Secretary's Advisory Committee on Genetic Testing

***Public Meeting: A Consultation on Genetic Testing*[*]**

Thursday, January 27, 2000

School of Nursing, University of Maryland, Baltimore

655 West Lombard Street

Baltimore Maryland

Overview

The Secretary's Advisory Committee on Genetic Testing (SACGT) was chartered to advise the Secretary of Health and Human Services (DHHS) on the medical, scientific, ethical, legal, and social issues raised by the development and use of genetic tests. As part of this charge, Dr. David Satcher, U.S. Assistant Secretary for Health and Surgeon General, has requested that SACGT assess, in consultation with the public, the adequacy of current oversight of genetic tests. This assessment requires consideration of the potential benefits and risks (including socioeconomic, psychological, and medical) to individuals, families, communities, and society. As part of a multifaceted effort to consult with the public on these issues, on January 27, 2000, the Committee held a public meeting to gather perspectives on issues in genetic testing, in particular on the adequacy of current oversight. The meeting was attended by a wide range of individuals with an interest in genetic testing, including patients, consumers, health professionals, scientists, genetic test developers, educators, industry representatives, policymakers, lawyers, students, and others, and it included representatives of a wide range of diverse ethnic and racial groups.

The meeting opened with a plenary session that began with introductory presentations by SACGT members; a keynote address by Dr. David Satcher; a presentation on the history of genetic testing, including its impact on diverse communities, by Robert Murray, Jr., M.D., Howard University College of Medicine, and a presentation on genetic testing and disability rights, by Andrew Imparato, J.D., of the American Association of People with Disabilities.

Several members of the Committee provided summaries of background information for the consideration of oversight of genetic testing. (Much of the background information regarding genetic testing that was provided in these presentations can be found in the document prepared by SACGT entitled *A Public Consultation of Oversight of Genetic Tests*.) Francis Collins, M.D., Ph.D., SACGT *Ex Officio* Member spoke on "The Future

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[*] The following SACGT members were part of the Steering Group that planned the January 27th meeting: Judith Lewis, Ph.D., R.N. (Chair); Patricia Barr; Ann Boldt, M.S.; Joann Boughman, Ph.D.; Mary Davidson, M.S.W.; Edward McCabe, M.D., Ph.D. (ex officio); Victor Penchaszadeh, M.D., M.S.P.H.; Michele Puryear, M.D., Ph.D.; and Reed Tuckson, M.D. The following individuals also served on the Steering Group: Maricela Aguilar, R.N., M.S.N.; Adrienne Asch, Ph.D., M.S.; Sylvia Au, M.S.; Thomas Bleecker, Ph.D.; Vence Bonham, J.D.; Mei-Ling Chang, M.P.H.; William Freeman, M.D., M.P.H.; Jane Lin-Fu, M.D.; Ilana Mittman, M.S./C.G.C.; Robert Murray, M.D.; Donna Olsen; Pilar Ossorio, Ph.D., J.D.; and Gisela Rodriguez, M.S.W. SACGT is grateful to the Steering Group members for outstanding contributions they made in the planning and conduct of this meeting.

of Genetics and Genetic Testing and the Impact of the Human Genome Project;" Victor B. Penchaszadeh, M.D., M.S.PH., presented "What are Clinical Validity and Clinical Utility of Genetic Tests and How Do They Affect Risks and Benefits of Genetic Tests and Oversight Categories;" Mary Davidson, M.S.W., and Barbara Koenig, Ph.D., discussed "Individual and Social Risk/Benefit Issues;" and Kate Beardsley, J.D., presented information on "Current Status of Oversight of Genetic Tests and Options for Additional Oversight." These presentations were followed by a facilitated panel discussion of public perspectives on issues involved in the development and use of genetic testing.

The afternoon session included facilitated discussion groups that allowed participants to provide their perspectives and to comment on the specific issues in genetic testing upon which the public is being asked to comment. Vence Bonham, J.D., Michigan State University, moderated a report-back session, during which the group facilitators and rapporteurs presented the major points of discussion to the larger group. The afternoon session also included a public comment session and a report regarding the Centers for Disease Control and Prevention (CDC) Genetic Consortium-Laboratory Workgroup.

PLENARY/MORNING SESSION

SACGT Member Joann Boughman, Ph.D., Vice President for Academic Affairs and Dean of the Graduate School, University of Maryland, Baltimore, welcomed attendees and noted that the University of Maryland was pleased to host this public consultation meeting. Judith Lewis, Ph.D., R.N., SACGT Member and Chair of the Steering Group for the public consultation meeting, also welcomed meeting participants and expressed the appreciation of the Committee to the staff of the University of Maryland for their extraordinary efforts in supporting the meeting. She explained the various mechanisms of outreach that the Committee is using in its public consultation efforts and noted that although all of these mechanisms are important, the public meeting is especially useful in reaching members of diverse communities and engaging members of the public directly regarding genetic testing and oversight issues. Dr. Lewis noted that although the public consultation for this part of the process officially ends on January 31, such consultation would become an ongoing and integral part of the Committee's work.

Edward McCabe, M.D., Ph.D., SACGT Chair, welcomed participants and commented that in developing appropriate public policy on an issue as complex as genetic testing, it is critical to have these kinds of gatherings at which the Committee can listen to and learn from members of the public, whose willingness to share experiences and perspectives is much appreciated. Dr. McCabe reviewed the day's agenda and noted that public input from all consultation sources will be considered in the Committee's deliberations.

Keynote Address: A Call for Broad Consultation on Oversight of Genetic Testing
David Satcher, M.D., Ph.D., Assistant Secretary of Health and Surgeon General of the United States

Georges Benjamin, M.D., Secretary of Health and Mental Hygiene, State of Maryland, introduced Dr. Satcher, who began his address by noting that the Committee was asked to make recommendations for oversight of genetic testing in consultation with the public because it is an area that will affect all of us, and it is important to make sure that the public understands and participates in this process. These are complex issues that encompass both highly technical and highly personal components, he continued, and it is particularly important to ensure that the science is tied to sound policies. Although there is good reason to celebrate our progress, Dr. Satcher noted, this is only the beginning of an era in which great advances likely will be made in using genetics to help cure disease and preserve health, and these advances will require new policies that will ensure the safety of genetic testing in health care and public health. He outlined three areas that require particular attention: ensuring that genetic tests are not introduced into clinical practice until they are ready for clinical use; ensuring that continuous and rigorous quality control practices are in place; and ensuring that the public understands genetic testing and its implications.

Dr. Satcher discussed the problem of health disparities between minority and majority populations and whether growing knowledge in the area of genetics might help the effort to eliminate the gap in health status. The benefits of genetic testing, which can help predict an individual's risk of developing a genetic disease and facilitate its diagnosis, must be available to all Americans, Dr. Satcher emphasized. And because broad and diverse involvement in these research activities and programs is essential, we must address issues such as lack of access to services as well as the fear and mistrust that leads many to forego participation in programs that are available to them, especially when these programs are sponsored by the federal government. In addition, Dr. Satcher continued, because genetics has the potential to revolutionize medicine, we must work together to maximize its benefits and prevent its harms. The need to address the issue of discrimination based on genetic information is particularly critical.

Dr. Satcher noted that today's meeting will explore important issues and questions regarding the oversight of genetic testing and provide essential input and advice to the Committee. Expressing confidence that the Committee's report will represent a balanced view that includes the range of perspectives presented, Dr. Satcher concluded by thanking attendees for taking part in this important public policy process and noted that "all of us will have vital roles to play in this work of integrating genetic testing into medicine and society."

Background on Genetic Testing

A Brief History of Genetic Testing, Including Its Impact on Diverse Communities

Robert Murray, Jr., M.D., Howard University College of Medicine

In this presentation, Dr. Murray compared two national genetic testing programs for Tay Sachs disease and sickle cell disease. Both of these diseases are inherited autosomal recessive conditions. However, Dr. Murray noted that the testing programs differed dramatically in how they originated, in how they were funded and managed, and in the populations they served. The population to which the first program was targeted was highly educated, with an above-average economic status. The other program served a less well-educated, significantly poorer population. Significant distinctions between the two diseases also affected the testing programs. Tay Sachs is a disease with clearly defined parameters, a limited life expectancy, and no effective clinical treatment. Little was known about its precise pathophysiology, and prenatal testing could identify its presence in the fetus. On the other hand, although there were no tests at the time to detect sickle cell disease prenatally, the genetic cause of the disease was well-understood and its pathophysiology well known.

The Tay Sachs testing program, Dr. Murray said, was established as a result of growing awareness of the frequency of the disease in Jewish individuals, and the project was initiated by researchers in genetics. The Jewish community was educated before testing, and an accurate test was available, which was critical because the mortality rate for this disease is 100 percent. The program was so successful that today Jewish couples often have themselves tested before marriage.

Sickle cell disease began to receive public attention in 1970, and in 1972, President Nixon signed the National Sickle Cell Anemia Control Act, which authorized $115 million for sickle cell research. However, funding was never received by sickle cell programs. In the meantime, said Dr. Murray, many people continued to hold misconceptions about the disease, resulting in stigmatization, and many African Americans feared the specter of genocide, because no reliable diagnostic test for sickle cell was then available. Although sickle cell centers were established to disseminate accurate information and to conduct testing, the sickle cell testing program, unfortunately, had become a model of how *not* to run a successful program. In some sickle cell testing programs, school children were tested without their permission, counseling was provided haphazardly, and results were not always kept confidential.

