Highlights of the Twelfth Meeting of the
Secretary's Advisory Committee on Genetic Testing
February 13-14, 2002
Bethesda, Maryland

The twelfth meeting of the Secretary's Advisory Committee on Genetic Testing (SACGT) was held in public session February 13-14, 2002, in Bethesda, Maryland. The Committee was briefed by agency representatives on the activities of their agencies regarding advancement of the knowledge of clinical validity and utility of genetic tests in response to a SACGT request. Dr. Eve Slater, Assistant Secretary for Health, conveyed greetings from the Secretary and Deputy Secretary and indicated that they, as did she, regarded the Committee's deliberations and recommendations as extraordinarily important. The National Institutes of Health (NIH) and the National Human Research Protections Advisory Committee (NHRPAC) updated the Committee on recent developments on third parties in human subjects research. SACGT received a report on the activities of the Ontario Provincial Advisory Committee on New Predictive Testing. The Informed Consent/IRB Work Group presented a draft report on issues in decision making and informed consent for clinical and public health genetic tests. The Committee heard three presentations on the economics of the genetic testing market. Finally, a panel of multidisciplinary experts helped the committee begin an exploration of the use, collection, and analysis of population data by race and ethnicity in genetic research and testing.

DAY ONE

The morning session began with an introductory presentation by Dr. Carol Greene, a policy analyst in the Office of the Science Policy at DHHS, who provided background about the origin of the agency reports. SACGT has had extensive discussions in previous meetings about the critical importance of supporting ongoing data collection and analysis of genetic tests in both the premarket and postmarket phases. Its July 2000 oversight report included recommendations about the need for coordinated efforts in data collection. Since issuing that report, SACGT, largely through the efforts of the Data Work Group and its chair, Dr. Wylie Burke, has sought to understand the challenge of achieving this goal in greater detail. At its August 2001 meeting, SACGT decided that more specific detail was needed about the efforts of the agencies in the Department of Health and Human Services (DHHS) represented on SACGT to support the advancement of knowledge of the clinical validity and utility of genetic tests. In the fall of 2001, SACGT sent a letter to the heads of Agency for HealthCare Research and Quality (AHRQ), Centers for Disease Control and Prevention (CDC), Centers for Medicare and Medicaid Services (CMS), Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA), NIH, and the Office of Human Research Protections (OHRP) requesting information on their activities regarding the support of efforts to advance knowledge of clinical validity and clinical utility of genetic tests.

SACGT *ex officio* members or their representatives presented their agency's response to SACGT: Dr. David Lanier, AHRQ; Ms. Judy Yost, CMS; Dr. Steven Gutman, FDA; Dr. Muin Khoury, CDC; Dr. Michele Puryear, HRSA; and Dr. Francis Collins, NIH. Since OHRP is not a funding agency, its representative did not present. Following the agency presentations, Dr.

Greene presented again with an overarching analysis of the responses at the conclusion of the agency presentations.

In its discussion of the agency efforts, the Committee recognized the complexity of classifying the information requested into the given categories of primary research, secondary analyses, summary information development and summary information dissemination, and acknowledged the possibility that there was under-reporting and over-reporting of activities. While the Committee was impressed with the range of activities underway in primary research on genetic diseases and conditions, contributing to the advancement of knowledge about clinical validity and utility of a genetic test, there was some concern about the much more modest efforts underway in the three other areas – secondary analysis, information summary development and dissemination. NIH, with the largest budget of all the DHHS agencies, contributed the majority of resources in all four categories. The Committee emphasized the importance of effective coordination and communication among the agencies to foster synergistic collaborations and avoid unnecessary overlap and duplication.

The Committee also discussed whether the Department had a clear vision of its role in genetics and genetic testing and whether it views genetics as a targeted programmatic area or an integral part of health and medicine generally. A proposal was made to send a letter to the Secretary requesting information on the Department's philosophy and overall strategic approach to genetics and genetic technologies, which would help SACGT understand the context in which it makes its recommendations. Further discussion occurred about the adequacy of support for projects that focus on the translation of genetic tests into health care services, the value of an overarching vision of the HHS role in advancing the integration of genetic tests, and the importance of coordination of agency efforts.

