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

Summary of 11th Meeting
September 17-18, 2007
Washington, DC

The Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children was convened for its 11th meeting at 9:05 a.m. on Monday, Sept. 17, 2007, at the Ronald Reagan Building and International Trade Center in Washington, D.C. The meeting was adjourned at 1:58 p.m. on Tuesday, Sept. 18, 2007. In accordance with the provisions of Public Law 92-463, the meeting was open for public comments on Sept. 17, 2007.

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I. WELCOME, OPENING REMARKS

R. Rodney Howell, M.D.
Chair, Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
Professor, Department of Pediatrics
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Agenda for the Meeting. Dr. Howell opened the meeting by welcoming participants and saying that he hoped that the Advisory Committee would finalize the nomination process adding conditions to the uniform newborn screening panel. Dr. Howell then gave a brief overview of the agenda:

- **Status of the process for nominating/evaluating candidate conditions for inclusion on the uniform newborn screening panel.** Dr. James Perrin, the chair of the new external Evidence Review Group (ERG) that will be involved in reviewing evidence for conditions nominated to the uniform newborn screening panel, and Dr. Nancy Green would present minor changes to the nomination form and gave an update on progress regarding the ERG.
- **Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS)—Task Force on Genetic Testing.** Dr. Ferreira-Gonzalez, the chair of the SACGHS Task Force on the Oversight of Genetic Testing, would give a report on its work.
- **Update from Federal agencies involved in newborn screening.** Ex officio members of the Committee from the Agency for Healthcare Research and Quality (AHRQ), Centers for Disease Control and Prevention (CDC), Health Resources and Services Administration (HRSA), and National Institutes of Health (NIH) would give updates on their agencies' activities related to newborn screening.
- **Subcommittee meetings and reports.** The Advisory Committee's Laboratory Standards & Procedures Subcommittee, Education & Training Subcommittee, and Followup & Treatment Subcommittee would meet on Monday, Sept. 17, 2007, and give reports to the full Committee on Tuesday, Sept. 18, 2007. All of the subcommittee meetings would be open to the public.
- **Federal legislative update**. Cindy Pellegrini from the American Academy of Pediatrics (AAP) would update the Advisory Committee on Federal legislative developments.
- **Report from the Advisory Committee's new Research Workgroup.** Dr. Michael Watson, the chair of the Advisory Committee's soon-to-be established Workgroup on (Infant, Childhood, and Adolescent Genetics and Screening) Research would give his first report.
- **Genetic Alliance.** Ms. Terry would report to the Advisory Committee on the recent activities and programs of the Genetic Alliance.
- **Four Genetic Alliance projects on consumer perspectives in newborn screening.** Ms. Terry would describe the Genetic Alliance's four HRSA-funded projects related to consumer perspectives on newborn screening.
- **Report on the Personalized Healthcare Initiative.** Dr. Gregory Downing would give an update on the Personalized Healthcare Initiative in the Office of the Secretary of Health and Human Services (HHS).

Finally, Dr. Howell explained that to allow time for the Committee to discuss the nomination process, Dr. Susan Berry would not give her scheduled presentation on the Inborn Errors of Metabolism Information System of the Region 4 Genetics Collaborative. The Advisory Committee will invite her to give her presentation at another meeting.

Two Nominations for Adding Conditions to the Uniform Newborn Screening Panel. Dr. Howell announced that HRSA had received two nominations for adding conditions to the uniform newborn screening panel: (1) one for Krabbe disease from Micki Gartzke, representing the Hunter's Hope Foundation; and (2) one for severe combined immunodeficiency (SCID) from Dr. Jennifer Puck, representing the SCID Newborn Screening Working Group; Immune Deficiency Foundation; and Jeffrey Modell Foundation. These nomination packages were provided to the Committee for informational purposes only.

Approval of Minutes. The minutes from the May 17-18th, 2007, meeting of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children [Tab #5 in the materials distributed to Advisory Committee members] were approved.

Letter & Certificates of Appreciation. Dr. Howell presented certificates of appreciation from the HHS Secretary to the following Advisory Committee members whose 4-year terms are ending in September 2007: Dr. Amy Brower, chair of the Laboratory Standards & Procedures Subcommittee; Dr. James Newton; Dr. Greg Hawkins, chair of Education & Training Subcommittee; and Dr. Peter Coggins. Dr. van Dyck then presented Dr. Howell with a certificate of appreciation from the HHS Secretary and thanked him for his leadership, vision, and contributions as the Advisory Committee's chair since the Committee's inception.

New Committee Members and Liaisons. Dr. Howell welcomed two new nonvoting organizational liaison representatives to the Advisory Committee: Dr. Timothy Geleske from the American Academy of Pediatrics (AAP) and Dr. Alan Fleischman from the March of Dimes. He also welcomed two new nonvoting organizations and their organizational liaison representatives to the Advisory Committee: Dr. Michael Watson from the American College of Medical Genetics (ACMG) and Dr. Barbara Burton from the Society for Inherited Metabolic Disorders (SIMD).

Committee Business. Dr. Howell referred Advisory Committee members to several materials included under TAB #17 of the materials in their notebooks and said that they would be discussed on the second day of the meeting: (1) an article about the recent increase in the incidence of congenital hypothyroidism in New York State by Katherine Harris and Kenneth Pass; (2) information about a U.S. patent involved in newborn screening; (3) the Advisory Committee's standard operating procedures ("ACHDGDNC: Policies and Procedures for Operation and the Development of Recommendations for Screening Newborns and Children for Heritable Disorders and for the Heritable Disorders Program"); and (4) the calendar for the Advisory Committee's 2008 meetings.

II. EVIDENCE-BASED REVIEWS OF CONDITIONS NOMINATED FOR THE UNIFORM NEWBORN SCREENING PANEL

James Perrin, M.D., FAAP
Professor of Pediatrics, Harvard Medical School
Director, MassGeneral Hospital Center for Child and Adolescent Health Policy
Director, MCHB Evidence Review Group, Systems of Care for Children and Youth with Special Care Needs

Nancy S. Green, M.D.
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Dr. Perrin, who chairs the Advisory Committee's external Evidence Review Group (ERG) that will review evidence on conditions nominated for inclusion on the uniform newborn screening panel, described progress since the June meeting of the Advisory Committee on plans for the ERG. In recent months, Dr. Perrin and his colleagues have worked on developing draft definitions of terms used on the nomination form, developing a draft template for the ERG's evidence reviews, and begun planning how to perform evidence reviews on nominated conditions. The plans are still very preliminary and have to be approved by the Advisory Committee. Nevertheless, the ERG is eager to get started and hopes to get an assignment soon, so that it can perform its first evidence review for the Advisory Committee's meeting in May 2008.

Background on the Nomination Process. Dr. Perrin reminded Advisory Committee members that the process Advisory Committee members approved for nominating and reviewing conditions nominated for inclusion on the newborn screening panel involves three steps:

- **Step #1:** Nomination form submitted by proponent(s) of adding a condition
- **Step #2:** Federal administrative review of the nomination form
- **Step #3:** Review by the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
    a. Advisory Committee review
    b. Evidence-based review by an external ERG (but no recommendations)
    c. Advisory Committee review and decision

The role of the external ERG is to 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 recommended by ACMG. The ERG will not itself make recommendations to the Advisory Committee.

Composition of the ERG. Dr. Perrin proposed that the ERG be based in Boston at the MassGeneral Hospital Center for Child and Adolescent Health Policy. He further proposed that the core staff of the ERG include in addition to himself Project Director Diane Romm, Ph.D. (epidemiology/methods); Trish Mullaley, R.N. (consumer); Lisa Prosser, Ph.D. (cost/benefit analysis); Marsha Browning, M.D., M.P.H. (genetics); Ellen Lipstein, M.D. (health services research fellow); Alex Kemper, M.D., M.P.H. (methods and screening); and Nancy Green, M.D. (consultant).

To give the ERG broader national representation and review, Dr. Perrin proposed that the ERG have its own external advisory group. Possible members include Ned Calonge, M.D. (a health officer at the Colorado State Health Department), Robert Davis, M.D., M.P.H. (a health services researcher at the Center for Health Research, Kaiser Southeast), Celia Kay, M.D., Ph.D. (a geneticist at the University of Colorado who represents the American Academy of Pediatrics (AAP) on the group), and Ed McCabe (a geneticist and chair of the UCLA Department of Pediatrics). The ERG would appreciate thoughts from the Advisory Committee about whether there should there be other types of people or other people among this group.

Dr. Perrin said that he expects the ERG will be further assisted by members of the Advisory Committee, as well as by individuals with ad hoc expertise for specific disorders. The procedures of the ERG will be very transparent so that people can understand what the procedures and processes are in the development of evidence. The ERG has a clear understanding of the importance of dealing with problems of conflicts of interest.

Draft Definitions of Terms on the Nomination Form. Dr. Perrin and his colleagues proposed draft definitions of several key terms (mostly from the nomination form) and asked for comments from Advisory Committee members on these definitions. The definitions were included under TAB #6 in the materials distributed to Advisory Committee members prior to the meeting.

- Severity of disease: (a) morbidity, disability, mortality; (b) burden of illness (family perspective); (c) vulnerability to morbidity, disability, mortality.
- Urgency: How soon after birth treatment needs to be initiated to be effective (to prevent complications or irreversible damage). Spectrum from life threatening to immediate to priority.
- Efficacy: (a) benefit: extent of prevention of mortality, morbidity, disability; (b) what are the treatment issues that may limit child or family acceptance or adherence?
- Risks of screening: (a) false positives, carrier detection, phenotypes with no or little morbidity; detection or suggestion of other disorders; (b) association—how strong is the reported relationship between a test result and a disease?
- Risks of treatment: Potential medical or other ill effects from treatment.
- Acceptability (invasiveness): (a) what tests/procedures are required; (b) how acceptable are these tests; (c) primary newborn screening and confirmatory testing.
- Availability: What is the availability of the (confirmatory) test in clinical practice?

After obtaining comments on these definitions from Advisory Committee members, the ERG will put the definitions out for public comment, so that the definitions can be revised and finalized prior to the Advisory Committee's next meeting in January 2008.

Draft Template for Evidence Reviews. Dr. Perrin and his colleagues proposed a template for the ERG to use in performing evidence reviews of conditions nominated for inclusion on the uniform newborn screening panel. That template, "Draft Template for Evidence Reviews," dated Sept. 17, 2007, was included under TAB #6 in the materials distributed to Advisory Committee members in advance of the meeting.

The components of the proposed evidence review template for the ERG are as follows:

1. Background
    - Information on the condition (prevalence, genetics, natural history, different forms of the condition)
    - Rationale for current review of the condition
2. Methods of review
    - Data sources: The ERG will limit studies to human studies only; will exclude case reports; will describe in reviews exactly how it obtained and evaluated data.
    - Decision model: The ERG will have a decision model that leads to evidence questions in each review.
    - Data abstraction: The ERG will describe actual methods of data abstraction and any new analyses it may do.
    - Focus groups of experts (investigators and families): To answer questions that cannot be answered via evidence review of either published data or available data from either principal investigators, the ERG will put together focus groups of experts to the ERG estimate severity and burden.
    - Screening and diagnostic testing. The ERG will describe in detail what is known about screening and diagnostic testing for the condition. It will define risks of screening such as false positives, carrier detection, phenotypes with little or no morbidity, and in some cases, the detection or suggestion of other disorders. It will also define risks of diagnostic testing.
    - Treatment. The ERG will describe in detail what it can determine from the evidence about the risks and benefits of treatment, and the applicability of treatment to specific condition groups, early versus late onset, etc.
3. Evidence review questions. The ERG will address questions about the natural history of the condition, including the variations of the condition, the differences between genotype and phenotype; what is known about prevalence of the condition and prevalence of subgroups; what is known about burden and severity of the condition; what is known about methods of screening and diagnosis; what is known about treatment effectiveness and variations; and to a degree what is known about costs of screening and treatment.
4. Lack of information. The ERG will indicate where data are absent, what the level of uncertainty is, and what new information or studies would be most critical to help the Committee make decisions about the condition.
5. Presentation of results. The ERG will present what evidence it can gather in summary and table form for the Advisory Committee to review in making its recommendations to the Secretary. The ERG will not make recommendations. The responsibility for making recommendations to the HHS Secretary about a particular condition will rest solely with the Advisory Committee.

