

Secretary's Advisory Committee on Heritable Disorders  
and Genetic Diseases in Newborns and Children

Summary of Eighth Meeting  
June 5-6, 2006  
Washington, DC

The Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children was convened for its eighth meeting at 9:00 a.m. on Monday, June 5, 2006, in the Rotunda Ballroom at the Ronald Reagan Building and International Trade Center in Washington, D.C. The meeting was adjourned at 1:53 p.m. on Tuesday, June 6, 2006. In accordance with the provisions of Public Law 92-463, the meeting was open for public comments for an hour on June 6, 2006.

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## I. WELCOME, OPENING REMARKS

**Rodney Howell, M.D.**

**Chair, Secretary's Advisory Committee on Heritable Disorders  
and Genetic Diseases in Newborns and Children**

Dr. Howell welcomed participants to the eighth meeting of the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children (ACHDGDNC, the Committee). He introduced Lt. Col. David S. Louder, III, M.D., Chief Consultant for Maternal-Child Medicine and Pediatrics at the Office of the Surgeon General of the Air Force, who was present for his first meeting as a representative to the Committee from the U.S. Department of Defense.

Next Dr. Howell asked all other Committee members to introduce themselves. He also indicated that Committee members have been asked to file conflict of interest statements with the Health Resources and Services Administration (HRSA) for review. As the Committee moves into evaluating specific newborn screening tests, it is important that any Committee member with a conflict of interest notify HRSA.

Dr. Howell also reported that there had been some important publications since the Committee's last meeting, including the May 2006 supplement to *Pediatrics* entitled "A Look at Newborn Screening: Today and Tomorrow," which was edited by Dr. Edwards, Dr. Howell, and Dr. Lloyd-Puryear. This supplement, produced with funding from HRSA's Maternal and Child Health Bureau, was passed out to Committee members.

Finally, Dr. Howell outlined the agenda for the 2-day meeting:

- **Update on federal agency and federal advisory committee activities relevant to newborn screening.** Representatives from several federal agencies and advisory committees would update the Committee on their activities.
- **Status of the states with respect to newborn screening.** Dr. Brad Therrell, who directs the National Newborn Screening and Genetics Resource Center (NNSGRC), would give his usual report on status of the states with respect to newborn screening.
- **Federal legislative update.** Dr. Green from the March of Dimes would report on several bills related to newborn screening that are being considered by Congress.
- **Nomination process for newborn screening candidate conditions to the Committee for evaluation.** The Committee would be considering whether to accept the proposed nomination form to be used by advocates to nominate conditions to be added to the newborn screening panel. Dr. Howell noted that the nomination form had been through much iteration. Committee members and a few people had been asked to fill it out as a pilot test, so he hoped that Committee members could make a decision about finalizing the form. In addition, Dr. Howell said the Committee needed to consider what type of external evidence-based review group it should use to evaluate the evidence related to adding conditions to the uniform newborn screening panel. He noted that he preferred developing a new group to using any existing body, because few existing bodies deal with rare diseases.
- **Subcommittee meetings and reports.** The Education & Training Subcommittee, the Followup & Treatment Subcommittee, and the Laboratory Standards & Procedures

Subcommittee would meet on Monday, June 5, 2006, and give reports to the full Committee on Tuesday, June 6, 2006.

- **Policies and procedures for Advisory Committee practices.** Dr. Lloyd-Puryear would be presenting the first draft of policies and procedures.
- **Updates from organizational representatives to the Committee.** Representatives to the Committee from the Child Neurology Society, U.S. Department of Defense, and Food and Drug Administration would update the Committee on their organizations' activities relevant to newborn screening. (Dr. Howell noted that Dr. Alexander would be addressing the President's Council on Bioethics on newborn screening at its upcoming meeting June 22-23 in Washington, D.C.)

**Approval of Minutes.** The minutes from the previous meeting of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children held February 13-14<sup>th</sup>, 2006, were unanimously approved.

## II. AGENCY AND FEDERAL ADVISORY COMMITTEE UPDATE ON ACTIVITIES RELEVANT TO NEWBORN SCREENING

In the first session, individuals from the following federal agencies and federal advisory committees gave updates on their organizations' activities related to newborn screening:

- **National Institutes of Health (NIH):** Duane Alexander, M.D., Director, National Institute of Child Health and Human Development (NICHD)
- **Centers for Disease Control and Prevention (CDC):** Colleen Boyle, Ph.D., M.S., Director, Division of Birth Defects and Developmental Disabilities
- **Health Resources and Services Administration (HRSA):** Peter C. van Dyck, M.D., M.P.H., M.S., Associate Administrator, Maternal and Child Health Bureau.
- **Secretary's Advisory Committee on Infant Mortality:** James W. Collins, Jr., M.D., M.P.H., Chairman
- **Secretary's Advisory Committee on Genetics, Health, and Society:** Joseph Telfair, Dr.P.H., M.P.H., M.S.W.

Dr. Dougherty from the Agency for Healthcare Research and Quality (AHRQ), who had been scheduled to give a presentation, was unable to arrive in time to give her presentation, but her slides were included in the briefing books (Tab 6) distributed to Committee members.

In response to a question, Dr. Lloyd-Puryear explained that unlike ex officio Committee members from CDC, HRSA, NIH, and AHRQ, liaison representatives to the Committee, including Dr. Collins and Dr. Telfair, do not vote.

## **A. National Institutes of Health**

**Duane Alexander, M.D.**

**Director**

**National Institute of Child Health and Human Development (NICHD)**

**National Institutes of Health (NIH)**

Dr. Alexander gave a progress report on some ongoing initiatives at NIH and NICHD and also discussed some new initiatives:

1. **NIH solicitation for developing treatments for conditions detectable via newborn screening.** NICHD, joined by the National Institute of Diabetes, Digestive, and Kidney Diseases and the National Institute on Deafness and Other Communication Disorders, has issued an ongoing solicitation that encourages the scientific community to submit applications to develop new treatment approaches for conditions that are detectable via newborn screening. Applications will be solicited over the next 3 years. The quantity, quality, and diversity of applications in the first group of applications was very good; after undergoing peer review and selection, some of these applications will be funded in FY 2007.
2. **NICHD request for proposals (RFP) to develop improved “Novel Technologies in Newborn Screening.”** NICHD’s contracting office has issued an RFP to industry and the academic community to design and develop multiplexed screening assays that can be automated and utilized in a high throughput environment for newborn screening. The response has been good. The proposals will be reviewed and negotiated by the review committee and are also scheduled for funding in FY 2007.
3. **NICHD support of development of the newborn screening test for spinal muscular atrophy (SMA).** NIH has made a substantial investment in developing the test for newborn screening for this condition, and Dr. Tom Prior is working on this.
4. **Planning for November 2007 conference on newborn screening in north Africa and the Middle East.** North Africa and the Middle East are characterized by a high degree of consanguinity, and there is great interest among senior government officials and biomedical researchers in the Middle East about newborn screening. NIH Director Dr. Elias A. Zerhouni, Dr. Howell, and U.S. State Department representatives went to Morocco this past year to discuss biomedical issues and newborn screening. As a result, NIH, HRSA, and the CDC are planning a November 2007 conference in Morocco to discuss strengthening newborn screening in North Africa and the Middle East. The European community, the World Health Organization, and other sponsors are involved, as well.
5. **Discussions about involving the Regional Genetics and Newborn Screening Collaboratives and their National Coordinating Center (NCC) in facilitating R&D related to new technologies and methods of newborn screening for disorders recommended by the Committee.** NICHD is in preliminary talks about involving the regional collaboratives and coordinating center to assist investigators with providing specimens, access to patients, and providing a way to field test screening methods and technologies.

## **B. Centers for Disease Control and Prevention**

**Coleen Boyle, Ph.D., M.S.**

**Director**

**Division of Birth Defects and Developmental Disabilities**

**Centers for Disease Control and Prevention (CDC)**

Dr. Boyle reported that CDC has been involved in the following initiatives related to newborn screening:

1. **Emergency response related to newborn screening following Hurricane Katrina.** CDC assisted the Louisiana Department of Health and Hospitals/Office of Public Health in conducting a rapid assessment to determine the extent of newborn screening disruption in August and September 2005 following Hurricane Katrina. In the short term, they were able to disseminate new instructions to ensure optimal screening procedures; prompt hospital staffs to check log books for missing screening results; and identify about 1,200 infants in 53 hospitals with missing newborn screening results to be contacted for testing.
2. **Study of the epidemiology of missed or delayed diagnoses for conditions detected by newborn screening (Henderson et al).** Dr. Harry Hannon's group at CDC (the Newborn Screening Branch in the Division of Laboratory Sciences) has been conducting a study to determine the number, reasons why, and health outcomes for children with missed diagnoses from 1984 to 2004. The study involves a survey of state newborn screening lab and followup personnel, metabolic clinics, and affected families via parent advocacy groups. They want to encourage routine sharing of such information and identify procedures for routine surveillance of missed cases.
3. **Examining the prevalence of severe combined immune deficiency (SCID) among deaths in children under 18 months in California (Vogt et al).** CDC and the California State Department of Health Services will analyze 4,000 newborn dried blood spots, including 3,500 who died at ages under 18 months and 500 control children. All positives will be reanalyzed to see if cause of death was consistent with SCID. The results from this mortality cohort will reveal the extent to which SCID is an underlying cause of death in infants and very young children. This study will help determine underlying prevalence of SCID.
4. **Early Hearing Detection and Intervention (EHDI) Program.** EHDI programs in states are designed to identify infants with hearing loss by universal screening to permit early intervention. CDC and state representatives developed seven national goals that for EHDI programs. In 2004, only 69.9 percent of such infants received an intervention.
5. **Public health practice in laboratory genetics.** CDC, in collaboration with the Wadsworth Center, New York State Department of Health, Association of Public Health Laboratories, and Mt. Sinai School of Medicine is developing a survey to assess the extent to which DNA testing is used in the reporting of results from newborn screening programs within state public health laboratories. In addition, CDC is exploring a model called "synoptic reporting" to accomplish DNA-based (molecular) genetic lab test reporting to primary care physicians. It will start with conditions like cystic fibrosis and fragile X syndrome.
6. **Reports published by CDC staff on newborn screening.** Dr. Boyle presented a list of recent publications by CDC staff on newborn screening.

## Questions & Comments

Dr. Howell asked whether the 3,500 infants in California who died at ages under 18 months were screened for conditions other than SCID. Dr. Boyle said no. Dr. Howell said he thought it would be good to include other conditions. Referring to the program in New York for DNA testing, Dr. Howell also asked what DNA tests New York was looking at. Dr. Boyle said she would get the list for him.

## C. HRSA's Maternal and Child Health Bureau

**Peter C. van Dyck, M.D., M.P.H., M.S.**

**Associate Administrator**

**Maternal and Child Health Bureau**

**Health Resources and Services Administration (HRSA)**

Dr. van Dyck begin his presentation by stating that the mission of HRSA's Maternal and Child Health Bureau is to provide national leadership and to work, in partnership with states, communities, public-private partners, and families, to strengthen the maternal and child health infrastructure, assure the availability and use of medical homes, and build the knowledge and human resources in order to assure continued improvement in the health, safety, and well-being of the maternal and child health population. This population includes all American women, infants, children, adolescents, and their families; it includes individuals across their life span, women of reproductive age, fathers, and children with special health care needs.

The vision of HRSA's Maternal and Child Health Bureau for newborn screening is as follows:

- Use of a systems approach with defined public health roles at the state and national levels
- Presence of quality assurance
- Public-private partnerships for assurance of systems approach and comprehensive, efficient care and management
- Equity for families

Initiatives related to newborn screening include the following initiatives in education, training, capacity (infrastructure and workforce) research, and public policy:

1. **National Newborn Screening and Genetics Resources Center (NNSGRC).** The NNSGRC serves as focal point for national newborn screening and genetics activities and provides related resources to benefit consumers, health professionals, the public, the health community, and government officials. The NNSGRC Web site is <http://genes-r-us.uthscsa.edu/>.
2. **Genetic services and health care delivery programs.** The Maternal and Child Health Bureau supports Hemophilia Diagnostic and Treatment Centers and Thalassemia and Sickle Cell Disease programs as models of comprehensive care for the delivery of genetic services: testing, counseling, education, and coordinated systems of services. A new program, the Sickle Cell Disease Treatment Program, seeks to develop and establish mechanisms to enhance the prevention and treatment of sickle cell diseases via the coordination of service delivery, genetic counseling and testing, bundling of technical services, training of health professionals, and other related efforts.
3. **Understanding, informing and educating parents about newborn screening.** The Maternal and Child Health Bureau has undertaken a number of efforts to educate parents

about newborn screening. An appendix to the May 2006 newborn screening supplement to *Pediatrics* presents pictures of brochures developed by Dr. Terry Davis and her colleagues to use in educating parents (“7 Things Parents Want to Know About Newborn Screening: Quick Reference Guide for Health Professionals,” “This Test Could Save Your Baby’s Life”). These materials have been distributed to pediatric and prenatal care providers (obstetricians, family practice physicians, and nurse midwives) in a partnership with the American Academy of Pediatrics (AAP), the American College of Obstetricians and Gynecologists (ACOG), and the American Academy of Family Physicians (AAFP).