By 1974, an omnibus genetics bill was introduced based upon a report of the National Academy of Science's Committee on Inborn Errors of Metabolism. The Committee identified four reasons for genetic screening: to treat or manage disease; to provide information for making reproductive decisions; to prevent the onset or manifestation of the disease; and to conduct research. It also recommended nine guidelines (derived directly from the successful approach of the Tay Sachs testing program for testing), five of which are now considered critical to any testing effort: prior education of the community, informed consent, accurate diagnosis, professional counseling, and

confidential test results. A presidential commission reviewed these guidelines in 1983 and ranked them, in order to place a greater emphasis on those questions of most concern to the scientific community and the public.

Dr. Murray concluded by expressing hope that those working in genetic testing have come to better understand the most effective approaches to implementing testing programs and that they now recognize the importance of community involvement from the very beginning of the process.

Genetic Testing and Disability Rights
Andrew Imparato, J.D., American Association of People with Disabilities

Mr. Imparato opened his presentation by summarizing the history and activities of the American Association of People with Disabilities (AAPD), which was founded in 1995 to promote the political and economic empowerment of the 54 million children and adults with disabilities in the United States. The founders used the AARP as the model for a large cross-disability membership-based organization, and AAPD now has approximately 11,000 members. He encouraged meeting participants to visit AAPD's Web site at http://www.AAPD-DC.org.

The issue of genetic testing, Mr. Imparato noted, is one of increasing concern in the disability community, because it could have a wide range of critical effects upon individuals with disabilities and their families. Most notably, it could cause discrimination in a number of areas.

He then discussed the differences between the social model of disability as opposed to the medical model, which tends to equate disability with illness and medical intervention. It also tends to associate any negative life consequences experienced by people with disabling conditions as inherent in the conditions themselves. The social or civil rights model, by contrast, encourages people to recognize those with disabilities as a minority group that experiences discrimination based on fears, myths, and stereotypes. This model recognizes that disability is a natural part of human experience and does not necessarily limit a person's ability to make choices, live independently, pursue a meaningful career, or participate fully in all aspects of society. It also acknowledges that many of the most isolating and harmful aspects of living with a disability derive not from the condition itself, but rather from society's repeated failure to accommodate individuals who differ from the norm in human functioning.

The potential for discrimination in genetic testing remains largely unexplored, he said. In relationship to prenatal testing, for example, one must ask what kind of assumptions counselors are making about the quality of life experienced by individuals with Down syndrome or spina bifida or about the quality of life for families with members who have these conditions. Couples should be asked to identify their goals as parents and their aspirations for their children and should be encouraged to discuss how those goals or aspirations will be affected by having a child with one of these conditions. Citing his personal situation, he noted that because he has bipolar disorder, it is his responsibility as a parent to be alert to the possible presence of the disease in his two young sons. But, he

asked participants, how can he be assured that information about his genetic condition will not be used by insurance companies and other organizations to discriminate against his sons?

Mr. Imparato concluded by telling participants that the overarching question he would like them to consider is whether the benefits that can be derived from genetic testing will ever outweigh the strong potential for genetic information to be used to discriminate against people with genetic conditions in the same way that human cultures have, for centuries, discriminated against children and adults with disabilities.

Facilitated Public Perspectives

Donna Olsen, Indiana State Coordinator for Family Voices, and **Reed V. Tuckson, M.D.**, Senior Vice President, American Medical Association and SACGT Member, facilitated this session, during which individuals from throughout the country shared their personal experiences regarding genetic testing and genetic testing issues. The presentations were followed by a brief question and answer period.

The first discussant was **Yolanda Aguilar, M.Ed.,** a special education teacher with a special needs children's program in San Antonio, Texas. Ms. Aguilar regularly deals with the concerns of parents and students regarding the meaning of their diagnoses of genetic disease and the risk of recurrence, as well as other issues. She also serves as a board member of the Texas Fiesta Educativa, an organization that educates Hispanic families, about the services that their children can receive through the San Antonio school system.

Ms. Aguilar's mother was exposed to rubella and had her gall bladder removed while she was pregnant with Yolanda, exposing both of them to the effects of radiation and anesthesia. Ms. Aguilar was born with severe visual impairments, having developed congenital cataracts. Because of difficulties in obtaining health insurance coverage, surgery for her condition was delayed for several years. However, she did receive appropriate care after her father became a civil servant and her family received health insurance benefits. She attended school with her peers and looked forward to attending college, marrying, and having children. However, it later became clear to Ms. Aguilar, who has developed glaucoma and asthma, that she had not realized the full implications of her mother's experience on her own life. For example, because of preexisting condition clauses in insurance policies, Ms. Aguilar has had a difficult time obtaining health insurance. In addition, during the process of attempting to get health insurance, she has been forced to provide companies with information about herself that has resulted in denial of coverage, an experience that has heightened her concern that insurance companies might use the results of genetic tests improperly. Ms. Aguilar also has had a difficult time selecting physicians and has found that health insurance companies do not always classify drugs similarly, sometimes placing a needed treatment out of reach because it is designated as experimental. In addition, while in high school and college, Ms. Aguilar, who has decided not to have children, saw two of her friends with similar problems give birth to children with severe blindness, even though they had both undergone genetic counseling when they got married and were told that their children

would be healthy. Now she has former classmates who are seeing their grandchildren born with the same problems.

It was through the process of learning more about the role of genetics in her life and seeing how it has affected others that Ms. Aguilar realized that although genetic testing is generally beneficial, there is a great need for people to know more about it. Ms. Aguilar emphasized the need for efforts to improve education about genetic testing among the general population as well as among educators.

Randy Alexander is Chairman of the Iron Disorders Institute based in Greenville, South Carolina. Mr. Alexander has spoken frequently on issues of genetic testing and hereditary hemochromatosis (HH). In 1990, after a year of undergoing blood tests, he was diagnosed with HH, a metabolic disorder that involves excess accumulation of iron in the body, and was told that he likely had only six months to live. He kept this diagnosis hidden from others for many years. However, the discovery of the gene for this disease in 1996 and the testing that then became available validated the disorder's existence for Mr. Alexander, and he has become involved in working to increase awareness about HH among consumers and health professionals. Currently, he is writing a book based on his experiences.

Mr. Alexander explained that his brother and sister were initially misdiagnosed. His brother was prescribed iron pills for two years for his symptoms, and his sister, who was not correctly diagnosed until she was able to be genetically tested, was nearly institutionalized as a result of her symptoms.

Mr. Alexander noted that especially after many years of promoting the benefits of iron in the body, the challenge of educating the public and medical professionals about the adverse effect of excess iron and iron imbalance, an underlying cause of many diseases, is a daunting one. Because HH is a metabolic disorder involving iron accumulation over a lifetime, there is nothing you can do about HH at a young age, said Mr. Alexander. Although some have called for newborn screening for HH, the Institute's position (guided by its scientific review board), and Mr. Alexander's personal opinion as well, is that such screening is not appropriate.

The Iron Disorders Institute has received a warm reception from the CDC, where it has generated a heightened awareness regarding HH, now one of the hottest topics in medicine. Mr. Alexander commented that with increased funding, great progress is being made in understanding and treating HH, and he concluded his presentation by stressing the importance of educating the public about genetic testing and of ensuring that testing is conducted appropriately, with the necessary privacy protections in place.

Mei-Ling Chang, M.P.H., is Executive Director of Hui No Ke Ola Pono, the Native Hawaiian Health Care system of Maui. She is the daughter of a Kanaka Maoli (Native Hawaiian) mother and a second-generation Chinese father. Currently, she leads a cancer research team on Maui that studies the health behavior patterns of the Kanaka Maoli, and her knowledge of the Native Hawaiian experience with research studies has greatly informed her perspective on genetic research.

Ms. Chang described the cultural perspective of many Native Hawaiians, which emphasizes the sacred nature of all life. In Hawaii, she explained, people are called the "flowers of Hawaii," the progeny of the gods, and they believe that by caring for one another—a central value—they are connected to each other and to all things in the earth and the cosmos. This represents a distinctly non-Western perspective that leads many Native Hawaiians to avoid participation in a health care system that they perceive not only as at odds with their culture, but as uncaring and even inhumane. Thus, most Native Hawaiians, who say they would "rather die than enter an uncaring health care system," do not take advantage of screening and treatment services for heart disease, diabetes, and cervical and breast cancer—even when those services are offered at no cost. Statistics bear this out. According to Ms. Chang, Native Hawaiians die more frequently of breast and cervical cancer and cardiovascular disease than members of any other ethnic group. Her message to the Committee was that it has a tremendous opportunity to ensure that cultural context is appropriately considered in bringing the message about the benefits of genetic testing to specific communities.

While living in Milwaukee, Wisconsin, **Christine DeMark,** who currently works full-time in a retail store in Livonia, Michigan, decided to undergo testing at the University of Michigan for the Huntington disease mutation, after she learned that her mother had been diagnosed with Huntington disease. She spoke about how her diagnosis has profoundly affected her both professionally and personally. For example, Ms. DeMark's employer, a self-insuring company, after learning of her test results, decided it would not be able to meet her future health care requirements and fired her. (Ms. Demark decided not to pursue legal action against her ex-employer for her termination, because of the difficulties such action might have created for her in finding employment in the relatively small town of Milwaukee.) In addition, Ms. DeMark's fiancé broke off their engagement soon after learning of her diagnosis.