Dr. Alex Kemper has written a paper on pitfalls in developing evidence in newborn screening in which he used Pompe disease as a prototype model. The ERG plans to share Dr. Kemper's paper with the Advisory Committee and to seek publication of the paper. In addition, Dr. Nancy Green, who chaired the Advisory Committee's workgroup on the criteria that were included in the nomination form, reported that she, Dr. Marie Mann from HRSA, Dr. Howell, and Dr. Lloyd-Puryear have a paper in press in *Genetics and Medicine* about the nomination process.

Questions & Comments

Advisory Committee members made several comments regarding the ERG's draft definitions of terms from the nomination form for evidence reviews:

- Page 1 of the nomination form: *Condition, severity of disease: (a) morbidity, disability, mortality; (b) burden of illness (family perspective); (c) vulnerability to morbidity, disability, mortality*. Dr. Boyle, noting that the terms "burden of illness" and "vulnerability" were rather vague, asked whether the ERG intended to make them crisper. Dr. Perrin said the ERG would welcome help in this area. Dr. Telfair, Dr. Boyle, and Ms. Terry suggested that the ERG consider defining these terms with reference to quality of life scales developed specifically for children with chronic conditions. Dr. Howell suggested that Dr. Boyle and Dr. Dougherty assist the ERG in specifying these terms.
- Page 2 of the nomination form: *Treatment, Efficacy (Benefits): (a) benefit: extent of prevention of mortality, morbidity, disability; (b) what are the treatment issues that may limit child or family acceptance or adherence?* Dr. Perrin asked for the Advisory Committee's help in identifying treatment issues that may limit child and family acceptance or adherence. Dr. Dougherty said that she thought such topics did not belong in a discussion of efficacy, which is an applicable term when using a treatment in a clinical trial, and would instead belong in a discussion of effectiveness, which is the applicable term when using a treatment with normal people in normal, everyday situations. Dr. Perrin disagreed, stating that if no one will accept treatment in a randomized clinical trial, there is a problem. He added, however, that perhaps the ERG and Advisory Committee might want to consider adding the term "effectiveness" of treatment to the nomination form and evaluation process.

Advisory Committee members made several additional comments related to the ERG's criteria and process:

- **Criteria for the quality of evidence reviewed**. Dr. Dougherty, noting that the ERG's work is going to be groundbreaking, emphasized that it is very important for the ERG have criteria for the quality of evidence it reviews. Dr. Perrin replied that the ERG will use standard measures of quality when it can but that such measures will be difficult to use in the case of (a) focus groups used to estimate burden of illness and severity, which raise issues of bias; and (b) data from unpublished sources or case reports. In the latter instances, however, the ERG will be able to put limits around the confidence levels.
- **Capturing benefits of treatment.** Dr. Howell asked how the ERG would capture benefits of for conditions like Fragile X, which don't have traditional treatments but for which screening and early detection might confer benefits from early intervention or counseling. Dr. Perrin said if early intervention improves outcomes, the ERG would include that as benefit of treatment. Dr. Howell asked whether the ERG would consider benefits for parents in terms of having other children. Dr. Perrin said one member of the ERG, Dr. Lisa Prosser, has worked on that problem, and the ERG believes it will be able to address that benefit to a degree; however, the available literature on that benefit to parents is more generic than condition specific.
- **Presenting evidence from focus groups.** Dr. Howell asked how the ERG would present evidence from focus groups to the Advisory Committee. Dr. Perrin said the ERG would probably negotiate that with principal investigators. In general, the ERG would provide a summary table rather than very specific tables on evidence.

- **Dealing with conflicts of interest.** Dr. Howell asked how the ERG would deal with the fact that many conditions detected via newborn screening are rare conditions, and most experts will have tremendous conflicts of interest. Dr. Perrin stated that the ERG would focus on the evidence that experts have to support their positions. He noted that the ERG may encounter bias when it uses experts to define burden, so it has to be especially careful and thoughtful in that area. The ERG will be very open about where the data it uses come from and will state recognized conflicts of interest. Dr. Howell underscored the importance of stating recognized conflicts of interest so they would be above the board. Dr. Green added that some questions related to conflicts of interest would probably have to come to the full Advisory Committee for additional deliberation.
- **Mechanism for assessing bias in evidence reviews.** Dr. Boyle suggested that the ERG develop some sort of mechanism for assessing and making bias explicit in its deliberations. Dr. Perrin agreed that this was a good suggestion. He noted that the Institute of Medicine, for example, has a bias statement for new committees in which people need to explain what their positions are, what their experience has been in a particular area, what statements they've made publicly about a particular piece of work, etc. The ERG could consider developing its own mechanism.
- **Readiness for the ERG to begin its deliberations**. Noting that HRSA had received two nominations for adding conditions to the uniform newborn screening panel—one for Krabbe disease and one for severe combined immunodeficiency (SCID)—Dr. Howell asked whether the ERG was ready to proceed with evaluating evidence. Dr. Perrin replied that the ERG would like to start with one condition first, and then take on another condition a couple of months later. Dr. Howell stated that he was eager to move forward as quickly as possible, but the evidence review is so critical—and in fact, groundbreaking—that it really has to be very carefully done.

III. COMMITTEE BUSINESS—DISCUSSION OF THE NOMINATION AND EVALUATION PROCESS FOR CANDIDATE CONDITIONS ON THE UNIFORM NEWBORN SCREENING PANEL

A. Fine-Tuning the Nomination Form

The Advisory Committee considered two changes to the form it has approved for nominating conditions to be added to the uniform newborn screening panel.

Adherence. The first change considered by the Advisory Committee was on page 2 of the nomination form in the “Treatment” section—namely, changing the word “compliance” in the definition of “Efficacy (Benefits)” to “adherence.” Dr. Green explained that the nomination form formerly said "Treatment limitations, such as difficulty with acceptance or compliance," and noted that that term compliance was value-laden and therefore not appropriate in this context. She and Dr. Perrin and their colleagues believed what the nomination group had intended was a more neutral term of such as "adherence" or “acceptance” and recommended using one of these terms.

The Advisory Committee accepted this recommendation and voted unanimously to approve the following motion:

- ***MOTION #1****: On the nomination form for adding conditions to the uniform newborn screening panel, the Advisory Committee approves changing the word "compliance" to "adherence" on page 2 under the "Treatment" category in the definition of "Efficacy (Benefits)."*

Effectiveness. The second change considered was also on page 2 of the nomination form in the "Treatment" section. Several members of the Advisory Committee underscored the importance of considering effectiveness in the ERG's evaluation of the evidence on conditions nominated for inclusion on the uniform newborn screening panel. Dr. Boyle explained that the "efficacy" of an intervention is the gold standard—a measure of how something works under ideal conditions of use such as a clinical trial; the "effectiveness" of an intervention is a measure of how something works in a real-world setting such as a newborn screening program.

Dr. Dougherty recommended adding a new line for "Effectiveness." Dr. Lloyd-Puryear explained that because the nomination form had already been approved by the Advisory Committee and released to the public, the Committee would have to make a proposal to change the nomination form and then formally vote on that proposal if it wanted to change the form.

Dr. Green instead suggested just adding the word "Effectiveness" in parentheses after "Efficacy." She explained that the distinction between effectiveness and efficacy is not generally known to the public, so adding a separate box for "effectiveness' might be confusing to nominators. To address that concern, Dr. Dougherty suggested changing the title of the "Efficacy" box to "Treatment Effectiveness" and then letting the ERG determine whether the studies cited were efficacy studies or effectiveness studies. Dr. Green recommended leaving the nomination form as it was and asking the ERG to address effectiveness in its evidence review document. Dr. Brower agreed with Dr. Green, and Dr. Dougherty stated that she was comfortable with having effectiveness dealt with in the ERG's evidence review.

Finally, Dr. Howell stated that it was the sense of the Committee that the nomination form would not be changed with respect to "Efficacy (Benefits)"and that effectiveness would be addressed in the ERG's evidence review.

- ***DECISION #1****: The external Evidence Review Group (ERG), in reviewing the evidence for conditions nominated for the uniform newborn screening panel, will consider and report on evidence pertaining to the effectiveness of treatment, as well as to the efficacy of treatment.*

Ms. Terry volunteered to help HRSA address technical issues for Mac users in submitting nomination forms. Dr. Lloyd-Puryear said she would welcome her help.

B. Process for Handling Nominations

Dr. Howell initiated discussion of how the Advisory Committee should proceed with the two nominations of conditions to be added to the uniform newborn screening panel that had already been received: one for Krabbe disease and one for severe combined immunodeficiency (SCID). Copies of these two nominations were provided to members of the Advisory Committee at the meeting.

Dr. Green suggested that the Advisory Committee advise the ERG on which of the two nominations should be considered first to ensure a robust test of the ERG's process and interaction between the ERG and the Advisory Committee. Because disorders for which there have been no pilot studies would be unlikely to traverse the entire review process, she recommended that the Committee pick a disorder for which there have been pilot studies.

Dr. Watson, on the other hand, noted that Krabbe and SCID are enormously different conditions and are likely to draw out very different issues and recommended that the Advisory Committee ask the ERG to perform evidence reviews for both conditions to evaluate its processes. Dr. Howell agreed, stressing the importance of getting the Advisory Committee to process nominations as quickly as possible. Otherwise conditions will rapidly be going before the public and be screened for widely before the Advisory Committee has had a chance to even look at them.

Dr. Lloyd-Puryear pointed out that in the process Advisory Committee members approved for nominating and reviewing conditions nominated for inclusion on the newborn screening panel, HRSA is supposed to perform the initial review of nomination forms. She noted that HRSA had not set up its own system of review yet and asked what criteria HRSA should use in deciding to send nominations forms ahead and how to prioritize the nominations received. Dr. Howell explained that HRSA's role is simply to confirm that the nomination form is ready to go forward, not to do a scientific or priority-setting or qualitative review.

Dr. Howell pointed out that the Advisory Committee had not yet given formal approval to the ERG proposal presented by Dr. Perrin. Dr. Green stated that what Dr. Perrin had presented to the Committee at this meeting was very, very preliminary and that he would submit a more formal proposal. His presentation today had not even been reviewed by the ERG's own advisory group.

Ms. Terry asked whether it was correct to tell potential nominators of conditions for inclusion on the uniform newborn screening panel to use the nomination form previously approved by the Advisory Committee even though there were going to be iterative changes to the form. She also asked what the timeline for considering conditions nominated would be, given that the ERG's process has not yet been approved. Several Committee members noted that it was important to build trust with the nominators by framing out when the process for reviews is going to be in place.

Dr. Green responded to Ms. Terry that groups with nominations of conditions they would like to see added to the uniform newborn screening panel should go ahead and submit the nominations. She added that Dr. Perrin would like to consider one condition before the Advisory Committee's next meeting in January 2008, but he is reluctant to set a timeline for evidence reviews, in part because the timeline is likely to vary by condition.

Dr. van Dyck and Dr. Alexander said that, much as they would like the Advisory Committee to move forward on reviewing nominations for adding conditions to the uniform newborn screening panel, it was not ready to do so for two reasons. First, HRSA had not established its own process for reviewing performing administrative reviews (not scientific or priority-setting or qualitative reviews) before sending nominations on to the Advisory Committee. Second, the Advisory Committee had not yet approved Dr. Perrin's proposal for the ERG and its process for reviewing the evidence.

To address the first issue, Dr. Alexander suggested that the Advisory Committee ask HRSA to develop its procedures for processing nominations; that the Advisory Committee consider the nominations for Krabbe and SCID as have been given to the Committee for informational purposes only and that the Committee ask HRSA to process the nominations and then formally submit them

to the Committee as soon as possible. That way the Committee might be able to make a recommendation about how to move ahead with the Krabbe and SCIC nominations at its next meeting in January 2008.

To address the second issue, Dr. Alexander recommended that the Advisory Committee ask Drs. Perrin and Green to move expeditiously to incorporate revisions and turn their draft ERG proposal into a final report and submit the final report to HRSA to distribute to the Committee members. He also recommended asking HRSA to schedule a conference call prior to January 2008 for the Advisory Committee to review and modify or accept the revised ERG proposal. Finally, he recommended that HRSA move expeditiously to establish the ERG and get it in place once the ERG proposal is approved by the full Committee.

