

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

Summary of 13th Meeting
January 14-15, 2008
Washington, DC

The Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children was convened for its 13th meeting at 9:40 a.m. on Monday, Jan. 14, 2008, at the Marriot Bethesda North Hotel & Conference Center in Bethesda, Md. The meeting was adjourned at 1:58 p.m. on Tuesday, Jan. 15, 2008. In accordance with the provisions of Public Law 92-463, the meeting was open for public comments on Jan. 15, 2008.

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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**

Professor, Department of Pediatrics

Leonard M. Miller School of Medicine

University of Miami

Agenda for the Meeting. Dr. Howell opened the meeting by welcoming Advisory Committee members and other participants and giving a brief overview of the agenda:

- **Introduction of new Advisory Committee members.** The five new Advisory Committee members, all of whom had received ethics briefings earlier in the morning, would be introduced.
- **Reports from newborn screening programs/systems using partnerships for newborn screening and followup.** There would be several presentations illustrating a variety of different approaches and supporting infrastructures used by newborn screening programs/system for screening and followup of newborns identified as having genetic or metabolic disorders.
- **Federal legislative update.** Emil Wigode, director of Federal affairs in the March of Dimes' Office of Government Affairs, would update the Advisory Committee on Federal legislative developments of interest.
- **Report from the Subgroup on Newborn Screening of the Personalized Healthcare Workgroup (PHC).** Dr. Stephen Downs would report from the Subgroup on Newborn Screening that was established by the PHC Workgroup. As noted at a previous meeting, the PHC Workgroup makes recommendations to an advisory body called the American Health Information Community (AHIC) that makes recommendations to the Secretary of Health and Human Services (HHS) related to the development of interoperable electronic health information systems.
- **Subcommittee meetings and reports.** The Advisory Committee's Laboratory Standards & Procedures Subcommittee, Education & Training Subcommittee, and Followup & Treatment Subcommittee would meet on Monday, Jan. 14, 2008, and give reports to the full Committee on Tuesday, Jan. 15, 2008. All of the subcommittee meetings would be open to the public.
- **Report on the Secretary's Advisory Committee on Genetics, Health, and Society's (SACHGS) ongoing study of the impact of gene patents and licensing practices on access to genetic tests.** Dr. James Evans would describe an ongoing study by the SACHGS Task Force on Gene Patents and Licensing Practices of the impact gene patents and licensing practices have on access to genetic tests in clinical practice and public health settings.
- **Updates from the Advisory Committee's external Evidence Review Workgroup and the Advisory Committee's Nomination Review & Prioritization Workgroup (NRPW).** Dr. James Perrin and Dr. Nancy Green would update Advisory Committee members on the status of the Evidence Review Workgroup headed by Dr. Perrin and deliberations by the newly established Nomination & Prioritization Workgroup headed by Dr. Green. Dr. Howell requested that Advisory Committee members review the two nomination forms

forwarded to the Committee by the HRSA's Maternal and Child Health Bureau for conditions to be added to the uniform newborn screening panel: one nomination for severe combined immunodeficiency (SCID) and one for Pompe disease.

- **Report on HRSA's process for administrative review of nomination forms.** Dr. Marie Mann would talk about the process that HRSA's Maternal and Child Health Bureau has established to review nomination packages submitted by proponents of adding conditions to the uniform newborn screening panel to ensure that they are complete.
- **Public comment session.** As usual, there would be an opportunity for members of the public to offer comments to the Advisory Committee.
- **Committee business.** The final agenda item for the day would be to wrap up any remaining Committee business. Committee members would be asked, among other things, to comment on current policies regarding the authorship of Committee and workgroup reports published in refereed journals. They would also be asked to make suggestions for the agenda for the Committee's next meeting in May 2008.

Approval of Minutes. The minutes from the Nov. 14, 2007, meeting of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children by conference call [Tab #5 in the materials distributed to Advisory Committee members] were approved. The minutes from the Sept. 17-18, 2007, meeting of the Advisory Committee [also under Tab #5] were approved with the following changes:

- Page 24, first bullet: Change "Luminex B" to "Luminex bead."
- Page 33, third bullet: Change "Dr. Dougherty disagreed, noting" to "Dr. Dougherty suggested."
- Page 42, second line: Change "reported on the Genetic Alliance's two other projects" to "reported on two other projects."

II. INTRODUCTION OF NEW MEMBERS

Dr. Howell welcomed five new voting members to the Advisory Committee and reported that the Secretary of HHS had appointed him to a second 4-year term as the chair of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. The five new Advisory Committee members are the following:

- Rebecca H. Buckley, M.D., J. Buren Sidbury Professor of Pediatrics at Duke University Medical Center, Duke, NC
- Bruce Nedrow (Ned) Calonge, M.D., M.P.H., Chief Medical Officer and State Epidemiologist, Colorado Department of Public Health and Environment, Denver, CO
- Kwaku Ohene-Frempong, M.D., Director, Comprehensive Sickle Cell Center, Children's Hospital of Philadelphia, Philadelphia, PA
- Tracy L. Trotter, M.D., F.A.A.P., Senior Partner, Pediatric and Adolescent Medicine, San Ramon Valley Primary Care Medical Group in San Ramon, CA
- Gerard Vockley, M.D., Ph.D., University of Pittsburgh, Professor of Pediatrics, School of Medicine, Professor of Human Genetics, Graduate School of Public Health, Chief of Medical Genetics, Children's Hospital of Pittsburgh of University of Pittsburgh Medical Center, Pittsburgh, PA

Dr. Telfair announced that he plans to leave the Advisory Committee on Heritable Disorders and Genetic Diseases but not until a person who can replace him as the liaison from the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) is found.

III. NEWBORN SCREENING SYSTEMS USING PARTNERSHIPS FOR NEWBORN SCREENING AND FOLLOWUP

In this session, several individuals gave presentations illustrating partnerships for newborn screening and followup of newborns identified as having genetic or metabolic disorders:

- Dr. Susan Berry discussed the Region 4 Genetics Collaborative's Inborn Errors of Metabolism Information System (IBEM-IS) for long-term followup of affected newborns in Illinois, Indiana, Kentucky, Michigan, Minnesota, Ohio, and Wisconsin.
- Mr. William Slimak from Pediatrix Screening described the Nebraska Newborn Screening Program's contractual arrangement with Pediatrix Screening for newborn screening and followup services.
- Dr. Roger Eaton reported on the partnership for newborn screening services and followup activities between the University of Massachusetts Medical School–New England Newborn Screening Program (NENSP) and two New England states for newborn screening and followup services. In addition, Dr. Anne Comeau, who previously made a presentation on an NENSP project to develop sustainable long-term followup initiatives, made some brief remarks about NENSP's short-term followup activities after newborn screening.
- Dr. Michael Skeels, the director of the Oregon State Public Health Laboratory, described the contractual arrangements under which Oregon's Northwest Regional Newborn Screening Program (NWRNSP) at the Oregon State Public Health Laboratory provides newborn screening and followup services to several sparsely populated states and other entities in the region.

A. The Region 4 Genetics Collaborative's Inborn Errors of Metabolism Information System for Long-Term Followup After Newborn Screening

Susan A. Berry, M.D.
Professor and Director
Division of Genetics and Metabolism
Department of Pediatrics
University of Minnesota

Dr. Berry discussed the evolution and future plans for the Inborn Errors of Metabolism Information System (IBEM-IS) developed by the Region 4 Genetics Collaborative. The Region 4 Genetics Collaborative includes seven states that are seeking to share the use of available newborn screening and genetic resources: Illinois, Indiana, Kentucky, Michigan, Minnesota, Ohio, and Wisconsin. All seven states perform newborn screening using tandem mass spectrometry (MS/MS).

Newborn screening can be effective in improving outcomes and saving lives of affected children, Dr. Berry explained, only if the treatment provided once disorders are detected is effective. The problem is that there is no good evidence base for how inborn errors of metabolism should be

treated. The challenges in developing evidence-based medicine to treat inborn errors of metabolism are well known.

Strategies for encouraging the development of evidence-based medicine pertaining to such disorders include collaboration among centers, with Federal and state support, and the publication of systematic reviews. There is substantial precedent for national collaboration in the treatment of other diseases (e.g., childhood cancer), and there is no reason that something similar cannot be done in the case of rare inborn errors of metabolism.

The Region 4 Genetics Collaborative has a partnership of metabolic clinicians and state health department newborn specialists who are committed to collaboration and have formed a team to create new ideas about how to improve long-term followup of infants found to have inborn errors of metabolism detected via newborn screening. They have established Region 4's Long-Term Followup and Clinical Outcomes Workgroup, whose charge is to develop and implement a rational action plan to address long-term followup after newborn screening and the evaluation of clinical outcomes. The workgroup's priorities are (1) developing standardized diagnostic and medical management protocols for disorders diagnosed by newborn screening/care plans for specific diagnoses; and (2) evaluating clinical outcomes through identifying critical elements for followup.

The Web-based IBEM-IS developed by the Region 4 Genetics Collaborative's Long-Term Followup and Clinical Outcomes Workgroup is the primary instrument by which these priorities will be achieved. The IBEM-IS includes the following data: (1) core data elements (e.g., initial or updated newborn screening results; confirmatory testing results, other); (2) disease-specific data elements; (3) interval data elements collected at each center (labs, ER/hospital, prescriptions, developmental evaluations) with prompts built in; and (4) additional data elements (e.g., care coordination). So far the collaborators have defined the data elements for 19 disorders of the primary and secondary uniform newborn screening panel.

The development of the IBEM-IS began with the development by Region 4 of a Web-based registry and data system with demographic and disease-specific data elements for a single disorder—MCAD (medium chain Acyl-CoA dehydrogenase) deficiency. Recently, the database has been expanded to include other disorders such as maple syrup urine diseases (MSUD), organic acidemias, and long-chain fatty acid oxidation disorders.

Rather than being built from scratch, the IBEM-IS was built using a commercial relational database platform called DocSite®, which allows people to connect health information from different sources (e.g., inpatient/ emergency rooms, public health, home, physicians' offices) for care, tracking, etc. DocSite® is compliant with the Health Insurance Portability and Accountability Act, allows relative ease of entry at the point of service, has reporting functions, permits adding elements into and amending those elements for data management and monitoring, and makes it relatively easy to export data for analysis.

Institutional review board (IRB) approval is in place in the states of Minnesota, Illinois, Wisconsin, and Ohio, and the Region 4 collaborators are enrolling clinic subjects as they obtain their permission. Patients who enroll in the registry are asked to sign a prospective consent to allow continuing contact. Thus, there will be a cohort of patients with specific questions on whom data are being collected and who can be engaged in future research projects.

Since June 2007, the Region 4 collaborators have enrolled 89 subjects in the IBEM-IS: 31 with MCAD deficiency, 5 with MSUD, 17 with organic acidemias, 17 with long-chain fatty acid oxidation disorders, and a handful of others. The investigators were surprised and happy to

discover that about 85 percent of the data elements for MCAD deficiency and MSUD—and probably other disorders—are identical, because they pertain to the general health and well-being of the child; only about 15 percent of the data elements in the IBEM-IS are disease specific.

The IBEM-IS will serve as the foundation for research regarding the long-term management of inborn errors of metabolism, help define the natural history of these conditions as prospectively treated diseases, and provide a platform from which to integrate other data that will be critical to the care of affected individuals. The next steps for Dr. Berry and her colleagues are to define their research agenda and strategy with the IBEM-IS. They also want to work toward integration of the data (e.g., to allow importing the data directly from the newborn screen into the database and vice versa, to allow departments of health to export the data for their long-term followup mandates, to allow families or emergency room doctors to get access to the Web-based emergency plans).

Questions & Comments

Advisory Committee members, including Dr. Boyle, Dr. Hinman, and others, expressed great enthusiasm for and interest in the Region 4 Genetics Collaborative's IBEM-IS. Many of them also asked questions about the system.

Dr. Ohene-Frempong asked: When families consent to enroll, is the consent open-ended and also with the understanding that they may become either eligible or at least approached about future research? Dr. Berry explained that one of the elements captured in the IBEM-IS itself is permission to contact. So if a person says yes, enroll me and keep my data but no, do not contact me, the data can be sorted for that. If a person does not want to continue participation, it is possible to stop gathering data on the person, but the data that have already been collected on the person will remain in the database. That is cited in the consent form. Another issue related to consent, Dr. Berry noted, is what to do when somebody who has been enrolled turns 18. Region 4 plans to re-consent children for the IBEM-IS when they become adults.

Dr. Boyle asked how the IBEM-IS captures all the medical events for a child. Dr. Berry said that at each visit, the family is asked: How many emergency room visits did you have? Were those related to your inborn error of metabolism? The IBEM-IS also counts the number of hospital days that affected children have in a given interval. Thus, the IBEM-IS uses surrogates to measure the impact of what happens in the lives of affected children.

Dr. Georgeanne Arnold, speaking from the audience, asked how Region 4 would keep the IBEM-IS updated. Dr. Berry replied that doing this is a challenge but extremely important. Right now, although the IBEM-IS is electronically based, they are asking people to fill out the visit planners and hold onto them so that if there are any problems with the data in the IBEM-IS, they can go back and capture it. This system is not perfect, but it is what they can do right now.

Dr. Calonge asked how Region 4 would fund maintenance of the IBEM-IS over time. Dr. Berry said the IBEM-IS is grant funded for 5 years; after that, the source of funding is unclear. She and her colleagues recognize that there may be other plans for what happens on a national scale, but they want to at least start standard mapping. They are trying to maximize the possibility that if there is a meta-database for the world, the data from the IBEM-IS database can be exported to it if need be.