4. **Heritable Disorders Program: Regional Collaboratives and Coordinating Center.**

The Maternal and Child Health Bureau funds seven Regional Genetics and Newborn Screening Collaboratives and the National Coordinating Center (NCC) for the collaboratives. The idea of the regional collaboratives, now in their third year, is to improve equity in the distribution of resources and facilitate common data collection common policy development in the regions. The NCC tries to promote consistency among the regional centers.

5. **Other projects**

- *Development of a consumer-based family history tool to increase the public’s awareness of genetics.* The Maternal and Child Health Bureau’s partners in this project are the Library of Congress, the Genetic Alliance, and the American Society of Human Genetics. The toolkit is to be piloted over the next 3 years.
- *Translational genetic services.* The Maternal and Child Health Bureau has a cooperative agreement with Washington State to analyze models of genetic services delivery, including economic and policy issues, and to develop an agenda to translate genetic research into practice.
- *Two newborn screening projects:* (1) to establish a quality, Performance Evaluation and Assessment Scheme (PEAS) for newborn screening programs (NNSGRC); and (2) to support a best practice model of a child health data integration project for newborn screening (with the Public Health Informatics Institute) This latter effort is a long standing activity to combine and coalesce newborn screening technology and computerized information systems at the state level.
- *Newborn screening ACTION (ACT) sheets and confirmatory algorithms.* Newborn screening ACT sheets that describe the short-term actions that a health professional should take in communicating with the family and determining the appropriate steps in the followup of a newborn who screens positive for a condition in the uniform newborn screening panel, as well as an algorithm that presents an overview of the basic steps involved in determining the final diagnosis in the infant, were developed through the American College of Medical Genetics (ACMG), with funding from HRSA. The materials, which have been approved by the ACMG Board, are available on ACMG Web site (<http://www.acmg.net>), as well as at HRSA’s Maternal and Child Health Web site (<http://mchb.hrsa.gov/>). The newborn screening ACT sheets and algorithms have also been adopted by the board of the AAP, and many states are adopting the materials for their programs for distribution to pediatric health professionals.
- *May 2006 Pediatrics supplement on newborn screening.* The May 2006 supplement to *Pediatrics* entitled “A Look at Newborn Screening: Today and

Tomorrow” was produced with funding from HRSA’s Maternal and Child Health Bureau and highlights key developments and issues in the past 6 years.

Finally, Dr. van Dyck noted that financial, program, and other data from HRSA’s Maternal and Child Health Bureau are available at the following Web site:

<https://performance.hrsa.gov/mchb/mchreports>.

### **Questions & Comments**

Dr. Green noted that March of Dimes has developed videos in concert with the brochures for parents developed by Dr. Davis under contract to HRSA. She suggested that the videos be shown at a future meeting of the Committee, so that the Committee could provide feedback. Dr. Howell agreed that this was a good idea.

Dr. Edwards said AAP would like to know whether it can state in a policy statement that pediatricians should check the ACMG Web site for updated versions. Dr. van Dyck and Dr. Lloyd-Puryear said yes, noting that ACMG will be updating the content on the front of the newborn screening ACT sheets with help from the National Coordinating Center (NCC) for the regional collaboratives. HRSA wants every state to send out the appropriate ACT sheet for every newborn screening result, adding state-specific information on the back of the sheets.

Dr. Howell, noting that screening for hemoglobinopathies will lead to the detection of a panoply of other hemoglobinopathies other than sickle cell asked whether the new HRSA sickle cell disease treatment center network had a mechanism to provide genetic counseling for all of the variants. Dr. Telfair and Dr. van Dyck said generally speaking, the answer to this question is that the counseling may not be available locally but can be provide through different levels of operation (the 17 sickle cell community-based grantees, a local advisory committee, SCDA, the NNSGRC, and the ACMG).

Dr. Green said she thought it would be useful to look at how the different hemoglobinopathies are coordinated through the seven Regional Genetics and Newborn Screening Collaboratives. Dr. van Dyck said that the coordination of the sickle cell disease network with the regional centers does not exist yet—the program will not start until September, but is something that needs to be encouraged. Dr. Howell suggested that ACMG Executive Director Dr. Michael Watson, who is the project director for the NCC, could work toward coordinating the sickle cell and thalassemia centers with the regional collaboratives. Dr. Watson said he wished it were that easy, adding that there is considerable variability at the level of the states, and the NCC and regional collaboratives are going to be doing ACT sheets, but they decided that it was not their job to decide what should be primary targets of screening or to go beyond what the ACMG report said about the secondary conditions.

## **D. Secretary's Advisory Committee on Infant Mortality**

**James W. Collins, Jr., M.D., M.P.H.**

**Chairman**

**Secretary's Advisory Committee on Infant Mortality (SACIM)**

Dr. Collins stated that the mission of SACIM is to identify and work on several important program issues deserving of exploration and concentrated committee work that can lead to recommendations to the Secretary of Health and Human Services (HHS) to reduce infant mortality and improve the health status of pregnant women and infants.

SACIM has three subcommittees:

- Eliminating Health Disparities in Infant Mortality
- Clinical and Public Health Practice
- Funding and Finance

The tasks for these subcommittees are to identify issues for which there are program inadequacies, identify issues that could benefit from program enhancements, and work with issues that require additional HHS efforts to make improvements in maternal and child health.

The SACIM subcommittees are meeting now, and there is an upcoming meeting in July to come up with a work position paper to address specific recommendations. The hope is that the recommendations being developed will be action oriented, practical in nature, and reasonably implemented.

According to Dr. Collins, the SACIM Subcommittee on Eliminating Health Disparities in Infant Mortality is most likely going to focus on race and ethnic group differences in infant mortality as it relates to prematurity and low birth weight; the Subcommittee on Clinical and Public Health Practice is probably going to be looking at recommendations to expand the concept of maternal health as it extends from adolescence and then to pregnancy itself; and the Subcommittee on Funding and Finance, which is likely to be most relevant for the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children, is going to be addressing ways to fund these programs, particularly via Medicaid.

### **Questions & Comments**

Dr. Green reported that the Institute of Medicine would be coming out with a report on issues related to premature births, a leading cause of infant mortality, later this month. She urged SACIM to amplify the report's recommendations. Dr. Collins indicated that SACIM would certainly be doing that.

## E. Secretary's Advisory Committee on Genetics, Health, and Society

**Joseph Telfair, Dr.P.H., M.P.W., M.S.W.**

**Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS)**

Dr. Telfair gave a very comprehensive overview of SACGHS' mandate, scope of work, current priorities, and work products to date. The committee, which is chaired by Reed Tuckson, M.D., has been in existence for 3 years and meets about 3 times a year.

SACGHS has a mandate to explore, analyze, and deliberate on the broad range of human health and societal issues raised by the development and use, as well as the potential misuse, of genetic technologies and to make recommendations to the Secretary of HHS and other departments upon request. The scope of committee's charge encompasses (1) integrating genetic technologies into health care and public health; (2) clinical, ethical, legal, and societal implications of new medical applications; (3) research and data collection; (4) misuse of genetics in bioterrorism; (5) patent policy and licensing practices; (6) broader social applications of genetics (forensics, education, etc.); and (7) emerging genetic applications and issues.

As of May 2006, the priorities for SACGHS were genetic discrimination, coverage and reimbursement, pharmacogenomics, large population studies, direct-to-consumer marketing, patents and licensing, oversight, genetics education and training, access, public awareness, and the Committee's vision statement. The SACGHS' work products to date are available on the SACGHS Web site: <http://www4.od.nih.gov/oba/SACGHS/reports/reports.html>. Among them are the following

- **Reports:** A Roadmap for Integration of Genetics and Genomics in Society: Report on the Study Priorities for SACGHS; Coverage and Reimbursement for Genetic Tests and Services; draft report on Policy Issues Associated with Undertaking a Large U.S. Population Cohort Project on Genes, Environment, and Disease.
- **Letters to the Secretary of Health and Human Services:** Three letters on genetic discrimination and compilation of public comments, DVD highlights of public testimony, legal analysis of existing federal laws; two letters on direct-to-consumer marketing of genetic tests; a letter on the national health information infrastructure; and a letter on family history. (Responses from the HHS Secretary, if available, are also on the SACGHS Web site.)

SACGHS' ninth meeting was held March 27-28, 2006, and focused on reviewing policy issues related to large population studies. The SACGHS Large Population Studies Task Force is revising and augmenting a draft report on a large population cohort project of genetic variation, the environment, and common diseases, as well as the associated policy issues and options for addressing them. SACGHS would like members of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children to comment on the draft report. Comments are due July 31, 2006. The report (*Policy Issues Associated with Undertaking a Large U.S. Population Cohort Project on Genes, Environment, and Disease*) is available on the Web at [http://www4.od.nih.gov/oba/SACGHS/public\\_comments.htm](http://www4.od.nih.gov/oba/SACGHS/public_comments.htm).

Other SACGHS task forces are dealing with other topics addressed at the March 2006 SACGHS meeting. The SACGHS Pharmacogenomics Task Force is developing a draft report on guidance for industry and the Food and Drug Administration regarding pharmacogenetic tests and genetic tests for heritable markers and will refine recommendations for consideration by the full SACGHS at its June 2006 meeting. The SACGHS Task Force on Genetic Discrimination is

organizing a meeting with the Coalition for Genetic Fairness, the Chamber of Commerce, and the National Association of Manufacturers to discuss unresolved concerns regarding H.R. 1227, the Genetic Information Nondiscrimination Act of 2005, which would prohibit discrimination in health insurance and employment on the basis of predictive genetic information. That task force will be writing another letter to the Secretary urging him to take specific actions to advance the passage of federal genetic nondiscrimination legislation. The SACGHS Patents and Access Task Force is planning an information session for the June 2006 meeting of SACGHS.

### **Questions & Comments**

Dr. Boyle asked two questions about the SACGHS large cohort study on genes, environment, and disease: (1) whether it has any relevance to what the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children is doing; and (2) how the SACGHS study is related to the National Children's Study examining 100,000 children. Dr. Telfair said the SACGHS study relates to the National Children's Study in that both are large studies that require resources. The report is also relevant because it has recommendations about what conditions should be reviewed.

Dr. Alexander stated his belief that the issue of genetic discrimination is the topic being addressed by SACGHS that is most relevant to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. He added that if parents cannot be assured of protection against discrimination from genetic testing (not just privacy) in employment and health insurance, they will not want such testing. The Senate has passed a bill to prevent genetic discrimination twice 99-0, but efforts to get the bill passed by the House are needed. Dr. Telfair said the biggest concerns are clarity, definition, and enforcement. SACGHS will have professionals and others provide input on these issues at its upcoming meeting in June.

## **III. STATUS OF THE STATES—UPDATE ON NEWBORN SCREENING PROGRAMS**

**Bradford Therrell, Ph.D.**

**University of Texas Health Science Center at San Antonio**

**National Newborn Screening and Genetics Resource Center (NNSGRC)**

Dr. Therrell distributed a 2-page grid entitled "National Newborn Screening Status Report—Updated 06/01/06"—showing state requirements with respect to the core American College of Medical Genetics (ACMG) panel of 29 conditions and secondary conditions amenable to newborn screening. He noted that the handout has several footnotes—for example, to indicate that screening is universally required by law or rule, universally offered but not yet required, offered to select populations or by request, etc. He explained that the fact that screening for a specific condition is not mandated by a state does not mean that screening is not provided.

Next Dr. Therrell noted that state newborn screening programs reported the following recent changes in response to a request asking what they would want reported by NNSGRC to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children:

- Alaska has universally mandated hearing screening.
- Arizona has expanded its newborn screening panel to include several additional conditions and now requires two screenings. It has also increased its fee from \$20/screen to \$30 (first screen) and \$40 (second screen) and taken on the responsibility of collecting

- the fees from insurance companies. Arizona requires hearing screenings to be reported so the Arizona Department of Health Services can do followup. In May, Arizona started pilot testing for five fatty acid oxidation disorders and nine organic acids, with reporting to begin in September 2006. Screening for cystic fibrosis will be added in 2007.
- Colorado has expanded its newborn screening panel to the core 29 recommended in the ACMG report. It is looking to limiting tandem mass spectrometry (MS/MS) to first of two required specimens. Colorado has increased its fee from \$5/baby to \$80/baby (two specimens).
  - The District of Columbia expanded its newborn screening panel to 53 conditions as of February 1, 2006, and reportedly is doing well.
  - Florida indicated it is not screening for variant hemoglobins. An advisory committee is to consider the question of 24 hours vs. 48 hours (used at present) for obtaining a satisfactory specimen.
  - Georgia had a major law change in May 2006. Previously, the state did not charge a fee for newborn screening; now the fee allowed is \$40/baby. Georgia will expand to the core 29 conditions in the ACMG uniform panel in January 2007. The state labs are to be used only if they are shown to be the most cost-effective; otherwise, the state is to go out for bids.
  - Idaho is planning to expand its newborn screening panel to include cystic fibrosis in 2007.
  - Kansas requires screening for relatively few disorders, including hearing, congenital hypothyroidism, hemoglobinopathies (sickle cell), and galactosemia. A Kansas state law required that the treatment of anything detected by newborn screening be covered in its entirety by the state, but the budget limits what the state can add to its newborn screening panel. In May 2006, the Kansas legislature authorized money for an advisory committee to look at the budget, and develop newborn screening guidelines and any rules or statutory changes necessary. The advisory committee is to the legislature by January 1, 2007. The state recently amended the law requiring payment for PKU treatment formula and required a sliding-fee scale.
  - Kentucky will expand its newborn screening panel to the 29 conditions in the core ACMG panel on January 1, 2007, and increase its screening fee from \$14.50 to \$53.50. The state has been considering whether to detect cystic fibrosis using an IRT/IRT protocol or an IRT/DNA protocol.<sup>1</sup>
  - Louisiana will expand its newborn screening panel to 28 of the 29 conditions in the core ACMG panel on August 1, 2006, and increase its fee from \$18 to \$30. The state will begin screening for cystic fibrosis in July 2007.
  - Maryland added cystic fibrosis to its newborn screening panel on June 1, 2006. It uses an IRT/IRT protocol for cystic fibrosis screening.
  - Nebraska began mandatory screening for cystic fibrosis and CAH (congenital adrenal hyperplasia) on June 1, 2006. It uses an IRT/DNA protocol for cystic fibrosis screening.