Dr. Howell and other Committee members accepted Dr. Alexander's suggestions.

- ***DECISION #2****: HRSA will move expeditiously to develop mechanisms for administrative review of nominations, so that it can process the nominations for Krabbe disease and SCID and any other nominations that come in.*

- ***DECISION #3****: Dr. Perrin and Dr. Green will submit a revised final document regarding the ERG and evidence-based review processes to HRSA as soon as possible. HRSA will distribute the document to Advisory Committee members and schedule a conference call with Committee members, so they can approve or modify the plan prior to the Advisory Committee's January 2008 meeting. Once the plan has been approved, HRSA will move expeditiously to establish the ERG.*

Another recommendation from Dr. Alexander and Dr. Boyle was that Dr. Howell appoint a subcommittee of the Advisory Committee to (1) determine whether nominations were ready for evidence-based review; and (2) develop criteria for prioritizing nominations, so that the full Advisory Committee could consider which nominations to send to the ERG at its upcoming meeting in January 2008. Dr. Howell agreed with this suggestion and asked Advisory Committee members to let him know if they would serve on the subcommittee. Dr. Lloyd-Puryear urged Committee members who were leaving the Committee but who had not yet been replaced to stay involved in the process until their replacements had been named.

- ***DECISION #4****: Dr. Howell will appoint a Nomination Review and Prioritization workgroup of the Advisory Committee (1) to review nomination forms processed by HRSA to determine the nominations' readiness for referral to the ERG; and (2) to develop criteria regarding the prioritization (if any) of the Krabbe disease, SCID, and other nominations received from HRSA. The workgroup will report to the Advisory Committee at the Committee's next meeting in January 2008.*

Ms. Terry proposed giving the Krabbe and SCID nominations to Dr. Perrin and his colleagues immediately, so that they could use them to fine tune the ERG's own processes while they were waiting for the nominations to be formally assigned to them for evidence-based review. Dr. Watson noted that both Krabbe and SCID were quite different from Pompe disease, which was used initially to develop the ERG's processes, so it would be useful for the ERG to have the nominations for the purpose Ms. Terry set forth.

- ***DECISION #5:*** *The nominations for Krabbe and SCID will be given to Dr. Perrin prior to being referred to the ERG formally, so that he and his colleagues can use them to fine tune the ERG's own processes.*

C. Inviting an FDA Representative to the January 2008 Meeting to Discuss Access to Data

Dr. Green explained that one reason Dr. Perrin is reluctant to set a timeline for evidence-based reviews by the ERG, apart from the fact that the timeline will vary by condition, is that the process for getting unpublished data from the Food and Drug Administration (FDA) is uncertain. She asked the Advisory Committee to discuss how to hasten getting such data in order to expedite the ERG's evidence review process.

Speaking as FDA's representative to the Committee, Dr. Hausman explained that many people have raised this issue over the past 20 to 30 years. He said there are different rules depending on which FDA center is involved, but any data that come in to FDA about drugs, foods, or biologics are proprietary, and FDA is limited in its capacity to share certain types of information. Dr. Hausman said that there was no way he could promise access to any data, but he would be happy to facilitate communications between the Advisory Committee and the policy people at FDA who could address questions on this topic.

Dr. Howell accepted Dr. Hausman's offer, saying he would like to have the appropriate FDA representative make a presentation to the Advisory Committee at its upcoming meeting in January 2008.

- ***DECISION #6:*** *With Dr. Hausman's assistance, an FDA policy person who can address issues related to gaining access to FDA data on newborn screening tests will be identified and asked to make a presentation to the Advisory Committee at its meeting in January 2008.*

IV. SACGHS TASK FORCE ON OVERSIGHT OF GENETIC TESTING

Andrea Ferreira-Gonzalez, Ph.D.
Professor of Pathology
Director of Molecular Diagnostics Laboratory
Virginia Commonwealth University

Dr. Ferreira-Gonzalez reported on the newly created the Task Force on Oversight of Genetic Testing of the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS). Dr. Ferreira-Gonzales is the chair of the task force, which was created in response to a mandate from the HHS Secretary in March 2007.

The HHS Secretary's overarching mandate for SACGHS is "to explore, analyze, and deliberate on the broad range of human health and societal issues raised by the development and use, as well as potential misuse, of genetic technologies" and "to make recommendations to the Secretary of HHS and other departments upon request." The scope of SACGHS includes the integration of genetic technologies into health care and public health; clinical, ethical, legal and societal implications of new medical applications; research and data collection; patient policy and licensing practices; broader social applications of genetics, and emerging applications and issues. Additional information about SACGHS is available at http://www4.od.nih.gov/oba/ SACGHS.htm.

In March 2007, the HHS Secretary gave SACHGS a new specific mandate related to genetic and genomic tests. Specifically, the Secretary directed SACHGS to undertake the development of a comprehensive map of the steps needed for evidence development and oversight of genetic and genomic tests, with improvement of health quality as the primary goal. The Secretary further directed SACGHS to look at information provided and resources needed for proficiency testing (which has been interpreted to include looking into the adequacy and transparency of proficiency testing processes); to look at potential communication pathways to guide test use and new approaches and models for private and public-private sector engagement in demonstrating clinical validity and developing clinical utility into effectiveness measures; and to look at the added value of revisions to and enhancements of government oversight of genetic and genomic tests.

The HHS Secretary's additional specific mandate led to the creation of the SACGHS Task Force on Oversight of Genetic Testing. The task force currently force has 33 members, including five SACGHS members, several ad hoc members, several Federal experts, and a few consultants. There have been six meetings of the full task force and additional meetings of the "steering committee" (the five SACGHS members) and meetings to prepare the report of the SACGHS Task Force on Oversight of Genetic Testing. The focus of activities has been on identifying gaps in knowledge, discussing real and potential harms, and developing policy options.

There have been numerous publications on genetic testing already done by other entities. A 2000 report from the SACGHS, for example, made several recommendations with respect to the Food and Drug Administration (FDA), the Clinical Laboratory Improvements Act (CLIA) and the CDC involvement in genetic testing. HHS accepted these recommendations and indicated that they would be implemented over time as resources allowed. In 2007, FDA issued guidance that clarifies what constitutes an ASR, as well as guidance extending its jurisdiction to a narrow subset of LDTs—in vitro diagnostic multivariate index assays (IVDMAs), but its position regarding its jurisdiction over LDTs is not entirely clear. CDC has halted plans to establish a genetic testing specialty under CLIA, stating that other measures would be undertaken instead.

The SACGHS Task Force on Oversight of Genetic Testing is trying to complete its report to the HHS Secretary. The Task Force will present the report to SACGHS on Oct. 15, 2007, and then release the report on Nov. 5, 2007, for a 45-day public comment period. SACGHS will devote part of its meeting on Nov. 19-20, 2007, to an extended comment period on oversight of genetic testing, and there will be a roundtable of professionals discussing the status of genetics education initiatives. The public comment period on the report will end Dec. 21, 2007.

The chapters of the report of the SACGHS Task Force on Oversight of Genetic Testing are as follows:

- *Ch. 1: Background* (defines oversight broadly for the purpose of the report; acknowledges genetic exceptionalism as a social and policy reality; discusses broad ethical issues/spectrum of harms and benefits; ties in to the HHS Secretary's Personalized Healthcare Initiatives; discusses roles of different entities; identifies peripheral issues not addressed in report.)
- *Ch. 2: Technologies* (defines genetic test for the purpose of the report; lists methodologies being considered; identifies future trends)
- *Ch. 3: Analytical Validity, Proficiency Testing, and Clinical Validity* (most extensive content area; explores governmental, public/private, and private oversight options)

- *Ch. 4: Clinical Utility and Evidence Development* (notes no regulatory oversight for clinical utility; no existing infrastructure; suggests big opportunity for improvement; adopts broad approach for identification of actionable items)
- *Ch. 5: Effective Communication and Clinical Decision Support* (effective communication portion includes discussion of pre- and post-analytic communication; roles of labs, providers, and patients; genetic specialty vs. nongenetic specialty providers and labs; direct to consumer; clinical decision support portion includes discussion of pre- and post-analytic support, passive vs. active support, incorporation of evidence-based clinical guidelines, opportunity to achieve greater impact based on experience another sectors of health care, clarify how clinical decision support will be regulated)
- *Ch. 6: Summary of Policy Options* (will follow Sept. 5, 2007, meeting; steering committee members will review, consolidate, and prioritize)

After public comments and revisions are incorporated to the report of the SACGHS Task Force on Oversight of Genetic Testing, SACGHS will meet on Feb. 15, 2008, to discuss them. Final substantive revisions will be made after that, and a revised draft report will be submitted to the HHS Secretary informally on Feb. 29, 2008. The final report will be formally submitted to the HHS Secretary on April 30, 2008.

Questions & Comments

Dr. Howell said he had understood that the SACGHS Task Force on Genetic Testing would be looking at newborn screening tests. Dr. Ferreira-Gonzalez explained that the task force would be looking only at generic issues and would leave issues specific to newborn screening to ACHDGDNC..

Dr. Lloyd-Puryear noted that Advisory Committee member Dr. Brower is representing the ACHDGDNC on the SACGHS Task Force on Genetic Testing. In addition, Dr. Marie Mann from HRSA is serving as a consultant.

Ms. Terry emphasized that there is no consumer/patient/parent advocate involvement in SACGHS, noting that she had pointed that deficiency out to SACGHS. Ms. Terry stated that SACGHS Executive Director Sarah Carr has assured her that consumers will be given the opportunity to make public comments, but Ms. Terry nevertheless believes that this is a significant issue. Ms. Terry also noted that the 21st Century Medicine Coalition has identified 70 commercial labs and academic labs working on 200 IVDMIA tests, so they are going to be more and more common, and that is something that the SACGHS Task Force on Genetic Testing ought to consider. A coalition she is involved has given the list to the HHS Secretary and to FDA.

V. UPDATES FROM FEDERAL AGENCIES

Representatives of the Agency for Health Care Research and Quality (AHRQ), the Centers for Disease Control and Prevention (CDC), the Health Resources and Services Administration (HRSA), and National Institutes of Health (NIH) gave reports on their agencies' activities related to genetics and newborn screening.

A. Agency for Health Care Research and Quality (AHRQ)

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

Dr. Dougherty, after noting that AHRQ's overall mission is to improve the safety, quality, efficiency, and effectiveness of health care for all Americans, reported on the activities of the U.S. Preventive Services Task Force (USPSTF) related to newborn screening, evidence reports issued by the Evaluation of Genomic Applications in Practice and Prevention initiative, and some other AHRQ activities related to newborn screening.

USPSTF, an independent body created by law that is staffed by AHRQ, recently issued its recommendations pertaining to screening lipid disorders (insufficient evidence to recommend for or against); screening for developmental dysplasia of the hip (insufficient evidence to recommend for or against); and screening for speech and language (insufficient evidence to recommend for or against). In addition, USPSTF has been updating its recommendations for newborn hearing screening, screening for hemoglobinopathies, screening for congenital hypothyroidism, and screening for phenylketonuria. The newborn screening recommendations have been completed and submitted to *Pediatrics* for publication. Additional information on USPSTF guidelines and three uncopyrighted articles that might be of interest to the Advisory Committee as it deals with how to communicate evidence reviews can be downloaded from AHRQ's "Clinical Information" Website [http://www.ahrq.gov/clinic/]: (1) an article in the *Annals of Internal Medicine* on current USPSTF processes (Guirguis-Blake et al.); (2) an article on how to read the new USPSTF recommendations statements (Barton et al.); and (3) an article with commentary on integrating clinical and community services recommendations (Ockene et al.).

The Evaluation of Genomic Applications in Practice and Prevention initiative, which is supported by a collaboration of AHRQ and CDC's National Office of Public Health Genomics, has issued three new evidence reports: one on ovarian cancer/genomic testing; one on depression/Cyp450 testing and one on colorectal cancer/HNPCC. These are also available on AHRQ's "Clinical Information" Website [http://www.ahrq.gov/clinic/].