She told the Committee that she felt extremely fortunate to have been able in 1995 to go through a testing protocol that included a strong counseling component with a genetics counselor at the University of Michigan. Ms. DeMark credits this protocol with saving her life, because it helped her to consider many practical issues, such as making sure that she had health and life insurance before receiving the test results and preparing her emotionally for the possibility of receiving positive test results.

At the same time, she said, the havoc that the test result has wreaked in her and her family's lives has been inestimable. For example, while caring for her mother, who died of the disease, Ms. DeMark, who at this time is still asymptomatic, believed she was witnessing her own future as she saw her mother being abandoned by family and friends. She commented that although counseling has helped her cope and modify her overall perspective, her mother's death and her own diagnosis are constantly on her mind and affect all of her relationships. She concluded by stressing to the Committee the importance of providing effective protocols that include counseling to those who are undergoing genetic testing.

The next presenter, **Robert Miyamoto, Ph.D.,** is Principal Physicist at the Applied Physics Laboratory at the University of Washington in Seattle. His 13-year-old daughter, Tamara, has neurofibromatosis (NF), and as a result of his experience with NF, Dr. Miyamoto has become involved in politics in Washington state and at the national level and has become active in the debate on genetic testing. Dr. Miyamoto said that because neither he nor his wife have NF (or have undergone NF testing), it was a shock to find that they are now involved with genetic issues.

In describing Tamara's diagnosis, Dr. Miyamoto explained that her pediatrician expressed concern about several suspicious-looking birthmarks when Tamara was born. When Tamara was about six months old, the pediatrician referred them to a local dermatologist (who also was a geneticist), who told Dr. Miyamoto and his wife that Tamara might have NF and began to explain the implications. However, although the pediatrician was able to say that Tamara, who still looked and acted like any other six-month-old child, might develop potentially disfiguring tumors on her skin, tumors in her central nervous system, optic gliomas, bone deformities, learning disabilities, and mental retardation, it was not possible to predict exactly how the disease would progress. Dr. Miyamoto explained that this meant that he and his wife had to make many decisions based on intuition and educated guesses. For example, they are currently debating whether Tamara should have surgery on tumors that are compressing her spinal cord, because they do not know whether the tumors will continue to grow.

Technically speaking, genetic testing is about statistical relationships, commented Dr. Miyamoto. However, most of us do not understand statistics or view this testing in terms of science, and the science of genetic testing is not the crucial element. Rather, he stressed, what is important is the way the information is used and the decisions that are made based upon it. He emphasized that the purpose of genetic tests is to help us make better decisions about these matters throughout our lives, and the important question to ask is whether better decisions can be made with improved genetic testing. Dr. Miyamoto emphasized that understanding what a genetic test means is critical; poor decision-making may result without such understanding.

If the issue before us is one of oversight, he concluded, it is essential that we determine how to best communicate this information to the user. Those responsible for oversight can continue to maintain a mystical view of genetics by allowing the use of genetic tests to be built upon a language that is hidden from common sense, or it can ensure that follow-through occurs that evaluates the process of genetic testing all the way through to the end user and the decisions that are made based upon the test.

Victoria Odesina, R.N.C., M.S., C.S., is a clinical nurse specialist at the Charter Oak Terrace/Rice Heights Health Center in Hartford, Connecticut. She has served as a representative of the Alliance of Genetic Support Groups on the Genetic Testing Task Force and is the past Co-Chair of the New England Regional Genetics Group. The mother of two children with sickle cell disease, Ms. Odesina's eldest daughter was diagnosed with sickle cell at the age of six months. At that time, Ms. Odesina learned that newborn screening had been available for the disease, but unfortunately, it was not

available in the state in which they were residing at the time. When her next daughter was born two years later, Ms. Odesina requested screening.

Originally from Nigeria, Ms. Odesina struggled with her decision to request testing, as she and her husband feared the stigmatization that might follow the results. But she realized that by having the test, her daughter would be able to receive treatment and take advantage of whatever medical advances were available. Unfortunately, the pediatrician did not provide much information about the advances in sickle cell management and simply gave Ms. Odesina instructions to monitor the children. Ms. Odesina explained that she received no pre-counseling, post-counseling, or disease education and experienced enormous difficulties obtaining information about sickle cell disease and its management.

In addition, Ms. Odesina has seen recent evidence of lack of informed consent for newborn screening. For example, in the past year, she said, newborn screening results for her brother-in-law's baby were positive for the sickle cell trait. The baby's mother, who knew after the heel stick was performed that her baby was tested for phenylketonuria (PKU) but not sickle cell, asked whether Ms. Odesina's work with sickle cell patients was the reason her baby had been tested. We must find a way, said Ms. Odesina, to educate the public about the conditions for which newborn screening is conducted. In addition, it is important to understand that informed consent is far more than a signature on a dotted line; informed consent must be educated consent, no matter what kind of genetic test is being conducted.

In addition to discussing other problems she has encountered with genetic testing, including discrimination, Ms. Odesina emphasized the importance of ensuring that providers are sufficiently knowledgeable to interpret test results and to refer patients to the appropriate services. It also is critical, she stressed, to ensure that sufficient numbers of providers are available and that genetic counseling, health services, and education provided to a community are culturally appropriate and sensitive. Oversight, she suggested, should be conducted by a consortium that includes all stakeholders, including the federal government, state governments, communities, consumers, insurers, and others.

Traci Powell, who is currently pursuing her doctorate in genetics at Stanford University, has Friedreich ataxia**,** a rare recessive neurological disorder. Ms. Powell, who now uses a wheelchair, experienced her first symptom, abnormal reflexes, at age seven. But because Friedreich ataxia is difficult to diagnose, and because she had no other symptoms, the diagnosis was not made at that time. By age 11, she began to experience problems with her handwriting and difficulties riding a bicycle and climbing stairs. However, she remained undiagnosed until she was 19 years when she began having trouble walking. Her physician, a neurologist, presented the diagnosis to Ms. Powell in a manner that was devastating to her, telling her that by age 35, she would be either a bedridden vegetable or dead.

Ms. Powell went on to explain that in her family, genetic testing is not considered a major issue. Both she and her mother have had genetic testing, and her siblings will have carrier testing when they get married. She emphasized that there is, however, a great need to

learn about how families and people are going to use testing. One of the main points Ms. Powell wished to make to the Committee is that policymakers need to hear more about people's experiences in this area in order to gain insight regarding how genetic testing is used and to understand the range of problems associated with it. In addition, she said, it is important to consider the usefulness of genetic testing for consumers within the context of their individual views and beliefs about the causes of disease, whether environmental or hereditary, and their different ways of understanding disease.

Brian Sydnor, who works as a Legislative Liaison for the Democratic Leader, Michigan House of Representatives presented the concerns and recommendations that were expressed by participants of two dialogue groups of middle-income African Americans in Lansing, Michigan. These groups are sponsored by the Communities of Color and Genetics Policy Project (a collaborative effort by Tuskegee University, the University of Michigan, and Michigan State University, sponsored by the National Institutes of Health [NIH], National Human Genome Research Institute, Ethical, Legal and Social Implications Branch). Mr. Sydnor's group met in November and December 1999 for five weeks, specifically to discuss the issues in SACGT's *Public Consultation on Oversight of Genetic Tests* document. Mr. Sydnor is the past President of a Community Service Organization, Omega Psi Phi Fraternity, Sigma Upsilon Chapter, and is a Community Advisory Board Member for the Communities of Color and Genetics Policy Project.

Mr. Sydnor commented that although participants in the dialogue groups expressed enthusiasm about the cutting-edge research that is occurring in genetics and the benefits that can be expected to emerge from it, they also expressed a number of concerns in the following areas.

Cost. This technology is expensive, and costs should be determined in a fair and equitable manner and should not include unnecessary add-on expenses. If the technology to conduct a test is too expensive, little will have been accomplished to improve detection and to determine methods of prevention and treatment for everyone. Mr. Sydnor commented that ensuring that tests are affordable is essential to getting large numbers of people to take them.

Access and confidentiality. It is vital that all communities have access to these tests, but access to the results should be limited only to those with a need to know, with the consent and knowledge of the test subject. Moreover, the results of these tests should not be sent to a medical information bureau, because doing so increases the likelihood that the patient could lose control of the test and be harmed by potential employers or insurers. Self-tests that could be taken at home might be a solution to this problem.

Education. Over the past several decades, the government has given the African American community many reasons to be skeptical of offers of assistance. These examples, particularly the Tuskegee experience in Alabama, are still fresh in the minds of members of the African American community. Therefore, to help reduce fear of these tests, a major educational component should be a part of all genetic testing, and

additional medical personnel will be needed, who must become involved in all levels of research.

To encourage African Americans to enter the field of medical research, the emphasis on having fun while learning science must occur at the earliest stages of education. This will help to break down the barriers that have existed for so long between the African American and scientific communities.

Clinical studies. Large numbers of African Americans must become involved in clinical studies. This would increase the likelihood that they will believe that such studies are genuinely intended to address their particular ailments and concerns, and it would enable researchers to gather reliable data applicable to the African American community.