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<sup>1</sup>An IRT/IRT protocol consists of an immunoreactive trypsin (IRT) protocol without mutation analysis of the cystic fibrosis transmembrane conductance regulator (CFTR) gene; an IRT/DNA protocol includes mutation analysis.

- New Hampshire, on May 1, 2006, after more than 2 years of work, finally added five conditions to its newborn screening panel: BIO (biotinidase), CAH, MCAD (medium-chain acyl-CoA dehydrogenase deficiency), cystic fibrosis, and sickle cell. New Hampshire was the last state to screen universally for sickle cell disease. There have been meetings trying to expand the state's panel further, but the process is hard in New Hampshire.
- New York is testing for Krabbe disease in a pilot program.<sup>2</sup>
- New Mexico's legislature expanded the state's newborn screening program in 2005. Following a evaluation process to determine best approach, New Mexico obtained bids from members of the Western States Buying Cooperative (California, Colorado, Oregon, Utah, and Minnesota) and decided to contract services to Oregon beginning on October 1, 2006. The fee is expected to increase from \$32 for two specimens to \$89 for two specimens.
- Ohio is adding cystic fibrosis and CUD (carnitine uptake defect) to its newborn screening panel on August 1, 2006.
- Oklahoma added MCAD to its newborn screening panel on June 1, 2006, and will add other conditions from the core panel by end of the year.
- Rhode Island expanding its newborn screening panel to include the 29 disorders in the core ACMG panel on July 1, 2006.
- Texas reissued a request for proposals for newborn screening services in 2006, but no bid was awarded, so services will be performed by the state lab. Texas anticipates the start of expanded testing in November 2006. The fee is expected to increase from \$19.50 to \$29.50 for each of the two required screens.
- Utah expanded to the entire MS/MS panel on January 1, 2006. It contracts with ARUP, a lab in the state, for services.
- Washington state raised its clinical surcharge by \$3.10 to \$6.60. The overall fee for newborn screening is now \$67.50. On March 15, 2006, Washington added cystic fibrosis screening using an IRT/IRT protocol.
- Wyoming is part of the Colorado region, so it will expand its newborn screening program to include the 29 conditions in the in the core ACMG panel as soon as Colorado does.

Next Dr. Therrell presented several maps. One set of maps showed what service delivery models states use for newborn screening. About half of states are using contract screening labs and half use their own public health labs. Another set of maps showed what how many conditions are required in states' newborn screening panels. Only 12 states mandate the 29 conditions in the core ACMG panel. Other states come close, but do not mandate screening for cystic fibrosis or congenital hearing loss. (As of June 1, 2006, Minnesota's newborn screening panel included 53 conditions, but not all 29 conditions in the core ACMG panel.)

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<sup>2</sup> A person in the audience, Ms. Katharine Harris, from the Wadsworth Center, New York State Genetics and Screening Program, stated that New York is doing anonymized specimens rather than a pilot program of Krabbe disease. She said New York expects to begin universal screening for Krabbe disease sometime this summer.

According to Dr. Therrell, current issues related to newborn screening in the states are as follows: (1) when to take a specimen—12 hrs. vs. 24 hrs. vs. 48 hrs. for unsatisfactory specimens; (2) required single screen vs. required two screens; (3) financing—fees, amount available from Medicaid; (4) best protocol for cystic fibrosis screening—IRT/DNA vs. IRT/IRT (carrier detection issues—the states that are doing IRT/IRT say they are doing it because it gets around the issue of carriers, so they don't have the carrier follow-up); (5) software developed with CDC funding at Oregon Health and Science University (OHSU) that is available for anybody free of charge if they want to use it to do long term followup and tracking (about 25 states have taken advantage of this software); (6) whether to mandate all conditions on the ACMG panel (detection and liability issues); (7) the quality of recall data in hearing screening; and (8) data sharing—some states are asking that they not share laboratory cut-off data because of patent issues.

Finally, Dr. Therrell noted the following three Web sites related to newborn screening:

- National Newborn Screening and Genetics Resource Center (NNSGRC) Web site: <http://genes-r-us.uthscsa.edu/>
- National Newborn Screening Data System Web site: <http://www2.uthscsa.edu/nnsis/>. This site, hosted by NNSGRC, is a data base for collecting and providing data on newborn screening in the states and U.S. territories.
- March of Dimes PeriStats Web site: <http://www.marchofdimes.com/peristats/>. This site, developed by the March of Dimes Perinatal Data Center, provides free access to U.S., state, county, and city maternal and infant health data. It allows users to create maps and graphs for specific maternal and infant health indicators.

### Questions & Comments

Mr. Robertson, noting that fees for newborn screening are going up significantly, asked how these are being paid for. Dr. Therrell explained that the fees are covered by most people's private health insurance in the maternity package. For Medicaid, he said, the coverage is different for every state; however, every state has a policy that says if someone is unable to pay, there is a way to provide screening at no charge. Dr. Howell said he noted that funding for treatment is very meager; most children with disorders end up at university settings and have no money. The costs related to newborn screening for confirmatory diagnosis and followup far exceed those of lab testing.

Dr. James Hanson, from the National Institute of Child Health and Human Development, asked whether there was any plan to start collecting data on premature babies. Dr. Therrell replied that there was no plan but it was a good suggestion and NNSGRC would consider it.

Dr. Kus asked for more information about the issue of recall data on hearing screening. Dr. Therrell explained that the problem is that not everyone is reporting their data; they know that a baby got screened and got a test, but they do not know whether the child got followup, so they do not report to the Centers for Disease Control and Prevention. Dr. Howell added there is no evidence that they are followed up.

Dr. Edwards, noting that 25 nontreatable conditions are evaluated as a result of screening for the 29 conditions in the core ACMG panel, asked: If states screen for the 29 conditions, are they doing all 53? Dr. Therrell replied no, adding that some states do not want the secondary conditions listed as mandated, because they do not want to be held responsible for them—hence NNSGRC added the following footnote (D) to the secondary conditions on the second page of the “National Newborn Screening Status Report—Updated 06/01/06”: “likely to be detected (and

reported) as a byproduct of MRM screening (MS/MS) targeted by law or rule.” Dr. Rinaldo called this distinction silly, saying there are only two conditions on the secondary panel that have no links to the primary targets; all the rest are differential for the primary targets.

Dr. Hawkins said he found Dr. Therrell’s report that some states are using a protocol for cystic fibrosis screening (IRT/IRT) so as not to have to deal with carriers counterintuitive, because we should *want* to identify carriers. Dr. Therrell said the question for states often comes down to one of whether they have the resources to find carriers and do genetic counseling. Dr. Howell said this is a very important question that the Advisory Committee may want to consider further at some point.

## **IV. FEDERAL LEGISLATIVE UPDATE**

### **Jo Merrill**

#### **Director of Public Policy and Government Affairs**

#### **March of Dimes**

After being introduced by Dr. Green, the March of Dimes Director of Public Policy and Government Affairs, Jo Merrill, reported that the March of Dimes Office of Legislative Affairs has been working very hard to engage and educate members of Congress about newborn screening, especially members of the relevant committees.

The two bills in Committee members’ briefing books dealing with small business health plans have been withdrawn, Ms. Merrill said, so her report to the Committee would focus on the status of federal appropriations bills and authorization bills pertaining to newborn screening. According to Ms. Merrill, if the March of Dimes Office of Legislative Affairs had to choose between working on appropriations or authorization bills, they would work on appropriations bills. Authorization bills provide legislative language, but what is really needed is the funding.

**Federal Appropriations (Funding).** Last year federal funding for health, education, and labor actually went down. For FY 2007, the likelihood is that funding will remain level:

- **President’s budget request.** President Bush’s FY 2007 budget request for health and human services, and education, and related agencies proposed eliminating federal funding for the newborn hearing screening program and did not include funding of other newborn screening programs that have been funded in the past via the Maternal and Child Health block grant. The Maternal and Child Health block grant was cut last year, and the President’s budget request for this year proposed level funding.
- **Congressional appropriations.** The House and Senate have each passed their own budget resolutions. The House resolution included level funding for health and education programs; the Senate resolution included a \$7 billion increase for health and education. Because the two resolutions have to be reconciled, the likelihood is that funding for FY 2007 will remain level.

**Federal Authorization Bill—Newborn Screening Saves Lives Act (S. 2663).** S. 2663 is an authorization bill introduced by Senators Chris Dodd (D-Conn.) and Mike DeWine (R-Ohio); even if the bill is passed by Congress, funding for the authorized programs would have to be obtained separately. S. 2663 authorizes giving states resources to expand newborn screening programs; to access those resources, the states would have to commit to screen for all 29 conditions in the core uniform newborn screening panel. The Dodd-DeWine bill also lists new

responsibilities for the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children—and asks the Secretary of Health and Human Services to accept or reject the Committee’s recommendations within 180 days. Finally, the bill authorizes grant programs for lab personnel; education of parents and patient advocacy groups; establishes a system of followup care for newborns; requires the Centers for Disease Control and Prevention (CDC) to ensure the quality of labs; and establishes a new system at CDC to analyze data from newborn screening programs to improve detection and prevention.

In conclusion, Ms. Merrill said there is good news and bad news. The bad news is that no appropriations bills are likely to pass Congress, and funding will remain level. The good news is that the March of Dimes is seeing a lot of interest in Congress in newborn screening as more reports are coming out. It has found a few key advocates in Congress and has been making some progress in getting others involved too.

### **Questions & Comments**

Dr. Kus asked what activities would be undertaken with respect to the Dodd-DeWine bill (S. 2663). Ms. Merrill said there was a press conference at which the March of Dimes brought an ambassador family, and various advocacy groups have been trying to generate support for the bill and would like to push for a hearing on this to update the Congress; however, Ms. Merrill does not expect that a hearing will be held any time soon.

Dr. Howell asked whether the Dodd-DeWine bill would authorize any money for research related to newborn screening and noted that the Florida legislature funded a research program on fragile X syndrome at University of Miami. Ms. Merrill responded that Dodd-DeWine bill focuses more on programs under the HRSA and CDC than on research; however, there is a separate reauthorization bill for the National Institutes of Health, and that may authorize money for research related to newborn screening.

Dr. Howell also asked how successful the March of Dimes had been in bringing advocacy groups in the area of newborn screening together. Ms. Merrill said the advocacy groups work together fairly well, signing “Dear Colleague” letters to members of Congress, etc. There is no specific coalition on newborn screening, but there are related groups (e.g., a parental Title V group, Friends of NICHD group, and the CDC Coalition).

Dr. Howell asked whether Senator Hillary Clinton (D-NY) had introduced a bill. Ms. Merrill said the March of Dimes and the American Academy of Pediatrics have been working with her office staff to discuss things, but her plans for introducing legislation are not yet clear.

Dr. Lloyd-Puryear asked Ms. Merrill to explain why the two bills that were withdrawn should be of interest to the Committee. Ms. Merrill said the first bill was a bill to provide health insurance to small businesses; it would eliminate state mandates (because state mandates vary), which includes mandates on covering PKU formula that vary in states and PKU would have been eliminated. The other bill was an alternative to providing insurance for small businesses.

## V. NOMINATION PROCESS FOR CANDIDATE CONDITIONS ON THE UNIFORM SCREENING PANEL

**Nancy Green, M.D.**  
**Medical Director**  
**March of Dimes Birth Defects Foundation**

Dr. Green reminded everyone that in October 2005, Dr. Howell appointed a Criteria Workgroup, headed by Dr. Green, to make recommendations to the Advisory Committee about what criteria should be used to evaluate conditions nominated for State newborn screening programs for screening newborns. Members of the workgroup are Dr. Howell, Dr. Brower, Dr. Boyle, Dr. Coggins, Dr. Dougherty, and Dr. Rinaldo, and Dr. Green. Dr. Lloyd-Puryear and Dr. Marie Mann are providing HRSA staff support to the Criteria Workgroup.