AHRQ's other activities related to genetics include an assessment in partnership with CDC of infrastructure needs to monitor the utilization and outcomes of gene-based applications in the U.S. health care system (in progress). In addition, AHRQ is supporting a study of the impact of gene expression profiling test on breast cancer outcomes (in progress); an evidence report on Her2neu, focused mostly on women who are Her2neu negative, for which there is no good evidence now on what to do if they have a recurrence of metastatic cancer (in progress); and a randomized clinical trial of the effects on genetic testing on warfarin dosing (Marshfield Clinic grant).

Several newer AHRQ initiatives may eventually be related to newborn screening and/or genetic testing. The Value-Based Health Care Initiative, for example, is a large initiative of the Secretary

of HHS to get people together to do quality improvement. The idea is that quality problems—that is, people not getting the right care at the right time—is a national problem, but that the solutions are local. Thus, AHRQ will be helping to develop a learning network of chartered value exchanges organized at the local community level [http://www.hhs.gov/valuedriven/communities/valueexchanges/exchanges.html].

Other new AHRQ initiatives that may be related to genetics and newborn screening include the potential expansion, depending on the appropriations bills, of the comparative effectiveness work that AHRQ has been doing for the last few years [http://effectivehealthcare.ahrq.gov/]; and the Healthcare Innovations Exchange, which provides user-friendly information about successful health care quality improvement initiatives [http://www.innovations.ahrq.gov/].

Finally, Dr. Dougherty noted that AHRQ will soon be making some new funding announcements related to patient safety, health information technology, quality improvement, etc.

Questions & Comments

Dr. Howell, observing that checking newborns for hip dysplasia is done routinely by physicians, asked whether the USPSTF report that found no evidence that this was beneficial had a recommendation on how to go forward. Dr. Dougherty said the findings from the USPSTF report feed to a research agenda, perhaps by NIH. Dr. Alexander from NIH said he would be reluctant to fund a randomized clinical trial in which children would *not* be checked for hip dysplasia, because checking for dysplasia has been done forever and seems to be beneficial.

B. Centers for Disease Control and Prevention (CDC)

William H. Hannon, Ph.D.
Chief, Newborn Screening Branch and Molecular Biology Branch
Division of Laboratory Sciences
Centers for Disease Control and Prevention (CDC)

Dr. Hannon explained that although several entities within CDC undertake activities in newborn screening and genetics, he would talk primarily about activities in CDC's National Center for Birth Defects and Developmental Disabilities (NCBDDD) and about a couple of activities of CDC's Newborn Screening and Molecular Biology Branch, which he heads.

Before describing the activities of these two entities, Dr. Hannon reported that NCBDDD (within CDC's Coordinating Center for Health Promotion) has recently gained a very exciting, enthusiastic new director, Dr. Edwin Trevathan. Dr. Trevathan, a neurologist who recently worked with the Missouri Department of Health as principal investigator on autism and development disability monitoring network in Missouri, is very enthusiastic about getting more involved in newborn screening issues.

Dr. Hannon also reported that Newborn Screening Branch in the Division of Laboratory Sciences, which he has headed for many years, recently merged with the Molecular Biology Branch. The decision to merge the two branches to create the Newborn Screening and Molecular Biology Branch was made in part because Dr. Hannon is about to retire and in part because of the importance of molecular biology to newborn screening. The newly merged branch has 47 people. Dr. Hannon is the acting branch chief of the new entity, but CDC will begin recruiting for his replacement in 2008.

CDC's National Center for Birth Defects and Developmental Disabilities (NCBDDD). NCBDDD's activities related to newborn screening include the following:

- **Pilot projects of screening for and diagnosis of Duchenne muscular dystrophy**. Pilot projects are being conducted to test the feasibility of newborn and infant screening for Duchenne muscular dystrophy. The screening of newborns and children from 6 months of age to 15 months of age is being done using a creatine kinase test on dried blood spots at several hospitals in Ohio. The project also involves surveys to look at some other issues, including the informed consent process, why parents accept or decline screening, health care providers' attitudes, etc. Information and reports coming out of this project are expected late this year or early next year.

- **Research related to screening for and determining the incidence of fragile X syndrome (FXS).** With support from NCBDDD's Division of Birth Defects and Developmental Disabilities, headed by Dr. Boyle, Emory University researchers have been developing an automated, high-throughput screening test for dried blood spots to identify FXS. Preliminary work indicates that the test has great sensitivity. Currently, the new test is being used on 70,000 to 100,000 deidentified dried blood spot cards from Georgia's newborn screening program to ascertain the incidence of FXS in the general population, as well as in specific ethnic and racial groups.

- **Assessing and evaluating historical data from the National Newborn Screening & Genetics Resource Center (NNSGRC) database**. The NNSGRC database contains a tremendous amount of information, and Dr. Vicki Stover Herztberg at Emory University and her colleagues are mining 1991 to 2000 data from the database to study the incidence of congenital hypothyroidism. The increased incidence of this disorder was discussed in a recent article by Katherine Harris and Kenneth Pass [included under TAB #9 in the materials distributed to Committee members]. Data from the NNSGRC database will allow Dr. Stover and her colleagues to examine this topic in greater depth.

- **Paper on lessons learned from the impact of Hurricane Katrina on newborn screening in Louisiana.** A paper by Dr. Emad Yanni and his colleagues entitled "Lessons Learned from the Impact of Hurricane Katrina on newborn screening in Louisiana" is coming out in the October 2007 issue of *Pediatrics.*

CDC's Newborn Screening and Molecular Biology Branch. Two activities of the newly merged Newborn Screening and Molecular Biology Branch in the Division of Laboratory Sciences (within the Coordinating Center for Environmental Health and Injury Prevention) at CDC are the following:

- **Newborn Screening Quality Assurance Program**. This program, which was initially started by Dr. Hannon with funding from HRSA, performs quality assurance and proficiency testing related to newborn screening. It provides services that include filter paper evaluation, reference materials, quality control materials, and proficiency testing, as well as trainings, consultations, and network resources. More than 400 laboratories in 72 countries participate in the program. More information about the program is available at the program's Website [http://www.cdc.gov/nsqap/Public/default.aspx].

- **Newborn Screening Translational Research Initiative.** This program was established at the CDC Foundation in collaboration with CDC's Newborn Screening Branch. To help ensure that research is translated into routine laboratory tests for newborn screening, this program will provide laboratory support and a knowledge base for a wide array of conditions such as lysosomal storage disorders, autism spectrum disorders, immune deficiency disorders, infantile colic, diabetes, cystic fibrosis, and other disorders.

C. Health Resources and Services Administration (HRSA)

Peter C. van Dyck, M.D., M.P.H., M.S.
Associate Administrator
Maternal and Child Health Bureau
Health Resources and Services Administration (HRSA)

Dr. van Dyck discussed HRSA's initiatives related to newborn screening for families and the general public, the National Newborn Screening and Genetics Resource Center (NNSGRC), the Regional Genetics and Newborn Screening Collaboratives and the National Coordinating Center (NCC) for the regional collaboratives, and some recent developments related to medical homes for children with special health care needs.

Initiatives Related to Newborn Screening for Families and the General Public. Four HRSA initiatives related to newborn screening for families and the general public are the following:

- **Family Health History Initiative**. In collaboration with the Genetic Alliance, HRSA has supported the development of two booklets that are designed to promote conversations about health within the family, translate family health history into health choices, healthy choices, and increase community involvement in health education: "A Guide to Family Health History" and "A Guide for Understanding Genetics and Health." The Genetic Alliance is partnering with 10 different communities across the United States to use and evaluate these tools, which are designed to be Web based and customizable. In addition, HRSA has supported the development of a "Health Provider Card" for individuals to fill out and take to their health care provider. One side of the card concentrates on concerns individuals may have about their family health history. The other side of the card provides information for providers to use a person's family history to figure out whether that person is likely to develop a disease. InterMountain Healthcare is conducting interviews with primary care providers to determine what kinds of information they want. InterMountain Health Care will integrate a customized version of the "Does It Run in the Family?" toolkit in its patient portal ("My InterMountain") and plans to link patients' input to their electronic medical records.
- **Community Genetics Education Network.** HRSA is supporting a 5-year project with the March of Dimes to work with four community-based organizations to improve genetic literacy, to increase access to culturally and linguistically appropriate genetics education programs and services in underserved and underrepresented populations and to promote lifestyle changes in these populations that reduce genetic health risks. The four community-based organizations are (1) the Dominican Women's Development Center in Washington Heights, N.Y (serving the Latin American community, including Dominican, Puerto Rican, South American, and Afro-Caribbean); (2) Charles B. Wang Community Health Center in New York, N.Y., serving a predominantly Asian-American community (Chinese, Korean and Vietnamese); (3) Genetic Science Learning Center at the University of Utah, serving Hispanic/Latino and Native American communities; and (4) National Human Genome Center at Howard University in Washington, D.C., serving African-American and West African immigrant communities. The Charles B. Wang Community Health Center has produced four bilingual brochures related to genetic testing and counseling. The project in Utah is conducting family genetics education and is working with the Hispanic and Latino community to teach children in grades 5 through 10 about the role genetics plays in causing disease.
- **Screening for Heritable Disorders in Children: Efficacy from a Family/Consumer Perspective**. HRSA is supporting a program is develop increased knowledge of family

perspectives that will assist genetic and newborn screening programs in planning for and supporting the constant involvement of parents and families. The Genetic Alliance and several other partners are involved in the program.

- **Family-to-Family Health Information Centers**. HRSA has provided grants for 30 Family-to-Family Health Information Centers last year and is funding 10 more this year, then 10 more next year. Thus, by the end of 2009, there will be one center in each State. Family-to-Family Health Information Centers are staffed by families of children with special health care needs and provide information to families and providers regarding the health care needs of and resources for children with special health needs; assist the families of such children make informed choices; develop partnerships with providers, managed care organizations, health care purchasers, and appropriate State agencies; provide training and guidance regarding the care of such children.

National Newborn Screening and Genetics Resource Center (NNSGRC). The HRSA-supported NNSGRC in Texas, which is headed by Dr. Brad Therrell, serves as a point of contact for newborn screening accessible to all (telephone, Website, listservs); provides expert consultative services to newborn screening programs that request it (telephone consultation, expert review teams, reports and recommendations); collects and reports national newborn screening data for program evaluation (the National Newborn Screening Information System has data on cases detected, births, presumptive positive tests, unsatisfactory specimens, etc.); and provides input into issues of national and regional importance (meetings of experts, white papers, funds for small projects, etc.).

HRSA's Heritable Disorders Program: Regional Genetics and Newborn Screening Collaboratives and the National Coordinating Center (NCC). HRSA has awarded 5-year grant awards (June 1, 2007, through May 31, 2012) through its Heritable Disorders Program to the seven Regional Genetics and Newborn Screening Collaboratives and the NCC for the regional collaboratives. The seven regional collaboratives have two objectives: (1) to strengthen communication and collaboration among public health, individuals, families, primary care providers, and genetic medicine and other subspecialty providers; and (2) to quantitatively and qualitatively evaluate outcomes of projects undertaken to accomplish their goals. The NCC, headed by Dr. Michael Watson, acts as a coordinating center and a bridge between the regional collaboratives and HRSA and other partners to identify and prioritize issues of importance.

Each regional collaboratives receives $500,000 in base funding per year. With this money, the regional collaboratives are working to develop partnerships with primary care providers, individuals, and families; seeking to develop practice models to facilitate coordination between genetic service providers and nongenetic health services professionals; working toward regional newborn screening State panel standardization and expansion and testing harmonization; and establishing newborn screening emergency preparedness plans.

Some regional collaboratives are receiving additional project grants from HRSA ($250,000 per project) for priority projects related to laboratory quality assurance (priority activity #1) or long-term followup (priority activity #2):

- *Laboratory quality assurance (priority activity #1*). The Region 4 Great Lakes, Southeastern, New England, and Mountain States Regional Collaboratives are receiving project grants to undertake specific newborn screening public health laboratory quality improvement projects such as enhancing the newborn screening analytical laboratory test performance across the country.

- *Long-term followup (priority activity #2).* The Region 4 Great Lakes, Southeastern, and New England Regional Collaboratives are receiving project grants for projects related to long-term followup. They are involved in collaborative health information technology and information exchange activities such as the creation and use of regional and national information systems designed to monitor health outcomes of infants and children identified with heritable disorders in newborn screening programs; to evaluate newborn screening performance; and to evaluate treatment protocols. They are also involved in collaborative activities between the public health newborn screening program and the service delivery system that build on existing child health information systems activities in the region and address issues of informed consent and family acceptance of screening and treatment.