Before coming to final conclusions and recommendations about these issues, the Committee agreed that additional data needed to be gathered in several selected areas to see how well interagency communication and coordination were working. Using a case study approach, the goal of this second phase of inquiry is to highlight the different steps in the translation process and identify successful approaches to coordination and collaboration among the agencies. The following conditions were suggested for the case studies: hemochromatosis, cancer, Factor V Leiden, newborn screening for sickle cell and other hemoglobinopathies, a rare disease to be determined in consultation with the Rare Disease Work Group, and medium chain acyl-CoA dehydrogenase deficiency (using tandem mass spectrometry). The Data Work Group will take the lead in developing the case studies and report back to SACGT at the May meeting. Following the deliberations on the outcomes of the case studies, the Committee will decide how to frame their request to the Secretary regarding the Department's outlook on genetics and genetic testing.

Dr. Eve Slater, Assistant Secretary of Health, made brief remarks to the Committee. She thanked the Committee for the past work on oversight of genetic testing, gene patents, and genetic discrimination, and other issues and looked forward to recommendations from the Committee on issues under deliberation such as health professional education and informed consent. At the conclusion of her remarks, Dr. Slater presented certificates of appreciation to four members of the SACGT whose terms were ending: Ms. Patricia Barr, Ms. Kate Beardsley,

Ms. Ann Boldt, and Dr. Barbara Koenig. She also announced that Dr. McCabe had been reappointed to serve as Chair of the Committee and that an announcement would be made in the near future about new appointments.

Next, the Committee was updated on recent developments on the issue of third parties in human subjects research. In June 2000, SACGT convened a panel of experts to discuss questions about whether third parties in research (at the time, referred to as secondary subjects) were considered human subjects under the Federal regulations governing the protection of human subjects. After subsequent deliberations, SACGT concluded that the mandate of NHRPAC was more appropriately suited to a fuller consideration of the issue and recommended to the Assistant Secretary for Health that NHRPAC be asked to carry out a review of Federal policy in this area. NHRPAC began studying the issue last year, deliberated for several months, and at its last meeting just a few weeks ago, finalized a consensus statement on the issue. NIH has also made recommendations on this issue in a report to OHRP.

Dr. Mary Faith Marshall, Chair of NHRPAC, and its Executive Director, Ms. Kate Gottfried, briefed SACGT on NHRPAC's statement on clarification of the status of third parties when referenced by human subjects in research. NHRPAC arrived at a consensus on the statement through deliberation on the issues by two working groups. According to Dr. Marshall, the crux of the issues was whether private information about an identifiable third party had to be referenced by the third party, or whether the third party could also be defined as those about whom information existed in tissue samples, medical records, or other sources. In the end, NHRPAC defined third parties as individuals "about whom researchers obtain information from human subjects but who themselves have no interaction with research investigators or their agents."

NHRPAC also advised that institutional review boards (IRBs) should consider how the research design might focus not only on the identified human subjects but on other persons as well. In cases in which a research project intends to collect a significant amount of private information in identified forms on third parties, the investigator and IRB should consider whether any of the third parties should be regarded and treated as research subjects themselves. In making this determination, IRBs should consider the following factors:

- The quality of information collected about the third party;
- The nature of the information collected;
- The ability of investigators to record information on third parties in a manner that protects the identity of those parties;
- The possibility that classification of a third party as a human subject may impact the rights or welfare of the originally designated human subject.

NHRPAC has posted the statement on their website[1] and will begin developing case scenarios to illustrate how to implement the guidance on third parties.

[1] NHRPAC's statement, *Clarification of the Status of Third Parties*, can be found at http://ohrp.osophs.dhhs.gov/nhrpac/mtg01-02/third.pdf.

Ms. Sarah Carr, Senior Policy Analyst at NIH, and Dr. James Hanson, Chief of the Mental Retardation and Developmental Disabilities Branch, at the National Institute of Child Health and Human Development, presented the NIH recommendations, which were developed at OHRP's invitation, to help address questions that had surfaced in the research community.[2] Dr. Hanson, who with Ms. Carr, co-chaired a subcommittee of the Trans-NIH Bioethics Committee, an internal trans-agency group that assists the agency's policy development and decision-making processes for issues involving the consideration of ethical, legal, and social implications of NIH-funded research, explained why and how NIH developed the recommendations, what the agency's goals were in developing them, the guiding principles on which they were founded, and the many issues that were deliberated by the subcommittee. Ms. Carr reviewed the recommendations, which are based on the Common Rule definition of human subject and are framed around four "rules of thumb."