Speaking from the audience, Dr. Nancy Green asked whether the IBEM-IS would accommodate data from prospective trials. Dr. Berry said the intent in setting up the IBEM-IS was to allow that. It would be possible to add data from a trial of a medication, for example, by adding a data element saying is this person on this trial and then add information. Dr. Green's also asked whether there

was some system for banking samples for people entered into the IBEM-IS. Dr. Berry stated that clinical samples are not being banked.

Several Committee members posed questions related to access to data in the IBEM-IS:

- Dr. Buckley asked who had access to all of the data in the IBEM-IS. Dr. Berry said that she and the epidemiologist are the only people with full access to all of the data. Dr. Buckley also asked how the consent form was handled. Dr. Berry explained that she wrote the consent form.
- Dr. Trotter asked whether primary care physicians had Web-based access to the emergency plan. Dr. Berry said yes, the primary care physician, the metabolic specialist, and the family all have access to the emergency plan.
- Dr. Boyle also asked how the IBEM-IS collaborated in public health functions. Dr. Berry said that in terms of access, the plan would be that because of the way the IBEM-IS is set up to allow the granting of permission to a user for access to certain sets of data, a department of health could be allowed access to all the data from their own state's activities for long-term followup. In terms of a larger-scale public health interest, obviously it's in our mutual interest to publish this information and share it. Dr. Berry added that if people have projects specific to this or information that we want to capture, it's not that hard to add or change the elements. So if there are better surrogates than just capturing days in the emergency room that should be added, that can be done.
- Ms. Terry also asked whether outside groups would be allowed to have access to the data collected via the IBEM-IS. Dr. Berry explained that Region 4 views the IBEM-IS as a public resource and will have a process by which groups like the Genetic Association Information Network can request access to deidentified data.

Dr. Hinman asked whether Region 4 had considered adding hemoglobinopathies or hearing disorders to the IBEM-IS. Dr. Berry said the beauty of the IBEM-IS is that you can add whatever disorders you want. Dr. Hinman also asked whether the IBEM-IS was being used to provide educational materials to primary care providers. Dr. Berry said no, but they could add this to the emergency plan, or add links to American College of Medical Genetics (ACMG) ACT sheets for professionals.

Dr. Kus asked for information about the tools being used for the expanded neurodevelopmental section of the IBEM-IS. Dr. Berry said that the Region 4 collaborators incorporated the results from several standard tools for a separate neuropsychiatric survey. Each disorder has an enrollment survey and an interval survey—and the neuropsychiatric survey is common to them all.

Ms. Terry expressed concern that Dr. Berry had implied that randomized clinical trials (RCTs) were the only type of evidence, despite the fact that other types of evidence are deemed acceptable in the case of rare diseases. Dr. Berry assured her that she had not meant to imply that RCTs were the only acceptable form of evidence. The IBEM-IS gathers data on the clinical history of what happens—and that in itself is evidence.

B. A Public-Private Partnership for Newborn Screening and Followup Services: Nebraska's Newborn Screening Program and Pediatrix Screening

William S. Slimak
Vice President of Operations
Pediatrix Screening

Mr. Slimak described partnership between Nebraska's newborn screening program and a commercial entity, Pediatrix Screening, under which Pediatrix Screening processes newborn screening specimens and helps drive systemic quality improvements in the state's newborn screening system.

Hospital and other birthing centers in Nebraska obtain newborn screening specimens and then send them by United Parcel Service (UPS) to Pediatrix Screening in Pennsylvania. Pediatrix Screening then analyzes the specimens and provides the results. In addition, Pediatrix Screening collects and analyzes data on various metrics related to newborn screening for Nebraska's newborn screening program. These include age of specimen at time of specimen collection, percentage of specimens found to be unsatisfactory and why, mean turnaround time from birth to specimen collection, average turnaround time from collection to receipt at the Pediatrix Screening lab in Pennsylvania, and average turnaround time from birth to results. For each metric, there is a state metric and a metric for each hospital.

The Nebraska Newborn Screening Program shares these metrics with hospitals to drive continuous improvement based on the phenomenon in human behavior known as the "Hawthorn effect" (i.e., if you start measuring something and you do nothing more than measure it and express those measurements to the user, you get improved service). In addition, when a problem is found, Nebraska talks with Pediatrix, and they apply Six Sigma principles to identify what the source of the problem might be so that corrections can be made.

This is the 5th year of the partnership between Nebraska and Pediatrix partnership in metrics-driven continuous improvement in newborn screening, and all of the metrics are moving in the right direction. Mr. Slimak cited data from the Nebraska Department of Health and Human Services' 2006 annual report *Newborn Screening in Nebraska: Newborn Screening for Metabolic and Inherited Disorders and Newborn Hearing Screening* to illustrate how data and analysis provided by Pediatrix Screening are used to drive continuous quality improvement in Nebraska's newborn screening program. The average turnaround time from specimen collection to receipt at the Pediatrix Screening lab in Pennsylvania, for example, now takes about 16 hours (with UPS deliveries 6 days a week). The turnaround time for laboratory testing of the specimens is about 1.1 days. And the average turnaround time from birth to the provision of results has been driven down to 5.2 days.

Questions & Comments

Speaking from the audience, Julie Miller from Nebraska's newborn screening program stated that she believes the relationship has been successful because of the contractual arrangement between Pediatrix Screening and the Department of Health, which clearly specifies expectations. She noted that quality improvement is built systemically into the Nebraska system. In response to a question from Dr. Rinaldo, Ms. Miller stated that Nebraska currently has 64 birthing places in its system, but the number fluctuates throughout the year.

Dr. Geleske asked when primary care physicians receive the laboratory results on newborn screening specimens. Mr. Slimak explained that all of the newborn screening results are available via the encrypted Internet. Abnormal results are called out either directly to the department or with one of Pediatrix Screening's genetic counselors, who are available 24 hours a day, 7 days a week.

Dr. Ohene-Frempong asked whether hemoglobinopathies are included in the system. Mr. Slimak said yes.

Dr. Calonge asked how Nebraska reduces its false-positive rates when they are higher than national rates while also making sure it does not have false negatives. Mr. Slimak explained that Pediatrix Screening looks at outcomes and testing algorithms. They come up with what they think are enhancements to the algorithm. They then take the data and new algorithms to the state advisory committees, which then decide how to proceed. Dr. Rinaldo asked what the false-positive rate for tandem mass spectrometry (MS/MS) in Nebraska's newborn screening program is. Mr. Slimak said the Nebraska Department of Health and Human Services' 2006 annual report talks about this. He believes that for overall MS/MS, the false-positive rate is something less than 0.1 percent. For things other than MS/MS, it is something less than 0.5 percent. Ms. Miller noted that the 2006 annual report is available online at the Nebraska Department of Health and Human Services' Web site at www.hhs.state.ne.us/nsp/.

Dr. Lavenstein asked about experience with cost. Mr. Slimak said his experience is that good, solid quality assurance and continuous improvement programs drive cost savings. When one starts a continuous improvement program, one can get immediate savings from "low-hanging fruit" that are as much as 10 or 15 percent of the cost. Then with a good established program, one can usually drive about a 5 percent reduction in costs annually. In response to a question from Dr. Howell, Ms. Miller said the screening cost per patient is \$25.75. The charges per infant screened are \$35.75, but \$10 of that is returned to the state and used to help pay for metabolic formula and foods.

Dr. Howell asked whether Pediatrix Screening plays any role in long-term followup of affected newborns. Mr. Slimak replied that Nebraska uses Pediatrix Screening's data system, so they could potentially be involved in long-term followup, but they are not involved in any significant way right now.

C. A Partnership between the New England Newborn Screening Program at the University of Massachusetts Medical School and two New England States for Newborn Screening and Followup

Roger B. Eaton, Ph.D., M.S.
Director
New England Newborn Screening Program (NENSP)
University of Massachusetts Medical School

Dr. Eaton described the arrangements under which the New England Newborn Screening Program (NENSP) provides newborn screening and followup services under contract to the states of Massachusetts and Rhode Island. NENSP is a program of Commonwealth Medicine, the service arm of the University of Massachusetts Medical School, and NENSP's senior staff is faculty members at the medical school.

The mission of Commonwealth Medicine is to apply knowledge to improve health outcomes for those serviced by public health and human service programs. According to Dr. Eaton, the model of having newborn screening services and followup provided under contract to the state department of

public health by a program affiliated with the service arm of a medical school offers a very good environment not only the delivery of newborn screening and short-term followup services, but also for technical research and development, for studying clinical outcomes and for clinical research, and for publications.

In Massachusetts, the contract between the state and the University of Massachusetts Medical School calls for NENSP to provide newborn screening and followup services from A to Z. In Massachusetts, therefore, NENSP screens every newborn, performs laboratory analysis and quality control, provides notifications when there are out-of-range results, and provides support and followup services. NENSP has standing specialty workgroups with specialists from outside the medical school and region (e.g., the metabolic workgroup, the cystic fibrosis workgroup, the hemoglobin workgroup) that provide day-to-day feedback, offer advice on implementing improvements in newborn screening and followup, and make recommendations on NENSP's more than 90 analyte-specific worksheets.

NENSP has both a short-term followup database and a long-term followup database for newborns. The short-term followup database is used to collect diagnostic and other information on newborns that undergo screening at birth. The long-term followup database for newborn screening grows out of the short-term database. It has tabs across the top for information captured from age 1 year, 1 to 3 years, 3 to 7 years, and up to 25 years.

If a baby born in Massachusetts has an out-of-range screen, NENSP notifies the pediatrician and specialist and coordinates the short-term followup. With three metabolic clinics in Boston alone, NENSP does not know when it first gets an out-of-range screening result where it would be most appropriate for the affected baby to be referred. Consequently, NENSP's first contact is with the baby's pediatrician. NENSP discusses the baby's out-of-range result with the pediatrician and what the next steps might be and determines what specialist that physician uses that the patient's insurance might cover. Then NENSP proactively notifies the specialist. The pediatrician sees the child and refers the child to the specialist. NENSP checks back later to ensure that everything actually happened as planned.

In Rhode Island, the contract between the state and the University of Massachusetts Medical School calls for NENSP to provide newborn screening services and to provide followup services in partnership with the Rhode Island Department of Health. Thus, if a baby in Rhode Island has an out-of-range screen, NENSP notifies the state health department. The health department takes over from that point on using its own contact algorithm. In most cases requiring urgent referral, the health department notifies its own contract specialist directly; and that specialist makes a referral to the pediatrician. It then has the responsibility to followup to ensure that the referral took place. If the NENSP lab gets results either during the holiday, during weekend, during an evening, when the Rhode Island health department staff may not be available, NENSP has all of Rhode Island's contact algorithms and notifies the appropriate specialist itself. NENSP then notifies the state health department of the contact, so the health department can do the followup later on.

Anne Marie Comeau, Ph.D.
New England Regional Newborn Screening Program
University of Massachusetts Medical School

Dr. Comeau made a brief comment about NENSP's role in interpreting newborn screening results for parents and professionals. She noted although there is generic information about newborn screening available on the Web such as the American College of Medical Genetics (ACMG) ACT sheets for professionals, STAR-G fact sheets for parents, HRSA-developed newborn screening brochures for parents, a person receiving a newborn screening result may require information that

is more laboratory specific. The lab that performed the newborn screening test is potentially a good source of such information. In Massachusetts, for example, such information is supplied by NENSP. NENSP has certified clinical geneticists and biochemical geneticists, endocrinologists, pediatricians, etc., on staff, so it is able to apply an experience-based laboratory analysis to help for anybody receiving a newborn screening result understand what that result might mean. NENSP gives advice as to urgency and next steps for newborns with positive screening tests and also provides relevant fact sheets.

Questions & Comments

Speaking from the audience, Kristi Zonno from Rhode Island's newborn screening program noted that Rhode Island is a small state. She said that the contractual relationship with the NENSP both helps reduce costs for the state and offers it the benefits of NENSP's expertise.

Dr. Ohene-Frempong asked Dr. Eaton to comment on how samples sent from Massachusetts and Rhode Island were tracked by NENSP. Dr. Eaton explained that the samples go from collection directly to the lab, and there are ways of tracking packages sent by UPS to make sure they get there. The NENSP makes sure it receives a package from every site in Massachusetts and Rhode Island at least once a day; if no package arrives from one of the sites, the program checks up on this.

Dr. Howell asked whether there were any problems in the handling of newborn screening specimens due to labs being closed on Sundays. Dr. Eaton said that NENSP does perform analyses of newborn specimens on Sunday. Furthermore, NENSP has an understanding that goal is to interface baby with effective care. Thus, if there is any issue that is outside the capability of the newborn screening program in Rhode Island, NENSP takes care of it.

Dr. Telfair asked Dr. Eaton to comment on NENSP's relationship with primary care providers in the community in performing followup activities with respect to affected newborns. Dr. Eaton said the initial contact goes to the pediatrician and educational materials go to primary care providers, but the NENSP generally works with tertiary care facilities.

D. Oregon's Northwest Regional Newborn Screening Program: Newborn Screening and Followup Services for States in the Northwest Region and the Pacific

Michael Skeels, Ph.D., M.P.H.
Director
Oregon State Public Health Laboratory
Committee Member

Dr. Skeels (by telephone) described the contractual arrangements under which Oregon's Northwest Regional Newborn Screening Program (NWRNSP) at the Oregon State Public Health Laboratory provides newborn screening and followup services to several sparsely populated states and other entities in the region.