At previous Committee meetings, it was agreed that there would be three steps in the process of nominating conditions for the Committee's evaluation:

- **Step #1:** Nomination form submitted by proponent(s) of adding a condition
- **Step #2:** Federal administrative review of the nomination form
- **Step #3:** Review by the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
  - a. Evidence-based review by an external body
  - b. Committee review

It was also agreed that the nomination process should be developed using the following concepts: (1) broad access to nomination process; (2) considered review; (3) streamlined processes; (4) transparency; (5) consistent criteria throughout the nomination process; and (5) three broad areas identified (Condition, Test, Treatment) and References.

According to Dr. Green, the Criteria Workgroup had identified the following tasks to be completed by the Committee with respect to the three steps in the nomination process:

- Step #1: Finalize the nomination form submitted by proponent(s) of adding a condition.
- Step #2: Clarify Federal administrative review of the nomination form.
- Step #3: Delineate the processes for review by the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children.
  - a. Delineate processes for evidence-based review by an external body.
  - b. Delineate processes for review by the full Committee.

Dr. Green explained that there would be two presentations in this session. First, she would be talking about the modifications to the draft nomination form for proponents of adding a condition that incorporated Committee members' input and about pilot testing of the revised nomination form by potential users. The hope was that the Committee could then finalize the nomination form (the task with regard to Step #1). Second, Dr. Dougherty would be talking about what the next steps should be to go about delineating processes for evidence-based reviews by an external body (one of two tasks related to Step #3).

## **A. Draft Nomination Form for Adding Conditions to the ACMG Uniform Newborn Screening Panel**

Dr. Green reported that the Advisory Committee's Criteria Workgroup had made considerable progress with respect to finalizing the nomination form to be used by proponents of adding a condition to State newborn screening panels since the Committee's meeting in February 2006:

- It had made modifications to the nomination form.
- It had piloted the nomination form to consumers (the Genetic Alliance has been very helpful) and geneticists.
- It had solicited additional input on the nomination form from consumer health advocacy groups.

**Modifications to the nomination form.** Dr. Green presented a revised nomination form dated 5/18/06) She noted that the Criteria Workgroup had based its revisions taking the following suggestions from the February 2006 Committee meeting into account: (1) keep the nomination form simple; (2) keep process for nomination consistent with downstream review; (3) include a tracking number for submissions; (4) streamline the process by funneling multiple applications on the or linked disorders); (5) allow only the full Advisory Committee to reject a nomination form application, even with expedited review; (6) include a conflict of interest disclosure with the nomination form and overall nominating process (for the Committee too); (7) think about how to prioritize (may want to start with the 84 disorders that were on the ACMG's original list; and (8) think about how to consider the economic impact of screening in the evidence-based review by an external body in Step #3. Dr. Green then reviewed each of the revisions to the form, which were marked in red (e.g., each statement should have a specific reference listed at the end; the severity of disease and spectrum of disease should be noted; under the test category, include the concept of secondary disorders; under treatment, include treatment limitations such as difficulty with acceptance or compliance).

**Pilot of the revised nomination form by potential users.** Dr. Green reported on several pilots of the nomination form without the last version and recent edits, noting that the SMA pilot was received over the weekend and the Committee has not seen it yet:

- **Consumers:** Sharon Terry, president, Genetic Alliance; Jill Fisch, president, Save Babies Through Screening (pilot of the nomination form using Wilson's disease with Kimberly Symonds, executive director, Wilson's Disease Association); Micki Gartzke, director, Hunter's Hope Foundation (pilot using Krabbe disease)
- **Health professionals:** Carol Greene, M.D. (pilot using glutaric aciduria type 1), Society for Inherited Metabolic Disorders; Jennifer Puck, M.D., University of California at San Francisco (pilot using SCID, severe combined immune deficiency); Priya Kishnani, M.D., Duke University (pilot using Pompe diseases); and Jill Jarecki, Ph.D., research director, Families of SMA (pilot using SMA, spinal muscular atrophy).

**Input on the nomination form from the Genetic Alliance.** Dr. Green reported that the Genetic Alliance had made the following suggestions with respect to the nomination form and process:

- Pilot the nomination form with a large, well-trained, savvy consumer committee.
- Have strict general guidelines for inclusion: (1) limits of age of onset for the condition, for which there is later childhood or adult onset; (2) reject disorders for which there are no treatments; and (3) define a minimum incidence.

- Define “treatment.” (For example, does treatment include genetic counseling?)

Finally, Dr. Green noted that the Genetic Alliance had offered to help work with consumers to determine the suitability of nominating a new disorder for inclusion on the uniform newborn screening panel, assist in completing a nomination form; and interpret decisions.

### Questions & Comments

Dr. Telfair said he thought the Criteria Workgroup had done an excellent job on the nomination form and asked if people who had piloted the nomination form could describe their experiences. At Dr. Howell’s request, reports on the following were given:

- **Pilot of the nomination form for Wilson’s disease.** Ms. Fisch said that Dr. Sharon Terry from the Genetic Alliance approached her about doing a pilot of the nomination form. Ms. Fisch, in turn, asked Ms. Kimberly Symonds from the Wilson’s Disease Association to do the form. Wilson’s disease is a condition with both a test and treatment. Ms. Symonds explained to the Committee that she sent the questions to three experts on the Wilson’s Disease Association’s medical advisory committee, then used their responses to fill in the nomination form and sent the form back to the experts to review. Ms. Fisch is concerned about the complexity of the form and she thought that the Genetic Alliance might serve well as an organization where consumers could go to get assistance in completing the form.
- **Pilot of the nomination form for Krabbe disease.** Ms. Gartzke said that although she first felt intimidated by the nomination form, she decided to fill it out herself using her own references for Krabbe disease rather than to go to scientists for each section. Overall, she thought the form was all right for her to fill out, but she would be a bit worried about other consumers with less information. She supports the idea of having the Genetic Alliance help advocacy groups and consumers complete the form.
- **Pilot of the form for glutaric aciduria type 1 (GA1).** Dr. Carol Greene, who piloted the nomination form using GA1 said she is a professional, and she made a phone call to find out what is published and where are the citations. She thought the forms could be done collaboratively. If there are no data out there and it is not obvious who the experts are, then the condition is not ready for being nominated for a core condition. She did not think an OMIM<sup>TM</sup> number<sup>3</sup> is needed.

Several Committee members agreed that it would be useful to have the Genetic Alliance provide assistance to advocacy groups and consumers in filling out the nomination form. Dr. Hawkins also suggested adding a one-page cover sheet to the nomination form giving consumers information about how to complete the form and where they can get help in completing the form. Dr. Green and Dr. Howell agreed that it would be useful to add a page of instructions to the form.

Dr. Rinaldo said he sees the nomination form as a group of 14 mini-abstracts that should be filled out by professionals and combine most up-to-date information coming from all the components. He particularly liked the pilot nomination form written by Dr. Jennifer Puck for severe combined immune deficiency.

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<sup>3</sup> Online *Mendelian Inheritance in Man* (OMIM<sup>TM</sup>) is a continuously updated catalog of human genes and genetic disorders. Each OMIM entry is given a unique six-digit number whose first digit indicates the mode of inheritance of the gene involved:

Dr. Rinaldo also said he hoped that the Committee would initially be dealing with nominations of conditions for which the treatment is quite well established (e.g., Krabbe, Pompe, Wilson’s disease)—and the test has been missing. He added that in his opinion, if no one is already doing the test for a condition in a prospective way, the condition is not a good candidate for adding to the uniform newborn screening panel.

Dr. Harry Hannon from the Newborn Screening Branch in CDC’s Division of Laboratory Sciences asked how transparent the evaluation would be, noting that eliminating demonstrated bias is very important. He also proposed giving nominators comprehensive feedback on strengths and weaknesses of their nominations; this feedback could be provided by simply modifying the nomination form to say “Acceptance/Rejection Form” and giving feedback on each section. Dr. Green said even though the Criteria Workgroup did not want quantitative weightings, it might consider qualitative feedback.

Dr. Alexander observed that the Committee is going to have to come to terms with how to handle nominations for condition for which there is no treatment, because families and other advocates are going to put forward such nominations. Ms. Gartzke confirmed this, emphasizing that from the families’ perspective, newborn screening is valuable even without treatment, because in the absence of screening, it is hard to get children with rare conditions diagnosed and the kids and their families suffer during what is often a long diagnostic odyssey.

Dr. Kus said the issue that has to be addressed is what constitutes treatment and whether the concept of benefit should be broadened from “medical benefit that improves a child’s health. Dr. Howell noted that Dr. Don Bailey, principal investigator on the Fragile X Project in North Carolina, has written on expanding the concepts of what constitutes a treatable disorder, and he suggested inviting him to give a presentation on this topic to the Committee, Dr. Green said this was a good idea, but she suggested having someone present the other side (e.g., a parent whose child had a false positive for fragile X syndrome). Dr. Howell agreed and asked everyone for help in identifying such a person. Dr. Boyle noted that fragile X syndrome is different from other disorders and said she thought the Committee might also like to hear from someone with Wilson’s disease or something that has a more immediate impact on the family.

Dr. Howell asked what was needed for Committee to move the revised nomination form ahead. Dr. Green said the Committee needed to respond. Committee members then engaged in a wide ranging discussion about the nomination form. Dr. Kahn said if Committee members knew what the external evidence-based review process was going to be (deal with risk, benefits, cost-efficacy, etc.) and used that process consistently, they could ask for less in the nomination form.

- **Finalize the nomination form.** Dr. Alexander reminded Committee members that the nomination form is a screening instrument to allow the Committee to see whether something goes to the next stage. He said he would feel very comfortable using the information on the revised nomination form in deciding whether a condition should go forward, as well as in prioritizing among conditions. He thinks the nomination form does the job. Dr. Rinaldo recommended that the Committee get to the point where it is reasonably comfortable with the nomination form and then go ahead and make a decision about it. He said the Committee could spend months to refine the form—in the end, though, it is what the nominators put in that makes the difference.
- **Finalize the nomination form but leave it open for change.** Dr. Dougherty suggested that the Committee could finalize the nomination form but leave open the possibility of revising the form in parallel with the development of the external evidence-based review group if new things need to be added. She added that conversations involving Dr. Green,

Dr. Howell, and others had led to the idea of having a meeting with some experts in evidence review to at least shape an outline of what the evidence review process in Step #3 in the process of nominating conditions to the ACMG uniform newborn screening panel would look like before going forward. She would be discussing this proposal in her presentation. Perhaps they should delay voting on the nomination form until they had heard her presentation. Dr. Lloyd-Puryear suggested that the nomination form could be revised to reflect input from the external evidence-based review group. Dr. Howell confirmed that the nomination form would not be set in stone if the Committee approved it at this meeting.

- **Add a new category like “benefits” for families to fill out.** Mr. Robertson proposed adding a category like “family impact” to the nomination form that family advocates could fill out. He explained that treatment “efficacy” is a scientific term and seems different from “benefits” to children and their families. Dr. Telfair agreed that a category such as that suggested by Mr. Robertson should be added, saying it might be labeled “quality of life.” Dr. Lloyd-Puryear observed that the ACMG newborn screening report included criteria related to impacts on children and families; noting that there is a category of “risks” associated with the test, she suggested possibly adding a category for “benefits” associated with the test. Dr. Gregg suggested that these issues were included in the concept of cost-efficacy and proposed having someone come back to talk to the Committee about this. Dr. Green raised the idea of including “benefit” as a subcategory under the section of the nomination form on “Treatment Efficacy.”
- **Add a one-page cover sheet with instructions.** Committee members agreed with Dr. Hawkins suggestion that a one-page cover sheet giving consumers information about how to complete the nomination form and where to get help in completing the form would be useful. Dr. Green said she would welcome suggestions about what should be included.

After hearing Dr. Dougherty’s presentation (see below), Dr. Alexander made the following motion, with the understanding that the nomination form might be modified by the Committee in the future, and the Committee approved it unanimously.

- ***MOTION #1: The Committee accepts the nomination form dated 5/18/06 to be used by proponents of adding a condition to the ACMG uniform newborn screening panel as a blank form to be sent to an evidence-based review entity for review and modification by the Committee as needed.***

## **B. Proposed Approach to Developing Procedures for an External Evidence-Based Review Group**

**Denise Dougherty, Ph.D.**  
**Senior Advisor, Child Health**  
**Agency for Healthcare Research and Quality (AHRQ)**

Dr. Dougherty discussed what steps the Committee should take to help delineate processes for evidence-based reviews by an external body in Step #3 of the nomination and review process. She said there is lack of clarity generally and debate on how to do evidence review in genetics and pediatrics both inside and outside Committee. To help the Committee make an informed decision on what a more evidence-based approach would look like in practice before contracting with an evidence review entity, therefore, it might be useful to hold a small meeting of Criteria Workgroup members, evidence review experts, and genetics and pediatric experts this year to

consider the nomination form and other materials and to propose a draft protocol for how to look at the evidence. The Criteria Workgroup would then look at the outcome from the meeting and develop a proposal for the full Committee to consider.