The section of the Common Rule definition that applies to third parties is the clause "identifiable private information." According to the Common Rule, a human subject is a person about whom information that is both private AND identifiable is collected. NIH's first rule of thumb suggests that a third party does not become a human subject unless and until the investigator obtains information about the third party that is both private and individually identifiable. The second and third rules attempt to clarify the concepts of identifiable and private when applied to third parties. The fourth rule of thumb reiterates the importance of maintaining the confidentiality of all research information about identifiable individuals, whether they are human subjects or third parties, as confidential. Such information should be kept secure and protected from inappropriate disclosure.

Following the presentations, the Committee briefly discussed the two reports. The Committee commended the processes that were employed to produce the documents and noted that the two documents are complementary and reach similar, though not identical, conclusions on the essential questions surrounding the third party issue. SACGT agreed that it would convey to the Assistant Secretary for Health its support of the development of guidance on third parties by OHRP based on the principles outlined in the NHRPAC and NIH papers. The Committee also indicated that specific illustrative examples would help clarify when third parties are human subjects and that OHRP should seek public comment on draft guidance.

In the afternoon, Dr. Anne Summers, Chair of the Ontario Provincial Advisory Committee on New Predictive Technologies, and Dr. George Browman, Chair of its Evaluation Subcommittee, briefed SACGT on the work of their committee. Dr. Summers presented an overview of genetic services in Ontario, the impact of genetics on healthcare, the goals and composition of the Ontario Advisory Committee, and the recommendations made by the Committee.

Dr. Browman reviewed the eight sections of the report of the Evaluation Subcommittee. The sections covered principles for decision-making, confronting gray zones in the evaluation and coverage of genetic testing services, and an evaluation toolkit. Dr. Browman noted that there are several elements to consider in the decision-making process, including the intended purpose of the proposed service, the effectiveness and usefulness of the service, and economic

[2] A copy of the NIH recommendations can be obtained by contacting Ms. Lora Kutkat (kutkatL@od.nih.gov), the Executive Secretary of the NIH Trans NIH Bioethics Committee.

considerations. He also suggested that certain conditions might need to be placed on tests that fall within a gray zone before coverage is approved.

The next group of presenters provided an economic analysis of the genetic testing market. In 2001, the marketing, consulting, and training firm of Frost and Sullivan released its analysis of the genetic testing market. Mr. Dorman Followwill, Vice President of Healthcare and Life Sciences Practice at Frost and Sullivan, presented an overview of the impact of discovery and diagnostics on the healthcare industry. Mr. Followwill discussed the three drivers of healthcare: patients; data and technology; and supply-side race to market. He predicted that there would be a demand/supply gap in the future as a result of having more and savvier patients on the demand side and an overburdened infrastructure on the supply side. He noted that genetics is changing the practice of medicine, for example, more rapid screening for genetic diseases and instantaneous diagnostics for microbial infections. However, these new genetic technologies and services will likely create unprecedented challenges.

Mr. Manoj Kenkare, research manager of Frost and Sullivan's Healthcare and Life Sciences Practice, presented the Frost and Sullivan 2001 analysis of the U.S. genetic testing market. The report covered four primary areas: prenatal/newborn screening, genetic predisposition testing, genetic cancer testing, and technology and regulatory assessment. The preliminary findings indicated that the genetic testing market is currently in the early stages of development but holds strong growth potential with revenues expected to reach $778 million in 2005. Some of the challenges facing the market are the ability to communicate the value of genetic screening, the change to a product-driven market, and reimbursement and coverage issues.

The final speaker of the session, Dr. Wade Aubry, senior advisor to the Health Technology Center (HealthTech), presented his group's forecast report for genetic testing. HealthTech predicted that the greatest impact of genetic testing on quality of care would be in the area of newborn screening in the next two to five years. Family history will continue to be an indication for genetic testing in the next two to five years. HealthTech predicted the demand for genetic testing will rise and impact the current delivery systems. For example, in order for the genetic counselor workforce to meet rising demands, alternatives to traditional counseling sessions should be considered such as group sessions or video counseling. In addition, health insurance coverage implications may serve as a barrier for underserved and uninsured populations.