NWRNSP serves as a regional center for newborn screening for six sparsely populated states (Oregon, Idaho, Nevada, New Mexico, Alaska, and Hawaii), for military facilities in Washington State and Korea, and for birthing facilities in Guam, Saipan, and Kwajalein. These states and other entities vary widely in their capacity to provide newborn screening program administration, management, education, and followup. Thus, the state departments of health and other entities enter

into contracts with Oregon's state health department (the Oregon Public Health Division) for the newborn screening services they need. Then each of the states operates as autonomous and state-centered a program as possible.

The continuum of newborn screening services that NWRNSP is able to provide are the following:

- Education of parents (e.g., via the parents' newborn screening brochure, which can be customized) and practitioners (e.g., via distribution of an online *Practitioner's Manual* to doctors, midwives, nurse practitioners and laboratorians who work with newborns)
- Lab screening and confirmation
- Short-term followup and tracking
- Medical consultation and referral
- Population-based public health model
- Cost-effective pooling of resources

As illustrated by several slides that Dr. Skeels presented, the newborn screening and followup services provided to the six states and other entities vary, depending on their particular needs.

Questions & Comments

Speaking from the audience, Sylvia Au from Hawaii's health department reported that contracting with Oregon for newborn screening services has been very satisfactory. Hawaii's newborn specimens are sent via Federal Express to Oregon, and the screening results are available within a week. Hawaii also pays Oregon to do data entry (including Neometrics software for followup) and shares educational materials and information with other states that have contracts with Oregon. The cost for the screening is \$47 per newborn, and that that includes the collection kit, education materials, initial screen, any repeat screens, confirmatory testing, and consultants. The entire state followup staff is funded through that fee, so the program is totally sustainable and does not use a penny of state money. Hawaii does quality assurance things via practice profiles, surveys with providers, and focus groups with families.

Dr. Calonge suggested that it would be interesting to catalogue how different states handle the issue related to newborn screening to develop a toolbox for other states. Dr. Howell agreed that having HRSA catalogue the different approaches was a good idea.

IV. LEGISLATIVE UPDATE

Emil Wigode

Director, Federal Affairs

Office of Government Affairs

March of Dimes

Mr. Wigode reported on Federal legislative developments of interest to Advisory Committee members. He noted, however, that newborn screening is a priority of the March of Dimes at both the Federal and state levels. March of Dimes chapters in the states have been trying to get the states to screen for the 29 core conditions on the uniform newborn screening panel recommended by the American College of Medical Genetics (ACMG). Currently, 16 states plus the District of Columbia are now screening for the 29 core conditions on the panel. In the months ahead, March of Dimes chapters in the other states will be trying to get them to screen for these conditions.

At the Federal level, at the end of 2007, after a few attempts to override President George W. Bush's veto of the State Children's Health Insurance Program (SCHIP), Congress extended SCHIP to March 2009. There were no policy changes, so SCHIP will cover about 6 million children rather than being expanded to cover 9 million to 10 million children.

The Labor, Health and Human Services, and Education (LHHS) appropriations bill that Congress passed in 2007, with good increases for HRSA and other agencies, was vetoed by President George W. Bush in November 2007. In the final wrap-up session, therefore, Congress passed an omnibus bill with funding for 11 of the 12 appropriations bills that are supposed to move separately. In the process \$6 billion was cut from the original LHHS bill sent to the President. For most programs, including HRSA's Heritable Disorders Program, funding remained level.

Congress is about to reconvene for 2008. President Bush will deliver his State of the Union address on Jan. 28, 2008, and he will deliver his Fiscal Year 2008 budget proposal by Feb. 4, 2008. This will be a difficult year in terms of getting things done in Congress, in part because there is a presidential election going on.

Nevertheless, there is an opportunity to move bills such as the Newborn Screening Saves Lives Act. The Senate version of this bill (S. 1858) passed the Senate unanimously, and the House version has 68 sponsors. The Newborn Screening Saves Lives Act would reauthorize activities authorized in 2000 in the Children's Health Act and expand a few areas. Specifically, it would do the following:

- Authorize a series of grant programs to help states expand their newborn screening programs to include the 29 core conditions in the uniform newborn screening panel.
- Authorize grant programs for educating and training health professionals, parents, and establishing a coordinated system of care.
- Renew the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children for an additional 5 years of work; require the Secretary of Health and Human Services to respond to the Advisory Committee's recommendations within 180 days; and add individuals with expertise in ethics and infectious diseases who have experience in the area of newborn screening as full members on the Advisory Committee.
- Authorize an Internet clearinghouse for information on newborn screening.
- Authorize the Centers for Disease Control and Prevention (CDC) to perform quality assurance for laboratories involved in newborn screening
- Require CDC in consultation with HRSA to develop a national contingency plan for newborn screening to be implemented in disasters.
- Authorize the National Institutes of Health to expand its research activities related to newborn screening via the Hunter Kelly newborn screening Research program.

The Genetic Information Nondiscrimination Act has passed the House but is delayed in Senate.

Questions & Comments

Dr. Lavenstein reported that on March 3 or March 4 of this year, the American Academy of Neurology has a "Neurology on the Hill Day." About 100 adult neurologists and a few child neurologists will be coming to speak to their representatives or to their senators about three different topics. One of the topics is newborn screening, and efforts there will focus on the House

and the Newborn Screening Saves Lives Act. Dr Lavenstein said he would like to get a copy of Mr. Wigode's remarks.

V. REPORT FROM THE PERSONALIZED HEALTHCARE WORKGROUP AND ITS SUBGROUP ON NEWBORN SCREENING

In this session, Dr. Gregory Downing, the project director for the Personalized Healthcare (PHC) Initiative in the Office of the Secretary of Health and Human Services (HHS), briefly summarized his presentation on the initiative at the Advisory Committee's meeting in September 2007. Then Dr. Stephen Downs, the co-chair of the PHC Workgroup's recently established Subgroup on Newborn Screening, gave a report on the activities of that subgroup.

A. Background on the HHS Secretary's PHC Workgroup

Gregory J. Downing, D.O., Ph.D.
Project Director
Personalized Healthcare Initiative
Immediate Office of the Secretary
U.S. Department of Health and Human Services (HHS)

Dr. Downing explained that the Personalized Healthcare (PHC) Workgroup is one of several workgroups of the American Health Information Community (AHIC), a public-private advisory body chartered in 2005 to make recommendations to the HHS Secretary on how to accelerate the development and adoption of health information technology for an interoperable nationwide health information system. AHIC is setting the stage for the integration of interoperable electronic health information in the U.S. health care system.

The PHC Workgroup has both a specific charge and a broad charge:

- Its *specific charge* is to make recommendations to AHIC to consider means to establish standards for reporting and incorporation of common medical genetic/genomic tests and family health history data into electronic health records, and provide incentives for adoption across the country including Federal Government agencies.
- Its *broad charge* is to make recommendations to AHIC for a process to foster a broad, community-based approach to establish a common pathway based on common data standards to facilitate the incorporation of interoperable, clinically useful genetic/genomic information and analytical tools into electronic health records to support clinical decisionmaking for the clinician and consumer.

The PHC Workgroup has identified four perspectives as being important to its vision of a consumer centric approach: clinician, researcher, health plan, and payer. It has also identified four priority areas across each of these perspectives: genetic/genomic tests; family health history; confidentiality, privacy, and security; and clinical decision support.

On July 31, 2007, AHIC accepted the PHC Workgroup's recommendations to develop a PHC "use case" (discussed further by Dr. Downs below) addressing genetic/genomic tests and family health history. The genetic/genomic tests portion will address common polymorphisms associated with specific diseases, and their coding and incorporation into electronic health records. Newborn screening tests are an important category of genetic/genomic tests. In October 2007, the PHC

Workgroup formed a Subgroup on Newborn Screening, chaired by Dr. Stephen Downs from Indiana University and Dr. Peter van Dyck from HRSA.

B. The PHC Workgroup's Subgroup on Newborn Screening

Stephen M. Downs, M.D., M.S.
Co-Chair, Subgroup on Newborn Screening
Personalized Health Care (PHC) Workgroup
American Health Information Community (AHIC)
Associate Professor and Director
Children's Health Services Research
Indiana University School of Medicine

Dr. Downs explained that the PHC Workgroup's Subgroup on Newborn Screening has a charge to develop "actionable recommendations around harmonization of standards for electronic health information reporting and exchange of state-mandated newborn metabolic, genetic/genomic, and hearing screening results." The specific tasks for the Subgroup on Newborn Screening are the following:

1. Make the case that AHIC should take up newborn screening as one of the areas in which to develop health information standards via a "use case." (A "use case" is a software development strategy to aid in the design of information systems. AHIC use cases are intended to be given or made available to software developers who can use it as a guide to develop software systems that will meet the specifications of the use case.)
2. Suggest a brief or high-level use case or use cases related to newborn screening that would help in the design of health information systems in support of newborn screening.
3. Consider some of the implementation issues that come into play when one envisions actually implementing a system in these use cases.

In general, Dr. Downs explained, an AHIC use case does the following: (1) it defines the *goal* for a particular use for which the information system is going to be put; (2) it treats the *system* as a black box (i.e., there is nothing about a use case that says how a particular program will be written or how a particular piece of software will be put together); (3) it describes the *actors*—people or the other information systems or other objects that need to interact with that information system—and identifies them as primary or secondary actors, depending on whether the system is acting on them or they are acting on; (4) it identifies what should trigger the information system to act; (5) it describes the general course of events when actors interact with the system; and (6) it identifies post conditions—the state of the information system and the actors when they are done.

The goals for the newborn screening use cases that Dr. Downs is envisioning, after discussions with the Subgroup on Newborn Screening, include the following:

- Record data collected with the blood spot, to record bedside hearing screening results.
- Transmit birth site data to public health and to newborn screening labs.
- Record blood spot test results, to transmit newborn screening results including quantitative values from laboratory tests.
- Create the ability to deliver appropriate information to the medical home, to families, to public health, to registries.

- Provide decision support to providers in the form of guidelines (e.g., information that providers can get such as the ACMG ACT sheets that might be appropriate to a particular case) or reminders (e.g., a reminder to a provider to check newborn screening results on a young child).
- Track positive screens to ensure diagnostic confirmation and clinical followup.
- Track confirmed cases to ensure long-term followup (across time and distance)
- Make data available (with appropriate precautions) for quality improvement and for research on testing and treatments.

The draft report from the Subgroup on Newborn Screening is undergoing review by the members of the subgroup and will be presented to the PHC Workgroup for its consideration on Jan, 30, 2008. Dr. Downing would like the members of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children to get copies of the draft so that they can provide comments on the draft prior to the next meeting of the Subgroup on Newborn Screening on Jan. 16, 2008. On Feb. 6, 2008, the draft recommendations will be provided to AHIC's Population Health and Clinical Care Connections Workgroup. Then on Feb. 26, 2008, once a consensus is reached, the co-chairs of the PHC Workgroup will advance their recommendations regarding the newborn screening use case to AHIC for a decision by that body on how to proceed.

Questions & Comments

Dr. Lloyd-Puryear asked whether Dr. Downs wanted formal comments from the Advisory Committee. Dr. Downing replied that he would like comments from Advisory Committee members to be provided informally before Jan. 30, 2008. Advisory Committee members could be further involved any time between now and when the use case prototypes come out at the end of February 2008. Once the use case recommendations are supported by AHIC, there will be additional opportunities to weigh in. The Subgroup on Newborn Screening would like some official action from the Advisory Committee.

VI. COMMITTEE BUSINESS—SUBCOMMITTEE REPORTS & DISCUSSION

The Advisory Committee's Laboratory Standards & Procedures Subcommittee, Education & Training Subcommittee, and Followup & Treatment Subcommittee held meetings that were open to the public from 1:30 p.m. on Monday, Jan. 14, 2008. On the second day of the meeting, Jan. 15, 2008, each of the subcommittee chairs gave a report to the full Committee, as discussed below.

The Laboratory Standards & Procedures Subcommittee is now headed by Dr. Gerard Vockley. The Education & Training Subcommittee is now headed by Dr. Tracy Trotter and Jana Monaco. The Followup and Treatment Subcommittee continues to be chaired by Dr. Coleen Boyle.

A. Laboratory Standards & Procedures Subcommittee Report

Gerard Vockley, M.D., Ph.D.

Chief of Medical Genetics

Children's Hospital of Pittsburgh of UPMC

Professor of Human Genetics and Pediatrics

University of Pittsburgh

Committee Member

Dr. Vockley, who is the new chair of the Laboratory Standards & Procedures Subcommittee, noted that he and Dr. Calonge are both new members of the subcommittee. Then he summarized what had transpired at the subcommittee's meeting the previous day.

Update on the Subcommittee's Study of Routine Second Specimens. Dr. Hannon updated subcommittee members on progress with respect to the study of routine second screens for congenital hypothyroidism (CH) and congenital adrenal hyperplasia (CAH) that was begun on behalf of the subcommittee about 15 months ago.

The routine second specimen study has both retrospective and prospective components. The goal is to enroll 12 states with 25 percent of births in the United States. Dr. Hannon indicated that getting state-specific institutional review board (IRB) approvals for the subcommittee's routine second specimen study has been challenging. So far, only three states' IRBs have granted waivers for retrospective study; only two of those states have granted waivers for prospective study. Other challenges encountered in trying to perform the routine second specimen study include difficulty identifying a qualified principal investigator in some states, different consent processes for each state, and a lack of consensus on the level of risk by different IRBs. Dr. Vockley said that the Advisory Committee's Research Workgroup chaired by Dr. Watson may be able to help with this problem, and one step that the full Committee might want to consider is advocating for a national approval process for newborn screening studies.