Specifically, Dr. Dougherty proposed the following approach:

1. A small meeting of Criteria Workgroup members, evidence review experts, and genetics and pediatric experts is convened this year (a) to review the Committee’s proposed nomination form for adding conditions to the ACMG uniform newborn screening panel; and (b) to develop a proposal for reviewing and grading evidence to take back to the Criteria Workgroup and then the full Committee with specific questions for consideration.
2. The Criteria Workgroup develops a proposal for the full Advisory Committee.
3. The full Committee discusses the proposal. It reviews the approach and gives guidance for revisions and approval.
4. Approved methods and criteria are integrated with the nomination form.
5. The Committee develops internal processes for dealing with post-nomination course of action.
6. An external evidence review group is formed to use the approved protocol for review of a nominated condition.

### **Questions & Comments**

Several Committee members spoke in favor of the meeting. Dr. Kahn, recalling presentations from the Advisory Committee on Immunization Practices and the U.S. Preventive Services Task Force, said he supported the effort to develop a process that is both transparent and based on a methodology that gains national acceptance. Dr. Telfair said he agreed with Dr. Dougherty that it made sense to pull together people for the meeting; he added, however, that there should be concrete deliverables related to the meeting itself.

Dr. Rinaldo said he thought such a meeting would require a significant expenditure of time and effort to come up with trivial changes.

Dr. Robertson asked whether the small meeting group would work on the nomination form. Dr. Dougherty said that it would not work on it very much, although it could say that the criteria would include “benefits” to children and their families from newborn screening when there is no treatment. Dr. Lloyd-Puryear said her understanding was that the meeting would have one specific outcome—i.e., the protocol for review of conditions nominated for inclusion in the uniform newborn screening panel (steps to follow)—and two general outcomes (an assessment of cost of the process for review and the general capacity of reviews).

Dr. Howell said he perceived that there was general support among Committee members for Dr. Dougherty’s suggestion that a small meeting be held to come up with a transparent protocol for reviewing the evidence.

- ***DECISION #1: A small meeting with experts in evidence-based review, pediatrics, and rare genetic diseases, as well as some people from the Committee, will be convened soon (a) to review the proposed form for nominating conditions to the Committee to evaluate for newborn screening; and (b) to develop a proposal for reviewing and grading evidence to take back to the Criteria Workgroup and then the full Committee***

*with specific questions for consideration. If possible, the meeting will be held in late summer 2006, so that the Criteria Workgroup is able to present a proposal to the Committee at its November 2-3, 2006 meeting.*

## **VI. COMMITTEE BUSINESS—SUBCOMMITTEE MEETINGS & REPORTS**

The Education & Training Subcommittee, the Followup & Treatment Subcommittee, and the Laboratory Standards & Procedures Subcommittee of the Advisory Committee held meetings that were open to the public from 3 p.m. to 5 p.m. on Monday, June 5, 2006. On the second day of the meeting, June 6, 2006, each subcommittee made a report back to the full Committee, as discussed below.

In addition, Dr. Howell noted that Dr. Jeffrey Brosco, a developmental pediatrician with a Ph.D. in history, had been given a federal contract to search the literature and do an oral history to produce an accurate document with respect to harms resulting from newborn screening. Dr. Howell said he hopes that the Committee will hear from him later.

### **A. Laboratory Standards & Procedures Subcommittee Report**

**Amy Brower, Ph.D.**  
**Executive Director**  
**Third Wave Molecular Diagnostics**  
**Medical Informatics and Genetics**

Dr. Brower, the chair of the Laboratory Standards & Procedures Subcommittee, first identified the members of the subcommittee: Dr. Alexander, Dr. Collins, Dr. Howell, Dr. Rinaldo, Dr. Harry Hannon from the Centers for Disease Control and Prevention, and Dr. Don Chace from Pediatrics, along with Dr. Marie Mann (HRSA staff).

She then reminded everyone that the charge of the Laboratory Standards & Procedures Subcommittee is to define and implement mechanisms for the periodic review and assessment of the following:

- the conditions included in the recommended uniform newborn screening panel
- infrastructure services needed for effective and efficient screening of the conditions included in the uniform newborn screening panel
- laboratory procedures utilized for effective and efficient testing of the conditions included in the uniform panel

One of the subcommittee's first priorities for the short term is to design a study to assess the utility of the routine second screen of newborns. Currently, 17 percent of babies born in the United States get a routine second screen. The subcommittee believes that if a routine second sample is valuable, every newborn should have one; and if it is not, no newborns should have one.

Thus, the Laboratory Standards & Procedures Subcommittee is seeking the approval of the full Committee to initiate a study of the utility of routine second screens of newborns for congenital

hypothyroidism (CH) and congenital adrenal hyperplasia (CAH) in February 2007. The proposed timeline for the study, which may take as long as 2 years to complete, is as follows:

- *February 2006:* Seek the approval of the Laboratory Standards & Procedures Subcommittee for the study.
- *March 2006:* Perform literature search for all publications regarding detection of cases by a routine second screen after a nondetection on the original screen.
- *May 2006:* Develop a draft protocol to help focus discussions of the subcommittee for pursuit of project goals.
- *May 2006:* Write a summary of information from the literature supporting a second screen; create a table of states and birth rates of states that perform routine second screens; and develop an outline of all variables that could contribute to cases identified only on the second screen (e.g., specimen collection variables, information about newborns, time and conditions for specimen transport to lab, specimen handling variables, variables associated with analytic methods, storage conditions for specimens, disorders and medical information for cases detected on first and second screen, severity of cases and treatment options).
- *June 2006:* Modify project protocol as required and seek Laboratory Standards & Procedures Subcommittee's approval to initiate project.
- *June 2006:* Submit project protocol to the full Advisory Committee to initiate the project.
- *Summer 2006:* Discuss project with the Association of Public Health Laboratories for support and approval.
- *August 2006:* Plan October/November workshop of stakeholders from states with second screens.
- *September 2006:* Designate participant list and issue invitations to attend (travel provided).
- *October/November 2006:* Hold workshop of stakeholders from states involved in routine second screens: (a) discuss state specific compromises/changes to match protocol to state activities; (b) solicit support for the project from participants and identify state programs willing to participate; and (c) identify a data review expert group to work with APHL to review the reported data quarterly.
- *January/February 2007:* Initiate the project. (NOTE: Duration will depend on the number of states participating and time to gather sufficient data to draw valid conclusions—calculations of the power of the study. A writing group will be formed to compile and analyze data after completion of the study for developing a publication.)

### **Questions & Comments**

Several Committee members complimented Dr. Brower and the Laboratory Standards & Procedures Subcommittee on their progress. In addition, several Committee members asked specific questions.

Dr. Boyle asked why the subcommittee had decided to do a prospective study of the utility of second screens rather than to do a study looking at data retrospectively. Dr. Hannon explained

that the decision was made for many reasons (e.g., there is a large expense in going back and pulling specimens, the specimens may not exist; the specimens may be compromised, etc., so best way is to do in real-time) that make it logistically easier to do a prospective study than a retrospective one. He noted that the Association of Public Health Laboratories would be collecting the data for the study.

Dr. Green asked what the literature of second testing indicated about why some things were picked up on a second screen but not the first. Dr. Hannon said the evidence is unclear.

Dr. van Dyck asked whether the intent of the subcommittee was to look only at CH and CAH or also to look at other conditions that might be looked at on a second test. Dr. Hannon explained that the intent was to look only at CH and CAH. Dr. Boyle and Dr. Kus asked whether there and utility in looking at all the tests even though power might not be there. Dr. Hannon said the idea was to simplify the issue and not make the study overwhelmingly complex—and to look at the two conditions that have historically been the driving force for the second test. Dr. Brad Therrell, from the National Newborn Screening and Genetics Resource Center, explained the history of second screens and said he thought a national study to resolve the issue was a good idea. Dr. Green said it struck her that CH and CAH might have been the conditions for which a second test was added only because they were among the first conditions screened for, but now 20 of 29 conditions are found using tandem mass spectrometry (MS/MS) and she thought that the study was missing an opportunity if it didn't include something like MCAD (medium-chain acyl-CoA dehydrogenase deficiency). Dr. Howell said he thought dealing with all the issues related to MS/MS would make the study too complex.

Several Committee members raised other methodological issues or questions. Dr. Dougherty and Dr. Boyle asked what the outcome measures for the study would be. Dr. Hannon and Dr. Rinaldo explained that the question being investigated is: Is a routine second newborn screening test of value or not, with no bias at the start. They will collect data on a wide range of variables and see which way the data are leading and what is contributing to specific outcomes. Dr. Hannon said that the study would not only capture the lab component; it also would be looking at the babies identified to see if anything is different about them. Dr. Lloyd-Puryear asked whether there would be uniform cutoff points and uniform technology. Dr. Hannon said, no, the investigators would capture the states' existing cutoffs and algorithms without changing anything. Dr. van Dyck asked whether there would be any advantage of looking at a group of states that do not do a second test as a control group. Dr. Hannon replied that the question had come up in the subcommittee's discussion, and Roger Eaton said they could use an algorithm and information from a database to answer the questions that would be answered by such a control group.

Dr. Howell asked the Committee if it would endorse the Laboratory Standards & Procedures Subcommittee's efforts to initiate a study of the utility of routine second screens of newborns for CH and CAH in February 2007. He noted that the subcommittee was proposing a meeting in conjunction with the American Public Health Laboratories, so it would not require any money.

Some Committee members said that although they eagerly supported the Laboratory Standards & Procedures Subcommittee's proposed study, they would like to have an opportunity to review and comment on the full protocol. Thus, Dr. Howell directed that the Laboratory Standards & Procedures Subcommittee's plan be sent to Committee members for their review and comment within 2 weeks. Committee members will be sent electronic copy of the final protocol and be asked to vote on it. If a majority agrees, the study will be approved and go forward. Any Committee member who expected to be going out of town should let Dr. Lloyd-Puryear know.

- **DECISION #2:** *The plan of the Laboratory Standards & Procedures Subcommittee for a study of the utility of routine second screens of newborns for CH and CAH will be sent electronically to Committee members so that they can comment on it within 2 weeks. If a majority of Committee members vote to approve the plan, the subcommittee will be authorized to proceed with the study.*

## **B. Education & Training Subcommittee Report**

**Gregory A. Hawkins, Ph.D.**

**Assistant Professor**

**Section on Pulmonary, Critical Care, Allergy, and Immunologic Diseases**

**Department of Internal Medicine**

**Wake Forest University School of Medicine**

Dr. Hawkins noted that he was substituting for the chair of the Education & Training Subcommittee Dr. Becker, who was attending an American Public Health Laboratories meeting. He reminded Committee members that the Education & Training Subcommittee's approved charges are as follows:

- Review existing educational and training resources for health professionals, parents, screening program staff, hospital/birthing facility staff, and the public.
- Identify deficiencies and make recommendations for action regarding the five groups.

Dr. Hawkins reported that for several months, the Education & Training Subcommittee has been reviewing all the educational resources related to newborn screening and genetics that already exist. Dr. Hawkins noted that the two major topics of discussion at the Education & Training Subcommittee's meeting on June 5, 2006, were the following:

- Methods to effectively get information on newborn screening to health care providers and parents: What are sources of information? Who should be responsible for disseminating the information? How should the information be disseminated?
- National spokesperson (s) for newborn screening: Who should it be? How should it be used?

Most of the educational resources on newborn screening that are needed for health care providers are already available, so a systematic organization of materials is all that is required. The following list of Web sites with genetic resources has been compiled by the Education & Training Subcommittee. The subcommittee would like Committee members and others to suggest other resources they may know that should be added (or deleted). To get information about newborn screening out to health care providers, Dr. Hawkins said, will probably require involving the states. The resources available for education are nearly unlimited, so a key question is which should be used as the core information.

### **Key Genetic Resources for Review**

- NLM's Genetics Home Reference <http://ghr.nlm.nih.gov>
- National Newborn Screening and Genetic Resource Center <http://gene-r-us.uthscsa.edu>
- March of Dimes <http://www.marchofdimes.com>

## Key Genetic Resources for Review

- AAFP <http://www.aafp.org>
- AAP <http://www.aap.org>
- ACOG <http://www.acog.org>
- ANA <http://nursingworld.org>
- CDC <http://www.cdc.gov>
- National Society of Genetic Counselors <http://www.nsgc.org>
- Genetic Alliance <http://www.geneticalliance.org>
- ACMG <http://www.acmg.net>
- ASHG <http://www.ashg.org/genetics/ashg/menu-educ-genedat.shtml>
- ISONG <http://www.isong.org>
- Save Babies <http://www.savebabies.org>
- Kansas University <http://www.kumc.edu/gec>
- University of Utah <http://www.genetics.utah.edu>
- American College of Physicians Foundation <http://nnlm.gov>
- OMIM <http://www.ncbi.nlm.nih.gov/Omim>
- Office of Rare Diseases <http://rarediseases.info.nih.gov>
- Star-G-Hawaii <http://newbornscreening.info/index.html>
- NCHEG <http://www.nchpeg.org>
- MCH Library <http://mchlibrary.info>
- Gene Tests <http://www.genetests.org>

Dr. Cathy Fomous gave an excellent presentation to the Education & Training Subcommittee on June 5<sup>th</sup> on the National Library of Medicine's (NLM) Genetics Home Reference Web site (<http://ghr.nlm.nih.gov>). This Web site, which explains genetic conditions, genes, and chromosomes, has been around since 2003, but many subcommittee members were not aware of it. More than 100 reviewers are used to keep the information accurate and current. Dr. Hawkins showed a slide of the home page for the Genetics Home Reference Web site, and explained that this is type of Web site the Education & Training Subcommittee envisions using as a platform for disseminating information. It has information about all 29 disorders in the American College of Medical Genetics (ACMG) uniform newborn screening panel, although some disorders are covered more directly than others. The site includes resources for families such as the "Help Me Understand Genetics" section, a glossary, and an "Ask the Geneticist" feature sponsored by Emory University.