HRSA's vision for the next 5 years is that all health care and public health professionals will have genetic resources readily accessible to them and will understand what it means to "think genetically." In addition, health care and public health professionals will know that the Regional Genetics and Newborn Screening Collaborative is the "go-to place" for information about genetic resources and services within the region.

Developments Related to Medical Homes for Children with Special Health Care Needs. Over the years, HRSA has supported policy initiatives to establish medical homes for children with special health care needs. There is growing interest in the medical home concept of comprehensive care.

Earlier this year, for example, the American Academy of Pediatrics, the American Academy of Family Physicians, the American College of Physicians, and the American Osteopathic Association adopted a consensus statement entitled "Joint Principles of the Patient-Centered Medical Home." That document defines a patient-centered medical home as "an approach to providing comprehensive primary care for children, youth, and adults. The [patient-centered medical home] is a health care setting that facilitates partnerships between individual patients, and their personal physicians, and when appropriate, the patient's family."

In addition, Section 204 of the Tax Relief and Health Care Act of 2006 (Medicare Medical Home Demonstration) calls for HHS to establish a medical home demonstration project to redesign the health care delivery system to provide targeted, accessible, continuous and coordinated, family-centered care to high-need populations.

D. National Institutes of Health (NIH)

Duane Alexander, M.D.
Director, National Institute
of Child Health and Human Development (NICHD)
National Institutes of Health (NIH)

Dr. Alexander updated the Advisory Committee on some ongoing and new initiatives related to newborn screening at NICHD and briefly discussed other NIH initiatives. For several years now, NICHD has had as one of its major initiatives the expansion of newborn screening. This initiative has two components: (1) the issuing of grants and contracts to develop improved newborn screening technologies and treatments; and (2) the development of a national Newborn Screening Translational Research Network based on the seven Regional Genetics and Newborn Screening Collaboratives funded by HRSA's Heritable Disorders Program.

NICHD Grants and Contracts Related to Newborn Screening. As Dr. Alexander reported to the Committee at previous meetings, one component of NICHD's initiative has been awarding grants and contracts to develop improved newborn screening technologies and treatments. Dr. Alexander updated the Advisory Committee on several of these.

- **Contracts awarded to develop improved newborn screening technologies.** The 3-year contracts NICHD awarded to the New York State Health Department and the University of Washington are now moving into their second year. Among the accomplishments is the development of what looks like a promising and definitive test for spinal muscular atrophy for newborn screening. Another is exploring the Luminex Bead technology as a possible improvement over microarray chips for application in newborn screening. Yet another is assessing expanded uses of tandem mass spectroscopy in newborn screening. The Luminex Bead technology could incorporate screening tests for severe combined immune deficiency (SCID).
- **Grant awarded to apply nanotechnology to newborn screening.** NICHD recently awarded a Small Business Innovation Research grant to the company that is using a nanotechnology that has some great promise for applicability into newborn screening. It was developed as a microfluidic technology for doing rapid chemical analyses even at the bedside with great accuracy and with a very small quantity of analyte. It has the advantage of being extremely rapid, producing answers within minutes, using a tiny nanoliter sample, the capability of doing multiple assays (20 to 30 analyses) from one tiny microchip at a low cost, being relatively simple to perform, and being highly accurate.
- **Grants awarded to develop treatments for conditions detectable via newborn screening.** As Dr. Alexander has reported previously, NICHD has a program announcement soliciting applications from investigators for developing new and innovative approaches to treatment for disorders that could potentially be screened for but for which there is no treatment at the present time. The response to this has been good but not great. NICHD has funded a number of grants in this area, including efforts to develop interventions for spinal muscular atrophy and a number of other disorders.
- **Grant related to newborn screening for fragile X syndrome (FXS**). NICHD has funded a grant looking at introduction of newborn screening for FXS. That has been held up because the process for screening that NICHD thought was going to work has not. It may be that other approaches to screening under development will allow NICHD to proceed with the grant.

NICHD's Newborn Screening Translational Research Network. The second component of NICHD's initiative to expand newborn screening— create a Newborn Screening Translational Research Network based on the seven Regional Genetics and Newborn Screening Collaboratives funded by HRSA's Heritable Disorders Program—is just getting underway. The goal is to make the regional collaboratives part of a research network to facilitate research on the introduction of screening for new disorders, to establish registries of patients who are diagnosed with these disorders for their availability for treatment, and to test new treatment interventions through the capacities of this network.

Other NIH Institutes' Initiatives to Develop Treatments. NIH Institutes other than NICHD are also undertaking work related to newborn screening, primarily trying to develop treatments for disorders that newborns are not screened for yet. The National Institute of Neurological Disorders and Stroke has several treatments under evaluation for spinal muscular atrophy. The National Human Genome Institute has screening techniques for severe combined immune deficiency (SCID) and the Office of Rare Diseases supports a network of 10 centers in rare disease research, most of

which have some innovative treatment approach under study for disorders that could potentially become conditions for newborn screening.

VI. PUBLIC COMMENT SESSION

Two individuals made public statements to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children on the afternoon of Sept. 17, 2007. The full text of their statements appears in Appendix A.

1. Micki Gartzke
Parent & Director of Education & Awareness
Hunter's Hope Foundation

Ms. Gartzke said she hoped that the Advisory Committee would resolve its process issues related to reviewing nominations of conditions to the newborn screening panel quickly, so that it could consider the nomination of Krabbe disease in the very near future. She noted that the New York State newborn screening program began screening for Krabbe disease on Aug. 7, 2006, using a two-tiered approach with tandem mass spectrometry (MS/MS) and DNA sequence analysis. To date, the New York program has tested approximately 300,000 specimens for Krabbe disease and referred 37 infants for confirmatory enzyme analysis. Two infants have been diagnosed with Krabbe disease and undergone a core blood transplant. A third infant is currently undergoing a neurological exam to characterize the disease. A fourth infant is thought to have a later-onset form of the disease and is being followed by a physician and a neurologist.

Ms. Gartzke also asked for more consumer representation on the external Evidence Review Group (ERG) headed by Dr. Perrin. In addition, she suggested that the ERG clarify its definition of "burden of illness." She believes the definition should specify the burden to the child or medical system, not the family, because a child is never a burden to the family. Dr. Howell asked Ms. Gartzke to give her comments regarding the ERG to Dr. Nancy Green, so that she and Dr. Perrin could have them as they finalized the ERG proposal for the Advisory Committee's review.

2. Jill Levy-Fisch
Parent & President
Save Babies Through Screening Foundation

Ms. Fisch said that she thought the Advisory Committee's proposed process for evaluating conditions nominated for inclusion on the uniform newborn screening panel generally seemed fine and that she hoped that the Advisory Committee would move forward with it as soon as possible. One change she would like to see in the proposed process is more consumer representation on the external ERG headed by Dr. Perrin. In addition, she said she would like the ERG to clarify its definition of "burden of illness," adding that families do not like the term burden.

Ms. Fisch said that she was excited that Krabbe disease had been nominated for inclusion on the uniform newborn screening panel. She said she hoped that Krabbe disease would be added to the uniform newborn screening panel soon, so that newborns diagnosed with the condition could receive transplants. She also would like to see secondary conditions moved expeditiously to the core panel. Dr. Howell asked Ms. Fisch to give her comments regarding the ERG to Dr. Green, so that she and Dr. Perrin could have them as they finalized the ERG proposal for the Advisory Committee's review.

VII. 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 2:00 p.m. on Monday, Sept. 17, 2007. On the second day of the meeting, Sept. 18, 2007, each subcommittee gave a report to the full Committee, as discussed below.

A. Laboratory Standards & Procedures Subcommittee Report

Amy Brower, Ph.D.
Executive Director
Third Wave Molecular Diagnostics

Dr. Brower, chair of the Laboratory Standards & Procedures Subcommittee, reported that the subcommittee had had an active meeting the previous day and been joined by 12 advocates. She then summarized the presentations and discussions that had occurred at the meeting.

Update on the Subcommittee's Routine Second Specimen Study. Dr. Harry Hannon updated the subcommittee on progress with respect to the study of routine second screens for congenital hypothyroidism and congenital adrenal hyperplasia. As reported in May 2007, the Centers for Disease Control and Prevention's (CDC) institutional review board (IRB) determined that the proposed retrospective study is category IV exempt and that the prospective study may not be considered human research.

In recent months, efforts have focused on getting State-specific IRB approvals for the study. Unfortunately, progress has been slow. So far only 1 of the 16 States involved in the routine second specimen study has gained its IRB's approval for the retrospective study, and none of the States have gained their IRB's approval for the prospective study. The electronic data form for the study is almost complete, though, and data from Delaware, the one State that has gained IRB approval, will be used to pilot the form.

The Laboratory Standards & Procedures Subcommittee discussed the challenges in getting IRB approvals in the States and will continue to work with the States to obtain the IRB approvals for the second-specimen study. The subcommittee notes, however, that the difficulty in getting State IRB approvals is an important issue for future multisite studies.

Report on a Planned DNA Training Course for Newborn Screening Laboratory and Followup Team Members. Dr. Hannon and Dr. Megan Latshaw from the Association of Public Health Laboratories (APHL) discussed a 1-week DNA training course they are putting together for laboratory and followup team members. The emphasis is on DNA or molecular testing using cystic fibrosis as the test case example. The course is sponsored by APHL, CDC, and the National Newborn Screening and Genetics Resource Center (NNSGRC), with input from the Cystic Fibrosis Foundation. The four potential sites for the course are Wisconsin, Texas, Massachusetts, and New York. The projected start date is February 2008.

Update on FDA Guidance Relevant to Newborn Screening. Dr. Hausman reported that the Food and Drug Administration (FDA), in the realm of medical devices, had released analyte-specific reagent (ASR) guidelines on Sept. 14, 2007 ("Commercially Distributed Analyte-Specific Reagents (ASRs): Frequently Asked Questions"). These guidelines have potential implications for newborn

screening for cystic fibrosis and other DNA-based tests, which the Laboratory Standards & Procedures Subcommittee plans to investigate in depth.

The Laboratory Standards & Procedures Subcommittee also discussed the fact that there is only a single source of specimen collection paper for newborn screening. Dr. Hannon has worked with CDC to produce generic collection forms for emergency purposes.

Update on Newborn Screening Proficiency Testing. Dr. Hannon updated the subcommittee on the CDC program that performs quality assurance and proficiency testing related to newborn screening. CDC is working on an expanded panel focusing on 12 primary analytes. Many of these are not available commercially, so a CDC lab is synthesizing them. The subcommittee also discussed changes to the proficiency testing challenges in the American College of Medical Genetics/College of American Pathologists program.

Recommendations Related to Newborn Screening for Cystic Fibrosis (CF). Dr. Phil Farrell, who has been involved with the European Consortium and the Cystic Fibrosis Foundation, reported to the subcommittee on the state of newborn screening for CF. He explained that newborn screening for CF was recommended by HHS, CDC, and the Cystic Fibrosis Foundation in 2004, and the emphasis today is on preventing the symptoms of CF rather than treatment. Dr. Farrell estimated that by 2008, 90 percent of babies would be screened for CF—a big change from 2000, when only 10 percent were screened.

According to Dr. Farrell, one problem with the implementation of newborn screening for CF is that the testing algorithms and the mutation panels vary in different States. To address this problem, Dr. Farrell asked the Laboratory Standards & Procedures Subcommittee to consider the following recommendations: (1) specify a uniform mutation panel across all different states for the newborn testing that includes only CF-causing mutations (including Class IV and Class V mutations that in the past have been considered mild CF-causing mutations and including CF-causing mutations in minority populations) and excludes CFTR polymorphisms that are not disease causing; and (2) let the Cystic Fibrosis Foundation and CDC determine content of uniform panel; with the assistance of regulatory agencies and industry.