Discussion of a Study of Routine Second Screens in Tandem Mass Spectrometry (MS/MS).

The Laboratory Standards & Procedures Subcommittee also talked a little bit about the potential for adding an evaluation of using a second screen in the MS/MS part of newborn screening. Subcommittee members thought that this should be a separate study if it were undertaken so as not to derail the routine second specimen study for CH and CAH. Possibly, however, the subcommittee may be able to leverage some of the information being collected from 41 states via Dr. Rinaldo's national collaboration on MS/MS screening standards. Dr. Rinaldo plans to make a presentation to the subcommittee about how it might either stage a new study or use information that is already available.

The Lab Subcommittee's Role in Reviewing Newborn Screening Technology. The Laboratory Standards & Procedures Subcommittee discussed whether more input of the subcommittee into the technologic aspects of adding disorders to the newborn screening panel was needed. This topic was reviewed a couple of years ago by the subcommittee. Subcommittee members decided that the process of reviewing the technology has been appropriately and adequately incorporated into the procedures of the Advisory Committee's external Evidence Review Workgroup headed by Dr. Perrin. A Laboratory Standards & Procedures Subcommittee member serves on the Evidence Review Workgroup, so the subcommittee decided that it did not need to revisit the matter any further at this time.

National Laboratory Standards for Newborn Screening Results. Subcommittee members noted that the national collaboration on MS/MS screening standards involving 41 states serves as excellent model for developing standards for other screening tests. The subcommittee agreed that it should concentrate on highlighting needs in the realm of laboratory testing standards through discussion and testimony. It hopes that raising these issues to the full Advisory Committee will focus attention on them and spur cooperation on testing standards.

Reexamining Disorders on the Uniform Newborn Screening Panel. The Laboratory Standards & Procedures Subcommittee discussed the process by which disorders should be removed from the uniform newborn screening panel recommended by the American College of Medical Genetics (ACMG). It was suggested that removing conditions from the uniform newborn screening panel would probably occur through a process that is very similar to adding conditions to the panel.

Improving Technology for Screening for Tyrosinemia Type I (TYR I). Dr. Rinaldo gave presentation to the subcommittee on TYR I as an example of a situation in there are data showing that the disease course for TYR I is significantly altered by screening and early therapy, but MS/MS experience indicates that tyrosine levels do not correlate well enough with TYR I to be reliable. Succinylacetone is reliable as a second-tier test and could be incorporated into a first-tier test for TYR I.

Subcommittee members agreed that a disorder that is already on the ACMG uniform panel should not be removed because of technological issues; rather efforts should be made by the Laboratory Standards & Procedures Subcommittee to focus attention on technological deficits and spur improvement. The subcommittee will invite broader discussion and make a specific recommendation for altering the technology used to screen for TYR I to full Advisory Committee at its next meeting in May 2008.

Role of Molecular Techniques in Screening. There are a growing number of genetic disorders that are amenable to molecular screening, and Laboratory Standards & Procedures Subcommittee members suggested that this was an area on which the subcommittee should focus in the future. Genetic disorders that are amenable to molecular screening fall into two categories: (1) disorders for which molecular screening is used as followup to the current newborn screening panel (e.g., the inborn errors of metabolism such as MCAD deficiency and galactosemia); cystic fibrosis; and the hemoglobinopathies; and (2) disorders for which molecular screening is likely to be the primary method of choice for some disorders as we move forward (e.g., hearing defects and some of the immunologic disorders that are receiving increasing focus).

Screening at Different Periods of Life. Finally, Dr. Eaton said that he had written a note to himself that even though the Advisory Committee has focused much of its energies on newborn screening, screening can actually occur in other periods of life. It is important to maintain that as a concept and think more about when it appropriate to start thinking about screening for some of these other disorders.

Questions & Comments

Dr. Howell stated that TYR I is a very serious and treatable condition and there should be no question about keeping this disorder on the uniform newborn screening panel. The current screening test does not identify patients with this disorder well, however, so the screening test must be changed.

In addition, Dr. Howell indicated that some research programs started by the National Institutes of Health (NIH) that involve states have had tremendous issues because of problems with state IRBs,

and he believes solving this problem and making the IRB approval process more efficient as we move forward is absolutely essential. At Dr. Howell's request, Dr. Hannon explained that the states were willing to defer to a central IRB, but the problem was that they could not decide which central IRB to defer to. For the routine second specimen study, part of the problem was the way the study was designed. If they had decided that the data were coming to CDC and that CDC would have a strong role in managing the data, they could have gone through to the CDC IRB process and had a central IRB to defer to.

Dr. Fleischman noted that the HHS Office for Human Research Protections, with the Association of American Medical Colleges and NIH is doing work on alternative models for IRB approvals—namely, “central IRBs” or “collaborative processes.” These alternative models are supported by Federal regulations, if people wish to defer. The *Code of Federal Regulations* has a section on "cooperative research" (45 C.F.R. 46.114) that allows any IRB to defer to a central or other IRB to allow for collaborative work and to shorten the process of IRB approvals. Dr. Fleischman suggested that Dr. Howell, on behalf of the Advisory Committee, request the assistance of the Secretary's Advisory Committee on Human Research Protections (SACHRP) in thinking about how to streamline this kind of very important collaborative work and how to create that kind of national collaboration. He also recommended that Advisory Committee members read some of the distinctions between public health surveillance and human subjects research that the Centers for Disease Control and Prevention (CDC) has published and have been opined on by the HHS Office for Human Research Protections.

Dr. Howell stated that the Advisory Committee would take Dr. Fleishman's advice and ask someone from SACHRP to address issues related to IRBs and other research process issues that are impeding research such as the routine second specimen study. Dr. Lloyd-Puryear and Dr. Telfair suggested inviting Hunt Willard or someone else from the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) to make a presentation to the Advisory Committee. Dr. Boyle noted that another possible mechanism the Advisory Committee might consider to use in thinking through IRB issues with public health emergency dimensions is the Epidemic Intelligence Service (EPI-AID) mechanism. This mechanism, which CDC uses for all its emergency response work, allows CDC to act quickly, responsibly and work with state health departments via an expedited IRB process. Dr. Howell indicated that the issue of IRBs would be on the agenda of the Advisory Committee's May 2008 meeting and that representatives of organizations that could shed light on issues of interest to the Advisory Committee would be invited to make presentations.

- **DECISION #1:** *The issue of IRB approvals will be on the agenda of the Advisory Committee's May 2008 meeting. HRSA will invite experts who can shed light on IRB and research process issues of interest to the Committee from the Secretary's Advisory Committee on Human Research Protections (SACHRP), the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS), and the Centers for Disease Control and Prevention (CDC) to make presentations.*

B. Education & Training Subcommittee Report

Tracy L. Trotter, M.D., F.A.A.P.
Senior Partner
Pediatric and Adolescent Medicine
San Ramon Valley Primary Care Medical Group
Committee Member

Dr. Trotter, one of the new co-chairs of the Education & Training Subcommittee, reported that the subcommittee's meeting on Jan. 14, 2008, had been very well attended, with many people attending for the first time. He then summarized the substantive discussions that had occurred.

Recommendation Regarding Creating a National Repository for Newborn Screening Educational Materials in Multiple Languages. Education & Training Subcommittee members continued to discuss the development of a national repository that would provide user-friendly access to newborn screening educational materials in multiple languages. Translations of newborn screening educational materials have been done by various states, regions, and individuals and are often not available to other states, regions, and individuals in a timely manner. In addition, there is considerable duplication of effort that seemingly could be avoided.

The idea is that a national repository that would provide user-friendly access to newborn screening educational materials in multiple languages would pull existing newborn screening educational materials in multiple languages and formats together from various sources, including the following:

- National Coordinating Center (NCC) and the Regional Genetics and Newborn Screening Collaboratives (RC)
- National Newborn Screening and Genetics Resource Center (NNSGRC) and the Genetic Education Materials (GEM) database that is maintained by NNSGRC
- Genetic Alliance (GA)
- National Library of Medicine (NLM)

After a spirited discussion, subcommittee members voted to make the following recommendation to the full Advisory Committee with regard to the repository:

- *Subcommittee's Recommendation Regarding the National Repository of Newborn Screening Educational Materials in Multiple Languages: The Education & Training Subcommittee recommends to the Advisory Committee that there be a specific section of the National Newborn Screening and Genetics Resource Center (NNSGRC) Web site that contain newborn screening educational material in multiple languages and information that is accessible to all of our five target audience—namely, health care providers, affected families; hospitals/birthing centers; screening program staff; and the general public.*

Future Directions for the Education & Training Subcommittee. The Education & Training Subcommittee discussed future directions with respect to its charge of identifying and addressing deficiencies in educational and training resources for the five groups that are part of its charge: health professionals, parents, screening program staff, hospital/birthing facility staff, and the public.

Subcommittee members thought that given the role of primary care physicians in newborn screening and the different roles that they play, targeting educational efforts to them might help with the education and training of the other four target audiences.

Dr. Trotter noted that a report in the current issue of *Pediatrics* entitled “Newborn Screening Expands: Recommendations for Pediatricians and Medical Homes—Implications for the System” (2008; 121; 192-217) made observations about pediatricians that are similarly applicable to other primary care physicians as well:

“advances in newborn screening...pose new challenges to primary care pediatricians, both educationally and in the management of affected infants. Primary care pediatricians require access to information... collaboration with local, state, and national partners is essential... to optimize the function of the newborn screening systems.”

Finally, Dr. Trotter indicated that the Education & Training Subcommittee would like guidance from the Advisory Committee about where to focus its efforts. One idea that the subcommittee had was to partner with the existing professional groups—including the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG)—to improve educational efforts related to the role of primary care physicians in newborn screening. The subcommittee also believes that improving genetic literacy at the primary care level is very important. Given the pervasiveness of genetics in the world of practicing medicine, primary care providers are going to require a lot of education and a lot of training on how to interpret genetic test results.

Questions & Comments

Dr. Howell asked what the Education & Training Subcommittee’s high-priority action items are. Dr. Trotter replied that the subcommittee’s priorities are (1) to get the national repository for newborn screening educational materials in multiple languages and multiple formats in place; and (2) to develop guidelines for translation and literacy requirements that could be used by the national repository; and (3) to launch the subcommittee’s efforts to address primary care physicians’ gaps in knowledge related to newborn screening and genetics with help from the AAP, AAFP, and ACOG, perhaps via workshops at annual meetings, continuing medical education credits for introductions to medical genetics, etc.

Dr. Buckley, noting that some pediatricians have no knowledge of genetics, said she thought it would be very helpful if the AAP got behind educational efforts related to newborn screening and genetics. Dr. Howell asked whether it would be useful for the Advisory Committee to request that the professional medical organizations do a workshop on issues related to genetics and newborn screening. He asked Dr. Trotter and the Education & Training Subcommittee to develop a recommendation on this topic during the break, so that the full Advisory Committee could act on it before the meeting ended. Dr. Trotter agreed to do this (and in fact, presented a recommendation in the last session of the day).

Dr. Telfair indicated that the Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS) had started a group similar to the Education & Training Subcommittee—namely, the SACGHS Education Task Force. He recommended that the Education & Training Subcommittee members talk to the chair of that committee, Dr. Barbara Burns McGrath.

Dr. Boyle emphasized that the development of the proposed national repository is a very complex issue. There are already lots of materials available, and an important question is whether there should be links to those materials or how they should be handled. Dr. Trotter agreed, saying that

the subcommittee discussed this matter at length and failed to resolve it. The subcommittee decided to first pull things together to see what is already available. Speaking from the audience, Dr. Brad Therrell from the National Newborn Screening and Genetics Resource Center (NNSGRC) said that he would give a report on providing access to the national repository for newborn screening educational materials in multiple languages and multiple formats on the NNSGRC Web site at the May 2008 meeting.

C. Followup & Treatment Subcommittee Report

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

**Director, Division of Birth Defects and Developmental Disabilities
National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention (CDC)**

Dr. Boyle, who has remained as the chair of the Followup & Treatment Subcommittee, reported that the subcommittee had had a very lively meeting the previous day and thanked everyone for participating. Dr. Boyle explained that the Followup & Treatment Subcommittee has been focusing on two major activities: (1) defining and characterizing long-term followup after newborn screening; and (2) examining issues related to insurance coverage of medical foods. She then reported what had transpired in these two areas at the Jan. 14, 2008, subcommittee meeting.

Activities Related to Long-Term Followup After Newborn Screening. In April 2007, the Followup & Treatment Subcommittee convened a meeting of stakeholders to look at two issues: (1) the components of long-term followup after newborn screening; and (2) the primary participants in long-term followup. Subsequently, the subcommittee prepared a white paper on the on the components of long-term followup. This paper, which was approved by the full Advisory Committee in the fall of 2007 for submission to *Genetics in Medicine*, sets forth the following with respect to long-term followup after newborn screening:

- *Goal of long-term followup:* To achieve the best possible outcome for children and their families
- *Definition of long-term followup:* Chronic disease management, condition-specific treatment, and preventive care
- *Components of long-term followup:* (a) evidence-based treatment; (b) coordination of care; (c) continuous quality improvement; and (d) new knowledge discovery

At the subcommittee meeting on Jan. 14, 2008, Dr. Alan Hinman led the Followup and Treatment Subcommittee in a discussion to prioritize a list of the roles and responsibilities of the four key participants in long-term followup. The four key groups participating in long-term followup identified by participants at the April 2007 meeting were (1) affected individuals/families, (2) primary care providers (PCPs), (3) specialty and subspecialty providers, and (4) public health agencies. At the meeting on Jan. 14th, the Subcommittee also identified several additional key participants in long-term followup, including the insurance sector, the education and social service sector, the information and technology sector, and policymakers at the state and Federal levels.