Following this presentation, the Education & Training Subcommittee discussed what the icon for newborn screening should be to get information to public and health care providers. One suggestion for the message for patients was something along the lines of: “Talk to your provider about importance of newborn screening” (or some derivation of this message to make the connection between patient and health care provider). It was generally thought that the message should be generalized to include doctors, nurse, nurse midwives, etc.

The subcommittee also considered who might be a spokesperson to best convey the importance of newborn screening. Possibilities discussed included the U.S. Surgeon General (Dr. Richard H. Carmona), nationally recognized celebrities (e.g., sports stars, movie stars who are pregnant), or regular individuals (including pregnant women and mothers and families from different ethnicities).

The Education & Training Subcommittee’s recommendation to the full Committee is the following:

*The U.S. Department of Health and Human Services (HHS) should investigate creating a contract mechanism to package current genetic resources to develop a point of learning/CME package using standardized templates:*

- Health care providers: *Create templates for Web-based, personal digital assistant (PDA), and pocket guide written materials; (b) state-specific materials (e.g., ACT sheets); (c) continuing medical education (CME) credits to entice providers to study the material.*
- Parents: *Create templates for Internet, written and video-based materials using normal individuals and families of various ethnicities to communicate the message.*

### **Questions & Comments**

Dr. Telfair said he thought the Education & Training Subcommittee’s decision to start with what educational materials already exist was a good one. He asked whether the subcommittee had considered not-for-profit advocacy groups as resources. Dr. Hawkins said that it had not directly considered them; he added that he believes that health care providers should link affected families to advocacy groups. There are links to some advocacy groups on the NLM’s Genetics Home Reference Web site.

Dr. Green, reiterating that the Education & Training Subcommittee was trying to identify reliable sources and to take advantage of existing resources, noted that HRSA had been able to enlist the collaboration of the American College of Obstetrics and Gynecology (ACOG), the American Academy of Family Physicians (AAFP), and American Academy of Pediatrics (AAP), and that they had volunteered to put together a point of care package on newborn screening for health care providers. Dr. Green said much more remains to be done with respect to educating consumers about newborn screening goes, but it may be possible for the ACOG, AAFP, AAP, the March of Dimes, and groups such as the Genetic Alliance or Family Voices to do the packaging for consumers.

Noting the centrality of states to the newborn screening educational effort, Dr. Howell asked whether the Education & Training Subcommittee had discussed involving the seven Regional Genetics and Newborn Screening Collaboratives and National Coordinating Center (NCC) for the collaboratives in educational efforts. Dr. Green replied that the subcommittee had discussed the regional collaboratives, but it would also be important to learn more about how the NCC could

help. Ms. Monaco noted that one of the regional collaboratives, the New York-Mid-Atlantic Consortium (NYMAC) for Genetic and Newborn Screening Services, is trying to develop more uniform materials on newborn screening for use by health care providers and consumers throughout the region.

Dr. Howell asked Committee members for comments on the recommendation from the Education & Training Subcommittee. Dr. Lloyd-Puryear said she was unclear on what the contract is to do, because the various sites it mentions are already linked. Dr. Howell said if the Education & Subcommittee wanted HHS to use a contract mechanism, the subcommittee probably needed to develop a more concrete idea for what it wants done.

Dr. Hausman suggested that with the recent supplement on newborn screening in the May 2006 issue of *Pediatrics*, it might be that *Pediatrics in Review* might do a continuing medical education (CME) course on this topic. Several Committee members agreed that this was a good idea. Dr. Dougherty pointed to a CME course on childhood obesity that the Agency for Healthcare Research and Quality (AHRQ) had worked on with the Centers for Disease Control and Prevention (CDC) as an example of what could be done.

Dr. Edwards, although recognizing the importance of CME courses and educational materials on the Internet, emphasized his view that when a family calls a pediatrician at 4 p.m. and says their child has a disease the pediatrician may never have even heard of, the pediatrician needs written materials on hand giving state-specific information (e.g., experts, whom to get in touch with), not just information on the Internet. He would like to see states encouraged to get the core material, laminated or whatever, into the hands of practitioners who may or may not be Web sophisticates. Dr. Howell reported that one project of the regional cooperatives is for laboratories to fax with the newborn screening results a newborn screening ACT sheet from the lab.

Ms. Micki Gartzke, a parent on the subcommittee, said she agreed with Dr. Edwards that physicians need written materials in their offices, so that when families call, they know what to do. The important thing is getting the information disseminated. That is one reason the subcommittee considered an HHS contract mechanism. Ms. Jana Monaco, another parent, noted that the state of Virginia had developed a healthcare practitioners' manual on newborn screening for every practitioner to have on shelf and had also developed parent brochures on newborn screening, which she could share with the Committee. Ms. Andrea Williams from the Children's Sickle Cell Foundation, Inc., agreed that getting information disseminated to health care providers is essential, but emphasized that there should be a balanced effort to ensure that parents are educated about newborn screening as well as providers.

Dr. Carol Greene from the Society for Inherited Metabolic Disorders said that the Education & Subcommittee should know that CDC is providing funds to the Genetic Alliance and other groups to build a national portal that offers accurate and scientifically valid information on individual single-gene disorders. This portal will be for individuals, families, and health care providers.

Finally, Dr. Boyle urged the Education & Training Subcommittee to take a look at CDC's health information campaigns—for example, campaigns for immunization or developmental screening (healthcare providers and daycare workers)—because it struck her that such campaigns might be a very good model for educating people about newborn screening. CDC's campaigns are collaborative and bring in lots of partnerships and use evidence-based dissemination measures. They cost several million dollars.

Dr. Howell said this was quite an appealing idea and Dr. Hawkins and Dr. Green agreed that it was worth pursuing. Thus, the following decision was made:

- ***DECISION #3: The Education & Training Subcommittee will hold a conference call in the very near future to discuss the concept of a broad national campaign for newborn screening along the lines of CDC's immunization campaigns.***

## **C. Followup & Treatment Subcommittee Report**

**Colleen Boyle, Ph.D., M.S.**

**Director**

**Division of Birth Defects and Developmental Disabilities**

**Division of National Center on Birth Defects**

**and Developmental Disabilities**

**Centers for Disease Control and Prevention (CDC)**

Dr. Boyle, the chair of the Followup & Treatment Subcommittee, identified the following as members of the Followup & Treatment Subcommittee: Dr. Dougherty, Dr. Telfair, Mr. Robertson, Dr. Kus, Col. Louder, Dr. Carol Greene, Dr. Newton, Jill Fisch, Dr. Brad Therrell, and Julie Miller.

Dr. Boyle explained that since the February 2006 Committee meeting, the Followup & Treatment Subcommittee had done a review of literature related to the goals and essential elements of newborn screening followup and treatment. After finding that what is currently available on long-term followup fits on half a page, the Followup & Treatment Subcommittee decided that as a small subcommittee, it could probably make the best contribution by focusing on long-term followup of individuals whose conditions were detected via newborn screening. Specifically, the subcommittee would like to do the following: (1) come up with definition of long-term followup of individuals with conditions identified by newborn screening; (2) specify the goals of long-term followup; and (3) identify key elements of long-term followup.

To facilitate this effort, Dr. Boyle explained, the Followup & Treatment Subcommittee would like to seek the Committee's approval to have a 1-day facilitated meeting to develop a logic model that describes the entire system of long-term followup and clarifies roles and responsibilities of all entities (family, individual, medical home, screening specialists, etc.). In preparation for the proposed meeting, the subcommittee has already drafted the following language as the goal of long-term followup: "*assure optimal health and development for an affected individual throughout the lifespan.*" It has also drafted the following as a definition of long-term followup: "*a comprehensive system of treatment and support, communication, data collection to optimize lifelong health and development for the individual, family and community.*"

The subcommittee believes that several perspectives should be represented at the 1-day meeting to develop the logic model for long-term followup, including some perspectives not already present among people involved with the subcommittee: the education or intervention perspective, healthcare systems perspective, nutritional perspective, and possibly some of the specialty care perspectives; people with such perspectives could certainly be identified in the Washington, D.C., metropolitan area, to keep the associated costs down.

Part of the plan would be for the subcommittee to review various models of care (for chronic disease, for cystic fibrosis, sickle cell, hemophilia, HIV, etc.) and to review what is being done in the seven Regional Genetics and Newborn Screening Collaboratives with respect to long-term

followup. Then subcommittee members would write up the product from the 1-day meeting and send out a report to get additional perspectives on long-term followup not represented at the meeting.

Dr. Boyle concluded her presentation by stating that the Followup & Treatment Subcommittee hopes that the proposed 1-day meeting can be held in the fall of 2006, perhaps in conjunction with the full Advisory Committee's meeting in November 2006. She said that the Followup & Treatment Subcommittee would like to present a proposal to the full Committee with more specifics about the proposed 1-day meeting to develop a logic model for long-term followup of affected newborns; then the Committee could provide feedback on the proposal and vote on whether to allow the subcommittee to proceed with the meeting.

### **Questions & Comments**

Several Committee members expressed support for the Followup & Treatment Subcommittee's focus on long-term followup. Dr. Howell said that it would help emphasize that newborn screening is far more than just a lab test.

Dr. Green, saying she was not sure that there was a standardized definition of short-term followup, asked whether Dr. Boyle thought the subcommittee should provide a definition of short-term followup before it tackles long-term followup. Dr. Boyle said maybe as a preamble, the subcommittee should clarify that.

Dr. Edwards urged the subcommittee not to overlook states as a key component of the followup and treatment system for newborns.

Dr. Dougherty mentioned that in coming up with a model for the long-term followup system, it would be a good idea to include the opportunity for research to know whether the treatments that come up later or are available now could be studied as part of the long-term followup system and part of continuously improving care. Dr. Howell recalled that Dr. Alexander's presentation the previous day suggested that the National Institutes of Health might have interest in such research.

Dr. Howell said he got the sense that the Committee was generally in favor of the Followup & Treatment Committee's proposal to have a 1-day meeting to develop a logic model for long-term followup. Although some Committee members expressed concerns that there might be too many Committee activities going on at once, Dr. Howell said he wanted the Committee accomplishing things. Thus the following decision was made:

- ***DECISION #4: The proposal of the Followup & Treatment Subcommittee to have a 1-day facilitated meeting— perhaps in conjunction with the November 2006 or February 2007 Advisory Committee meeting—to develop a logic model that describes entire system of long-term followup for newborn screening will be sent electronically to Committee members so that they can comment on it. If a majority of Committee members vote to approve the proposal, the subcommittee will be authorized to proceed with the meeting.***

## **VII. POLICIES AND PROCEDURES FOR ADVISORY COMMITTEE PRACTICES**

**Michele A. Lloyd-Puryear, M.D., Ph.D.**  
**Health Resources and Services Administration**  
**Chief, Genetic Services Branch**  
**Maternal and Child Health Bureau**  
**U.S. Department of Health and Human Services (HHS)**

Dr. Lloyd-Puryear reported that at the Committee's previous meeting in February 2006, Dr. Howell had asked her to convene a group to develop a written set of policies and procedures governing the operation of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. Since then, a group consisting of Dr. Becker, Dr. Boyle, Dr. van Dyck, Dr. Howell, and herself had developed a first draft of such a document. The draft was developed after the group reviewed the policies and procedures of the Advisory Committee on Immunization Practices, the Federal Advisory Committee Act's requirements, the Institute of Medicine's standard operating procedures pertaining to issues of conflict of interest, and the HHS handbook for the governance of advisory committees.

The draft policies and procedures document that was distributed to Committee members was entitled "The Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children (ACHDGDNC): Policies and Procedures for Operation and the Development of Recommendations for Screening Newborns and Children for Heritable Disorders and for the Heritable Disorders Program." The document had two major sections:

### **I. Development of ACHDGDNC Recommendations for Screening Newborns and Children**

- A. Purpose. This section gives background on the Committee and its purpose.
- B. Membership. This section specifies that the Committee consists of 15 regular members, including 4 ex officio members from federal agencies (HRSA, CDC, NIH, and AHRQ) and 2 nonvoting liaisons from the Secretary's Advisory Committee on Genetics, Health, and Society and the Secretary's Advisory Committee on Infant Mortality. It also specifies how additional Committee members are selected for membership.
- C. Financial interests. This specifies the financial forms that Committee members must file.
- D. Liaison representatives. This section specifies the process for appointments of liaison representatives, primarily from professional organizations.
- E. Voting. This specifies what constitutes a quorum for voting by the Committee and how conflicts of interest are to be addressed in voting.
- F. Meetings. This section specifies the number of regularly scheduled meetings of the Committee and procedures for notifying people about the meetings. It also specifies that meetings are generally open to the public for their entire duration, although there may be occasions when a closed meeting is required. It further specifies that meetings will comply with all provisions of the Federal Advisory Committee Act and Government in the Sunshine Act. It also discusses procedures for public comments.

