, April 5-7, 2001

II. Genetic Policy Formulation Meeting Summary Report

III. Publication of Genetic Policy Formulation Meeting Summary Report

IV. Development of primers – for tribes, researchers, Institutional Review Boards,

and funding agencies – each to include the following structure:

Primers:
- Background
- Standard Principles and Recommendations
- Risks and Benefits (Reciprocal)
- Advantages and Disadvantages
- Common Concerns
- Resources
  - Websites
  - Bibliographies
- Opportunities to Network
  - Education
  - Conversation
  - Action
  - Assistance

A. Workgroup for Primer for Tribes
- Carolyn Robbins -- co-Leader
- Michael Zwick -- co-Leader
- Connie Garcia
- Debra Harry
- Marla Jasperse
- Philip Lowenthal
- Terry Powell
- Brett Shelton

B. Workgroup for Primer for Researchers
- Dena Davis -- co-Leader
- Marla Jasperse -- co-Leader
- Tom Drouhard
- Bill Freeman
- Roger Gollub
- Jeff Henderson
- Jeff Long
- Ben Muneta
- Carolyn Robbins
- Brett Shelton

C. Workgroup for Primer for Institutional Review Boards
- Bill Freeman – co-Leader
- Brett Shelton – co-Leader
- Malcolm Bowekaty
- Jay Butler
- Dena Davis
- Thomas Drouhard
- Roger Gollub
- Philip Lowenthal
- Mike Zwick

D. Workgroup for Primer for Funding Agencies
- Brett Shelton -- co-Leader
- Chester Clarke
- Debra Harry
- Carolyn Robbins -- co-Leader

V. Governor Bowekaty is taking the lead in identifying tribal leaders who may be interested in participating in an international meeting of tribal leaders about genetics research. Ms. Commanda is assisting Governor Bowekaty in identifying Canadian leaders.
- Governor Bowekaty--Leader
- Laura Commanda

Once leaders have been identified, individuals interested in helping organize the meeting include:
- Mae-Ling Chang
- Debra Harry
- Francine Romero

VI. Posting of workgroup notes on NIGMS and NHGRI website
- Judith Greenberg
- Clifton Poodry
- Francine Romero

VII. Grants Writing Workshop – A training opportunity for individuals interested in ELSI grants. The grants writing workshop potentially can be tacked on to other regional meetings which would draw large numbers of American Indian and Alaska Native audiences.
- Francine Romero
- Jean McEwen
- Judith Greenberg
- William Freeman
- Clifton Poodry

VIII. Follow-up conference tentatively scheduled for late August in Portland, Oregon (topics and individuals to be incorporated include: genetic case studies, IRB members, Tribal leaders from the United States and Canada, and genetic counselors)
- Francine Romero
- Jean McEwen
- Judith Greenberg
- William Freeman
- Clifton Poodry

IX. Two follow-up primers:
- A. Primer for University Students and Faculty
- B. Primer on How to Promote Research by Native Students and Communities.

Report Summary: Formulating the Genetics Research Policy

With unprecedented advances in genetics research in the past few decades, the need for the formulation of genetics research policy specific to AI/AN continues to be unmet. A meeting of 29 individuals was convened in Rio Rancho, New Mexico, February 7-9, 2001, to discuss tribal concerns, tribal expectations, the process of research, existing genetic studies, research codes, and existing genetics policies. The purpose of the meeting was to begin the process of creating documents that could be instructive to both tribal communities and researchers about the conduct of genetics research studies. The meeting was not organized as a summit of representative genetics research issues, but was intended to be an intense round-table work session.

The genetics research policy formulation meeting was conducted in four segments. During each segment, individuals representing each of the respective areas of tribal perspectives, researcher perspectives, or review board perspectives were provided with opportunity to express their concerns, ideas, or experiences regarding genetics research. There was an ongoing question and answer session as each individual spoke within a given segment. After all the individuals within a segment had spoken, general discussion ensued for the remainder of time within each respective segment. The fourth segment concentrated on the synthesis of the ideas and needs presented at the conference with concentration on the next steps.