State Practices on Analyzing and Reporting Nonmandated Conditions in Newborn Screening. Colleen Buechner from the National Newborn Screening and Genetics Resource Center (NNSGRC) reported on an NNSGRC survey on State practices with respect to analyzing and reporting conditions that are not mandated in the ACMG uniform newborn screening panel. Forty-one of the 51 newborn screening programs surveyed responded to the survey, and 34 programs of these stated that they do report results for nonmandated conditions. In addition, 25 of the programs responding to the survey reported concerns about reporting tyrosinemia type I (TYR I), which causes severe liver disease and death if untreated.

Report of Increased Prevalence of Congenital Hypothyroidism. Dr. Marie Mann gave a report on the increased incidence of congenital hypothyroidism cases based on data from the NNSGRC, which was described in a recent article by Katherine Harris and Kenneth Pass [included under TAB #17 in materials distributed to Advisory Committee members]. The NNSGRC's director Dr. Brad Therrell is convening a workgroup to review this issue and will give an update to the subcommittee in January 2008.

Questions & Comments

Dr. van Dyck asked what concerns States had about TYR I that led some of them to remove it from their newborn screening panels. Dr. Brower stated that the format of the NNSGRC survey did not allow States to specify what their concerns were and that it would be important to do followup to find out.

Kathy Harris from New York and Colleen Buechner from NNSGRC reported that what led some States (e.g., New York) to remove tyrosinemia from their newborn screening panels were concerns about missing some cases of TYR I, because although the States were using dried blood spots to screen newborns for elevated blood tyrosine levels, tyrosine is not a specific marker for TYR I, and the programs were not screening them for succinylacetone, which is a specific marker for TYR I but not detectable via routine newborn screening. Dr. Green and Dr. Hannon added that some States (e.g., North Carolina) were also concerned about false positive rates, noting that elevated blood tyrosine levels are very common in some babies but do not necessarily indicate TYR I.

Dr. van Dyck pointed out that the nomination form approved by the Advisory Committee for nominating conditions to be added to the uniform newborn screening panel can also be used to nominate conditions that should be removed from the uniform panel. Dr. Howell agreed.

Dr. Watson suggested that the Advisory Panel might want to consider TYR I as a condition that should be re-reviewed in light of the problems reported in the NNSGRC survey. He noted that Dr. Piero Rinaldo and his colleagues have described a method of modifying succinylacetone to be run using tandem mass spectrometry newborn screening tests that would get at TYR I. Dr. Eaton said the succinylacetone method requires adding another injection and therefore raises economic questions. Mr. Bill Slimak from Pediatrix encouraged the Advisory Committee to consider the logistics of moving samples, stability of samples, capital investment, etc., in its deliberations.

Dr. Howell emphasized that it is important to screen for tyrosinemia because the condition is very treatable. He suggested that the Advisory Committee address the current state of affairs with the diagnosis of TYR I at a subsequent meeting. He noted that the Advisory Committee would also have to decide what to do about nominating the condition for reconsideration as a condition on the uniform newborn screening panel.

Finally, Dr. Howell expressed his belief that the informed consent issue in newborn screening research is going to be one of the biggest single things the Advisory Committee has to deal with. He said that the National Institutes of Health (NIH) has found it extremely difficult to get some newborn screening research programs going, because many State health departments have not been involved in research in the past, and the way they relate to research institutions with whom they partner is very complicated.

Dr. Lloyd-Puryear suggested that perhaps the Advisory Committee should try to work with the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) to see if the Advisory Committee could come up with some guidelines that would facilitate the process of gaining informed consent. Dr. Fleischman added that the HHS Office of Human Research Protection and the HHS Secretary's Advisory Committee on Human Research Protection might be assets in this conversation.

B. Education & Training Subcommittee Report

Gregory A. Hawkins, Ph.D.
Assistant Professor
Section on Pulmonary, Critical Care, Allergy, and Immunologic Diseases
Department of Internal Medicine
Wake Forest University School of Medicine

Dr. Hawkins, chair of the Education & Training Subcommittee, said the primary purpose of the subcommittee's meeting the previous day was to review and discuss three draft documents (included under TAB #10 in the materials provided to Advisory Committee members) that subcommittee members have been working on developing in recent months.

- **Subcommittee's newborn screening education and training communication plan (working document).** This is a document for the use of the Education & Training Subcommittee that outlines plans for working toward the subcommittee's goals for a newborn screening public education program directed to five primary target audiences: health professionals, affected families, screening program staff, hospital/birthing facility staff, and the public. In developing the plan further, the subcommittee will identify current education efforts and the most critical gaps in public knowledge, attitudes, and practices. Dr. Hawkins asked Advisory Committee members to read the plan and give the Education & Training Subcommittee feedback.
- **Subcommittee's proposal asking HHS to fund a study of the utilization of and response to newborn screening educational materials provided in the context of health care provider-parent interactions, along with a proposed study plan.** The Advisory Committee has not received any response to its 2006 letter to the HHS Secretary asking him to "develop and fund a mechanism to study the distribution of existing newborn educational materials and acquisition of knowledge about newborn screening by expectant parents in the context of the health care provider-patient relationship." The Education & Training Subcommittee would like to move forward with the proposed study as soon as possible, and in this document, it outlines specific methods, participants, and expected timelines for the study. The subcommittee has identified an expert in health care communications who is willing to work with it on the proposed study, so if funds for the study are provided, the study's results could be reported to the Advisory Committee in the fall of 2009.
- **Subcommittee's proposal to develop guidelines and a national repository for the translation of newborn screening educational materials in multiple languages and multiple formats**, paying close attention to health literacy, cultural diversity, and quality translation that is available for nationwide access. At the May 2007 meeting, the Education & Training Subcommittee proposed creating a repository where all seven Regional Genetics and Newborn Screening Collaboratives could access newborn screening educational materials in multiple languages and multiple formats. Having had discussions with Dr. Brad Therrell and Colleen Buechner at the National Newborn Screening and Genetics Resource Center (NNSGRC), the subcommittee now recommends modifying the Genetic Education Materials (GEM) database maintained by NNSGRC: [http://www.gemdatabase.org/gemdatabase/DetailedSearch.asp] to make it the proposed national repository. The subcommittee also recommends the development of criteria for depositing materials into the repository such as those used by California's Newborn Screening Program. To do additional planning for the repository and nail down some of the specifics, the Education & Training Subcommittee requests permission to hold a 1-day

working group meeting in the Washington, D.C., area with members from the Education & Training Subcommittee, Dr. Therrell and Ms. Buechner, and other invited members.

Questions & Comments

Feedback on the Subcommittee's Communication Plan. Dr. Howell asked Dr. Hawkins to specify a deadline for Advisory Committee members to give the Education & Training Subcommittee feedback on its newborn screening education and training communication plan. Dr. Hawkins set a deadline of Dec. 31, 2007.

- ***DECISION #7****: Members of the Advisory Committee are to review the Education & Training Subcommittee's newborn screening education and training communication plan and provide feedback to the subcommittee by Dec. 31, 2007.*

Proposal for a Study of Newborn Screening Educational Materials Provided in the Context of Health Care Provider-Parent Interactions. Dr. Howell indicated that if the study proposed by the Education & Training Subcommittee is in the purview of existing HHS existing agencies and the issue is simply a matter of funding, no formal approval for the study is needed from the HHS Secretary. Dr. Lloyd-Puryear and Dr. van Dyck said that if the subcommittee wanted HRSA or another Federal agency or group of agencies to undertake its proposal, it make that recommendation to the full Advisory Committee to get its approval.

Dr. Telfair asked whether the Education & Training Subcommittee had discussed performing an environmental scan to ascertain whether similar projects are already being conducted. Dr. Hawkins stated that the subcommittee was not aware of any similar study in which the materials are being evaluated in the same context that the subcommittee is proposing.

Dr. Watson noted that every subcommittee has vast information needs, so it is important that the Advisory Committee figure out how to prioritize requests for studies. How does this study fit in to the overall priorities? Dr. Boyle suggested that one mechanism for prioritizing research might be the Committee's new Workgroup on (Infant, Childhood, and Adolescent Genetics and Newborn Screening) Research, which Dr. Watson chairs. Several other Advisory Committee members agreed. Dr. Telfair recommended that Dr. Watson's Workgroup on Research look at a report by the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) that outlines how to go about prioritization of research issues. The report is online at the SACGHS Website [http://www4.od.nih.gov/oba/sacghs/reports/SACGHSPriorities.pdf].

Following this discussion, Dr. Howell directed the Education & Training Subcommittee to provide its detailed study proposal to HRSA, so that HRSA could circulate it electronically to the full Advisory Committee. He asked Dr. Watson and the Workgroup on (Infant, Childhood, and Adolescent Genetics and Newborn Screening) Research to begin to evaluate how the study fits in with the Advisory Committee's other research priorities and to report back to the full Committee. The Advisory Committee will then make a determination of how to proceed.

- ***DECISION #8****: The Education & Training Subcommittee will submit its proposal for funding a study on newborn screening education in the context of the health care provider-patient relationship to HRSA, so that HRSA can circulate it via e-mail to Advisory Committee members. The new Workgroup on (Infant, Childhood, and Adolescent Genetics and Newborn Screening) Research, chaired by Dr. Watson, will then help the Advisory Committee determine how the study fits in with its other research priorities.*

Plans for a National Repository of Newborn Screening Educational Materials in Different Languages. Dr. Howell authorized the Education & Training Subcommittee to proceed with the 1-day meeting in Washington, D.C., to plan the expansion of the GEM database to be the national repository for the translation of newborn screening educational materials in multiple languages and multiple formats. Ms. Terry reported that the Genetic Alliance, with funding from HRSA, has set up a repository with consumer and provider information. The repository is very flexible and very open and has a lot of capacity. It also has material in probably about 30 languages right now. It is run off some software called Digital Commons, which is what universities use. Ms. Terry also reported that the Genetic Alliance is developing its "Access to Credible Genetics Resources Network," which is building tools to assess whether or not information is worth depositing in a repository. Dr. Howell suggested including Ms. Terry in the 1-day meeting, and Dr. Hawkins agreed that this was an excellent idea.

- ***DECISION #9****: The Education & Training Subcommittee is authorized to proceed with a 1-day meeting in Washington, D.C., with a subgroup of subcommittee members, Dr. Therrell, Ms. Buechner from NNSGRC, Ms. Terry, and other invited individuals to plan the expansion of the GEM database to be the national repository for the translation of newborn screening educational materials in multiple languages and multiple formats.*

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, the chair of the Followup & Treatment Subcommittee, reported on the subcommittee's ongoing efforts related to long-term followup and treatment after diagnosis following newborn screening. She also reported on the subcommittee's efforts to ensure that families of children with metabolic conditions are able to obtain medical foods and formulas for their children.

Draft Paper on Long-Term Followup After Newborn Screening. As mentioned at the May 2007 meeting, the Followup & Treatment Subcommittee held an expert panel meeting in April 2007 to discuss the goals, definitions, and major components of long-term followup after newborn screening. Since then, the subcommittee and Dr. Alex Kemper have developed a white paper summarizing the consensus at the April meeting: "Long-Term Followup After Diagnosis Resulting from Newborn Screening: Statement of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children" (dated 9/12/07) [which was handed out to Committee members]. Dr. Boyle said that the Followup & Treatment Subcommittee would like the Advisory Committee to formally endorse the paper: The subcommittee also hopes to get the paper published in *Genetics in Medicine*.

According to the paper, the goal of long-term followup is to achieve the best possible outcome for children and their families. The definition of long-term followup is "chronic disease management, condition-specific treatment, and preventive care." The components of long-term followup are evidence-based treatment, coordination of care, continuous quality improvement, and new knowledge discovery. The concluding section of the paper states that the Advisory Committee's next steps will be to develop a roadmap for implementing long-term followup following newborn screening and diagnosis. Subcommittee member Dr. Alan Hinman guided the Followup & Treatment Subcommittee in thinking about roles and responsibilities of various sectors, including

families, the health sector (primary and specialty), and the public health sectors. The subcommittee is now developing a position paper on implementing long-term followup and hopes to bring something back to the full Committee at its next meeting in January 2008 meeting. It might first identify and analyze effective models in the public health sector.