Strict regulation of testing and the results. Because it is likely that a host of genetic tests will be available in the future, and because these tests will be varied and diverse, the highest degree of scrutiny and protection should be applied to all of them. It is better to err on the side of caution, rather than risk that results will fall into the hands of those who may use them in unintended and possibly harmful ways.

Message delivery. It is important to remember that getting the word out to the African American community no longer depends so heavily on using the African American church. Other outlets, which could include popular entertainers and sports figures, must be tapped in order to disseminate vital messages to the masses. It is important to use the messengers of yesterday as well as today in order to effectively reach the community.

Protection of samples. Protection and proper disposal of blood samples are essential. One member of a dialogue group expressed concern, after having undergone many different types of tests for prostate cancer, about the possibility of his sons and grandsons being discriminated against in employment and insurance because of a possible predisposition to prostate cancer. Others expressed concern about what happens to blood samples that are drawn by law enforcement agencies. Will the DNA samples of individuals who are found to be innocent be placed in a huge databank, or should those samples and all data identifying the individuals from whom they were taken be destroyed? Group participants strongly encouraged that these samples and identifying data be destroyed.

Mr. Sydnor concluded by emphasizing that strict controls must be in place to ensure that the public is protected from those who may use this technology and the results in harmful ways. He also commented that “we wish to emphasize that we share the same concerns that majority communities express in the area of genetic testing. We, too, want what is best for society as a whole.”

The last presenter, **Dorothy Thomas**, of Albuquerque, New Mexico, is an elementary school teacher working for the Bureau of Indian Affairs. She shared some of the perspectives of the Native American community regarding issues that involve genetic testing, as well as some of her personal experiences as a breast cancer survivor. Ms. Thomas was diagnosed with breast cancer 14 months ago and is the only member of her family, including her four sisters, to have this disease. During a routine exam, a lump in

her breast was found, and after undergoing a lumpectomy and being diagnosed with cancer, she was advised to have chemotherapy but decided instead to have a radical mastectomy. Fortunately, her lymph nodes were clear. Ms. Thomas explained that she knew intuitively that her tumor was not fatal and chose to take a five-year course of tamoxifan instead of undergoing chemotherapy. One year has now passed with no evidence of recurrence.

Her message to the Committee was to listen to the individual involved—the one who has to make treatment decisions—and to respect that individual's intuition about his or her condition. It is also important, she said, to consider cultural context in these decisions. Native Americans, for example, do not typically focus on what may have caused an illness. Instead, they accept those who are ill and/or different into the community and do the best that is possible. For example, Ms. Thomas had a student with Lang syndrome who was not expected to live past the age of 10. He is now 25 years old and, because he was accepted into the community, he routinely participates in all of its ceremonies. It is also important to provide education about genetic testing, said Ms. Thomas, who observed that many in the Native American community who have undergone genetic testing were unaware that the testing was being conducted or did not understand its significance.

Question and Answer Period

- Arthur Holden, who is involved in genetic research, leading the largest private effort to detect single-nucleotide polymorphisms (SNPs), asked members of the panel to explain practical ways in which education about genetic testing could be improved. In response, several panelists stressed the importance of ensuring that information about genetic testing is available and understandable to the public and that this information is useful to all parties, including insurance companies and the medical community. Panelists also suggested that educational materials should be provided to different groups for their review and comments regarding readability and understandability and that it is important to understand and appreciate the variety of adult learning styles.

Another suggestion was to use other models, such as the one used for immunization, to educate people about genetic testing. The work of the Genetic Awareness Coalition and the National Coalition of Health Professional Education in Genetics was also mentioned. Panelists agreed that educational materials do not need to be overly technical and that identifying sources for help and referrals is more important than providing detailed technical knowledge. Panelists also stressed the importance of becoming involved in schools, where the science of genetics is being taught, and of teaching what the numbers mean and how they affect lives. One panelist commented that how the information is being used, rather than simply its technical meaning, must always be kept in mind.

- Dr. Kathleen Rand-Reed, a practicing applied bicultural anthropologist with a background in marketing, commented that in working to help foster dialogue between scientists and families, she has found that some groups prefer to be spoken to in a common language, so that they are assured that discrimination is not occurring, but that

some populations want to hear tailored messages so that they know that there is sensitivity to their particular situation and needs. She asked the panel to identify what messages should be universal and what messages should be directed to specific populations.

Mr. Sydnor commented that a community wants to be informed of the risks and benefits of genetic testing, but it wants the message to be relayed with sensitivity and does not want to receive this information through scare tactics. There is a need to be both sensitive and culturally sensitive. Ms. Chang suggested that it also is important to know how long a program will be in existence and what will happen when the funding disappears for a particular program.

- Lee Brown, of Howard University, commented that there appears to be a great deal of apprehension regarding the ability of science to attend to the real needs of people, and he wondered if panelists could explain what science has to do to treat people more humanely and how the new procedures of genetic testing can be conducted in a way that will facilitate healing.

Ms. Chang replied that there needs to be a recognition that science does not exist for the sake of science; rather, it exists as a tool for people. Science, she said, must learn the heart and the core of what it means to be a human being. Ms. Chang commented that the knowledge of what it means to be human from both spiritual and scientific perspectives is important in closing the gap that is keeping Native Hawaiians from being healthy and living longer. Perhaps, she suggested, "we can offer science a little bit of humanity."

- Ms. Sasa Ewaliko from Hawaii explained that a number of her family members have been diagnosed with a rare disease called CADASIL. She said that it has been extremely difficult to find information about this disease and to get appropriate referrals. She asked the Committee for assistance. Dr. Tuckson thanked her for "ending this session in a very human and poignant way" and asked members of SACGT to provide her with information and assistance.

Ms. Olsen ended the session by noting that a common thread throughout these presentations was the importance of education. She encouraged the forming of partnerships between medical professionals and families to improve the education of community members and health care professionals about genetic testing. She also suggested that families and community groups must become part of any sort of consortium that is created to address genetic testing oversight issues.

Wrap-Up of Morning Session and Charge to Afternoon Discussion Groups
Patricia A. Barr, SACGT Member
Judith Lewis, Ph.D., SACGT Member

After Dr. Lewis provided a brief overview of the format for the afternoon discussion groups, Ms. Barr expressed appreciation to the discussants for sharing their personal experiences and perspectives with SACGT. She pointed out how enormously helpful the session was in illustrating the importance of placing science in a social context and that

we must always consider the perspectives and points of view of the people who will use these tests. Although different points of view will always exist, she concluded, all of us want quality health care, and there is no doubt that the quality of the care that is provided must match that of the best possible science.

AFTERNOON DISCUSSION SESSIONS

Discussion Groups

Each participant attended one of 11 discussion groups that were formed to provide meeting participants the opportunity to consider the specific issues and questions regarding oversight for genetic testing that are outlined in the SACGT document, *A Public Consultation on Oversight of Genetic Tests*. Each group had at least one facilitator, a rapporteur, and when needed, a science advisor. Facilitators and rapporteurs presented results during a continuation of the general session later in the afternoon.

PLENARY/AFTERNOON SESSION

Report of the CDC Genetic Consortium-Laboratory Workgroup

Patricia Charache, M.D.

Dr. Charache, who is a member of both SACGT and CLIAC, explained that at the SACGT meeting in October, CDC agreed to convene a meeting of public and private groups to explore the question of whether a public-private consortium could provide additional oversight of genetic testing and whether it was feasible option. Although the January 25-26 meeting was cancelled because of inclement weather, some of the participants met to discuss issues. They included Dr. Edward Baker of the CDC, and representatives from the American College of Medical Genetics, the Association of Molecular Pathologists, the CDC, the College of American Pathology, the Genetics Working Group of the Clinical Laboratory Improvement Advisory Committee (CLIAC), the Health Resources and Services Administration, the National Newborn Screening and Resource Center, and NCCLS. The meeting of the full workgroup was rescheduled for February 23 in Washington, D.C.

Public Comments

Carol Isaacson Barash, Ph.D., Principal, Genetics, Ethics and Policy Consulting, Consultant to Orchid Biocomputer, Inc.

Dr. Barash noted that the SACGT consultation document does not acknowledge several uses for genetic tests, including pre-implantation diagnosis, SNP testing, and multiplex testing, and she commented that the need for recommendations relevant to these tests must be addressed. Dr. Barash also noted that decisions about the degree of oversight for specific genetic tests should be based upon the value of the information that a test result provides. In addition, the value and significance of the information and the test's medical benefit must be weighed against the potential for that information to be used *against* the

person being tested. She commented that a tendency to rank genetic risks can create confusion, because not all genetic risks are the same.

Sandra Brandley, Executive Director, Alpha 1 Association

Ms. Brandley explained that the Alpha 1 Association is an advocacy and education organization created to benefit those affected by alpha-1 antitrypsin deficiency, a common genetic disorder that affects at least 100,000 people in the United States but that remains largely underdiagnosed. Alpha-1 antitrypsin deficiency manifests itself most commonly as lung disease in young adults and less commonly as liver disease in infants and children. Unlike other genetic disorders (such as Huntington disease), the presence of the alpha-1 gene defect does not necessarily mean that the individual will develop symptoms of the disease. Still, the earlier a patient is diagnosed, the more opportunities are available for treatment and lifestyle changes to halt or slow the progression of the disease. An even greater problem, however, is that many individuals must battle not only the effects of the disease but discrimination. Ms. Brandley emphasized that genetic privacy laws must be in place and enforced in order to ensure that discrimination cannot occur. Using the model developed by the HIV/AIDS community (although alpha-1 is not a communicable disease), blind genetic testing can be done, so that individuals can be informed of their genetic results without risk of discrimination. Ms. Brandley concluded that individuals considering this test should seek guidance and genetic counseling from trained health care professionals, because there are significant risks and benefits to genetic testing for alpha-1.