The perspectives represented in the round table discussions underline the dangers of generalization and emphasize the need for greater responsibility by the research community and funding agencies.

- Researchers should never assume that the tribal concerns, customs, and expectations are the same from one tribe to another.
- Researchers need to negotiate with the tribal communities.
- The informed consent made with individuals and communities must include ongoing communication. Each time the question changes, there should be feedback to the individuals and the communities involved to keep them informed and to renegotiate as necessary.
- Researchers need to explain the state of the art for their particular area of research, including the technology, and explain the eventual benefits the researchers expect of their research for tribal communities and individuals. The potential need of keeping samples for these eventual projects needs to be part of the initial discussion and negotiation.
- Researchers need to know that tribes are looking at control issues for samples and want to be at the table when these issues are being discussed.
- Researchers should never assume that tribal concerns and expectations are similar to their own, especially with respect to the use of body specimens.
- Researchers must always have respect for data and samples. The storage of all data must be secure and respectful. The disposal of samples must also be done respectfully and safely.
- All uses of specimens must be clearly stated within the consent form. The IRB does not condone blanket approvals for future uses of body specimens.
- Researchers should not permit a community with wishes for a cure to assume that their decision to participate in a research project will soon cure or prevent the condition. Rather, the community should understand that the research may only contribute to an eventual cure.
- Researchers and institutions have not taken full steps to minimize and repair the disruption of genetics research on individuals, family, and community. Individual researchers and institutions need to consider their agreements with the tribes as contracts, and they must honor, comply with, and fulfill what was agreed with the tribe. Institutions need to take responsibility for the unethical behavior of their students and faculty.
- Researchers need to be honest with individuals and communities about the actual vs. potential benefits of a research project. There should be initial true and complete disclosure of the risks and benefits of the proposed research. Researchers must disclose all possible conflicts of interest.
- Researchers need to identify problems as soon as possible.
- Researchers need to recognize the expertise of tribal health boards and the IHS IRBs. Investigators often think of IRBs as another hurdle to get over rather than as a resource.
- Funding agencies need to be responsive to the needs of non-traditional grantees.

- Researchers should actively develop community research capacity and capability.
- All research that is reviewed by the National IRB must also receive tribal approval.
- Lay versions of protocols and manuscripts should accompany all submissions.
- The IRB encourages pre- and post-test genetic counseling to minimize risk and harm.
- Studies should be designed to look at both genetics and environment.
- The general public needs to be aware that complex diseases have strong environmental components.

Acknowledgements

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--Francine C. Romero

Appendix A. Resources Distributed *Prior* to the Meeting

Author(s)	Year	Title	Journal	Volume: Pages
American Indian Law Center, Inc	1999	Model Tribal Research Code		
American Society of Human Genetics	1996	Statement on Informed Consent for Genetic Research	American Journal of Human Genetics	59:471-474
Burgess M, Brunger F		Negotiating Collective Acceptability of Health Research		
Chakravarti A	1999	Population Genetics--Making Sense Out of Sequence	Nature Genetics Supplement	21:56-60
Foster MW, Bernstein D, Carter TH	1998	A Model Agreement for Genetic Research in Socially Identifiable Populations	American Journal of Human Genetics	63:696-702
Foster MW, Sharp RS, Freeman WL, Chino M, Bernsten D, Carter TH	1999	The Role of Community Review in Evaluating the Risks of Human Genetic Variation Research	American Journal of Human Genetics	64:1719-1727
Freeman WL	1997	IHS Guidelines about the Collection and Use of Research Specimens.		
Freeman WL	1997	The Role of Community in Research with Stored Tissue Samples.		
Freeman WL	1994	Making Research Consent Forms Informative and Understandable: The Experience of the Indian Health Service.	Cambridge Quarterly of Healthcare Ethics	3:510-521
Indigenous Peoples Council on Biocolonialism	2000	Summaries of Selected Genetic Studies involving Indigenous Peoples		
Indigenous Peoples Council on Biocolonialism		Indigenous Research Protection Act		
Inuit Tapirisat of Canada	1993	Negotiating Research Relationships in the North		
Juengst ET	1998	Human Genetics '98: Ethical Issues in Genetics. Group Identity and Human Diversity: Keeping Biology Straight from Culture	American Journal of Human Genetics	63:673-677
Kaufert J, Commanda L, Elias B, Grey R, Young TK, Masuzumi B	1999	Evolving Participation of Aboriginal Communities in Health Research Ethics Review: The Impact of the Inuvik Workshop	International Journal of Circumpolar Health	58:134-144
Lander ES, Schork NJ	1994	Genetic Dissection of Complex Traits	Science	265:2037-2048
Macaulay AC, Commanda LE, Freeman WL, Gibson N, McCabe ML, Robbins CM, Twohig PL	1999	Participatory Research Maximises Community and Lay Involvement	British Medical Journal	319:774-778