A roundtable discussion following the presentations was held with the presenters and Committee members. Among the topics discussed were the similarities between the Canadian committee and SACGT, the different types of categories of genetic tests, the different perspectives of the presenters on whether the end product is the actual test (Frost and Sullivan) or a service in which the test is just one element (Canadian committee), the potential impacts of direct-to-consumer marketing and information dissemination, and the balance of supply and demand.

Dr. Patricia Charache, liaison to the Clinical Laboratories Improvement Advisory Committee (CLIAC), updated SACGT on the issues addressed by CLIAC at its January 30-31 meeting. Dr. Charache briefly discussed CLIAC's work with regard to waived testing, premarket review, requirements for Ph.D. laboratory directors, and HIPAA-required contracts for private CLIA surveys. She discussed in detail a CDC proposal for a Quality Institute. The Quality Institute

would be established to provide ongoing data collection and analysis. Prior to the establishment of the Institute, a conference would be convened to develop a framework for a national report on the health laboratory system. Based on the outcomes of the conference, a report would be drafted to describe the laboratory system and outline a set of quality indicators.

The final presentation of the day was by Dr. Michael Watson, executive director of the American College of Medical Genetics (ACMG). Dr. Watson presented the outcomes of a survey on CLIA compliance conducted by ACMG and the American Society of Human Genetics (ASHG). The online survey was sent to members of ASHG and ACMG. Thirty-five of the 99 responding research laboratories were not CLIA certified and eight were not genetic testing laboratories. Of the 35 non-CLIA certified laboratories, 16 were not aware of the Federal regulations that apply to clinical laboratories. Twenty-seven felt that it was too difficult to obtain a CLIA license. Among the types of assistance needed were protocol books, quality assurance programs, and help to identify clinical laboratories willing to take on new tests. Ms. Judy Yost of the Centers for Medicare & Medicaid Services requested a copy of the comments after they had been anonymized to help her office develop technical assistance and educational programs. Dr. McCabe suggested that the Rare Diseases Work Group assist Ms. Yost to develop such programs since many of the non-certified laboratories were providing testing for rare diseases.

DAY TWO

Dr. Barbara Koenig and Dr. Benjamin Wilfond, co-chairs of the Informed Consent/IRB Work Group, began the second morning with a presentation of the group's draft report, *Issues in Decision Making and Informed Consent for Clinical and Public Health in Genetic Tests.* Dr. Koenig presented an overview of the issues considered by the work group in the development of the report and described the importance of informed consent in genetic testing and hence the need for the report. Dr. Koenig explained that informed consent referred to the informed decision making process followed by the informed consent of the patient. Dr. Wilfond then described the patient/test characteristics that influence informed consent, including purpose of the test, disease severity, clinical validity and utility, and psychological and social implications. The four consent components are information disclosure, assessment of comprehension, provider input regarding test decision, and documentation. Dr. Koenig concluded the presentation by reviewing the group's recommendations, which were directed to three major groups: HHS, FDA, and the private sector.

In general, the Committee concurred with the conceptual framework of the report -- that certain test characteristics were key to considering the nature of the consent process -- as well as the report's explanation of those factors and the way they can affect consent. They also thought that the report provided an excellent discussion of the important points that health professionals should consider about informed consent for genetic tests. Although most members agreed that certain tests might warrant a more robust informed consent process, some concerns were expressed about how that determination would be made and implemented, and what impact it might have on the practice of consent in general.

In addition, many members of the Committee expressed concerns about the proposal that FDA be involved in the determination of the consent process and in assuring that a robust consent

process was performed when determined necessary. The Committee reasoned that the involvement of FDA in this role could interfere with the patient/provider relationship and may undermine the primacy that the needs of individual patients should have in determining the nature of the consent process. The Committee concurred with most of the recommendations pertaining to the private sector regarding development of guidance for specific tests, off-label use, and coverage of professional services in facilitating the process of informed consent and decision-making. The Committee also supported three of the recommendations directed to DHHS regarding a conference to discuss the types of informed consent processes and to explore methods that should be practiced for different types of tests, requirement of test developers to submit information to FDA that can be used in the informed consent process, and Medicaid and Medicare coverage of professional services in facilitating the patient's informed decision-making.