Medical Foods and Formulas. As noted in May 2007, a subgroup of the Followup & Treatment Subcommittee is developing strategies to gather facts about insurance coverage for metabolic foods and formulas. The problem of variable and incomplete insurance coverage for metabolic foods and formulas is well known to the patient community and the nutrition and dietician communities, but there is no source of systematic data on what the gaps and needs are. Currently, therefore, the subgroup is concentrating on the development of a survey of families of affected children to get better information on their needs. The expert subgroup is helping to develop the survey. The survey will include focus groups of parents and be implemented in two regions. In addition to developing this survey, the another subgroup is gathering information about State legislation and its impact and evaluating existing professional policies and medical food requirements and the need for coverage of medical formulas and foods.

Questions & Comments

Several people made comments on the draft paper "Long-Term Followup After Diagnosis Resulting from Newborn Screening: Statement of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children"(9/17/07, v.2):

- **Goal of long-term followup**
    - Page 2, line 34: Dr. Watson said add "and their families" before the period after newborn screening.
- **Definition of long-term followup**
    - Page 4, lines 69-72: Dr. Watson said insert "counseling and social support services" here.
    - Page 2, lines 39-40: Dr. Anne Comeau from New England Screening Program Comeau said the definition of long-term followup, as stated, is simply the provision of care, and she believed that the definition should be the assurance of *good quality* care. For that reason, she proposed changing "the provision of chronic disease management, condition-specific treatment and age-appropriate preventive care" on lines 39-40 with "assurance of access to quality care and disease management." She thought that the definition needed to push people to thinking about this whole feedback loop of long-term followup. Dr. Boyle said there is a statement in line 42: "Integral to assuring appropriate long-term followup are activities related to improving care delivery, including continuous quality improvement through the medical home and research into pathophysiology and treatment." Dr. Carol Greene said the definition of long-term followup had been carefully wordsmithed in the spring meeting—and was worded not to say assurance of access to treatment. The second sentence is meant to include all those parts. Part of the consensus at the spring meeting is that *treatment*, not *assurance of access to treatment*, is part of the long-term followup of somebody with a positive screen. Dr. Dougherty said she tended to agree with Dr. Comeau, because one still gets the sense from the definition as worded that things may continue to be fragmented rather than all working together; by putting treatment in the definition, the subcommittee may have negated the other components of long-term followup that go beyond treatment—including coordination.

- **Components of long-term followup care**
    - Page 3, line 55: Ms. Monaco suggested removing "when appropriate" before "the patient's family." Other people noted that it was not possible to make this change, because the wording is part of a quote from the March 2007 consensus statement on the medical home adopted by the American Academy of Pediatrics, the American Academy of Family Physicians, the American College of Physicians, and the American Osteopathic Association, which is available on the Web at http://www.medicalhomeinfo.org/ Joint%20Statement.pdf.

    - Page 3, lines 57-60: Dr. Geleske stated that it is incorrect to say that a "medical home" can be provided through mechanisms other than a physician because the March 2007 consensus statement on the medical home, which is referenced at the top of page 3, specifies that every patient has a relationship with a personal physician and that the medical home is physician directed. Dr. Dougherty suggested that noting that families' preference may not always be to have a physician be the center of everything and that this topic was discussed by the subcommittee. Dr. Geleske stated that he would agree to changing lines 57-60 to say, "The medical home is often considered to reside within a medical practice and be physician directed, but additional care could also be provided through other mechanisms such a public health department and community-based organizations." Speaking from the audience, Julie Miller suggested saying: "Although the medical home is considered to reside within a medical practice and be physician-directed, a medical home could also be supported through other mechanisms, such as a public health department or other community-based service." Dr. Dougherty recommended that the Committee read the March 2007 consensus statement again before approving the paper, noting that it might be preferable to change the document to say that the medical home is a promising concept without referencing the specific definition in the joint principles.

Dr. Hinman, observing that the Advisory Committee supported the thrust of the paper presented by the subcommittee but had some concerns about how the medical home is referred to, suggested that the Committee approve the paper in principle pending revisions and final approval by telephone. Dr. Howell agreed that this was a good approach. Following some discussion, the Committee voted unanimously to approve the following motion:

- ***MOTION #2****: The Advisory Committee approves the paper "Long-Term Followup After Diagnosis Resulting from Newborn Screening: Statement of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children" in concept, with the understanding that the subcommittee will revise the document to address specific concerns raised at this meeting. HRSA will circulate the revised document by e-mail, and then schedule a conference call for the Advisory Committee prior to its meeting in January 2008 to review and vote on whether to approve the revised document.*

Finally, Dr. Kahn suggested that the Committee might benefit from presentations regarding the movement toward a patient-centered medical home, the promise of practice-based research networks, and the incorporation of evidence-based treatment and quality improvement into practices. Dr. Howell agreed that such presentations would be worthwhile, and Dr. Kahn said he would communicate to the Committee about presentations he thinks the Committee might learn from.

- ***DECISION #10:*** *Dr. Kahn will advise the Committee on presentations on the movement toward a patient-centered medical home, the promise of practice-based research networks, and the incorporation of evidence-based treatment and quality improvement into practice.*

VIII. FEDERAL LEGISLATION: AN UPDATE

Cindy Pellegrini
Associate Director
Department of Federal Affairs
American Academy of Pediatrics (AAP)

Ms. Pellegrini gave an update on the status of Federal authorizing legislation related to the State Children's Health Program (SCHIP). Labor, Health and Human Services, and Education (LHHS) appropriations bills, newborn screening bills, and other legislation of interest to the Advisory Committee. She noted that the AAP is working in strong partnership with many of the other organizations, including the March of Dimes, Genetic Alliance, American College of Medical Genetics, American College of Obstetricians and Gynecologists, American Academy of Family Physicians, Association of State and Territorial Health Officials, and others on these issues.

Authorization of the State Children's Health Insurance Program (SCHIP). Ms. Pellegrini stated that the health issue at the top of the congressional agenda was SCHIP—a program created to help states provide health coverage to low-income children. There are currently 9 million uninsured children, but SCHIP is in a very tenuous situation. When SCHIP was enacted in 1997, its authorization was set to expire on Sept. 30, 2007, and the program cannot continue with an expired authorization.

The House and Senate have each approved a SCHIP reauthorization and expansion bill, and a conference committee is working to resolve the differences between two versions. The conferees seem to be going with the Senate bill, which would provide SCHIP with about $35 billion more funding over the next 5 years and allow it to cover an additional 3 million to 4 million children. One reason the Senate version is being used as the model by conferees is that this bill passed the Senate by a veto-proof majority.

President George W. Bush has threatened to veto any bill with more than $5 billion in additional funding for SCHIP. Congressional leaders have said that they will send a SCHIP authorization bill to the White House by Sept. 30, 2007, but it appears that President Bush will veto the bill. In that case, there will probably be a short-term extension of the program, which is something no one really wants, least of all the governors and the administrators of SCHIP because it is almost impossible for them to continue this program effectively on a week-to-week and month-to-month basis. The situation is very fluid and changing day to day. Ms. Pellegrini encouraged Advisory Committee members to keep a close eye on it and engage in or support advocacy efforts if they could.

Labor, Health and Human Services, and Education Appropriations. The Federal funding process is well underway. The House passed an LHHS appropriations bill in July 2007. The Senate Appropriations Committee has produced an LHHS bill, but the full Senate has not acted on it yet.

Both the House and the Senate bills reject the cuts in the Administration's proposed budget for LLHS ($7.6 billion below last year's funding level) and, in fact, would increase LHHS funding

appropriations. The House bill provides for about $147 billion in LHHS appropriations—an increase of $4.3 billion over last year, but still $2.9 billion below FY '05. The Senate bill provides $9 billion over the President's request.

Furthermore, the House and Senate bills would spare HRSA from a number of cuts proposed by the Administration. The Administration requested level funding for the Maternal and Child Health Block Grant; the Senate bill would also level-fund it, but the House bill would fund it at an increase of $57 million. The Administration proposed eliminating the universal newborn hearing screening program; both the House and the Senate bills restore the program and give it modest funding increases.

The Administration issued a formal veto threat of the House LHHS appropriations bill on July 17, 2007, and is saying that President Bush will veto any number of appropriations bills that are above the President's request. The White House has reportedly directed the secretaries of numerous cabinet-level agencies to send letters to Congress rejecting the increases in funding for their programs. The fact that HHS Secretary Leavitt recently sent a letter to Capitol Hill rejecting increases for Health and Human Services programs illustrates just how difficult this process is going to be. The fiscal year ends on September 30, but no LHHS appropriations bill will have been passed by then. In fact, it may be near to the end of the year before an LHHS appropriations bill is signed into law.

Newborn Screening Saves Lives Act. Two newborn screening bills—the Newborn Screening Saves Lives Act sponsored by Senator Chris Dodd (D-CT) in the Senate and the Screening for Health of Infants and Newborns (SHINE) Act sponsored by Senator Hillary Clinton (D-NY)—have been combined into a single package that has been introduced in the Senate. The new bill (S. 1858) has the same name as the Dodd bill—the Newborn Screening Saves Lives Act—and the Senate Health Committee hopes to mark it up in the next 4 to 6 weeks. S. 1858 would do the following:

- Authorize about $75 million in new newborn screening activities, which includes $5 million in grants for education and training of health care personnel and laboratory personnel, $15 million in State newborn screening grants (for states that have adopted or are in the process of adopting the uniform panel), and $15 million for the evaluation of newborn screening programs at the state level.
- Renew the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children (although it mistakenly refers to the Committee by its original name) for an additional 5 years of work and authorizes $1 million per year in spending.
- Establish a new online clearinghouse on newborn screening information which would include "current educational and family support and services information, materials, resources, research, and data on newborn screening," funded at $2.5 million per year.
- Authorize $5 million for the Centers for Disease Control and Prevention (CDC) to perform quality assurance in labs that do newborn screening, $15 million for an interagency group that would coordinate and expand surveillance and research, $10 million for grants for education of parents, families, and advocacy groups.
- Require a national contingency plan to be developed within 180 days for newborn screening continuity in the event of a public health emergency such as that that happened along the lines of Hurricane Katrina.
- Provide $7 million for the Hunter Kelly Newborn Screening Research Program to expand and coordinate research particularly on conditions that could be added to the panel in the future.

Other Bills of Interest. The Genomics and Personalized Medicine Act (S. 976), sponsored by Senators Barack Obama (D-IL) and Richard Burr (R-NC), has not seen any meaningful action to date. There are no additional cosponsors and no companion bills in the House.

In May 2007, Senator Obama had just obtained an amendment that was added to the Senate's Food and Drug Administration (FDA) reform bill that would require the Secretary of HHS to contract with the Institute of Medicine to study the overall safety and quality of genetic tests and report on that. There has been no resolution on this, because the FDA reform bill is still in conference negotiations.

The Laboratory Test Improvement Act (S. 736), sponsored by Sen. Ted Kennedy (D-MA) and Gordon Smith (R-OR), would provide for regulation of home-brew laboratory tests by the FDA. This bill has not seen any meaningful action to date. There are no additional cosponsors and no companion bills in the House.

The Genetic Information Nondiscrimination Act, which would prohibit discrimination on the basis of genetic information with respect to health insurance and employment, passed the full House (H.R. 493) earlier this year and seemed to have a great deal of momentum. Unfortunately, the Senate version (S. 358) is now is stalled in the Senate Health Committee. One Senator has a hold on this bill, and what the Senator is requesting would fundamentally change the underlying bill, so there is currently an impasse on the legislation.

IX. COMMITTEE BUSINESS—PLANNING THE COMMITTEE'S NEW RESEARCH WORKGROUP

Michael S. Watson, Ph.D., FACMG
Executive Director, American College of Medical Genetics (ACMG)
Director, National Coordinating Center (NCC) for the Regional Genetics and Screening Collaborative Groups

Dr. Watson reported that, at Dr. Howell's request, he recently agreed to chair the Advisory Committee's new Workgroup on (Infant, Childhood, and Adolescent Genetics and Newborn Screening) Research. The workgroup has not yet been formed, and Dr. Watson will be seeking the advice of the full Advisory Committee in defining its mission and priorities. He will also be seeking input from Advisory Committee members about how to integrate subcommittees' activities into what the workgroup is going to be doing.

The Research Workgroup will identify current and future research needs pertaining to infant, childhood, and adolescent genetics, as well as to newborn screening. Dr. Watson cited many examples to give a general sense of the vastness and the breadth of questions that arise around a research agenda around newborn screening and infant, child, adolescent genetics. There are enormous communication and information needs for many parties, including families, providers, public health authorities, and others.