Author(s)	Year	Title	Journal	Volume: Pages
Royal Commission on Aboriginal Peoples	1993	Integrated Research Plan		
University of Victoria	2000	Protocols & Principles for Conducting Research in an Indigenous Context		
Weijer C, Emanuel EJ	2000	Protecting Communities in Biomedical Research	Science	289:1142-1144
Weijer C, Goldsand G, Emanuel EJ	1999	Protecting Communities in Research: Current Guidelines and Limits of Extrapolation	Nature Genetics	23:275-280

Appendix B. Resources Distributed *During* the Meeting

Author(s)	Year	Title	Journal	Volume : Pages
Cochran P (Alaska Native Health Commission)	2001	Guidelines for Respecting Cultural Knowledge		
Day L (First Nations Chief's Health Committee)	2001	Continuing the Dialogue: Genetic Research with Aboriginal Individuals & Communities		
First Nations and Inuit Regional Health Survey National Steering Committee	1997	First Nations and Inuit Regional Health Survey	www.afn.ca	
Harry D, Howard S, Shelton B	2000	Indigenous Peoples, Genes, and Genetics: What Indigenous People Should Know About Biocolonialism	www.ipcb.org/pubs	
Kaufert J, Commanda L, Elias B, Grey R, Masuzumi B, Young K	2001	Community Participation in Health Research Ethics	Pushing the Margins: Native and Northern Studies	50-61
Kimball E	1994	Researcher Sensitivity and Responsibility to American Indian and Alaska Native Communities		
National Institute of General Medical Sciences	2001	Policy for the Responsible Collection, Storage, and Research Use of Samples from Identified Populations for the NIGMS Human Genetic Cell Respository	http://locus.umdnj.edu/nigms/comm/submit/collpolicy.html	
National Institute of General Medical Sciences	2001	Report on the First Community Consultation on the Responsible Collection and use of Samples for Genetic Research, September 25-36, 2000	http://www.nigms.nih.gov/news/reports/community_consultation.html	
National Institutes of Health and Indian Health Service	1999	Roundtable Conference on American Indian Research and Training Needs		
Romero FC	2001	Genetic Research and Native Cultural Issues, A Model of Community Based Genetic Research		
Terry S (PXE International)	1995	Lay Advocacy Organization's Blood and Tissue Bank Accelerates Research		

Appendix C. IHS Guidelines for implementing and complying with IHS Policy on specimens, draft as of April 25, 2001

I. Basic Principles, Special Concerns, and Objectives.

These IHS Guidelines are based on **three basic principles**.

1] **Tribal approval is required for all research involving the tribe.**
2] **Institutional Review Board [IRB] approval is required to all human research.**
3] **A "best practice" for IHS, researchers, and IRBs is to work in partnership with tribes.**

The IHS Guidelines are simply the *detailed steps to implement* those three basic principles. These Guidelines are a proposed floor, not ceiling; tribes or IRBs may require stricter steps.

The IHS has seven special **considerations, circumstances, and concerns**.