The Followup & Treatment Subcommittee's plan between now and the next Advisory Committee meeting in May 2008 is to develop a draft white paper on key participants' roles and responsibilities in long-term followup after newborn screening; circulate the paper to participants at the Jan. 14, 2008 subcommittee meeting, Advisory Committee members, and others for comments; and ultimately develop another white paper that the full Advisory Committee approves for

submission to *Genetics in Medicine*. The subcommittee hopes to have a draft white paper for the full Committee's consideration at the May meeting.

Issues Related to Insurance Coverage for Medical Foods for Children with Disorders

Detected via Newborn Screening. At the Followup & Treatment Subcommittee meeting on Jan. 14, 2008, the Medical Foods and Formulas Workgroup reported on its recent activities:

- *Survey of families' barriers to obtaining medical foods.* Dr. Mary Kay Kenney reported that she and others have been refining the survey tool to get information from families of affected children to characterize the problems with respect to insurance coverage of medical food. There has been some cognitive testing of parents in New York. In the coming months, additional work and testing will be done to increase the reliability and validity of the survey tool and make it more literacy sensitive and appropriate. It is hoped that the HRSA-funded Regional Genetics and Newborn Screening Collaboratives will be involved in validating and implementing the survey.
- *State legislation pertaining to medical foods.* Alissa Johnson, formerly at the National Conference of State Legislatures, reported that 36 states have some legislative language pertaining to medical food. The statutory language varies from state to state, and the translation of the statutory language into practice is unknown. Ms. Johnson suggested doing a survey at the state level to see how state laws pertaining to medical foods translate into practice, and this will probably be the subcommittee's next step in this area.
- *Evaluation of professional policies on medical foods.* Dr. Rani Singh gave an overview of the professional endorsements of insurance coverage for medical foods. The American Academy of Pediatrics (AAP) had a 1994 statement endorsing insurance coverage for medical foods, and the Society for Inherited Metabolic Disorders (SIMD), and the Genetic Metabolic Dieticians International (GMDI) similarly endorsed coverage more recently.

The Followup & Treatment Subcommittee is now considering doing a state-level survey to get a better sense of how legislative mandates pertaining to medical foods translate into practice. The subcommittee will also try to engage the insurance industry as an active participant in the subcommittee.

Questions & Comments

Dr. Howell asked whether the Followup & Treatment Subcommittee had considered how research would be integrated into long-term followup to track the outcomes with regard to treatment, novel treatments, etc. Dr. Boyle replied that the subcommittee talked about it in terms of the active engagement of key participants in long-term followup in new knowledge discovery, but the subcommittee will do additional work in this important area in the future.

Speaking from the audience, Julie Miller from Nebraska's newborn screening program stated that at the Followup & Treatment Subcommittee's discussion of roles and responsibilities for long-term followup at the meeting on Jan. 14, 2008, some people thought that there was an important role for the Federal Government in addition to a role for state and local governments. The reason is that policy development and core public health functions at the Federal level have a large influence at the state and local level.

A second person speaking from the audience, Sylvia Au from the Hawaii Department of Health reported some of the states in her region have or are seeking mandates on medical food, but the problem is that most large group insurers are under ERISA and therefore do not have to follow state mandates. Hawaii has very broad legislation that covers medical foods and formulas

regardless of age, up to at least 80 percent of the cost. Still insurance companies either make families pay for these items ahead of time and wait months to get reimbursed or they just decline to pay because they are under ERISA. Ms. Au said she believes that Hawaii is probably moving toward a model where the state provides the medical foods and formulas and then bills the insurance companies.

A third person speaking from the audience, Dr. Bob Kaslovsky, a pediatric pulmonologist from Charleston, W. Va., who treats patients with cystic fibrosis, said that an important issue for long-term followup is addressing the needs of patients transitioning into adult care whose coverage under state programs ends at age 21. Dr. Telfair replied that several members of the Advisory Committee are transition advocates and fully understand the importance of addressing the transition into adult care and issues related to adult care from pediatric into adult care.

D. Research Workgroup Report

Michael S. Watson, Ph.D., FACMG

Executive Director, American College of Medical Genetics (ACMG)

Director, National Coordinating Center (NCC) for the Regional Genetics and Newborn Screening Collaboratives

Dr. Watson, who is chairing the Advisory Committee's newly established Research Workgroup, reported that the Research Workgroup did not meet on Jan. 14, 2008, when the various subcommittees were meeting, because some members of the Research Workgroup are subcommittee members and would have been unable to attend. Because of this scheduling conflict, the Research Workgroup will probably do much of its work offline.

The members of the Research Workgroup are still being selected. So far Drs. Rinaldo, Fleischman, Burton, and Vockley have agreed to be members. Dr. Watson would also like to involve other entities, including the data collection workgroup of the HRSA-funded Regional Genetics and Newborn Screening Collaboratives; the National Institute of Child Health and Human Development (NICHD), which has been developing a Newborn Screening Translational Research Network; and the National Newborn Screening & Genetics Resource Center (NNSGRC).

Dr. Watson observed that research needs cut across every one of the Advisory Committee's subcommittees. The Research Workgroup is developing a mechanism to go to the subcommittees to identify areas in which it can have some involvement.

In addition, Dr. Watson and his colleagues are organizing a meeting that is partially funded by NICHD and partially funded by HRSA through the National Coordinating Center for the HRSA-funded Regional Genetics and Newborn Screening Collaboratives to bring state officials together to discuss how to move from sovereign state control of data and information to national data collection activities. They want to look at the possibility of developing a dried blood spot repository that can be used in research and all the data collection that the various subcommittees want.

During the past couple of months, the Research Workgroup has been starting to figure out how to identify what is going on in research related to newborn screening and genetic activities. Some research projects can be found in the CRISP (Computer Retrieval of Information on Scientific Projects) database of federally funded biomedical research projects maintained by the National Institutes of Health (NIH). Dr. Watson said he would like to be able to learn what is going on in research not only at the Federal level, however, but also at the state level, where pilot studies and

other forms of translational research are being done. He asked Advisory Committee members for their suggestions about how to get information on research pertaining to newborn screening and genetic activities.

Questions & Comments

Dr. Dougherty recommended that Dr. Watson clarify what “research pertaining to genetic activities” is. She also recommended that the Research Workgroup include contract, as well as grants, in its research inventory. The Agency for Healthcare Research and Quality (AHRQ) funds quite a bit of research under contracts, which are not in the CRISP system maintained by NIH, and Dr. Dougherty said it might be useful for Dr. Watson to meet with some people from AHRQ to clarify the terms that they use.

Dr. Telfair asked whether the Research Workgroup had a statement of purpose or set of goals and outlines. Dr. Watson replied that the workgroup did not yet have a statement of purpose or goals in part because of staffing issues. The plan is that the Research Workgroup will have co-chairs, with a secondary chair coming from NICHD or NIH, but the secondary chair has not been selected yet. Dr. Lloyd-Puryear is going to be the primary HRSA staff person for the Research Workgroup, and they are planning a conference call of the core group sometime in the next 4 weeks to better define the workgroup’s mission and expand its membership. He promised to provide an update at the Advisory Committee’s May 2008 meeting.

Speaking from the audience, Andrea Williams from the Children’s Sickle Cell Foundation, Children’s Hospital of Pittsburgh, commented that the Research Workgroup should include consumers as members. Dr. Watson said he agreed.

VII. THE SACGHS STUDY OF THE IMPACT OF GENE PATENTS AND LICENSING PRACTICES ON ACCESS TO GENETIC TESTS

James P. Evans, M.D., Ph.D.

Chair, Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS) Task Force on Gene Patents and Licensing Practices

Professor of Genetics and Medicine

Director of Clinical Cancer Genetics and the Bryson Program in Human Genetics

Departments of Medicine & Genetics

University of North Carolina at Chapel Hill

Dr. Evans reported on an ongoing study by the Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS) Task Force on Gene Patents and Licensing Practices of the impact of gene patents and licensing practices on access to genetic tests. The SACGHS Task Force on Gene Patents and Licensing Practices that Dr. Evans chairs is a group of 17 people that includes SACGHS members (including Dr. Telfair), ad hoc members, and experts from Federal agencies. Issues related to gene patents and licensing engender great passion, and a concerted effort was made to achieve a balance of experts and stakeholders on the task force.

According to Dr. Evans, SACGHS identified gene patents and licensing as an SACGHS priority in 2004, but it deferred its efforts in this area because it was awaiting the completion of a report on intellectual property rights in genomic research by the National Academy of Sciences (NAS). After the NAS report came out, SACGHS formed a small group to review the NAS report, and the

general feeling was that the report was excellent, but one area the report did not fully address was the impact of gene patents and licensing practices on patients' access to genetic tests.

In 2006, therefore, SACGHS decided to move forward with an in-depth study of how gene patents and licensing practices affect patients' access to genetic tests. It established the SACGHS Task Force on Gene Patent and Licensing Practices to guide the study, and a workplan for the study was approved by SACGHS in November 2006.

The purpose of the SACGHS study of gene patent and licensing practices is to identify the positive and negative effects of current gene patenting and licensing practices on patients' access to health-related diagnostic tests, predictive tests, and tests for other clinical purposes. The effects include effects on "clinical access" (defined as health professionals' ability to provide genetic test for patients), "patient access" (defined as patients' ability to obtain needed genetic testing), and translational research. The SACGHS study is *not* focusing on patents that are related to drug or product development. Most of the concerns that people have in the realm of patient access, at least proximally, have to do with diagnostic tests, and the task force thought that it was beyond the scope of its efforts at this point to also look at drug development.

The SACGHS study of how gene patents and licensing practices affect patients' access to genetic tests plan has three parts, which are being done concurrently:

- **Part 1: Data Gathering and Analysis.** Measuring the impacts of gene patents on patient access to testing is extremely challenging, and the SACGHS task force is relying on indirect measures of impacts. It is gathering data by performing a literature review, consulting with experts in the field, conducting case studies, and possibly performing additional research. The case studies that the task force is focusing on, with help from colleagues at Duke University, are hemochromatosis, congenital hearing loss, cystic fibrosis, breast and colon cancer, Tay-Sachs and Canavan's disease, Alzheimer's, and spinocerebellar ataxia. The hope is that these case studies will yield general lessons with regard to diagnostic development, commercialization, communication and marketing, adoption by clinical providers and third-party payers, and ultimately consumer utilization or patient access. The case studies are also related to what the Advisory Committee on Heritable Disorders and Genetic Diseases does.
- **Part 2: Gathering Public Perspectives.** Few topics, aside from the issue of genetic discrimination, raise as many passions among the public as the issue of gene patenting. Thus, public perspectives are very important to take into account. The SACGHS task force is soliciting and compiling public comments by various means.
- **Part 3: Gathering International Perspectives.** Although the U.S. patent system is enshrined in the U.S. Constitution, the task force believes that it can learn a lot from how other countries have dealt with similar issues especially, for example, in the realm of licensing. It has identified experts engaged in data gathering, had a roundtable discussion on international practices in gene patenting and licensing by Jorge Goldstein, Claire Driscoll, and Lin Sun-Hoffman and a review of U.S. patent reform initiatives by Judge Pauline Newman in July, and is in the process of analyzing those perspectives.

The SACGHS Task Force on Gene Patent and Licensing Practices will analyze and synthesize these various aspects of the study and come out with a draft report for the HHS Secretary, which will then ultimately be finalized. The next steps for the SACGHS task force are to wrap up the literature review and case studies by January 2008; utilize the information gathered to date to develop a draft report and recommendations to the HHS Secretary, gather public input regarding

the issue and draft report; and then discuss and revise the report to the HHS Secretary with input from the public and full SACCHS. The release of the SACGHS report on gene patent and licensing practices is anticipated in September/October 2009.

Questions & Comments

Dr. Buckley asked Dr. Evans to comment on differences between patenting and licensing. Dr. Evans noted that the patent system is in the U.S. Constitution. For that reason, although there are also patent laws and patent reforms being undertaken, Dr. Evans believes it will be easier to get traction and to impact the access to genetic tests by addressing licensing issues. People at the National Institutes of Health (NIH) are generally in favor of fairly broad licensing arrangements, and Dr. Evans believes that there is a lot to be said for that position, but it does have to be balanced with the intent of a patent which is a monopoly for a limited period of time in exchange for publishing the patent. He thinks that at least some degree of broad licensing is a good thing.

Speaking from the audience, Dr. David Ledbetter from Emory University said the process of encouraging nonexclusive licensing of genes in diagnostic tests needs to be up front when families and others that discovered the gene get a patent, because once there is an exclusive license, it is hard to get it changed to a nonexclusive license. Most genes are discovered with NIH funding, and most investigators would like to have the technology for genetic testing available as broadly as possible, but they usually do not participate in the technology transfer process. When the academic investigator who cloned the gene, in partnership with families and family support groups, makes a disclosure to the institution's technology transfer office, if the investigator does not participate in the process, the technology transfer people will often negotiate an exclusive license to the highest bidder. The investigator should stay involved with that process and encourage the technology transfer office and institution to consider broader, nonexclusive licensing for the diagnostic field of use for that gene discovery, because the financial investment of any genetic testing lab to develop a test is relatively modest compared to the huge investment in drug development where an exclusive license might be a reasonable consideration. Institutions with NIH funding or funding from any other source are free to choose how to commercialize their inventions in an exclusive or nonexclusive way and to separate diagnostic from therapeutic fields of practice for the technology.