- G. Working groups and subcommittees. This section addresses the composition of subcommittees of the Committee, as well as working groups.
  - *Subcommittees*: This specifies that the charge of each subcommittee is established by the full Committee; membership must include two or more Committee members; must include HRSA staff; and may include ex officio members and, as consultants, liaison representatives. On occasion, other people who are not government employees, Committee members, or liaison representatives may be asked to serve as consultants to a committee.
  - *Working groups*: This specifies that working groups are used for gathering, analyzing, and preparing information for the Committee. The Advisory Committee's chair person appoints working group members, and such members need not be Committee members.
- H. Member responsibilities. This section discusses topics such as attendance at meetings, standards of conduct, media interactions, and Committee correspondence.
- I. Selection of topics. This specifies procedures for the identification and selection of agenda items for the Committee.
- J. Process for developing recommendations. There is still considerable work to be done on this section. The section will have three sections: (a) technical recommendations, (b) policy analysis; and (c) developing the recommendations.
- K. Publication of recommendations. This section notes that recommendations are published on the Committee Web site and may occasionally be reprinted in other publications.
- L. Implementation and evaluation of the recommendations. This section notes that the implementation and evaluation of the impact of the recommendations is the responsibility of the relevant HHS program, not the Advisory Committee.

**II. ACHDGDNC Recommendations for the Heritable Disorders Program.** This sets out a separate process for the development of recommendations for the Heritable Disorders Program based on the unique statutory authority for the program established by Title XI, Section 1109 of the Public Health Service Act, 42 U.S.C. 300b-8 and 9.

Dr. Lloyd-Puryear asked Committee members to make comments about the draft document, including what they would like to see expanded, etc.

### **Questions & Comments**

Dr. Dougherty said she thought that having a document of policies and procedures for the Committee was a great idea. In addition, she made several specific points. First, noting that the draft document included procedures for two broad categories of recommendations—recommendations for screening newborns and recommendations for the Heritable Disorders Program—she asked where recommendations such as a public awareness campaign would fit. Dr. Lloyd-Puryear said that the document identifies three types of recommendations: technical recommendations, policy recommendations, and recommendations pertaining to the Heritable Disorders Program.

Second, Dr. Dougherty said that it would be helpful for the document to clarify in any statement of policy and procedures, which items are "musts," which are "shalls," which are "mays," and

which just describe the state of what the Committee is doing. Dr. Lloyd-Puryear agreed that such language should be added but indicated that the document is a work in progress, and these and other specifics remain to be worked out by the Committee.

Third, Dr. Dougherty said it would be helpful to working groups and subcommittees to include the rules governing their meetings and actions (e.g., Do subcommittees have to have open meetings? Does the Followup & Treatment Subcommittee have to invite all members to the meeting in fall or just some? Who pays for such meetings?). Dr. Boyle noted that the document does not indicate that subcommittee meetings must be open. Dr. Lloyd-Puryear explained that the tradition—which she believes is a good one—has been that subcommittee meetings are open. Minutes for workgroup or subcommittee meetings must be made publicly available. Dr. Green asked how the chairs of subcommittees were selected. Dr. Howell said that they were appointed by him in his capacity as Committee chair.

Dr. Green and Dr. Boyle asked Dr. Puryear to clarify what the procedures for handling the conflicts of interest by members of the Advisory Committee are and whether they give the whole Committee access to members' potential or perceived conflict of interests as the Institute of Medicine's procedures do. Dr. Puryear explained that the procedures for the Advisory Committee go back to the provisions of the Federal Advisory Committee Act. Individuals' financial conflicts of interest are reviewed by a special Ethics Office in HHS. People with a conflict of interest can serve on the Committee if the need for their services outweighs the potential conflict of interest. If a person is found to have a focused conflict of interest, the HHS Ethics Office may provide a waiver for the person that obligates the person to remove himself or herself from specified situations in which that conflict arises.

Dr. Boyle said she did not think the Advisory Committee had dealt with any challenging issues with conflict of interests, but they might come up. She noted that if conflicts of interest for the for the Advisory Committee are limited to financial interests, then the Advisory Committee will not have as transparent or rigorous a process as the Advisory Committee on Immunization Practices. Section E. on Voting in the draft document indicates that Advisory Committee members are supposed to announce their conflicts of interests prior to any voting to determine if they can vote. A question that arises is: How is Dr. Howell going to handle this? Dr. Howell replied that since the formal conflict of interest process is handled at HHS, he could ask routinely before any vote whether anyone has a conflict of interest. Dr. Boyle also noted that the following sentence on page 7 in Section G. Working Groups and Subcommittees should be deleted: "Members with a potential conflict of interest cannot serve on a subcommittee."

Dr. Telfair, focusing on Section I. Selection of Topics, suggested that the Committee might want to go back to what the charge of the Committee when selecting topics is to ensure that work is done that relates most to that charge. He noted that other committees he serves on do this.

In response to a question from Dr. Edwards, Dr. Lloyd-Puryear said there is nothing in the draft document that specifies which subcommittee members can vote.

Dr. Puryear concluded the discussion by stating that she would like to get comments from Committee members on the document over the next several months. Thus, the following decision was made:

- ***DECISION #5: Over the next several months, Dr. Lloyd-Puryear and others will continue to work on the draft policies and procedures document for the Advisory Committee and will incorporate Committee members' suggestions.***

## VIII. UPDATE FROM ORGANIZATIONAL REPRESENTATIVES TO THE COMMITTEE

Representatives to the Committee from the following organizations gave updates:

- Child Neurology Society (CNS): Hugo W. Moser, M.D.
- U.S. Department of Defense (DoD): David S. Louder, III, M.D., Lt. Col., USAF, MC
- U.S. Food and Drug Administration (FDA): Ethan Hausman, M.D.

### A. Child Neurology Society

**Hugo W. Moser, M.D.**

**Director**

**Neurogenetics Research Center**

**Kennedy Krieger Institute**

Dr. Moser, appearing on behalf of Dr. Bennett Lavenstein of the Child Neurology Society (CNS), stated that Dr. Lavenstein and the CNS have great interest in newborn screening programs and would like to make contributions to ensure that newborn screening works well. The following written statement from Dr. Lavenstein was made available to Committee members:

“The Child Neurology Society supports universal newborn screening and legislation that promotes its implementation throughout the United States. The CNS supports the position of the American Academy of Pediatrics advocating universal newborn screening. The CNS recommends that federal funds be appropriated for programs to insure clinical followup and research on those current and future disorders identified. The CNS will also recommend from time to time that additional disorders be added to the list where they meet the scientific criteria as demonstrating that identification and treatment are advisable. The CNS will work with HHS, the American College of Medical Genetics, the American Academy of Pediatrics, the American Academy of Neurology, and other organizations to promote this goal.”

In many neurological disorders, Dr. Moser said, if one waits for symptoms to develop, the battle for therapy has already been lost. Thus, newborn screening that allows diagnosis before symptoms appear will radically change the whole approach to therapy for neurological disorders. This opportunity is very exciting. CNS feels that it can make a contribution by helping to evaluate the therapeutic approaches—both in terms of clinical appraisal and the increasing use of noninvasive neuroimaging techniques and biochemical approaches.

Dr. Moser noted that in recent years it has been found more and more that many of the disorders, which in the past were thought to be childhood disorders, also manifest later on or in adulthood, and with manifestations that are often totally different from the classical childhood presentations. These adult forms have been recognized only recently and are probably underdiagnosed. This has a profound implication for newborn screening because people with adult-onset disorders will be identified by newborn screening, and a major challenge will be to differentiate whether an asymptomatic child has the childhood phenotype or the adult phenotype and whether to provide what may be an invasive therapeutic approach.

According to Dr. Moser, CNS has been involved in a spinal muscular atrophy (SMA) program. It is also interested in Pompe's disease screening and Fabry disease screening. And the points he

has made apply to all of these. Finally, Dr. Moser noted that in last few months, a procedure for doing newborn screening for adrenal leukodystrophy (ALD) has been developed. There are plans to do a study with Dr Rinaldo to evaluate this technique.

### **Questions & Comments**

Dr. Howell said one issue that concerns people with Pompe's disease and Krabbe disease is identifying adults with enzyme deficiencies in the newborn period and figuring out what to do about them. He asked whether Dr. Moser thought that expert neurologists would be able to differentiate between the adult and childhood phenotypes. Dr. Moser said he thought there was some promise of being able to differentiate them with a fair degree of probability.

## **B. U.S. Department of Defense**

**David S. Louder, III, M.D., Lt. Col., USAF, MC**  
**Chief Consultant for Maternal-Child Medicine and Pediatrics**  
**AFMSA/SGOC**

Col. Louder gave a presentation on the U.S. military health care system and its role in newborn screening. He explained that although he was the Chief Consultant for Maternal-Child Medicine and Pediatrics in the Air Force, he was representing all three branches of the military (Army, Navy, Air Force).

The U.S. military health care system has 411 clinics and 70 hospitals with 9 million beneficiaries and 106,000 newborns annually. In terms of the number of babies delivered, the military system would be the 12<sup>th</sup> largest state. The military health care system has “federal supremacy” to exceed state requirements; the default newborn screening system is the host state’s newborn screening system. Current requirements for TRICARE state reimburse for newborn screening services endorsed by American Academy of Pediatrics.

The military health care system offers several advantages for newborn screening. It has public health experts, policymakers, rule makers, reimbursement authorities, delivery hospitals, baby doctors, and genetic disease experts all under one virtual roof around the world. It has a collegial global network of subspecialty support and expertise for remote locations. It can look at quality and prevention. It can control a large volume of testing. It has a single computerized medical system that can integrate with labs. It has the ability to create/manage a newborn screening registry.

On the other hand, there are several challenges for the military health care system in doing newborn screening. The military has 500 facilities and hundreds of local systems/processes. There are complicated relations between labs, the civilian sector, and the military. There is little local institutional memory, and program oversight changes frequently. Overseas newborns, both on and off base, represent unique logistic challenges. The military population and medical staff are constantly moving. Rural and overseas locations are distant from laboratories, so there is the possibility of delays in newborn testing and results. Nearly half of newborns are delivered in civilian hospitals. There is inconsistent support for what to do with newborns that screen positive. There are challenges with geographic and time zone differences. Testing expenses are borne by local budgets.

To improve and coordinate newborn screening in the military better, the Department of Defense created a team “to promote and validate the execution of a comprehensive, expanded, and

uniform newborn metabolic screening program for all DOD infants.” The components of the program are the following:

- A uniform military health care system policy and requirement for newborn screening
- Education regarding the testing program
- Timely tandem mass spectrometry (MS/MS) testing and results
- Registry for tests and followup of positives
- Management of patients with positive screens

The team deliverables are the following: (1) recommendations for an expanded newborn screening policy; (2) recommendations for requirements for a centralized laboratory and newborn registry; (3) recommendations for a direct care implementation and training plan; and (4) recommendations for civilian hospital participation.

Col. Louder said that with assistance from Dr. Lloyd-Puryear and Dr. Marie Mann at HRSA and Scott McLean, an Army geneticist in San Antonio, they had formed a committee of experts in clinical care, clinical program management, laboratory contracting, computer systems, data management, and genetics to figure out what they needed to do and how to get that relayed to decisionmakers. The committee will develop recommendations to include a financial “Independent Cost Estimate”; develop a statement of work for proposal requests; develop and leverage educational materials; and evaluate service and facility financial impacts.

In the near future, they will gain approval of TRICARE and the military services; publish a request for proposals; create a mandate within the direct care system (implementation instructions within each service and program funding within each service); get the registry active; and develop implementation strategies for uniform comprehensive newborn screening program for locations that “deliver downtown.” After that, they will reevaluate, refocus and redefine.

### **Questions & Comments**

Dr. Howell opened the discussion by noting that the military was actively involved in the ACMG newborn screening report and that military is a wonderful system for research efforts.

Dr. van Dyck asked whether most babies in the military health system were getting newborn screening. Col. Louder said yes, and the effort he described is an attempt to coordinate things better. The biggest challenge for the military health system is dealing with infants who screen positive. In response to a question from Dr. Rinaldo, Col. Louder said they hope to have a request for proposals out later this summer with implementation in FY 2007.

Dr. Kus asked Col. Louder to comment on how the Army, Air Force, and Navy are able to work collaboratively across jurisdictional lines. Col. Louder explained that the Navy took lead and used a contract lab to show a better way of doing things. For the most part, pediatricians from the different services are involved, and they work well together to help babies. Dr. Hawkins asked where the Marines and Coast Guard fit into the system. Col. Louder explained that the Marines are part of the Navy, and the Coast Guard is under the U.S. Department of Homeland Security.