- Tribal governments legally control research done within their jurisdiction. IHS Guidelines must work with each tribe's Codes and procedures about research.
- Many AI/AN people have special cultural values and concerns related to patenting of genes, cloning, and the use of blood and other tissues.
- Some tribes have been stigmatized or harmed by research recently, that reinforces the fears and distrust of many AI/AN people about research.
- Most tribes want to receive maximal benefits from research in which they are involved, and want to add to their knowledge base for unto "their seventh generation" from now.
- Most tribes see their role in research differently from some researchers. For instance:
  - "Secondary analysis of data requires fresh tribal review"--but some researchers assume that secondary analysis does not need tribal approval because the data are already public or the original research had been approved;
  - "Tribal approval may be an on-going process, not just a one-time decision"--but some researchers assume that tribes do not want at least to be informed when a new genetic test is added to the original protocol, and that tribes do not want to make the decision for themselves about the level of ongoing reporting to and approval by the tribe (see [11] of The IHS Guidelines);
  - "We need ways to deal with researchers who violate our trust, because a few researchers have recently violated our trust"--but some researchers assume that tribes trust the stated intentions of researchers (see [14] of The IHS Guidelines).
- Confidentiality and anonymity are more difficult to achieve and maintain in small rural communities than in large urban areas, and when clinical data are computerized.
- Although IHS can help protect tribes, the primary protectors are each individual tribe.

The objective of these IHS Guidelines is to define **best practices**, that is, to support:

- fully informed tribal review and approval of research that will save specimens for future research, or that will use saved specimens;
- negotiations between the tribe and researcher about research procedures and the level of researcher-tribal communication acceptable to the tribe for the specific protocol;
- fully informed complete review and approval by all IRBs with jurisdiction;
- fully informed consent by each potential volunteer participant of the research that obtains specimens to be saved;
- the proper obtaining, retention and use of saved specimens that observe the limits and intents of the informed consent by the people from whom the specimens were obtained, and of the approval by the tribal government[s] and IRB[s]; and
- the future use of specimens that is based on and limited by the health priorities, values, and concerns of the tribe[s] involved, and the merits and soundness of the science.

II. The IHS Guidelines *(i.e., the detailed steps to implement the three basic principles).*

[1] All research involving tribes must have tribal approval. "Tribal approval" means a resolution by the Tribal Council or by an authority delegated by the Council.

[2] All researchers who obtain or use, and all entities that store, specimens obtained with IHS involvement must agree to these Guidelines. IHS will distribute to researchers, specimen banks, and IRBs both the Guidelines and model consent forms for specimens.

[3] If blood or tissue will be obtained directly from volunteer participants under a research protocol, both the consent process (using lay language) and protocol must specify:

- the tests to be done under the protocol;
- if any specimens will be saved.

[4] If any specimens will be saved, both the protocol and consent process must state the nature of future "secondary uses," and the process to seek approval of the future uses:

- whether the stored and maintained specimens will include identifiers;
- class[es] of tests or procedures that may be done on the saved specimens, including DNA tests, or other genetic tests, or growth of perpetual cell lines;
- if the PI or other researchers may contact volunteer participants in the future;
- location, duration, and procedures of storage and of disposal;
- if the specimens are from placenta or umbilical cord, other tissues with strong social meaning or value, or other aspects about which tribal members may be concerned, e.g., cloning, patenting specimens or material derived from them.

[5] Researchers must not engage in, and must not permit others to engage in, secondary use of specimens until they comply with all steps. "Secondary use" includes:

- tests or other uses not explicitly mentioned, either by name or as a class, in the original protocol and consent; or
- giving or loaning specimens to anyone. (That does not include another laboratory doing tests for the original researcher, if tests and laboratory were stated in the protocol. It does include another laboratory doing its own tests, doing tests not specified in the protocol, or retaining specimens.)

[6] The tribe[s] with jurisdiction must beforehand: A] be notified about (if it agrees), or review and approve, all proposed secondary uses within the original research purpose and consent; and B] review and approve all other uses. The original protocol that will store specimens must include such notification, review, and approval, in its procedures.

[7] Researchers of the original protocol, and of a new protocol receiving specimens, must track and comply with the limits on the use of each specimen imposed by IRB[s] and tribe[s], and by the consent of the person from whom it was obtained, even if the specimen is anonymous or if the person has died.