Dr. Ledbetter said professional societies and family support groups who are involved as collaborators in the research also can be helpful in encouraging institutions to make broad use of their discoveries in diagnostic tests, because they are named as inventors on the patent although the university owns all of the rights but shares the income and revenue of that invention and royalties with the individual investigators. He thinks everybody needs to be more aware and up front that when a discovery is made, they are committed to nonexclusive licensing strategy as the first priority and only if that cannot succeed, which would be rare in diagnostic testing, will they revert to an exclusive license.

Finally, Dr. Ledbetter said it had always struck him as odd that the NIH intramural research program has a rule that all discoveries must be disclosed and they seek commercialization, but they must seek commercialization through nonexclusive licensing unless that fails, and then they can revert to an exclusive licensing. So 10 or 15 percent of the entire NIH budget research is committed to that nonexclusive, greatest access licensing strategy. But when NIH gives money extramurally to an institution under the Bayh-Dole Act, the institution is then free to commercialize without any rules about how they develop the licensing models. But on a volunteer basis, the institution and individuals can influence that.

Dr. Howell observed that many of the conditions that the Advisory Committee deals with largely are very rare, and he is aware of circumstances where when a gene was patented and when there

was an effort then to license that particular patent, only one party would come to the table because of the rarity of the disease.

Ms. Terry, expanding on Dr. Ledbetter's comments, said that even when patient advocacy groups and investigators are aware of the patent and licensing issues, things are difficult. She is a patent holder now, as are several advocates, and their biggest problem is working with the university technology transfer offices, which think there are cash cows in diagnostic testing and want to double the cost of the diagnostic tests to increase profits. She and other advocates have said that that doing that is completely unconscionable, because we want the patients to have the greatest access, and they are in fact, subsidizing the test, but the advocates had to get pro bono lawyers to fight the issue.

Dr. Lloyd-Puryear asked why tandem mass spectrometry (MS/MS) had not been included as a case study, given that there is a patent issue. Dr. Evans said the SACGHS Task Force on Gene Patents and Licensing Practices is focusing on gene patents—the patenting of nucleic acids and information. Thus, it is out of their purview to look at MS/MS and other technology patents, which do not have some of the novel nuances of gene patenting.

Dr. Watson observed that one of the things the Laboratory Standards & Procedures Subcommittee discussed at its meeting on the previous day was the question of when one begins to integrate genetic testing, not the functional tests, into the algorithm of the screening test itself, one can begin to move into diagnostics by bringing some mutation testing into the newborn screening algorithm itself. He asked whether the SACGHS case studies on cystic fibrosis and hearing loss extended to the effect on public health vs. the diagnostic sector. Dr. Evans said yes, that was part of the analysis.

Speaking from the audience, Dr. John Johnson from the Mountain States Genetic Network said that they have found obstacles for Medicaid patients to getting tests because only a few labs do tests and may not be Medicaid providers. He added that this could be a patent issue or just a rarity issue and there are only a few labs that want to do the test. Dr. Johnson urged the task force to take this access issue into account in its research. Dr. Evans said that is an important and difficult issue to consider.

VIII. UPDATE ON THE ADVISORY COMMITTEE'S NOMINATION AND EVALUATION PROCESS FOR CONDITIONS ON THE UNIFORM NEWBORN SCREENING PANEL

In this session, there were two presentations related to the Advisory Committee's process for evaluating nominations submitted by proponents of adding conditions to the uniform newborn screening panel recommended by the American College of Medical Genetics (ACMG).

- Dr. James Perrin, chair of the Advisory Committee's external Evidence Review Workgroup that will review and report on the evidence relevant to the Advisory Committee in making recommendations about which conditions to add or remove from the uniform newborn screening panel, gave an update on the workgroup's composition and plans.
- Dr. Nancy Green gave a report from the Advisory Committee's Nomination Review & Prioritization Workgroup (NRPW), a small group of the Advisory Committee established in September 2007 that looks at nominations forwarded by HRSA and makes recommendations to the full Advisory Committee about whether the nominations are ready to go to the Evidence Review Workgroup and the order in which they should proceed.

A. Report on the Evidence Review Workgroup's Plans

James Perrin, M.D.

**Professor of Pediatrics, Harvard Medical School Director, Division of General Pediatrics
Director, Center for Child and Adolescent Health Policy, Harvard Medical School
MassGeneral Hospital for Children**

Dr. Perrin updated Advisory Committee members on the status of the external Evidence Review Workgroup that was established to review the evidence for conditions nominated to the uniform newborn screening panel. The core Evidence Review Workgroup, which is based in Boston at the MassGeneral Hospital (MGH) Center for Child and Adolescent Health Policy, now consists of the following individuals:

- Marsha Browning, M.D., M.P.H. (genetics)
- Anne Comeau, Ph.D., University of Massachusetts Department of Public Health (state perspective)
- Nancy Green, M.D., Columbia University
- Alex Kemper, M.D., M.P.H., M.S., Duke University (methods/screening)
- Lisa Prosser, Ph.D. (cost/benefit analysis)
- Denise Queally, Consumer (PKU Family Coalition)
- Shira Goldenholz, M.D., M.P.H., MGH/Harvard (project coordinator)
- Ellen Lipstein, M.D., MGH/Harvard (health services research fellow)
- Diane Romm, Ph.D., Project Director (epidemiology, methods)
- James M. Perrin, M.D., MGH/Harvard (policy, chronic conditions)
- Marie Mann, M.D., HRSA (HRSA staff person and ex officio member)

In addition, a small external advisory group headed by Jannine Cody, Ph.D., University of Texas, has been set up for the purpose of giving the Evidence Review Workgroup broader national representation and review. This small advisory group, called the Evidence Advisory Group, also includes Harvey Cohen, M.D., Ph.D., Stanford University; Robert Davis, M.D., M.P.H., Kaiser Atlanta; and Celia Kay, M.D., Ph.D., University of Colorado. Its membership may be expanded in the future.

Recent activities by the external Evidence Review Workgroup include the development of an abstract form, as well as the development of conflict of interest forms based on the Institute of Medicine's (IOM) approach. The conflict of interest forms for all staff, consultants, and collaborators ask individuals to provide information on direct intellectual conflicts of interest and self/family financial conflicts. Individuals who have a conflict of interest are not necessarily prohibited from participating in the activities of the Evidence Review Workgroup, but they must make the conflict explicit. Condition-specific consultants can provide testimony to the Evidence Review Workgroup and review the workgroup's analyses for accuracy; however, they will not be permitted to review the workgroup's analyses for interpretation.

The structure of the evidence review that the Evidence Review Workgroup will develop for the Advisory Committee will be as follows:

1. Rationale and objective

- Specify rationale for review at this time:
 - Nomination form and consideration by the Advisory Committee of prospective pilot data re population-based assessment; spectrum of disease well described; screening test capable of identifying the condition; treatment is well described
 - Recent changes in treatments and/or screening
- Objectives of review: To provide timely information to the Advisory Committee to guide recommendation decision for a specific screening protocol

2. Questions for review

- Natural history (including variations in phenotype)
- Prevalence (including genotype, phenotype, and phenotypic variations)
- Impact and severity
- Methods of screening and diagnosis (in screen-positive individuals)
- Benefits of treatment (both efficacy and effectiveness in screen positive individuals and individuals diagnosed in other ways)
- Harms or risks of screening, diagnosis, and treatment
- Costs (screening, diagnosis, treatment, late treatment, failure to diagnose in newborn period) if available

3. Evidence review model and methods

- Describe decision model and development of evidence questions
- Describe search methods

4. Systematic review and additional data collection and review

- Study selection and data abstraction and review:
 - Inclusion/exclusion criteria for peer-reviewed literature (will exclude single case reports, but will do analyses of multiple case reports); will review consensus statement for guides, not abstraction
 - Data abstraction and equality assessment (standard quality assessment methods, but will also apply some other ones; will perform additional analysis of raw data from unpublished sources if possible)
 - Focus groups of experts (investigators and families) to estimate impact and severity estimates if there are no data (probably not a large number of these)
 - Data synthesis

5. Evidence review results and summary

- Results (follow order and content of main questions; decision analyses/decision model findings (outcomes tables)
- Summary (key findings in summary and table form; indicated where evidence is absent and what evidence would be most critical)
- All decisions are to be made by the Advisory Committee. The Evidence Review Workgroup makes no recommendations.

Dr. Perrin concluded his presentation by stating that the Evidence Review Workgroup is eagerly awaiting its initial assignments. He and his colleagues would like to begin with an evidence review of one condition, then start a second evidence review 3 or 4 months later. They estimate that a single evidence review might take about 6 months (including 3 months for a literature review and abstracting, the identification of key investigators in the first 2 months; focus groups, if needed in month 3 or 4; and data synthesis and report development in months 4 to 6. If additional data analysis is needed, the time required to complete an evidence review might be longer.

Questions & Comments

Dr. Howell said he was happy to hear that the Evidence Review Group might be able to take on two assignments in a fairly short time and hoped that it could shorten the 6-month review process if possible. Reminding everyone that the plan had been that two members of the Advisory Committee would serve as liaisons to the Evidence Review Workgroup, Dr. Howell asked Dr. Calonge and Dr. Rinaldo to serve as the Committee's liaisons on the Evidence Review Workgroup's small external advisory group.

- **DECISION #2:** *Dr. Calonge and Dr. Rinaldo will serve as serve the Advisory Committee's liaisons to the Evidence Review Workgroup's small external advisory group headed by Dr. Jannine Cody.*

Dr. Howell then asked Advisory Committee members to comment on the Dr. Perrin's proposal. There were not very many comments. Dr. Dougherty asked how the Evidence Review Workgroup would report to the Committee on the quality of the evidence that is reviewed. Dr. Perrin said the plan had originally been to embed the description. Dr. Dougherty suggested that the workgroup include a summary paragraph at the end on the review, and Dr. Perrin agreed to do that.

- **DECISION #3:** *The external Evidence Review Workgroup headed by Dr. Perrin will include as part of its evidence reviews a summary paragraph on the quality of the evidence.*

Dr. Boyle noted that the Evidence Review Workgroup was venturing into new territory, because it would be considering proprietary information. She asked whether Dr. Perrin and his colleagues had given any thought to addressing conflict of interest issues related to proprietary information. Dr. Perrin replied that the Evidence Review Workgroup has benefited from the experience of the IOM with respect to addressing conflicts of interest. People serving on IOM committees often have explicit conflicts of interest, yet are able to vote. The Evidence Review Workgroup is using a somewhat different strategy. It will be responsible for the interpretation of proprietary data, and although it will share its analyses with the people who provide such data, those people will be asked only to confirm the accuracy of the data, not for their opinion of the workgroup's analyses.

Finally, Dr. Calonge urged the Advisory Committee to think beyond the evidence reviews about what its construct for taking the evidence review and recommending it or not recommending that a

condition be included in the uniform newborn screening panel should be. He identified three possible approaches: (1) the task force which looks at this concept of net benefit of screening; (2) the community guide that the Centers for Disease Control and Prevention (CDC) runs, which talks about sufficiency of evidence, which is a different construct and looks at the quality and the number of studies in a slightly different way; and (3) the work done by a group called GRADE, which is an update international approach to taking systematic evidence reviews and turning those into recommendations. The Advisory Committee's goal should be to minimize its chances of being wrong and maximize its chances of being correct and get a consistent process prior to getting a report from the Evidence Review Workgroup.

Dr. Boyle recommended forming a workgroup headed by Dr. Calonge to recommend such a process. Dr. Howell agreed that this was a good idea. He said that they would establish a workgroup to come up with a construct for the Committee's recommendations pertaining to conditions nominated for the uniform newborn screening panel and try to get a report from the workgroup at the Advisory Committee's next meeting in May 2008.

- **DECISION #4:** *The Advisory Committee will establish a Recommendations Workgroup headed by Dr. Calonge to recommend a construct for the Advisory Committee to use in making recommendations after receiving reports on the evidence for conditions nominated for inclusion on the uniform newborn screening panel. The workgroup will report to the Committee at its next meeting in May 2008.*

B. Report from the Nomination Review & Prioritization Workgroup

Nancy S. Green, M.D.

Associate Dean for Clinical Research Operations

Associate Professor of Clinical Pediatrics, Division of Hematology

Associate Director, Irving Institute for Clinical Translational Research

Columbia University Medical Center

Dr. Green gave a report from the Nomination Review & Prioritization Workgroup (NRPW), the small group that was created by Dr. Howell at the September 2007 Advisory Committee meeting (1) to develop criteria to determine the readiness of nominations of conditions to be added to the uniform newborn screening panel for referral to the Advisory Committee's external Evidence Review Workgroup; and (2) to develop criteria regarding the prioritization (if any) of nominations forwarded to the Advisory Committee after being administratively processed by HRSA's Maternal and Child Health Bureau.

Overview of the Advisory Committee's Process for Adding Conditions to the Uniform Newborn Screening Panel. As background for new members of the Advisory Committee, Dr. Green first briefly reviewed the Advisory Committee's process for evaluating nominations and adding conditions to the uniform newborn screening panel. The basic principles underlying the process, she explained, are broad access to the process, considered review, streamlined process, transparency, consistent criteria throughout the nomination process, a structured evidence-based review through an external workgroup (the Evidence Review Workgroup headed by Dr. Perrin), and three main areas for consideration (condition, test, and treatment).