For the next session, SACGT convened a panel of experts to consider issues associated with the collection, use and analysis of population data in genetic research and genetic testing; to broaden understanding of these issues; and to explore their policy implications and whether SACGT should take steps to address them. The inclusion of diverse populations during the development of genetic tests is critical to enhancing the validity of genetic tests, ensuring their appropriate use and application, and assuring access to the benefits of new genetic technologies

The goals of the panel were to explore how and why racial and ethnic population data are collected, analyzed, and used in social and health policy; how and why the categories are used in genetic research and in the provision of genetic testing services; what the concerns are about the use of race and ethnicity categories in genetic research and clinical practice; and whether other approaches should be considered as efforts to increase collection and analysis of genetic testing data are undertaken. There may be important differences to consider depending on whether the data are being collected as part of genetic research aimed at the development of a genetic test or as part of the application of a test in clinical practice and public health. Distinguishing between genetic tests for disease mutations and genetic tests for responses to medications may also be important in some contexts.

Dr. Claudette Bennett, Chief of the Racial Statistics Branch at the U.S. Census Bureau, presented an overview of the types of data collected by the Census Bureau, explained why these data are collected and why the categories were changed recently, and provided preliminary analysis of the 2000 Census data. The Census Bureau collects data on race (American Indian and Alaskan Native tribes; detailed Asian; detailed Pacific Islander), Hispanic origin (detailed ethnicities), and ancestry (either single or multiple). The data are collected to fulfill a variety of legislative and program requirements such as those used for state redistricting. In the Census 2000, the overwhelming majority of the U.S. population reported only one race (97.6 percent) of which 75.1 percent responded White.

Dr. Olivia Carter-Pokras, Director of the Division of Policy and Data in the HHS Office of Minority Health, presented an overview of why racial and ethnic data are needed and how they are collected and used. Racial and ethnic data are needed for a number of reasons such as monitoring demographic trends at national, state, and local levels and identifying high-risk populations to target interventions. DHHS collects race and ethnicity data through the Directory of Health and Human Services Resources, Medicaid managed care, and other entities. Some of

the issues involved in the collection of such data include the absence of a requirement by the Federal government to collect such data, concerns about confidentiality and privacy, and discrepancies between self-identification and observer identification. With respect to genetic testing, race and ethnicity data have been used, for example, to determine the prevalence of a condition in a screened population (e.g., neural tube defects, sickle cell anemia), to assess attitudes about autonomy and confidentiality with breast cancer predisposition testing, and to assess response to pre-test education for breast cancer predisposition testing.

Dr. Robert Desnick, Chair of the Department of Human Genetics at Mount Sinai School of Medicine, discussed the use of ethnicity in genetic research and testing with examples of prenatal and premarital screening for genetic diseases that affect Ashkenazi Jewish populations and broad, population-based carrier screening for cystic fibrosis (CF). A number of inherited diseases with a high prevalence in the Ashkenazi Jewish population may be attributed to founder effect, a selective advantage to carriers, and/or consanguinity. By using ethnicity data in genetic research, it is generally easier to identify disease/susceptibility genes in groups with high disease prevalence. For example, genes for an inherited form of breast cancer, Crohn disease, and pycnodysostosis were positionally cloned in groups with high disease prevalence. Prenatal screening for Tay-Sachs disease in the Jewish population in the U.S. has resulted in a decline in the number of cases in this group. In 2001, preconception and prenatal carrier screening for CF was recommended and a core mutation panel was defined. The detectability rate of the CF screen based on the recommended core mutation panel is greater than 80 percent for individuals of Northern European and Ashkenazi Jewish descent but much lower for Hispanics and Asian Americans (57 percent and 30 percent, respectively). Some of the issues associated with genetic testing and screening are group and individual stigmatization, confidentiality and privacy, and insurance and employment discrimination.

Dr. Steven Mack, Visiting Scientist at Roche Molecular Systems, discussed how issues of race and ethnicity apply to pharmacogenetics, autoimmunity and transplantation, and genetic diagnostics. Genetic differences distinguish populations in two ways: private (individually unique) polymorphisms are geographically restricted and often represent mutational events whereas allele frequency distributions of public (common) alleles differ between populations and can be used to differentiate between closely and distantly related populations. Dr. Mack reviewed the global distribution of cytochrome P450 variant alleles, a family of genes involved in drug metabolism that have been intensively studied in the pharmacogenetics field. Depending on the P450 variant, individuals may be extensive metabolizers (possessing at least one normal allele) or poor metabolizers (carrying two mutant alleles resulting in loss of drug metabolism), or intermediate or ultrarapid metabolizers. For example, the prevalence of CYP2C19 poor metabolizers is greater than 50 percent in the Vanuatus, Polynesian outliers, and North-Central Vanuatus whereas it is less than 5 percent in European Americans, Saudi Arabians, and some African countries. Dr. Mack concluded that data can be organized on several levels (species, race, ethnicity, population, and individual), but studying genetic variation on the individual level would likely be the most informative way.