[8] Proposed secondary uses of nonrenewable specimens must be reviewed for community and scientific values. There are two obligations: 1] nonrenewable specimens should be used up only by research with high value; 2] specimens should be shared if they would benefit a volunteer or family, tribe, or society. Those two obligations are especially important for specimens not easily obtained, e.g., by surgery or biopsy. The original protocol that stored the specimens must include procedures for review.

[9] All proposed secondary uses of specimens must be reviewed and approved by all participating institution that hold, send, or receive the specimens, using their IRB or Human Research Protection

(HRP) procedures. The researcher of the new protocol must send copies of a consent form and of the tribal and IRB approvals of the original protocol, as part of the new protocol submitted for IRB review or HRP procedures. (IRBs may develop cooperative agreements to avoid duplicated IRB review.)

[10] Many "anonymous" specimens have clinical or demographic information about the people from whom the specimens were obtained. IRB review must assess if true anonymity is achieved and maintained, i.e., that identifying some people cannot occur due to combination of demographic or clinical data or linkage to other databases.

[11] If all proposed uses are within the original truly informing consent, see **Table 1**. Within the original truly informing consent means the consent cited the uses as a class (e.g., "kidney function tests") or by name. Related to original study means the stated purposes for which the specimens were obtained. A proposed use is eligible for expedited IRB review as a minor modification of protocol if it is both within the original consent and related. All other proposed uses within the original consent require full IRB review. (The IRB itself or institution's HRP procedure, not the researcher, assesses that it meets both criteria.) If the specimens are not anonymous, then: 1] the researcher must not contact individuals without their prior consent; and 2] reports identify individuals only with their consent.

TABLE 1

When all proposed uses of specimens are within the original truly informing consent:

Related to original study	Standard conditions for the new research protocol or plan:
yes	Review and approval for community and scientific value and merit; & each institution's IRB review and approval of the modification of the old protocol (or of the new protocol), potentially by expedited review; & notification to, and possibly review and approval, by the tribe; & reports (e.g., publications) identify the tribe only with the tribe's approval.
no	Review and approval for community and scientific value and merit; & full review and approval by each institution's IRB--not expedited review; & formal review and approval by the tribe; & informed [re]consent by each volunteer participant--unless 1] waived by the IRB and tribe, or 2] for anonymous specimens; & reports (e.g., publications) identify the tribe only with the tribe's approval.

NOTE: Negotiated agreements between the tribe and research may supersede what the Table has concerning tribal notification, review, and approval. (See also Discussion, below.)

[12] Proposed uses are outside the original consent, usually for one of three reasons.

- o The original consent did not include future use at all.
- o The original consent was too broad--a blanket consent to do any test--and thus was not truly-informing by today's standards. (These two consents are frequent in clinical care or older research.)
- o The future use is beyond a reasonably detailed truly-informing consent.

Future possible uses or protocols outside the original consent are so varied that a table of standard conditions is not feasible. Every proposed use must be approved by all tribe[s] and IRB[s] involved, and by the review of community and scientific value.

[13] Many new tests, like genetic tests, require pre-test counseling. If the protocol will do new tests with clinical relevance to people from whom the specimens were obtained, and if the specimens are identifiable, the researchers must specify how and when they will obtain the informed consent of each person to receive--or to not receive--the test results. (Some new tests are not CLIA approved; generally the results of non-CLIA approved tests are not given directly to the volunteer participants or their physicians.)

[14] The entities retaining specimens, and all researchers of every protocol, that obtain, store, test, or use the specimens must sign a copy of the following. The signed agreements extend these Guidelines to laboratories, specimen banks, and researchers that receive, hold, test, or secondarily use any specimen; the original researcher must obtain the same written agreement from them. The original agreements are sent to the IRB[s] and tribe[s] involved. If the new protocol is receiving specimens for secondary use, copies of the signed forms are sent to the original researcher. The tribe[s] and IRB[s] should notify funding agencies, supporting institutions, and publishers or editors of violations of these Guidelines that are not resolved.