Dr. Green also explained that the paradigm for the Advisory Committee's evaluation of conditions nominated for inclusion on the uniform newborn screening panel is as follows:

1. A condition is nominated for inclusion on the uniform newborn screening panel by proponents.
2. HRSA's Maternal and Child Health Bureau administratively reviews nominations submitted by proponents.
3. If nomination packages are deemed complete, HRSA forwards them to the chair of the full Advisory Committee.
4. There are interactions between the Advisory Committee and the Evidence Review Workgroup regarding the nominated condition.
5. The Advisory Committee makes recommendations regarding the nominated condition to the Secretary of Health and Human Services (HHS) (e.g., universal newborn screening, targeted screening, pilot study, critical studies needed, no recommendation, or recommend against newborn screening).

The Evolution of the Nomination Review & Prioritization Workgroup (NRPW). Dr. Green gave a brief history of the Advisory Committee's NRPW. She said that in 2005, Dr. Howell appointed a Nomination Workgroup that included Advisory Committee members Dr. Nancy Green (chair), Dr. Coleen Boyle, Dr. Amy Brower, Dr. Peter Coggins, Dr. Denise Dougherty, Dr. Piero Rinaldo, and Dr. Marie Mann (HRSA staff).

This workgroup was given two tasks. One task was to design a nomination process for adding disorders to the uniform newborn screening panel. Such a process was developed and approved by the full Committee. It was recently described in a report from the Committee written by the workgroup (Green et al.) in *Genetics in Medicine* (9:792-796, 2007). The second task was to create a nomination form that proponents could use to nominate conditions for inclusion on the uniform newborn screening panel. The nomination form was developed and has been posted online by HRSA at <ftp://ftp.hrsa.gov/mchb/genetics/nominationform.pdf>.

In the fall of 2007, having completed its initial tasks, the workgroup was reconfigured as the Nomination Review & Prioritization Workgroup, again chaired by Dr. Green. The NRPW was given two tasks. One was to recommend criteria for the Advisory Committee for the readiness for referral of a nomination to the Evidence Review Workgroup headed by Dr. Perrin. The other task was to perform a preliminary review of completed nominations forwarded to the Committee by HRSA's Maternal and Child Health Bureau and make recommendations to the Advisory Committee about the order in which the nominations should be considered.

The process with the NRPW, therefore, is that when the Advisory Committee receives a completed nomination that is deemed complete by HRSA's Maternal and Child Health Bureau, it refers the nomination to the NRPW. The NRPW then makes its recommendations about whether nominations are ready to be considered by the Advisory Committee and in what order. The Advisory Committee considers those recommendations and makes its own decision about which nominations to assign to the Advisory Committee's external Evidence Review Workgroup and in what order. The Evidence Review Workgroup reports its findings with respect to the evidence back directly to the Advisory Committee. The Advisory Committee then considers this information and makes its own recommendations regarding the nominated condition to the Secretary of HHS.

Recommended Criteria for Determining a Nomination's Readiness for Referral to the Evidence Review Workgroup. At the Advisory Committee's special meeting via teleconference on Nov. 14, 2007, the Advisory Committee accepted the NRPW's recommendations that conditions with the following six criteria be used to determine a nomination's readiness for referral to the Evidence Review Workgroup and for prioritizing nominations:

1. Nominated conditions are medically serious.
2. Disorders for which prospective pilot data (U.S. and/or international) are available for population-based assessment.
3. The spectrum of the disorder is well described to help predict the phenotypic range of those children who would be identified through a population-based screening process.
4. The characteristics of screening test are acceptable.
5. If spectrum of disease is broad, be able to identify those most likely to benefit from treatment especially if onerous or risky.
6. There are defined treatment protocols, use of U.S. Food and Drug Administration approved drugs (if applicable), and treatment is available.

Recommended Order in Which Nominations for SCID and Pompe Disease Received Should Be Processed. Dr. Green reported that two nomination packages from proponents of adding conditions to the uniform newborn screening panel had been forwarded to the Dr. Howell by HRSA's Maternal and Child Health Bureau: one for severe combined immunodeficiency (SCID) and one for Pompe disease. These had been forwarded to the NRPW.

In January 2007, the members of the NRPW (Dr. Green, Dr. Howell, Dr. Rinaldo, and Dr. Skeels) agreed that both the SCID and Pompe disease nomination packages had met all six of the criteria of a nomination's readiness for evidence-based review. Thus, the members of the NRPW voted unanimously to recommend that the Committee send both SCID and Pompe diseases for evidence-based review.

The next question the NRPW had to consider was which nomination it should recommend that the Advisory Committee send to the Evidence Review Workgroup for the first evidence review. Two members voted to recommend that the SCID nomination go to the Evidence Review Workgroup first, and two voted to recommend that the Pompe disease nomination go first. Thus, the NRPW is reporting that there was a split decision among the four NRPW members in its recommendations about which nomination—SCID or Pompe disease—the Advisory Committee should send to the Evidence Review Workgroup first.

Questions & Comments

Process improvements. Noting that this was the first time the process for considering nominations had been used, a few Committee members suggested improvements:

- Dr. Boyle requested that Committee members have access to the forms *before* the Committee meeting, so they can review the references.
- Dr. van Dyck said he had expected the Advisory Committee would receive a written summary about the six criteria the NRPW went through in the review or concerns about each, not just a verbal report. Dr. Green said this request was entirely reasonable, but the NRPW was not able to give a written report right now. Dr. Vockley and other Committee members said they did not need to have a written report for the SCID and Pompe disease nominations but would like to have a succinct summary from the NRPW in the future.

Dr. Vockley proposed that the Advisory Committee vote to send the Pompe and SCID nominations forward for evidence review and to require that the suggested process changes suggested by Dr. Boyle and Dr. van Dyck be implemented for any future nominations. After some discussion, the Committee voted to approve the following motion (2 abstaining; all others for):

- **MOTION #1:** *The Advisory Committee directs the external Evidence Review Workgroup headed by Dr. Perrin to consider the nominations for severe combined immunodeficiency disease (SCID) and Pompe disease to the uniform newborn screening panel with due speed. In the future, Advisory Committee members will be provided with nomination forms in advance of the meeting at which the Nomination Review & Prioritization Workgroup makes its recommendations. In making its future recommendations, the Nomination Review & Prioritization Workgroup will provide a succinct written report to the Advisory Committee with the rationale for its recommendations.*

Which nomination package should be sent to the external Evidence Review Workgroup first.

Dr. Dougherty asked for more information about why NRPW members differed in their recommendations about whether to recommend that the Advisory Committee consider SCID or Pompe disease first. Dr. Rinaldo explained that he supported having SCID go first because there is a U.S. pilot-screening program for SCID in Wisconsin and because population-based screening results for Pompe disease in Taiwan suggested a 0.5 percent false-positive rate. Dr. Green reported that the pilot-screening program for SCID in Wisconsin is still in its very initial phases, and she thought that it would not be sufficiently mature in terms of the experiences, the false positives, the ability to detect disorders, and other vicissitudes with population-based screening. Dr. Howell said he favored having Pompe disease go first, because population-based data on Pompe disease have been obtained in Taiwan, although he agreed that U.S. studies still needed to be done.

Dr. Calonge said he was ready to vote and suggested that there be a straw vote among Advisory Committee members on which nomination to send to the Evidence Review Group first. The straw vote showed that the great majority of Committee members favored sending the SCID nomination first. On the basis of this straw vote and the previous vote, Dr. Howell directed External Evidence Review Workgroup headed by Dr. Perrin to perform an evidence review for the SCID nomination first and for the Pompe disease nomination second but as soon as possible.

- **DECISION #5:** *The external Evidence Review Workgroup headed by Dr. Perrin will perform an evidence review for the SCID nomination immediately and perform an evidence review of the Pompe disease nomination second, but as soon as it possibly can.*

Other issues.

- Dr. Dougherty noted that what Dr. Green had called the Nomination Workgroup was actually called the Criteria Workgroup on which both she and Dr. Boyle served. That workgroup discussed criteria for evaluating nominations, not just the way the nomination formed looked.
- Dr. Burton asked what had happened to the nomination form for Krabbe disease that had been submitted previously. Dr. Lloyd-Puryear explained that HRSA received a series of nomination packages, but it did not forward some of them to the Advisory Committee because they were incomplete.
- Dr. Vockley, noting that the dates on the two submitted nominations were May and September 2007, asked whether there was a timeline for HRSA's administrative review.

Dr. Lloyd-Puryear explained that Dr. Mann would be explaining the process for HRSA's administrative review, but it is a very simple review for completeness with signed letters and signed conflict of interest forms, so it would generally be very rapid.

Reconstituting the Nomination Review & Prioritization Workgroup (NRPW). Dr. Howell explained that the NRPW established at the September 2007 Advisory Committee meeting and chaired by Dr. Green needed to be reconstituted with members of the Advisory Committee, because some members of the NRPW, including Dr. Green, are no longer members of the Advisory Committee. Dr. Howell said that he and Dr. Rinaldo had served on the NRPW previously, but he would like Dr. Ohene-Frempong and Dr. Buckley to serve on the reconstituted NRPW. Dr. Ohene-Frempong and Dr. Buckley both agreed to serve on the NRPW. Dr. Boyle recommended that someone with a public health perspective be added to the NRPW. Dr. Howell said he thought that was a very good idea and appointed Dr. Boyle to serve in that capacity. Dr. Howell also asked Dr. Green to continue to serve as a very active liaison between the External Evidence Review Workgroup headed by Dr. Perrin and the Nomination & Prioritization Workgroup.

- **DECISION #6:** *The Advisory Committee's Nomination & Prioritization Workgroup is to be reconstituted with the following Advisory Committee members: Dr. Howell (chair), Dr. Boyle, Dr. Buckley, Dr. Ohene-Frempong, Dr. Rinaldo, and Dr. Skeels. Dr. Green will serve as a liaison between the External Evidence Review Workgroup headed by Dr. Perrin and the Nomination & Prioritization Workgroup.*

IX. UPDATE ON HRSA'S PROCESS FOR ADMINISTRATIVE REVIEW OF NOMINATIONS OF CANDIDATE CONDITIONS FOR THE UNIFORM NEWBORN SCREENING PANEL

**Marie Mann, M.D., M.P.H.
Genetic Services Branch
Maternal and Child Health Bureau
Health Resources and Services Administration (HRSA)**

Dr. Mann outlined the process that HRSA's Maternal and Child Health Bureau has developed since the September 2007 Advisory Committee meeting for its administrative review of nomination packages submitted by proponents of adding conditions to the uniform newborn screening panel recommended by the American College of Medical Genetics (ACMG).

HRSA's role is simply to confirm that all the requested information is present on the nomination form and that the form is ready to be sent to the full Advisory Committee. The questions addressed by HRSA in its administrative review of nomination forms that are submitted are the following:

- Is there a signed cover letter by nominator(s)?
- Are all requested information for the condition/test/treatment present?
- Is there a signed formal conflict of interest statement for nominator(s)?
- Is there a list of supporting reference and copies of references, and are copies of the references included?

If some information is missing, the staff of HRSA's Maternal and Child Health Bureau requests that the nominator(s) supply the missing information. When the nomination package is completed,

it is forwarded by HRSA to the chair of the Advisory Committee, Dr. Howell, so that the full Advisory Committee can make a decision about how to proceed.

As of Jan. 14, 2008, HRSA's Maternal and Child Health Bureau had received and reviewed five nomination packages. The staff judged two of the nominations—one for severe combined immunodeficiency (SCID) and one for Pompe disease—to be complete and therefore forwarded these nominations to Dr. Howell. The other three packages were returned to the nominators for completion. One of the three should be finished shortly.

All of the nomination forms submitted were very complete in terms of having the boxes filled in. The areas that proved to be a challenge for the packages that were sent back to the nominators were (1) submitting a *signed* cover letter from the nominator(s); and (2) submitting a *signed* conflict of interest form from *all* of the nominators (not just the primary nominator); and (3) submitting *copies* of the references used for substantiating the statements made on the nomination form.

To help avoid similar problems in the future, HRSA has revised the instructions to be more explicit about the need for signed letters and conflict of interest forms from proponents. The revised nomination form is available online at the Advisory Committee's new Web site: <http://www.hrsa.gov/heritabledisorderscommittee/nominate.htm>.

Questions & Comments

Ms. Terry asked whether HRSA could provide templates of the cover letter and the confidentiality agreements could be put on the Advisory Committee's Web site. Dr. Mann said that HRSA could do that, but the issue was just getting things signed, so she did not think templates were necessary. Ms. Terry said that the Genetic Alliance could help make the instructions clearer to advocacy groups.

Dr. Fleischmann asked whether there is a standardized conflict of interest form, noting that it was important to make it clear to people that there are conflicts of interest other than just financial conflicts. Dr. Mann said that there was a brief description of the types of conflicts that nominators should include but that HRSA staff could explore that to see if additional guidance was needed.

Dr. Perrin, emphasizing that it was important for the Evidence Review Workgroup to be aware of what nominators' conflicts of interest are, asked whether information about nominators' conflicts of interest was made clear to the Evidence Review Workgroup. Dr. Puryear and Dr. Mann replied that the two nomination packages forwarded to the Evidence Review Workgroup (via the full Committee) were nominations with signed conflict of interest letters.

X. PUBLIC COMMENT SESSION

Several individuals made public statements to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children on the afternoon of Jan. 15, 2008. The text of their written statements appears in Appendix A.