Dr. Charles Rotimi, Director of Genetic Epidemiology at the National Human Genome Center at Howard University, discussed why the study of human genetic variation is being debated and the dilemma of explaining individual and group differences. One of the conclusions of the Human

Genome Project is that humans are 99.9 percent the same and that every population group overlaps genetically with every other. However, medical interests in the sequence of the human genome have focused on differences between people and media headlines have highlighted group differences as significant. For example, a medical article in 1997 reported an association between a genetic polymorphism in the aldehyde dehydrogenase gene in Asian-American men that affected alcohol metabolism. Dr. Rotimi stated that in order to explain genetic variances without suggesting that groups are inherently different, three points should be recognized: 1) human groups are extremely fluid; 2) the word "race" is misleading and does not capture commonalities and differences of a shared history; and 3) group attributes evolve with the alacrity of culture, not genes.

Dr. Joseph Graves, Professor of Evolutionary Biology at Arizona State University West, discussed the inappropriate use of social categories in biological study. Natural selection and genetic drift contribute to the determination of disease frequency. But in areas made up of individuals of different geographic origins, these factors will vary. For example, a wide range of mutations, which are likely to be carried by unrelated families, causes Hemophilia A. Genetic drift is a major determinant of a population's frequency of a certain allele. Dr. Graves also reported that individuals may carry genes of diverse geographic origins and presented data on admixture estimates in African Americans. Identifying the genetic components in complex diseases such as hypertension requires the analysis of gene/environment interactions. Dr. Graves stated that the hypertension difference noted between African Americans and other groups is the result of a biological response to social and cultural factors. Dr. Graves concluded that genetically based, racial differences are non-existent in most disease categories and that long-standing differentials in health and mortality are not predicted by underlying human genetic variation.

Dr. Lisa Brooks, Program Director of the Genetic Variation and Genome Informatics Programs at the National Human Genome Research Institute (NHGRI), presented an overview of NHGRI's haplotype map project. The haplotype map is an organizational map of haplotype blocks that are defined by single nucleotide polymorphisms (SNPs) and their common haplotypes, or clusters of SNPs. Preliminary findings indicate that most SNPs are in haplotype blocks and that each block is made up of a few common haplotypes. The common haplotypes are found in all populations but there are some population differences in haplotypes. The haplotype map will serve as a resource for future association studies.

Dr. Jean McEwen, Program Director of the Ethical, Legal, and Social Implications (ELSI) Program at NHGRI, concluded the presentations with a review of research that is underway to advance knowledge of the ELSI implications of genetic variation research. In April 1999, a request for applications was released requesting studies on the ELSI implications of research into human genetic variation. Nine projects were funded comprising the Genetic Variation Consortium. Among the project topics are interpreting genetic differences, race and public communication about human variation, pharmacogenetics and population groups, and concepts of race and ethnicity in genetics research.

A roundtable discussion following the presentations was held with the panelists and Committee members. Among the topics discussed were how to classify data without reifying the idea of

race, targeted marketing to populations, individualized medicine and counseling, and distinguishing when race is useful in a social context but not in a biological or genetic context. SACGT invited the panelists back to continue the Committee's discussion of the issues more in-depth and provide cogent examples for the Committee to use to illustrate the issues at hand.

Before adjourning, Dr. McCabe reviewed the preliminary agenda for the May meeting to be held in Baltimore, Maryland. The one-day education conference, *Genetic Testing and Public Policy: Preparing Health Professionals*, will take place on May 13. The SACGT meeting will be held on May 14-15, and the expected topics on the agenda include a briefing of the proceedings of the education conference, review of draft papers from the Access Work Group and the Rare Disease Work Group, report on the case studies from the Data Work Group, and a roundtable on the history of the development and implementation of the cystic fibrosis screening guidelines.