Michael Sprinker, CIH, Director, Health and Safety Department, International Chemical Workers Union Council

Mr. Sprinker began by commenting that there is a saying in labor that "you leave a lot of your rights at the door when you walk into work" and that this seems to be true when it comes to genetic testing. He noted that the concept of "industrial psychology" has come to be interpreted as "behavioral safety" (emphasizing fixing the worker rather than fixing hazards in the workplace) and that the union is concerned that employers will implement genetic testing in an effort to identify "safer employees or employees less susceptible to illness and injury." The selling of "quick fix" approaches to workplace safety and health will increase quickly with unproven genetic testing methods and with the misinterpretation of certain alleles indicating somewhat elevated risk ratios. He urged the Committee to focus on the issues surrounding the potential problems of testing for workplace "suitability" as well as the possible effects of genetic information being used in worker compensation systems. At this time, he said, worker compensation carriers routinely require that anyone submitting a claim for any injury or illness must release all medical records.

Suzanne Feetham, Ph.D., R.N., F.A.A.N., American Academy of Nursing

The American Academy of Nursing (AAN), Dr. Feetham said, concurs in general with the considerations of the Committee. Increasingly, she said, patients will expect nurses

and other health professionals to clarify and interpret information gained from genetic tests. She continued by noting that nurses advocate for the right of all to have accessible health care, including genetic testing and counseling services; however, at the same time, it is necessary to assess the actual benefits and utility of genetic testing and through oversight to protect the confidentiality of this information. In addition, AAN argues that although advances in knowledge about genes, genetic research, and genetic testing are beginning to bring benefits to the public health, a number of major ethical, legal, social, economic, and educational issues remain unaddressed. Dr. Feetham further noted that the public understanding of genetic testing tends to be in terms of gene discovery and the expectation of developing better treatments and cures for specific diseases, even though the potential in these areas is often not accurately presented.

The AAN views the issues of informed consent and the privacy of genetic information as major factors in its recommendations, which Dr. Feetham summarized as follows: "that sensible, systematic, and meaningful regulation of genetic tests and genetic test kits must be developed. The marketing of tests should be allowed, but only after proper clinical validation and clinical utility; full disclosure of risks must be provided; the public must be assured that genetic testing will remain voluntary; and health care coverage must include the desired genetic testing and counseling services." In addition, AAN has identified seven categories of tests that fall into what it considers the "higher scrutiny areas:" new tests or tests not yet validated in diverse populations; tests that are predictive rather than confirmatory; tests for disorders with no available treatment; tests that will be applied to a large segment of the population; tests to be used on children to detect the likelihood of their developing later onset disorders; tests for disorders with low penetrance; and widespread testing for low-incidence conditions.

Michele M. Schoonmaker, Ph.D., Director, Medical Reimbursement and Government Affairs, Vysis, Inc.

Dr. Schoonmaker opened by noting that Vysis, Inc., is the only manufacturer of genetic tests that offers five Food and Drug Administration (FDA)-approved *in vitro* diagnostic kits using DNA probes. She called the Committee's attention to three major points. First, all genetic tests are designed to identify a particular genetic marker. However, although the detection technologies will differ depending upon whether the target is a nucleic acid or a protein, the development of the actual tests will be the same as those in clinical chemistry or any other laboratory testing market, and some tests will be performed as laboratory services, while others will be developed by manufacturers and sold as kits. Any additional burdens of proof beyond those currently required by the FDA are likely to create a disincentive for companies to standardize quality control and commercialize genetic tests and will reduce the genetic test manufacturer's ability to compete in the medical testing market.

Second, the FDA's risk-based classification scheme for diagnostic devices also works for genetic tests. Thus, if a clinical trial can economically and feasibly be completed, then the test should undergo FDA review, regardless of whether or not the developer intends to distribute the test to other users. Otherwise, current oversight regulations are adequate.

Finally, diagnostic tests are evaluated primarily to obtain regulatory approval and insurance coverage. For a kit manufacturer, these processes are separate, time consuming, and expensive. Dr. Schoonmaker urged the Committee to consider an oversight option that would allow a test developer to request concurrent payer and regulatory review, in order to increase the efficiency and lower the cost of collecting data in the time currently allotted for regulatory review alone. In addition, although cost data should not be a criterion for obtaining approval, a test developer should have the option to submit cost data voluntarily. Following approval, any additional data required beyond the scope of the trial could be collected during a post-market surveillance period.

Christine Brunswick, Vice President, National Breast Cancer Coalition

Ms. Brunswick began her remarks by noting that she is not only the vice president of the coalition, a grassroots advocacy organization, but a breast cancer survivor as well. She added that the coalition recognizes that genetic testing offers great opportunities for the advancement of the diagnosis and treatment of disease. But, she added, the coalition is also concerned about the limitations of genetic testing and the need for the federal government to ensure that the public is effectively protected. The coalition believes that all genetic tests must meet a rigorous approval process similar to that used for kits, and that the FDA must play a major role in this process. The coalition also believes that legislation must be promulgated to protect individuals against genetic discrimination.

Ms. Brunswick emphasized four major points. First, all genetic tests, including "home brews," must meet federal minimum standards before being approved and used outside of a research setting. Each intended use of a test must be validated, and for genetic tests that predict life-threatening, chronic, or disabling diseases, a particularly stringent level of scrutiny must be applied. Genetic tests that fall under this stringent scrutiny category must be made available only if and when the clinical validity of the test is fully established. Second, the FDA must use its current regulatory authority to increase oversight of all genetic tests, including "home brews," and the process must include expanded oversight for the protection of human subjects participating in all genetic test research. Third, health care professionals and Institutional Review Boards (IRBs) must be educated about genetic testing and its implications, because the value of genetic tests will be realized only if the professionals who administer and interpret those tests, as well as the IRB members who review them, understand their benefits and risks. Finally, before they consent to undergo testing, individuals must be fully informed of a genetic test's benefits and risks. They must also understand the social, psychological, medical, and economic impact that the test's results may have on themselves and their families. "Although incredible scientific advancements in genetics hold great promise and hope," Ms. Brunswick concluded, "we must be mindful of the speed and manner by which we adopt and use genetic tests in the delivery of medical care."

Emily Winn-Deen, Ph.D., American Association for Clinical Chemistry

Dr. Winn-Deen opened her remarks by informing the Committee that the American Association for Clinical Chemistry (AACC) is a professional organization that represents nearly 11,000 professional laboratory scientists, including physicians and medical technologists. The primary objectives of AACC are to improve clinical laboratory science, to further the public interest, to educate, and to help maintain high professional standards. AACC also shares the objective of SACGT to ensure that genetic testing is performed accurately and that results remain confidential. The association believes, however, that the current framework—as administered by the CDC, the Health Care Financing Administration, and the FDA—adequately protects patients. The group's primary message, she said, is to urge the Committee not to make an artificial distinction between genetic and other kinds of laboratory testing, because all clinical testing uses analytical techniques that isolate, characterize, and/or quantify clinical analyses, and all analytical techniques can be subject to imprecision and inaccuracy. In addition, safeguards against these errors already exist under CLIA.

The members of AACC also agree that it is not feasible to implement differing levels of scientific and analytical scrutiny based on the intended use of a test. The association agrees that patients have a right to be informed of the reasons for and the possible implications of their genetic tests and supports greater physician education in this area. Dr. Winn-Deen concluded by referring Committee members to her written comments.

Tene Hamilton, National Center for Bioethics in Research and Health Care, Tuskegee University

Ms. Hamilton began by stating that the goal of the Communities of Color and Genetics Policy Project (a collaborative effort by Tuskegee University, the University of Michigan, and Michigan State University) is to elicit policy recommendations regarding genetic technologies. Tuskegee, Alabama, is well known for the United States Public Health Service (USPHS) Tuskegee Syphilis Study, she noted, and even today, in this part of the country, a significant lack of trust of health care providers and the health care profession in general still exists. Ms. Hamilton informed the Committee that Tuskegee University is in the process of holding public group discussions about genetic testing and research. The concerns expressed by participants led to the project's recommendations that those being tested should be assured access to accurate genetic information, in both clinical and research areas; that professionals should be educated about genetic testing so that they can convey accurate information to their patients; and that informed consent should be considered integral to ensuring the rights of consumers. In addition, the demographic makeup of the community should be represented on local IRBs so that the community can adequately be represented and informed about all aspects of genetic research. Implementation of these recommendations, Ms. Hamilton concluded, will help foster a relationship of trust with researchers and the community, which will help ensure that another tragedy such as the USPHS Syphilis Study at Tuskegee does not occur.