1. Mei W. Baker, M.D.

**Newborn Screening for SCID Project in Wisconsin
Science Advisor, Newborn Screening Program
Wisconsin State Laboratory
University of Wisconsin-Madison**

Dr. Baker reported that she and her colleagues recently conducted a study to evaluate the feasibility of quantitating the number of T-cell receptor excision circles (TRECs) using dried blood spots from deidentified newborn screening specimens for use as a statewide newborn screening test to detect newborns with severe combined immunodeficiency (SCID). They optimized the use of reverse transcription polymerase chain reaction (RT-PCR) to quantitate TRECs and found real-time PCR for TREC quantification to be highly sensitive and specific for SCID screening in newborns. The Wisconsin Department of Health has given approval for this test to be implemented on all infants born in Wisconsin as part a 2- or 3-year pilot study beginning in January 2008. The hope is that SCID will subsequently be put on the newborn screening panel.

2. John Adams

Parent and Volunteer with the Canadian Organization for Rare Disorders

Mr. Adams, the father of a son with phenylketonuria (PKU) who volunteers with the Canadian Organization for Rare Disorders, noted that his son a beneficiary of American policies and the only non-American in the early drug therapy with Kuvan™. His response to this drug is remarkable: after just 2 days of treatment, the phenylalanine in his blood was reduced by 75 percent. Mr. Adams celebrated the advances in screening for and treating PKU that have been made since the discovery of PKU 75 years ago. He thanked the Advisory Committee for its work on heritable disorders and genetic diseases, which he again emphasized, has importance beyond U.S. borders.

3. Kym Wigglesworth

**Co-Chair Committee on Federal Legislation
National MPS Society**

Ms. Wigglesworth explained that the National MPS Society is an advocacy/family support group that is seeking to find cures for mucopolysaccharidoses (MPS) and related diseases. While the search for cures for MPS and related conditions continues, the National MPS Society tries to help families live and manage these disorders. For some forms, there are no treatments, but families say knowing diagnosis early on would benefit them greatly. Thus, the National MPS Society is willing to be a partner in supporting newborn screening efforts. Ms. Wigglesworth herself is the mother of a daughter with MPS1 who would have benefited from newborn screening.

4. Andrea Williams

Executive Director, Children's Sickle Cell Foundation

Ms. Williams emphasized that expectant mothers, mothers of small children, and the parents of affected children and persons who are of child-bearing age who could benefit the most should be a focus of newborn screening educational efforts, as well as physicians. She noted that sickle cell trait and disease are not uncommon conditions: About 1 in 12 African Americans carries sickle cell trait, and about 1 in 400 has sickle cell disease. Newborn screening for autosomal recessive

conditions has a natural byproduct—carrier identification. Noting that followup with families with babies identified as having sickle cell trait via the newborn screening program is widely ignored across the United States, Ms. Williams encouraged the Advisory Committee to address the need for followup testing and genetic counseling for such families.

5. Kelly Leight

President & CEO, CARES Foundation, Inc.

Parent of Child with Congenital Adrenal Hyperplasia

Ms. Leight urged the Advisory Committee, as it moved into an era where long term followup was part of the newborn screening system, to include more representatives of families and affected individuals, as well as representatives of social services, early intervention providers, and the insurance industry on the Committee. She also asked that funding for travel expenses for subcommittee members not be cut as proposed, because she feared that cutting it would negatively affect the ability of families, advocacy groups, and others to continue their participation.

6. Victoria Odesina

Parent

Citizens for Quality Sickle Cell Care, Inc.

Ms. Odesina, whose comments were submitted for the record by Jill Levy-Fisch, made points about (1) clarifying the roles of primary care providers in newborn screening; (2) including mid-level providers such as physician assistants and nurse practitioners in newborn screening educational programs; (3) developing a repository of annual family continuous quality improvement (CQI) reports for the newborn screening long-term followup programs; (4) addressing the issue of transition to adult care; (5) encouraging newborn screening projects to be inclusive and adopt the community-based participatory research model to evaluate program outcomes at all levels; and (6) being aware of the National Coalition for Health Professional Education in Genetics' (NCHPEG) educational resources for professionals and families.

7. Jill Levy-Fisch

President of Education and Awareness

Save Babies Through Screening Foundation

Parent in SCADD Family

Ms. Levy-Fisch made several points. First, noting that newborn screening samples in Georgia were not always being handled in a timely manner, she urged that steps be taken address this problem in Georgia and elsewhere. Second, echoing Ms. Leight, she recommended that the Advisory Committee increase the representation of families on the Committee, as well as to add a public health newborn screening person or followup manager. Third, again echoing Ms. Leight, she urged that funding for travel expenses for subcommittee members be maintained. Finally, she thanked the Committee for continuing to move this process forward and would recognized the efforts being made by the subcommittees.

XI. COMMITTEE BUSINESS

Rodney Howell, M.D.

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

Professor, Department of Pediatrics

Leonard M. Miller School of Medicine

University of Miami

In the last session of the day, Dr. Howell asked the Advisory Committee to wrap up a number of items that had been discussed earlier and to propose agenda items for the Committee's next meeting in May 2008.

Proposed Committee Resolution Regarding Newborn Screening Education & Training by Professional Medical Organizations. Earlier in the day, Dr. Howell had asked the subcommittee to develop a recommendation on newborn screening education and training by professional medical organizations for the full Committee to consider at this meeting. Dr. Trotter, speaking on behalf of the Education & Training Subcommittee, proposed that the Advisory Committee adopt the following resolution on this topic:

- ***Proposed Resolution on Professional Medical Organizations' Provision of Newborn Screening Education and Training to their Members:*** *First, the Advisory Committee acknowledges the importance of the American Academy of Pediatrics (AAP) clinical report, "Newborn Screening Expands: Recommendations for Pediatricians and Medical Homes—Implications for the System." Furthermore, the Advisory Committee recommends that the AAP and American Academy of Family Physicians (AAFP) develop a seminar or workshop for their 2008 annual meetings and a series of educational initiatives to address the roles of the pediatrician in the newborn screening system. To improve the knowledge of genetic testing and systems of care, the Advisory Committee considers it especially important that the AAP consider newborn screening in discussions of the future of pediatrics.*
- Second, recognizing the importance of ACOG and AAFP membership in prenatal education, the Advisory Committee recommends to the American College of Obstetricians and Gynecologists (ACOG) and AAFP that under their continuing medical education (CME) or other educational activities that have a genetic medicine focus, the design of those programs include newborn screening issues.*

Advisory Committee members discussed this resolution and suggested a few amendments, which Dr. Trotter and the Committee accepted:

- Involve other participants of the newborn screening community—e.g., public health—in the development of the training program, linking what happens in the pediatrician's office with public health.
- Change 2008 to "earliest possible date," because the professional medical associations' agendas for 2008 are already set.
- Encourage the AAP, AAFP, and ACOG to make some of their newborn screening and genetics educational materials available on a permanent basis by using their Web sites, so that when pediatricians or obstetricians have a specific question or an issue about a child, they can use the Web sites as referral sources.

With no further discussion, the Committee voted unanimously to approve the motion:

- **MOTION #2:** *The Advisory Committee approves the resolution on education and training by the AAP, AAFP, and ACOG that was proposed by the Education & Training Subcommittee (see above) as amended.*

Dr. Howell indicated that letters with the Advisory Committee's resolution would be sent out to the relevant professional organizations in the near future.

Request from the Association of Public Health Laboratories (APHL) to Send an Organizational Representative to the Advisory Committee. Dr. Howell noted that Dr. William Becker, formerly APHL's president, had sent a letter to him dated Oct. 25, 2007, requesting that APHL be permitted to send a nonvoting organizational representative to the Advisory Committee. (Dr. Becker's letter was included under Tab #5 of the materials distributed to Advisory Committee members for the meeting).

Committee members engaged in an extended discussion of whether to accept this request. There was general agreement that APHL is a constituency that would be able to contribute to the Advisory Committee's deliberations. The primary concern was allowing the size of the Committee to get too big. Dr. Rinaldo noted that Dr. Becker is no longer the president of APHL, so his replacement should be asked to reaffirm the request.

Dr. Vockley, as a new Committee member, asked for clarification of the rules governing appointments of liaison representatives from professional organizations. Dr. Lloyd-Puryear said the Advisory Committee is limited to 15 regular members by law. There are now 15 regular Committee members and 11 liaisons. Her recollection was that the Committee had agreed to have no more than 12 liaisons. Dr. Lloyd-Puryear and Dr. Howell stated that liaison members serve at the pleasure of the Advisory Committee and can be replaced if the Committee wants to ask someone else to serve to meet its need for expertise. The ground rules for the Committee are set forth in the Committee's standard operating policies and procedures (<ftp://ftp.hrsa.gov/mchb/genetics/policiesandprocedures.pdf>), and Dr. Lloyd-Puryear said she would include these in the Committee Members' meeting binders in the future.

The question of whether APHL would duplicate representation from the Association of State and Territorial Health Officials (ASTHO) was raised. Dr. Kus said that ASTHO does include lab functions, but he thought that public health representation and lab representation were both important. Dr. Calonge agreed. The question of whether Dr. Skeels filled the role of public lab representation for the Committee was raised. Dr. Lloyd-Puryear noted that Dr. Skeels is a member of the Committee as an individual; he is not representing APHL and cannot facilitate the transmission of messages to APHL.

Several Committee members, including Dr. Calonge, Dr. Ohene-Frempong, Dr. Dougherty and Dr. Boyle, Dr. Buckley, Ms. Monaco, and Dr. Rinaldo, said they thought it would be useful to have organizational representation of APHL if it was feasible. In addition, Dr. Rinaldo noted that his recollection that in the period of public comments about the American College of Medical Genetics newborn screening report, APHL felt they were not adequately involved in the process. Implementation of newborn screening recommendations will require substantial buy-in of public health labs, so having an APHL representative would help with that.

Following this discussion, the Committee voted to unanimously to approve the following motion:

- **MOTION #3: *The Advisory Committee will invite the Association of Public Health Laboratories (APHL) to send a nonvoting organizational liaison representative to the Committee.***

Other Items Discussed.

- ***Recent articles on newborn screening.*** Dr. Howell drew attention to several recent articles published about newborn screening under Tab #16 in the materials distributed to Advisory Committee members for the meeting.
- ***Authorship of Committee-endorsed reports in peer-reviewed journals.*** Dr. Howell asked for Advisory Committee members to voice their opinions on the way the authorship of reports prepared by subcommittees and endorsed by the full Advisory Committee should be handled. He and Dr. Lloyd-Puryear noted that two Committee-endorsed reports by subcommittees—an article on the process for reviewing the evidence on conditions nominated for inclusion in the uniform newborn screening and an article on the goals and components of long-term followup after newborn screening—have been submitted to *Genetics in Medicine*. For both of these two reports, the people on the subcommittee who actually did the work are listed as the authors, with a note that the report was prepared for and endorsed by the full Committee. Dr. Telfair said he thought the approach that had been used to date was more than fair but appreciated the discussion. He agreed that the people who actually did the work on the papers should be recognized. Hearing no further comments, Dr. Howell said that the same approach would continue to be used for future reports of a similar nature.
- ***Subcommittee members' travel expenses.*** Dr. Boyle echoed concerns voiced by public presenters that subcommittee members' travel expenses would no longer be paid for. She said she understands that funding is a challenge, but she would hope that subcommittee members' travel expenses could continue to be supported, because the 3-hour meetings are very beneficial. Dr. Howell said that Dr. Puryear and Dr. van Dyck had heard the recommendations and would see what they could work out.
- ***Response to the SACGHS report on oversight of genetic testing.*** Dr. Dougherty asked whether the Advisory Committee's response to the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) on the report on oversight of genetic testing is available. Dr. Lloyd-Puryear replied that it was available and she would send it out to Committee members.

Agenda Items Proposed for the Committee's May 2008 Meeting. Dr. Howell asked Advisory Committee members for suggestions for agenda items for the next meeting on May 15-16, 2008:

1. Dr. Burton recommended inviting Maria Escolar or Joann Herschberg to talk about long-term outcomes following stem cell transplantation for Krabbe disease. Dr. Howell said he agreed that clarifying the long-term outcomes for such children was essential. He said he thought it would be desirable if there could be some sort of a workgroup before the Advisory Committee's May meeting of all the involved people, and that workgroup would report to the Committee.
2. Dr. Dougherty asked that Dr. Calonge report from the newly established Committee Recommendations Workgroup on a recommended construct for the Advisory Committee to use in developing recommendations after receiving reports on the evidence for

conditions nominated for inclusion on the uniform newborn screening panel. Dr. Howell said that this would certainly be on the agenda.

3. Dr. Howell suggested that the Laboratory Standards & Procedures Subcommittee headed by Dr. Vockley have a working group on this topic and make a specific recommendation for altering the technology used to screen for tyrosinemia type I (TYR I) to the full Advisory Committee at the May meeting.
4. Dr. Lloyd-Puryear suggested that there be a report from the Evidence Review Workgroup headed by Dr. Perrin on the nomination for severe combined immunodeficiency (SCID) and perhaps the nomination for Pompe disease.
5. Dr. Hannon, speaking from the audience, suggested a presentation on the intent and scope of the National Institutes of Health (NIH) Newborn Screening Translational Research Network at the National Institute of Child Health and Human Development (NICHD).
6. Ms. Monaco asked for an expert on medical foods to present to the Advisory Committee, noting that such foods are still considered food supplements, but parents of children who need medical foods view them as a medication for their children. Dr. Boyle suggested holding off on such a presentation until the Followup & Treatment Subcommittee got more survey data in first. Ms. Monaco agreed to that proposition.

Finally, with no other business at hand, Dr. Howell adjourned the meeting at 2:40 p.m.

**

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.
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