Dr. Therrell asked whether civilian hospitals were also involved in this effort. Col. Louder said that might involve them, but the plan was to focus on the direct care system first in hopes that states would speed up and catch-up and differences between the military and civilian facilities would diminish.

Dr. Telfair asked how the military health system manages newborns following a positive screen, saying this question came up in the Followup & Treatment Subcommittee. Col. Louder replied that the goal is to get pertinent information for the provider and families on what to do immediately and pertinent information on a confirmatory test to determine whether the initial positive is false or true; and then bring in appropriate resources to help take care of the child. The resources may vary from location to location, but phone resources will be a part of the overall system. It is important to get things happening quickly (e.g., by having a health expert on the phone right at that time).

Dr. Kus asked what the military health system is doing with respect to long-term followup of newborns diagnosed with a condition. Col. Louder said the military has several mechanisms. Depending on complexity of the child's condition and health care needs, the military can assign the family only to places where they can receive those services. In response to a question from Dr. Green, Col. Louder said that the military does not yet have written guidelines pertaining to short-term and long-term followup that could be shared with the Committee.

Finally, Dr. Green asked whether issues related to the sharing of genetic information were an issue in the military more than in a civilian population. Col. Louder said the military has a great health care benefit; beneficiaries generally trust the military.

## **C. U.S. Food and Drug Administration**

**Ethan Hausman, M.D.**

**Medical Officer**

**Division of Gastrointestinal Products**

**Office of New Drugs, ODE-3**

**Center for Drug Evaluation and Research (CDER)**

Dr. Hausman stated newborn screening, genetics/genomics, and inborn errors of metabolism are on the map at FDA and interest in these topics occurs at multiple levels: top down, bottom up, and middle out. He then went on to describe the following pertinent FDA initiatives:

- **FDA's Critical Path Initiative for New Medical Products.** From the top is FDA's Critical Path Initiative. This is FDA's effort to stimulate and facilitate a national effort to modernize the scientific process through which a potential human drug, biological product, or *medical device* is transformed from a discovery or "proof of concept" into a medical product." Genomics is one of multiple components of the Critical Path.
- **FDA's Center for Devices and Radiological Health (CDRH).** CDRH helps ensure that medical devices are safe and effective. Medical devices are defined in the *Code of Federal Regulations* [21 CFR 201(h)] as intended for use in the diagnosis of disease; or in the cure, mitigation, treat or prevention of disease; OR intended to affect the structure or any function of the body, and does not achieve any of its primary intended purposes through chemical action within or on the body, and which is not dependent on being metabolized for the achievement of any of its primary intended purposes.
  - **Office of In Vitro Diagnostics (OIVD) Device Evaluation and Safety.** Medical devices include in vitro diagnostic devices—generally clinical laboratory tests of biological tissues such as blood, urine, or spinal fluid. Newborn screening in vitro diagnostic devices are generally biochemical tests. In

vitro diagnostic devices must undergo premarket review and are regulated by OIVD.

- **Voluntary Genomics Working Group.** One exciting development is establishment of a voluntary Genomics Working Group with a variety of participants by job description and training (statistics, internal medicine, pathology, etc.) who have a common interest in genetics and genomics and individual interests in things such as newborn screening, pharmacogenetics, and pharmacogenomics. This is like a big journal club. Members attend professional meetings and cultivate relationships with professional organizations and across sectors within the U.S. Department of Health and Human Services (HHS). If outside presenters from academia or industry wish to make a presentation, they may.
- **FDA's Center for Drug Evaluation and Research (CDER).** CDER has undergone a reorganization in recent years. Treatments for inborn errors of metabolism are now reviewed by the Division of Gastroenterology Products instead of by several different offices. Soon, the division will have an Inborn Errors of Metabolism Team of about six people to review treatments and therapies under one roof. Examples of drug treatments that have already come up for review are Myozyme, Fabrazyme, Cerezyme, Naglazyme, Buphenyl, and Orfadin.

### **Questions & Comments**

In response to a question from Dr. van Dyck, Dr. Hausman explained CDRH's Office of In Vitro Diagnostic Device Evaluation reviews medical devices for the diagnosis of inborn errors of metabolism. A device such as a DNA chip or microarray, for example, might be reviewed by the Office of In Vitro Diagnostic Device Evaluation.

## **IX. PUBLIC COMMENT SESSION**

The following individuals made public statements to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children on the afternoon of Tuesday, June 6, 2006. The written text of their statements appears in Appendix A.

### **1. Jana Monaco Parent & Board Member Organic Acidemia Association**

Ms. Monaco, the parent of a child with isovaleric acidemia, said she was very excited about the advances in newborn screening thanks to the efforts of the Committee. She noted that Virginia recently expanded its screening panel to include additional disorders included in the American College of Medical Genetic (ACMG) uniform screening panel and has found additional babies with disorders.

Ms. Monaco reported that she recently attended a meeting of the Northern Virginia Perinatal Counsel meeting and previewed a healthcare practitioners' manual on newborn screening for every practitioner in Virginia, as well as parent brochures distributed in newborn kits after delivery. She has shared these materials with Committee members and will share them with New York-Mid-Atlantic Consortium (NYMAC) for Genetic and Newborn Screening Services workgroups, where they are tackling different issues to try to bring uniformity to that region.

Ms. Monaco stated that she agreed with Dr. Alexander that more attention needs to be paid to privacy issues. DNA testing and newborn screening are confused—and when people say that newborn screening is an excuse to inventory the DNA of children, this threatens strides in expanding newborn screening. A few months ago, for example, a situation arose in which Minnesota screening was somewhat threatened by an individual who insisted on calling newborn screening DNA testing and was lobbying to make the program an opt-in process rather than an opt-out.

With regard to the nomination form for adding conditions to ACMG uniform newborn screening panel, Ms. Monaco agreed with Mr. Robertson’s suggestion that a question related to quality of life or something parents could answer should be added to the nomination form.

Finally, she said, although she realizes that there must be criteria, she struggles with the issue of whether there should be testing when there is no treatment that can cure a condition; she thinks most families want to know their child’s diagnosis even if there is no treatment or cure.

## **2. Micki Gartzke**

### **Parent & Director of Education & Awareness Hunter’s Hope Foundation**

Ms. Gartzke thanked the Advisory Committee and everyone associated with it for working on newborn screening, noting that as the parent of a child who died from early infantile Krabbe disease after a long diagnostic odyssey, she lives her life for that every day. Each advance means another child and family will be spared.

Ms. Gartzke reported that the Hunter’s Hope Foundation worked with Save Babies Through Screening and the March of Dimes in Kansas to get the state to expand its newborn screening program and had also been involved in the opt-in vs. opt-out situation in Minnesota described by Ms. Monaco.

Ms. Gartzke also reported that she had recently witnessed the effectiveness of education on newborn screening at a recent American Academy of Pediatrics (AAP) meeting, where Dr. Howell and Jim Kelly gave a presentation, “Rapidly Expanding Horizons of Newborn Screening” at a SuperCME session. It was exciting to see that physicians recognized that they needed to learn about newborn screening. Finally, Ms. Gartzke said that the Hunter’s Hope Foundation has been working on newborn screening for Krabbe disease—something close to her heart.

## **3. Jill Levy-Fisch**

### **Parent & President Save Babies Through Screening Foundation**

Ms. Fisch had to leave the Committee’s meeting early because of family obligations, so Ms. Gartzke made her comments. Ms. Gartzke reported that Dr. Sharon Terry from the Genetic Alliance had asked Ms. Fisch to help pilot test the draft nomination form for adding conditions to the uniform newborn screening panel. Ms. Fisch contacted the Wilson’s Disease Foundation to complete the form. She is concerned about the complexity of the proposed nomination form and would like a mechanism to help people such as parents and advocacy groups fill the form out. She and Dr. Terry had discussed the possibility of having the Genetic Alliance serve as such a mechanism.

Finally, Ms. Fisch urged the Committee to view the Save Babies through Screening Foundation as a resource and partner. It is the only parent resource devoted to newborn screening and makes materials available free of charge via the Save Babies Through Screening Web site (<http://www.savebabies.org/index.php>).

**4. Paula Brazeal  
President  
United Leukodystrophy Foundation (ULF)**

Ms. Brazeal noted that the ULF is committed to the identification, treatment, and cure of all leukodystrophies through programs of education, advocacy, research, and service. It was founded in 1992 and now represents 12,000 families and individuals in the United States and 73 foreign countries.

Ms. Brazeal explained that she lost two sons and a brother to adrenoleukodystrophy (ALD) several years ago. Just getting a diagnosis for her sons required going to multiple institutions. Her family wanted to keep the children at home to die, but the emotional and financial costs (even with insurance) to the family were very high.

The ULF has supported the Newborn Screening Project for ALD since its inception. Newborn screening for ALD offers the first chance to give hope for life to boys with ALD gene. If a child is diagnosed with ALD at birth, it is possible to prevent the development of Addison's disease, begin a dietary therapy with Lorenzo's oil, and monitor for changes in the brain with annual magnetic resonance imaging (MRI) to see whether the child should be considered for bone marrow transplantation.

**5. Francis "Bob" Evanosky  
Parent & Founder  
The Evanosky Foundation**

Mr. Evanosky, in his first appearance before the Committee, explained that he and his wife Sonya have three sons: John and Christopher, who are identical twins age 4 1/2, and Jack, who is age 2. All three boys were diagnosed with metachromatic leukodystrophy (MLD) in early 2005. The twins were born prematurely, and when they were about 15 months old, they began to experience rapid degradation in their abilities.

After several months of searching for a diagnosis, it was finally determined that the twins had the late infantile form of MLD. Unfortunately, it was too late for a stem cell transplant, and their condition was terminal. Fortunately, Jack was tested for MLD the next week, was found to have the condition, has received a stem cell transplant, and is now thriving.

Mr. Evanosky stated that he would like to see the word "benefit" associated with treatment of conditions detected via newborn screening. For families of affected children, regardless of whether there is a treatment or not, there is a benefit of knowing the diagnosis. There are many Ys in the road, and the earlier families know what they are up against, the better choices they can make. For example, he and his wife might never have had Jack, knowing how difficult his life would be, if they had known about the twins earlier.

The Evanosky Foundation would like to establish a relationship with the Committee to help with expanding newborn screening for all diseases for which there is a benefit from such screening

The foundation was formally established in June 2005 to spare others the experience that Mr. Evanosky and his family have been going through for any type of childhood disease that can be determined within the first couple of weeks of life. Its mission is to fund MLD research and develop programs to enhance the overall quality of life for families affected by MLD or other leukodystrophies.

Mr. Evanosky said he would like to write a letter giving a father's perspective to Dr. Howell. Dr. Howell said that the letter would be put in the minutes with the public comments.

**6. Carol Greene, M.D.  
Society for Inherited Metabolic Disorders (SIMD)**

Dr. Greene said that SIMD appreciated the Committee's efforts with regard to developing a process for adding conditions to the ACMG uniform newborn screening panel and was happy to have been able to help pilot test the draft nomination form. SIMD again urged the Committee to devote attention to issues related to followup, including access to quality treatment and the evaluation of long-term outcomes.

In the May 2006 issue of *Pediatrics*, Botkin et al. made a statement that "some children with benign conditions were seriously harmed by unnecessary restrictions in diets." SIMD does not dispute this statement, but wants to emphasize that the harms with amino acid restricted diets are not recent (they date back to when newborn screening was implemented three decades ago) and there were not large numbers of the children harmed. The science base for current treatments for inborn errors of metabolism would avoid overtreatment that led to rare instances of harm.

SIMD cautions, however, that harm may still occur when appropriate specialists are not involved in the care of affected newborns. To avoid harms from inappropriate treatment, babies with disorders detected should be seen by the appropriate specialist—whether a hematologist, endocrinologist, neurologist, audiologist, or genetic or metabolic specialist. Dr. Greene noted that issues in diagnosis and management following a positive newborn screen, including possible psychological harms from false positive screens, will be the focus of a joint ACMG/SIMD educational session at the ACMG meeting in the spring of 2007.

## **X. COMMITTEE BUSINESS**

**Rodney Howell, M.D.  
Chair, Secretary's Advisory Committee on Heritable Disorders  
and Genetic Diseases in Newborns and Children**

Dr. Howell asked whether Committee members had any further comments. Hearing none, he directed Committee members to notify Dr. Lloyd-Puryear if they had any items they would like to see put on the agenda for future meetings. He also noted that the Committee's next meeting would be November 2-3<sup>rd</sup> at the Washington Hilton near Dupont Circle in Washington, D.C.

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We certify that, to the best of our knowledge, the foregoing meeting minutes of the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children are accurate and correct.

/s/ \_\_\_\_\_

R. Rodney Howell, M.D., Ph.D.  
ACHDGDNC, Chair

/s/ \_\_\_\_\_

Michele A. Lloyd-Puryear, M.D., Ph.D.  
ACHDGDNC, Executive Secretary

These minutes will be formally considered by the Committee at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.

## **APPENDIX A: WRITTEN PUBLIC COMMENTS**