Deborah Kent

Ms. Kent told the Committee that the purpose of her comments was to offer a different perspective—that of the consumer. She was born with a condition which caused her to be completely blind from birth. However, because her family was loving and encouraged her to take part in every aspect of life, she felt "very normal" about herself, and eventually became a professional writer of children's books. When she and her husband considered becoming parents, they knew that their child could inherit her condition and also be blind, but they did not believe that the lack of sight would deny their child the potential to live a fully meaningful life. "As we think about the uses and implications of genetic testing," she said, "I hope that we can always be aware that human beings are so very much more than their medical symptoms or their physical limitations and that every human life has potential." What must be kept in mind, she concluded, is that because a great deal of misperception about disabilities is based on fear, it is critical that all those in the field of genetic testing consider the ways that society perceives individuals with disabilities or medical conditions and creates roadblocks in their lives.

Gualberto Ruano, M.D., Ph.D., CEO, Genaissance Pharmaceuticals

Dr. Ruano informed the Committee that his purpose was to address the questions of how the transition from research to actual clinical practice is made and how genetic associations are validated. Genaissance, he said, is pursuing genetic associations to drug response as an area of pharmacogenetics. First, he argued that markers should not be considered individual polymorphisms but as haplotypes, the given organization of polymorphisms. Second, he argued that a genetic association must be subject to a statistically rigorous analysis. Third, it is necessary to look at population substructure, to examine the lineage of populations, and to identify markers that specify the lineage so that appropriate control studies can be done and so that treatment and placebo groups can be identified. He concluded that the world is in the midst of a revolution in the use of genetic tests; soon, he said, these tests will be used to predict such simple conditions as high cholesterol, as well as complicated diseases such as schizophrenia. It is absolutely essential, Dr. Ruano insisted, that as this new wave of genetic testing enters the medical marketplace, its uses are fully validated. He concluded that it is important to bear in mind these technical issues or "the emerging field of pharmacogenetics is going to be troubled by the same lack of variability and reliability that has been a problem in classical epidemiology."

Paula Trahan Rieger, R.N., M.S.N., C.S., A.O.C.N., F.A.A.N., President-Elect, the Oncology Nursing Society

Ms. Rieger informed the Committee that the society is a national organization of more than 29,000 registered nurses and other health care professionals dedicated to excellence in patient care, teaching, research, administration, and education in the field of oncology. Oncology nurses with specialized training and skills provide cancer genetic counseling, and they are adding to the evolving body of cancer genetics knowledge. She noted that in cancer care, certain categories of genetic tests require a higher level of oversight. For

example, although molecular tests used currently in cancer diagnostics and prognostics have a sufficient level of oversight with respect to clinical validity and reliability (even though questions remain regarding utility), cancer predisposition genetic testing (which determines disease susceptibility) should be held to a higher level of scrutiny because of the ethical, legal, and psychosocial implications associated with the tests. For example, patients often make irrevocable decisions regarding medical management, such as the decision to have prophylactic surgery, based on the results of these tests.

The society believes that at present, oversight mechanisms that address the clinical validity and utility of cancer predisposition testing are insufficient and recommends that workable criteria for oversight (including quality assurance procedures) be implemented in order to guarantee safe and appropriate testing. All stakeholders should be involved in the formulation of these standards and procedures. The society also recommends that voluntary informed consent be obtained in all settings in which cancer predisposition genetic testing occurs and that standards be developed to delineate the minimum information that should be reviewed during the process of informed consent. Furthermore, the society believes that cancer predisposition genetic testing must occur within the context of cancer genetic counseling to assure that consumers receive sufficient education to make informed decisions. It is also important that health care providers have sufficient knowledge and expertise in this area. Thus, the society recommends that standards of minimum competencies be set for the provision of cancer genetic counseling.

Ms. Rieger concluded by remarking that oncology nurses with specialized education have much to offer in helping people before, during, and after genetic testing, and their work will be affected profoundly by the use of genetic information in the management of cancer. The society supports the active inclusion of nurses and other health care professionals in delineating future guidelines for cancer predisposition genetic testing.

Neil A. Holtzman, M.D., M.P.H., Johns Hopkins University

Dr. Holtzman commented that the most critical lesson that his research team has learned is that when faced with a decision about a genetic test, people need information about what that test will mean to them; how good a predictor it will be of whether they will get the disease; and if the test is positive, what can be done to help them. However, the difficulty with tests that are available today—particularly predictive tests for common disorders—is that these data are not always available and that for laboratories that market tests as services, there is no regulatory requirement to collect them. He noted that the situation is different for genetic tests marketed as kits, because a manufacturer of a kit must collect data on clinical validity before the FDA allows that manufacturer to market it. By requiring data for kits and not for genetic tests marketed as services, he said, a double standard—of which the public is the victim—has been created. He noted that his written comments elaborate upon this concern.

Jean Jenkins, the International Society of Nurses in Genetics

Ms. Jenkins opened her remarks by noting that the International Society of Nurses in Genetics (ISONG) includes approximately 300 members, representing nearly every state in the United States, as well as Canada, Brazil, Israel, and Japan. ISONG members, she said, are involved in all aspects of the delivery of genetic services, and they have seen firsthand how genetic disorders and risk for inherited conditions affects individuals, their families, and even their communities. ISONG affirms that genetic testing should be conducted voluntarily, that testing should be based upon informed consent, and that absolute confidentiality should be maintained. The society recommends that teams and representatives from public and private sector laboratories and federal oversight agencies, as well as consumers, should be assembled to review laboratory performance, recommend new procedures, and design modifications in oversight guidelines. Unannounced surveillance of laboratories should be conducted annually, at a minimum, and laboratories also should be expected to contribute to public health and professional education, as well as to community-based research about genetic testing. In addition, protections should be equitable across the board, and comprehensive and consistent laboratory policies that address the interests of children and their families must be developed. These policies should be bolstered by regulations that require parental informed consent forms, children's assent forms, and evidence that the families have been offered counseling with trained health care professionals. Counseling and support services should be offered before, during, and after genetic testing, and information should be culturally sensitive and delivered in multiple formats, including different languages. In addition to indices of clinical validity, a minimum set of outcome measures should be used to measure short-term clinical utility and long-term utility of genetic testing, including psychological, social, family, and cost-benefit outcomes.

Barry Berger, M.D., F.C.A.P., Vice President, Laboratory Medicine, Exact Laboratories, Inc.

Dr. Berger told the Committee that his company develops DNA-based tests for identifying sporadic somatic mutations that are known to be associated primarily with colon and rectal carcinoma. The analytical methods that are used for looking at these SNPs, he said, are well regulated by CLIA and current FDA regulation. He argued that physicians should be informed fully in the use of these somatic mutations for the current presence of tumor or adenoma neoplastic events, so that they can provide their patients with accurate information about these specific mutations. However, he added, because these are screening rather than diagnostic tools, the standards for informed consent should not be as rigorous.

Lisa Salberg, Founder/President, the Hypertrophic Cardiomyopathy Association

Ms. Salberg established the Hypertrophic Cardiomyopathy Association (HCMA) in 1996, after the death of her sister from hypertrophic cardiomyopathy (HCM). She noted that she has lost four members of her family to the disease and that other family members as well

as she herself are living with it at present. HCM, which affects both men and women and spans all nationalities and ages, has a prevalence of between 1 in 500 and 1 in 1,000. Although approximately 360,000 Americans are affected and HCM is a leading cause of sudden death in young people, most commonly young athletes, few are aware of the disease. However, Ms. Salberg noted, having HCM does not mean that an individual cannot live a normal life. On behalf of the HCMA, she urged the Committee to emphasize the importance of high-quality pre- and post-screening counseling, because, in many instances, HCMA members have sent samples to laboratories without knowing what screens would be conducted and without understanding what implications their test results might hold. In addition, the association is concerned that there have been instances when women have been persuaded by medical providers to abort their pregnancies as a result of positive test results, even though the mothers' health was not in danger. Genetic fear, she said, is a powerful tool. "Although it is necessary to evaluate the potential socioeconomic, psychological, and medical harm that may result from genetic testing," she said, "no committee, medical provider or governmental agency can decide what is in the best interest of any particular person." In the opinion of HCMA, patients deserve respect and complete confidentiality, as well as the right to make their own health care decisions.

Alice Cornelison, Ph.D., R.N., Howard University Division of Nursing

Dr. Cornelison told the Committee that "while we at Howard University are educating nursing students to care for the world's population, our mission includes a commitment to providing care to underserved communities, and it is from that perspective that I make the appeal for a real, rather than token, inclusion of diverse cultures. Be assured that while you are eyeing certain groups for inclusion or exclusion, these groups are also watching you." She recommended to the Committee that successes and failures of human testing should be publicized without violating the individual's confidentiality. It is the responsibility of health care educational institutions, Dr. Cornelison said, to keep abreast of current genetic research so that nurses, doctors, social workers, and genetic counselors, among others, can speak from a scientific and informed basis.

Wendy Uhlmann, M.S., President, National Society of Genetic Counselors

Ms. Uhlmann explained that the National Society of Genetic Counselors (NSGC), which represents and advocates for more than 1,700 genetic counselors, commends the efforts of SACGT in preparing a comprehensive and thoughtful paper, one that addresses the complexities of genetic testing and raises pertinent issues to consider in developing appropriate oversight strategies, and one that identifies a key concern—that health care providers and patients often have limited knowledge of genetics and the implications of testing.