All researchers will comply with the following for specimens and data in this project:

1. *NOT use the specimens and data received for any purpose other than those stated in this protocol and approved by the tribe[s] and IRB[s];*
2. *NOT release the specimens, or their associated raw data, to any other person or study, without the prior approval by the IRB[s] and tribe[s] involved;*

3a. *If the specimens or data are supposed to be anonymous, NOT attempt in any way to establish the identity of the subjects of the specimens or data received.*

3b. *If the specimens are not anonymous, NOT try to contact any individual or family other than as stated in this protocol, without the prior approval by the IRB[s] and tribe[s] involved, and without the prior approval of the individual.*

3c. *If the specimens are not anonymous, NOT try to obtain clinical or other information from anyone's medical or other records other than as stated in this protocol, without the prior approval by the IRB[s] and tribe[s] involved.*

The researchers understand and agree that noncompliance with this signed agreement will mean at least that the researchers should not publish or disseminate results of the research, and that the IRB[s] or tribe[s] will notify relevant funders, institutions, journals, publishers, and conferences of the noncompliance with this agreement.

[15] Storage of all specimens must provide physical security from unauthorized or inappropriate access. The disposal of specimens must be respectful.

[16] Researchers of the new protocol to use existing specimens have the same obligations as do the researchers of the original protocol. Those obligations generally include:

- to present the results of the research to the tribe[s] involved; and
- to seek tribal review of publications.

[17] Researchers must report all secondary uses, and status, of specimens in the Annual (Periodic) Re-Review to the IRB[s].

[18] Research teams must insure "institutional memory" to comply with requirements after the PI has left. Research teams should also have written agreements with their institutions to define control and responsibility over the storage and disposition of the specimens. The tribe[s] and IRB[s] involved may need to know those agreements.

[19] These Guidelines should be re-examined as experience develops, and may be modified.

III. Discussion.

Secondary research on blood or tissue specimens is increasingly sophisticated and frequent. It may benefit in the future the people and communities whose specimens are tested. For specimens that both are anonymous and exist before the research use, 45 CFR 46 § 101(b)(4) permits research on them without the informed consent of the people from whom they were obtained, because the research appears to carry no risk to them even if the tests are sensitive. However, individual members of a community may be harmed even though the specimens are anonymous for individuals, if the specimens retain the community's identification or are known to come from that community. The community at risk may be a specific tribe, a group of tribes (e.g., "tribes in the Northwest"), or ethnicity (e.g., "American Indians"). Specimens for which IHS was or is involved in collection or storage are not anonymous for ethnicity because they are known to be from AI/AN people, with the group of tribes also known. In the IHS policy, therefore, "anonymous" specimens means "anonymous only for individuals"; the specimens are identified at least as from the larger AI/AN community.

The term "anonymous for individuals" means that it is impossible for the researcher to identify individuals either:

- o directly (e.g., by name); or
- o by a combination of data elements.

The term also means that it is impossible for the researcher to identify individuals either:

- o from only the data at hand; or
- o with other information (e.g., medical records) to which the researcher has access; or
- o with information from other people (e.g., people who have access to medical records).

For specimens to be anonymous for the individual, therefore, the researcher must neither have any data, nor have access to any data with the possible cooperation of others, that alone or in combination identify one or more people from whom the specimens were obtained.

Many people fear that their specimens will be used in cloning. Cloning requires a live fresh human cell, to put that cell's nucleus into an ovum (woman's egg) to become a baby. Usual blood draws and specimens do not have or keep living cells; the nucleus of a perpetual cell is not fresh. Neither routine blood draws, specimen collections, and perpetual cell lines can be used to make a clone. To avoid an unnecessarily long consent document, it need not state that clones will not be made, unless the tribe or researcher wants that statement included.