Although much attention has focused on the tests themselves, genetic counseling is an important aspect of ensuring the development of safe and effective genetic testing. Before a genetic test is ordered, Ms. Uhlmann stressed, an accurate assessment of the patient's risk must be conducted—an assessment that can be complicated by the fact that a specific

genetic condition can be inherited in more than one way, can involve more than one gene, and can result from any one of a number of mutations within a gene. In addition, laboratories use different methods, even when testing for the same genetic condition, each with specific limitations and implications for the interpretation of test results. Therefore, a solid understanding of genetic principles is necessary for selecting the laboratory and determining who should be offered testing. The society agrees with the Committee that determining the degree of oversight will be a complex process, one that will require weighing the benefits and risks for each genetic test.

Ms. Uhlmann emphasized that genetic counselors have coordinated genetic testing and educated patients about these testing issues for more than 25 years and that the society encourages the involvement of genetic counselors in determining oversight for different genetic tests. However, given the rapid advances in genetic testing, she noted, the ability to offer genetic tests is exceeding the ability of such professionals to understand fully the implications of these tests. In fact, she added, the demand for genetic tests is such that testing may be offered even as long-term data is still being collected. Informed consent is therefore an important aspect of genetic testing, and it should include the limitations and implications of genetic testing from both the laboratory and clinical perspectives and should address the personal and family impact of genetic testing. Ms. Uhlmann concluded by re-emphasizing that genetic counseling is an integral part of genetic testing and that genetic counselors have much expertise to offer in addressing these important issues and in establishing oversight criteria for genetic tests.

Benjamin Dubin, Member, Executive Committee, the Alexander Graham Bell Association for the Deaf and Hard of Hearing

Mr. Dubin, whose daughter Rachel was born deaf, told the Committee that the Alexander Graham Bell Association for the Deaf and Hard of Hearing represents children who are deaf and hard of hearing, adults with hearing losses, and professionals who serve children with hearing loss. Today, the association is the largest national organization focused on the needs of deaf and hard of hearing children who use auditory communication approaches. The association addresses a wide range of issues important to people with hearing loss of all ages, and it emphasizes giving children and adults the skills to function within mainstream society.

Like most people with a hearing loss, Mr. Dubin continued, our members do not view themselves as part of a different culture; however, for most families, pediatric hearing loss presents extraordinary challenges, regardless of whether the child communicates auditorially or manually. Also, it is well known that more than half of all cases of hearing loss have a genetic component. The association, he said, vigorously supports any means of overcoming hearing loss that allows children to communicate with the larger world, whether through use of technology, medical intervention, or strategies such as speech reading**.**

Janine Cody, President, Alliance of Genetic Support Groups

Ms. Cody informed the Committee that one of the guiding principles of the Alliance is that meaningful progress in genetics is not possible without consumer involvement. The Alliance, she said, looks forward to being an active participant in the development and implementation of a plan to inform consumers of available genetic technologies and services.

William L. Freeman, M.D., M.P.H., Director, Indian Health Service Research Program

Dr. Freeman, based on 21 years of working with and listening to members of native communities, offered his assessment of the morning's plenary session. He expressed concern regarding the dangers of minimizing the harms that can be caused as a result of genetic testing and emphasized the need for genetic counseling and comprehensive support services. He called the Committee's attention to remarks made earlier that day by a woman from Hawaii who has CADASIL. In this case, he said, there was limited availability of genetic services for the patient and her family because of her rural location. In addition, they could not afford adequate services because they lacked health insurance, and what care was available was not only culturally inappropriate but inadequate. These weaknesses, he noted, in addition to an inappropriate over-reliance on the medical model of disabilities—one that is frequently imbedded in prenatal screening—create more fear and distrust and have more potential for harm than problems with clinical validity and clinical utility. Dr. Freeman recommended that the Committee address social factors related to genetic testing in greater detail and commented that the federal government should involve affected communities in developing programs for genetic testing, genetic research, and genetic care. Dr. Freeman stated that SACGT in its report should emphasize clinical validity and utility in the context of the potential benefits and harms of genetic testing to diverse ethnic, socio-economic, educational, geographic, and social communities.

Discussion Group Reports

Vence Bonham served as moderator for this session, during which the discussion group facilitators or rapporteurs shared the main ideas, concerns, and recommendations of their groups. Mr. Bonham noted that the main goal of these discussion groups was to ensure that everyone had an opportunity to provide his or her perspective and be heard.

Group A: Benefits and Risk Criteria

- This group did not focus mainly on the questions presented for discussion, but instead discussed the benefits and risks of genetic testing that are related to clinical utility, as well as other issues related to genetic testing and oversight.
- Knowledge is power, and there is a need to disseminate knowledge that is more accurate. One way to do this is through "true" informed consent, which includes providing accurate and understandable information about the medical and the

psychosocial implications of a test. It also is important to emphasize that people have a right to know or to "not know" this information

- Education about genetic testing is critical. It can be improved through targeting physicians, genetic counselors, and students in the primary grades through high school. Strategies for educating the public may include mailings, on-site visits, and use of radio and television.
- Participants discussed the implications of personal versus private information, noting that it is important to find accurate and reliable ways to centralize information about genetic testing.
- In considering criteria for assessing benefits of genetic testing, there is a need to ensure that appropriate psychosocial planning, economic planning, and reproductive options will be available for everyone.
- Unresolved issues included the complexity of evaluating genetic and environmental influences of disease. The group also thought that it was important to consider the definition of a genetic test, as well as the relative value a specific test should be given.

Group B: Benefits and Risk Criteria

- This group also discussed a range of genetic testing issues.
- One of the major benefits of genetic testing is that it can allow patients to make informed medical decisions and life choices. The availability of treatment itself is not necessary in order to make testing valuable, because the knowledge itself is beneficial. Risks of tests are related to the limitations of the tests themselves, and include poor positive predictive value or low sensitivity, insurance discrimination, and lack of informed consent.
- Informed consent must be considered an ongoing process of communication by all parties involved, including physicians, nurses, and patients, instead of simply a form that needs to be filled out. Certain kinds of testing, such as routine diagnostic testing (for example, chromosome studies on a newborn with a Down syndrome phenotype) may require less stringent informed consent requirements. However, consent should always be fully informed for predisposition or presymptomatic testing.
- Education of health care providers about genetic testing and specific genetic tests is critical. Physicians should recognize when it is necessary to refer to others with more expertise regarding a specific test. In addition, the education of patients concerning genetic tests should be a collaborative effort between physicians, counselors, nurses, and laboratories.
- The responsibility for ordering genetic tests and for interpreting the results must be shared by laboratories and physicians. The fact that all physicians may not be knowledgeable about all genetic tests may be considered a risk of genetic testing.
- IRBs must be more knowledgeable and responsible regarding the risks and benefits of genetic testing.
- A participant of the discussion group who was a member of a minority group commented that genetics and genetic testing, like other areas of health care, really does seem to be insensitive, in many ways, to the caring aspects of health care. She noted that "her people certainly would be ignoring genetics," which would be unfortunate, because it is potentially a beneficial tool with much to offer.

Group C: Test Categorization

- There was some resistance in this group to using the categorization scheme of "high risk" versus "low risk." Other useful categorization schemes might be germline versus somatic; levels of test validity and utility (areas in which test quality can be improved and risks reduced at the outset); the individual impact of a test, which should include a consideration of disease severity and treatment options; personal values and lifestyles; and cultural and familial context. Those who provide counseling must take all of these issues into account and must devote enough time to counseling to ensure that people have time to process and understand the information they are receiving as well as its implications.
- Additional education of consumers and all providers—not just physicians—is essential. Education must be broad and directed to the general public, rather than only to those who have already been diagnosed with genetic conditions.
- The categorization of tests is a complex and problematic issue. Each genetic test is different, and counseling must be individualized. Inappropriate categorization of tests can result in stigmatization. Thus, it is important to proceed slowly and get it right, especially in the areas of assuring the quality of tests and in considering oversight issues related to test development. Also, oversight should go beyond the laboratory level; guidelines are needed for providers as well. A consortium may be the best approach to oversight, but it must include everyone—policymakers, providers, and consumers. In fact, one idea that the group discussed was that of consumers themselves determining where their disorder falls in a risk categorization scheme.

Group D: Test Categorization

- Tests that are of minimal risk, such as a test for male-pattern baldness, may not require oversight. However, even for this test, clinical utility and clinical validity must be established. Predictive tests, as well as those for screening—including prenatal screening—and for pre-implantation diagnosis, require oversight. However, these tests are not created equal and should be classified according to the gravity of the condition and the information available about it (availability of treatment; potential impact on family dynamics and lifestyle; long-term implications; and the need for counseling); the severity of the disease; the potential for stigmatization and discrimination; the degree to which the information about the disease changes over time; and clinical validity.
- The group was divided regarding concerns for specific populations. Some commented that genetic testing is an overarching social issue that requires additional education and training across the board. Others commented that historical experience has shown that oversight is needed to protect certain populations from discrimination.
- The characteristics of diseases are what should be classified into categories, not the diseases themselves, and these categories should be fluid in order to take new technology into account.
- Increased and more effective education of the general public and health care providers is needed, as are more effective informed consent practices.