A special consideration applies once specimens are in research, i.e., specimens either obtained directly from volunteer participants under a research protocol, or gathered originally by a process of care and now under a research protocol. The original IRB[s] must review and approve every modification of a protocol, by either expedited or full review; see 45 CFR §s 46.103(b)(4) and 46.110. Later activities modify the research protocol, if they were not stated in the original protocol. Such activities include: giving or lending the specimens to another researcher; using them for tests other than those listed in the obtaining protocol; or seeking a patent. The original IRB[s], therefore, must review and approve such activities as modifications to the original protocol; the IRBs must also determine the potential harms of the proposed modifications, and if they are within the limits of the original informed consent.

There are three basic approaches for informed consent to store specimens.

[A] One approach is a blanket consent, that permits all future uses of specimens. It maximizes future testing and flexibility, which benefits future progress in science; however it does not recognize possible harms to communities or individuals, e.g., tests for stigmatizing conditions. For example, a protocol and consent process that leftover blood will be stored for "future tests about diseases of importance to AI/AN people" is a blanket consent. It covers too much, from otitis media to alcoholism, from non-stigmatizing to highly stigmatizing conditions. Potential participants being asked to consent to such future use would be uninformed about the risks and benefits.

[B] Another approach is a detailed consent: when the specimen is obtained, participants decide whether to permit saving a specimen, what future tests can and cannot be done, and whether to be contacted about results of future tests. The approach maximizes participant control; however the control is exercised when participants lack needed information about the future. Detailed consent has three major problems: future tests are too unknown and too varied to list; future potential harms and benefits may differ from those at present; and the current circumstances and values of potential volunteer participants may change in the future, rendering a decision based on current circumstances and values invalid for the same person in the future.

[C] These Guidelines take a third approach. Each participant decides to permit or not only future use *related to the current research* to which s/he is consenting--uses with values, risks, and benefits likely similar to those of the current research. For instance, consent about specimens left over from a vaccine trial would ask for narrow future uses, e.g., "future tests about infections important to AI/AN children." As a check, the tribe must approve or be notified, and IRBs must approve, all future proposed uses. As a second check, if the future tests use identifiable specimens for purposes beyond the original consent, the volunteer participants may be asked to reconsent for the new use.

Five examples will help clarify Table 1. Consider sera from a community project screening adults for diabetes (DM), stored with identifiers; the consent permitted future tests related to diabetes or related conditions such as atherosclerotic heart disease or chronic renal failure.

(1) First row--anonymous. Researchers want to use the sera (but anonymized), to determine the prevalence in the tribe of a newly found risk factor for DM.

(2) First row--with identifiers. Researchers want to run the tests on the same sera but with identifiers, to match results with each person's chart whether or not they have DM.

(3) Second row--anonymous, important to public health of the tribe. CDC wants to test the sera anonymously for antibodies to a newly-discovered fatal infection that broke out in the tribe, to see if there have been subclinical infections in the past. (The tribe and IRBs must approve the research; reconsent is not possible due to anonymity.)

(4) Second row--anonymous, without public health importance. Researchers want to test anonymously for the prevalence of a possible new Alzheimer disease gene in this tribe with a rate of disease 1/10 the U.S. rate, to see if the gene also is less prevalent. (Because the specimens are anonymous, the requirements are the same as for [3]. The tribe could decide to not allow the research, either due to its low importance to the tribe, or simply because it is outside the original study and consent.)

(5) Second row--with identifiers, with public health importance. A new blood test to detect early cancer of the cervix has been proven in non-AI/AN women but not in AI/AN women. Researchers want to run the test on the same stored sera, and get from each women's chart who had cervical cancer. The tribe's rate of cervical cancer is 10 times the U.S. rate. (The tribe and IRBs must approve the research; reconsent by each volunteer participants may be necessary. It may be possible, however, to link clinical information about cervical cancer to specimens without seeking reconsent while satisfying the concerns and requirements of the tribe and IRBs.)

NOTE: These Guidelines were developed with both formal and informal consultation and input by tribes, tribal IRBs, Area Indian Health Boards, the National Indian Health Board, Native specimen banks, researchers, and funders.

PLEASE GIVE COMMENTS, SUGGESTIONS, OR CRITIQUES TO:

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