Group E: Data Collection, Evaluation, and Dissemination

- Large longitudinal studies are needed so that scientists have access to population data on health. However, a host of complicated issues are involved in trying to collect information on identifiable samples so that people's health status can be tracked over time.
- Central themes were the issue of confidentiality and the consequences and dangers associated with breach of confidentiality (due to the identifiability of DNA). This issue must be addressed before any methodology regarding the collection, evaluation, and dissemination of genetic tests can be designed, as it constitutes a significant barrier to participation in these kinds of studies. In addition, because it is difficult to control how society will use this information, genetic testing should be optional and results should be handled at the discretion of the patient. The knowledge and consent of test subjects are always necessary.
- IRBs can work effectively for an individual institution, but in the private sector, standards of review and confidentiality vary greatly. If assurances regarding confidentiality can be made to individuals from the beginning, genetic testing is more likely to be accepted and less likely to result in stigmatization.
- Despite risks, there is value in genetic testing, which can offer reassurance that one does not or will not have a particular disease or disorder or which can confirm a diagnosis. Such information is valuable to many, even if treatment is not currently available, and the individual should have the option of having this information.
- HIV/AIDS testing may provide a useful model for applying a process of pre- and post-test counseling, for laboratory rigor, and for the development of an oversight body.

Group F: Data Collection, Evaluation, and Dissemination

- Members of this group considered the questions to be beyond their knowledge base and noted that this may serve as one example of the gaps that sometimes exist between the issues in genetic testing and the public's understanding of those issues. For example, from the perspective of the discussion group members, there was a lack of information and knowledge upon which to base their consideration of the first question, "Given that collection of data is an ongoing process, what type of system or process should be established to collect, evaluate, and disseminate data about the analytical validity, clinical validity, and clinical utility of genetic tests?" It also was not clear to discussion group members why data are not being shared, and group members believed they did not have the necessary information about how data is currently being collected and coordinated in order to address this question.
- An important consideration is who will receive the genetic tests. Also, the existing number identification systems used with HIV/AIDS testing seem to have been somewhat successful and might provide a useful model.
- Informed consent is critical; however, its design and implementation must consider cultural diversity, level of literacy, and the relationship between the consumer and genetic professionals.
- Different confidentiality issues arise when intervention is available, as opposed to when it is not. In addition, informed consent must cover the possible use of samples for

other studies, and samples must remain anonymous to prevent insurance and employment discrimination.

- An oversight process is needed, but it is not clear whether it should be conducted by a public or a private entity. Some thought that the federal government would be an appropriate oversight provider, but others noted that many do not consider the federal government to be a trustworthy steward of such personal information.
- Oversight functions should include standardization of IRBs, the development and implementation of a process for complaints from the public and from health care professionals, and the development and implementation of meaningful consequences for violation of oversight policies.
- Consumers should receive feedback after participating in research activities. After giving freely of their time and energy, consumers are entitled to some form of feedback and should have the option of receiving it.

Groups G: Oversight Options

- Some sort of central oversight would be useful, and a consortium of public and private groups might be an effective arrangement, although such a system could become a burdensome bureaucracy. It is important that some group be in place to consider genetic testing issues.
- The general sense of the group was that home testing might not be the best approach, although it would assure the preservation of privacy and confidentiality. Most agreed that gatekeeper involvement, such as that of a physician or a genetic counselor, is important, and that practitioners must keep informed of developments in the field.
- Oversight should include a component that addresses education and counseling, not merely the tests themselves.
- The degree of oversight may differ depending on the disease involved and the purpose of the test.
- It is important to gather data about the validity and utility of genetic tests.

Group H: Oversight Options

- As part of the process of determining what needs to be done in the area of oversight, it may be valuable to conduct a baseline needs assessment in order to evaluate existing mechanisms in genetic testing and the effectiveness of the current infrastructure. In such an effort, it would be important to involve professional organizations in determining existing genetic testing practices. Based on the needs assessment, evidence-based guidelines could be developed, and another needs assessment could be conducted to determine the impact of those guidelines.
- Education is essential. Consumer education must be culturally sensitive, and genetic and cultural competency education must be delivered to providers, insurance companies, and managed care companies. In addition, sufficient numbers of well-trained genetic counselors (as well as consumer support and advocacy organizations) must be available, and test participants must be aware that they are available.
- Informed consent is of critical importance; however, there are many barriers to effective informed consent.

- The resources to disseminate information to the public in a meaningful way are limited, and the information itself is enormously complex. Consumers must be aware of a test's limitations, as well as its utility, validity, and accuracy.
- Oversight should be provided not only for the tests themselves, but for the manner in which they are used. We must expand the existing mechanisms at the federal and state levels and also involve professional societies and consumers as well as other stakeholders in the oversight of this new technology.
- For each test, we should weigh the benefits of immediate application against what may be lost if the test is not performed. That is, does sufficient utility exist to use the test as it is, or would anything be lost by delaying its availability until more is known about the test?
- In evaluating when a test is ready for general use, it must be determined who will perform the test and how the results will be used. It is important to determine why tests are being ordered in order to allow for a proper interpretation of test results from the various private laboratories. Therefore, clinical information should accompany test samples.
- Before a test is performed, consumers must have information about why a test is being conducted, the potential treatment or cure for the disease for which the individual is being tested and possible implications of the test results, including social and economic implications.

Groups I/J Combined: Related Genetic Testing Issues

- Informed consent should be an interactive process between the provider and the consumer and should be used as a tool for provider and consumer education. The consent form should be understandable and should include as little legal terminology as possible. It should clarify the purpose of the test, provide basic information about it, and discuss its risks and benefits. Different criteria for research and clinical testing may be needed. In addition, informed consent should include information about how the test sample will be disposed of and whether patients will be recontacted if the sample is used for additional research. Coercion in any form should never be part of the informed consent process, and it should be the provider's, not the laboratory's, responsibility to ensure that informed consent is obtained before testing is conducted.
- Different levels of informed consent are needed for different categories of genetic testing. Routine and mandated genetic screening tests, such as newborn screening and tests to confirm clinical findings, may not require informed consent. However, presymptomatic testing, such as for Huntington disease, requires informed consent, as does predictive testing.
- The group considered how informed consent procedures could be standardized throughout the different states and various institutions involved. DHHS could create and promote a model of best practices in this area, which could be adopted on a state-by-state basis. Federal legislation might not be appropriate, because it may not be sufficiently adaptable.
- It was questioned whether any genetic testing is truly anonymous, considering that DNA acts as an individual's "fingerprint."

- Some regulation of insurance companies and employers may be needed to assure the public that genetic testing will not result in discrimination.

Groups K: Oversight Issues for Diverse Cultural Communities

- The best way to minimize the potential harms of genetic testing and maximize its potential benefits to diverse communities is through education. Educators should represent the diversity of the communities being offered genetic testing; however, it is just as important to be humane and compassionate in offering and conducting tests. There may be insufficient numbers of genetic testing professionals from diverse communities engaged in counseling and testing.
- Some genetic tests raise more ethical, legal, medical, and social concerns than do others. Tests that may raise these additional concerns are mainly those that predict diseases, specifically those for which treatment is not currently available, or those that do not with certainty predict that disease will occur.
- It is important to be aware that generalizations may be made about specific communities as a result of being able to test for one or more disorders in a specific population and that as genetic testing becomes increasingly mainstream, professionals and the public will focus less on the environmental contributions to disease and instead focus on hereditary influences.
- The public must understand that each individual carries some genetic mutations: No human being is genetically perfect. In addition, all individuals and communities must have equal access to genetic counseling and testing, and treatment information should be provided along with testing information, whenever possible.
- An equal balance of positive and negative stories about testing should be available to all who undergo testing.

Group L: Oversight Issues for Diverse Cultural Communities

- This group focused on how, for diverse communities, the potential harms of genetic testing can be minimized and the potential benefits maximized and also discussed concerns about the roles of the community in oversight and how the oversight process can be structured to include these communities.
- Diverse cultural groups can be defined in many ways (including according to language, religion, family structure, and geographic region), not just by ethnicity or race. A thorough understanding of these variables is essential before the initiation of any testing program. Many mistakes have been made because of a failure to understand this complexity among ethnical and cultural groups.
- Ethnic and cultural groups want to be included in the development and oversight of any genetic testing that will affect them, beginning with the research and development stages. Such inclusion is essential to the success of a testing program because it fosters a sense of trust. Commitment and concern about a community must be demonstrated by investigators and those conducting testing in order to ensure continued trust.
- It may be necessary to recruit representatives from different cultural groups to help explain the issues that face a particular community, as well as the primary desires and concerns of that community. These advisors also could determine the applicability of

general testing policies to a particular group and suggest the level and extent of information that should be disseminated.

- The importance of people who are trusted by the community communicating information about these tests cannot be overstated. The messenger is as important as the message.
- It is important to understand how best to enable genetic professionals, including researchers, clinicians, counselors, and advocates, to become ethnically and culturally sensitive to the values of diverse cultural communities. The development of this skill could be adopted as part of a set of core competencies required for genetic professionals.

Closing Comments

Dr. Lewis thanked those who presented public comments and others who had participated in the meeting for helping the Committee better understand oversight issues in terms of some of the special concerns that people have about genetic testing. She emphasized that obtaining the views of all stakeholders was an important part of this process and that SACGT is committed to continuing this dialogue with the public.

Dr. McCabe informed participants that the upcoming SACGT meeting on February 24 and 25 will in large part be devoted to considering the public comments gathered today, as well as through the other outreach mechanisms. He noted that the Committee has learned much from today's meeting and that SACGT looks forward to the continuing involvement of the public in this process.