When looking at a multiyear project like this, Dr. Watson said, he considers how to take advantage of where our health care system is going and how to we build an infrastructure and a set of tools today that actually fit into that and allow us to get at many of the kinds of questions that public health interests, private sector interests, and providers have. He believes that the health system will have to move toward an interoperable electronic health records, it is not going to be able to address the challenges it faces.

To develop the evidence base for newborn screening and genetic diseases, one of the most important things seems to be how to develop the infrastructure to do long-term followup of individuals found to have genetic conditions. It is going to take a different level of information to get at the evidence base about a disease than might be required by the State to document the outcomes from long-term followup programs of infants in newborn screening. What is needed is to build an integrated national information system.

The Research Workgroup will probably focus considerable attention on building the infrastructure to capture information that useful for national application for the greater good of the public in the United States. Dr. Watson believes that the development of an electronic information technology-enabled U.S. health system, a topic to be addressed by Dr. Greg Downing in his presentation on the HHS Secretary's Personalized Healthcare Initiative, will be essential to this effort. Information systems are being developed that allow for a number of people to participate in the delivery of information about outcomes, not just providers but families and public health authorities. Interoperable electronic communication systems between primary care providers, specialist providers in private or institutional environments, and State programs can help aggregate information that is going to be useful from a national perspective.

A number of players can help build an integrated newborn screening and infant, child, adolescent genetics data collection infrastructure. The Regional Genetics and Newborn Screening Collaboratives and National Coordinating Center have a head start in developing relationships between public health, primary care, and specialists that positions them well as a system to be able to contribute. HRSA, the National Institutes of Health (NIH) and the National Institute of Child Health and Human Development (NICHD), the Centers for Disease Control and Prevention (CDC), the States, and other organizations involved in newborn screening and infant, child, adolescent genetics can also help. Dr. Watson believes that it is important to consider models that try to integrate as many kinds of data as possible and meet the needs of as many of these entities as possible.

A number of challenges will undoubtedly have to be addressed in building an integrated data collection infrastructure. State sovereignty is an issue. What do legislation and other rules within States permit? Can a State share its dried blood spot repositories as national resources? How do we get through these institutional review board (IRB) issues that are individualized in every State and in institutions within States? Developing databases with standardized laboratory and clinical languages to permit electronic interoperability is going to be critical. There are also many systems issues to be addressed.

Given the vastness of the potential research agenda in newborn screening and infant, childhood, and adolescent genetics, Dr. Watson believes that one of the first things the Research Workgroup ought to do is figure out research is already going on so that resources are not wasted duplicating efforts. Dr. Watson has begun to look at what is already going on. NICHD, for example, is developing a national Newborn Screening Translational Research Network, as described by Dr. Alexander. CDC has a newborn screening translational research initiative too, as described by Dr. Hannon. The Institute of Medicine has a translational genomics committee that is beginning to look at the broader translational issues, and it will have a lot of recommendations about research agendas. These are but a few examples of all the work that is going on.

Dr. Watson plans to organize meetings with various entities to bring together people to discuss what is going on and what the gaps are. He will also try to ascertain what the major gaps are being identified in evidence-based reviews at the national level. In addition, he will seek input from the Advisory Committee's Follow-up & Treatment Subcommittee, the Laboratory Standards &

Procedures Subcommittee, and the Education & Training Subcommittee about what their major research interests are, what research gaps they face in moving ahead with their agendas, etc. Thus, various pieces of information will inform the Research Workgroup's proposed research agenda.

Finally, Dr. Watson identified three immediate tasks in organizing the Research Workgroup: (1) defining participants; (2) capturing research needs identified by the Advisory Committee's subcommittees; and (3) identifying knowledge gaps as identified by evidence-based reviews.

Questions & Comments

Dr. Dougherty asked what the purpose of the Research Workgroup is and how long it is expected to last. Dr. Watson responded that the Research Workgroup will help the Advisory Committee set priorities for research. Dr. Lloyd-Puryear added that the Research Workgroup's mission would be defined more explicitly by the full Committee. She explained that the Research Workgroup was constituted as a workgroup rather than a subcommittee because its mission is overarching.

X. GENETIC ALLIANCE

Sharon F. Terry, M.A.
President and Chief Executive Officer
Genetic Alliance

Ms. Terry explained that Genetic Alliance is an international coalition of about 600 genetic disease advocacy organizations that represent the interests of about 25 million individuals in the United States and other countries who are living with any of about 1,000 genetic diseases. Since the time of its founding 21 years ago with a HRSA grant, the Genetic Alliance has undergone a very dynamic evolution—moving from providing support groups for individuals with genetic conditions and their families to driving public agendas and research on genetic conditions. The organization has forged many partnerships with governmental, provider, nonprofit, and other organizations to achieve its goals. Its motto is: "How do we get to the place where we can shut the lights off and go home?"

A short time ago, the Genetic Alliance decided to undergo a paradigm shift—changing from a membership organization in which the Genetic Alliance was the hub to a network. The Genetic Alliance recently mapped its network and created an interactive map, so that you will soon be able to pick your organization, and pull it out so that the world spins all around you. Membership dues have been abolished, and organizations can now join the Genetic Alliance without charge.

One of the Genetic Alliance's major initiatives is the Web-based National Consumer Center for Genetics Resources and Services (NCCGRS), which was established recently with funding from HRSA. Developed using concepts like "The Long Tail," the NCCGRS is a consumer network center built on the principles of facilitating the sharing of information and resources and infrastructure by advocacy organizations, professional societies, universities, academic institutions, industry, and others.

The Genetic Alliance is very excited about the NCCGRS, which offers access to many, many open-access resources, including the following:

- **Disease InfoSearch** is a Web portal designed accessed through the "Disease InfoSearch" function on Genetic Alliance's Website [www.geneticalliance.org] to help patients,

caregivers, health professionals, and others easily locate and navigate the vast array of information on genetic disorders.

- **WikiGenetics** [http://wikigenetics.org/] is an open source, user-generated encyclopedia that provides information on human genetics for the lay public. It is run by Wikimedia, which also runs Wikipedia.
- **WikiAdvocacy** [http://wikiadvocacy.org/] is a free, interactive, reader-built guide to advocacy.
- **The Resource Repository** [http://www.resourcerepository.org/]is a Web-based repository for information aggregated from partners of the Genetic Alliance. The Genetic Alliance is very excited about this. The repository was built using a version of Digital Commons software, which allows organizations to upload their own information.

The NCCGRS also coordinates some very large programs of the Genetic Alliance that preceded the establishment of the NCCGRS:

- **The Access to Credible Genetics Resources Network** [http://www.geneticalliance.org/ws_display.asp?filter=atcg]. The Access to Credible Genetics Resources Network is funded through a grant from the Centers for Disease Control and Prevention (CDC), is a project in partnership with the University of Maryland, National Coalition for Health Professional Education in Genetics, FRAXA Research Foundation, and Parent Project Muscular Dystrophy. The goal of the Access to Credible Genetics Resources Network is to provide accurate information about rare genetic disorders for families and health care providers. The project has created three tools: (1) one that looks at what constitutes credible information; (2) a metric to rank the quality of evidence based information; and (3) a tool to help present that information.
- **Community-Focused Family Health History**. The Genetic Alliance, with funding from HRSA, has developed two booklets—"A Guide to Family Health History" (with family health history, folklore, genetics) and "A Guide for Understanding Genetics and Health"—that are designed to promote conversations about health within the family, translate family health history into health choices, healthy choices, and increase community involvement in health education. As discussed by Dr. van Dyck in his presentation, these tools are designed to be Web based and customizable for families. Copies of the booklets were distributed to Advisory Committee at the meeting.

Finally, Ms. Terry noted, the Genetic Alliance is working in the policy arena on issues such as discrimination in insurance and employment, genetic testing, lab services, Medicare reform, newborn screening, innovation, disease priorities, etc. On Sept. 20-21, 2007, it will hold a 2-day meeting, "Eyes on the Prize: Truth Telling about Genetic Testing," to propose solutions to advance the field of quality diagnostics and improve human health. About 200 people will be attending the meeting, including CEOs, all the major people involved in the government in terms of regulation and oversight of genetic testing, lots of policy think tanks, etc. Earlier this summer, the Genetic Alliance sponsored the Genetics Day on the Hill on July 10, 2007, and then held its annual conference on July 11-13th.

XI. GENETIC ALLIANCE PROJECTS RELATED TO CONSUMER PERSPECTIVES ON NEWBORN SCREENING

Sharon F. Terry, M.A.
President and Chief Executive Officer
Genetic Alliance

Ms. Terry reported that the Genetic Alliance is currently undertaking four HRSA-funded grant projects to develop increased knowledge of family perspectives that will assist genetic and newborn screening programs in planning for and supporting the constant involvement of parents and families. She and her colleagues then described the conceptual model for the studies, as well as the studies themselves.

Conceptual Model. In writing its proposals to HRSA for these studies, Ms. Terry reported, the Genetic Alliance recognized that the current "Information Age" requires models based on economic constructs that differ from those of our grandfather's "Industrial Age." The new models include open means of production, an abundance of information, networks and collaboration, organic and dynamic processes, win-win paradigm, and a demand from consumers for information at their fingertips that will start to drive the health care system the same way consumer demand has driven other "Long Tail" things like YouTube and iTunes.

In addition, the Genetic Alliance identified two distinct consumer perspectives in newborn screening in its proposals: (1) that of individuals affected by genetic conditions and their families ("advocates"); and (2) that of individuals who are unaffected by genetic conditions ("the general public"). Advocates appreciate the benefits of newborn screening tests that go beyond the medical model (i.e., testing only for conditions with treatments) and generally want the full use of all available technology. The general public is concerned about aspects of newborn screening such as "false positives" that may cause trauma to the family, carrier identification, and education. It is important to recognize the importance of balancing the interests and needs of both advocates and the general public.

Two Consumer-Focused Newborn Screening Studies. Two of the HRSA-funded consumer-focused newborn screening studies being undertaken by the Genetic Alliance are (1) a qualitative assessment focusing on the experience of families and professionals with respect to false-positive screens and carrier identification; and (2) a quantitative study of the public's awareness of issues inherent in newborn screening, how available it is, what is happening with the expansion of newborn screening, what is happening with followup, and changes in parental attitudes and responses with increased education about newborn of screening.

The qualitative and quantitative consumer-focused newborn screening studies are being run by the Genetic Alliance as a single project. Both studies engage a Consumer Task Force on Newborn Screening, a 10-member group which includes parents who have experienced a range of newborn screening outcomes (carrier identification, false positive screening, and typical/normal screening), as well as parents who have a child with a condition for which there is no medical treatment at this time, and parents whose child did not have access to screening for the condition she/he has. Both also have a National Advisory Council.

Qualitative study: experiences with false positives and carrier identification. For the qualitative assessment of experiences with respect to false positive screens and carrier identification in newborn screening, the Genetic Alliance is partnering with the University of Maryland. At Ms.

Terry's request, Dr. Carol Greene from the University Of Maryland School Of Medicine described the study.

Dr. Greene explained that the study would examine the impact of false positive screens and carrier identification on newborns and their families (including the psychologic, emotional, financial time spent) and on the newborn screening system (including the primary care physician, the public health laboratory or whatever laboratory does the screening). During the course of the 3-year project, the plans for the qualitative assessment of experiences with respect to false positive screens and carrier identification in newborn screening are as follows:

- *Year 1:* The project team will develop an annotated bibliography and conduct a combination of semi-structured interviews and focus groups in three States (Maryland, Georgia, and one other State to be determined). The goal is to identify issues and explore themes. Next the team will build a data collection instrument and pilot the instrument, using the semi-structured interviews and the focus groups. It will identify gaps in information and review its communication strategies.

- *Year 2:* The project team will use the data collection instrument to interview people who have either had a screen that was a false positive or had a child identified as a carrier as a result of newborn screening—control subjects who may not even remember the newborn screening process. It will also look at people who have experienced other sorts of false positives or interactions with the medical system. The team will also hold a Newborn Screening Conference

- *Year 3:* The project team will analyze interview results, and then use that information to identify problems and to develop models to resolve the identified problems in the newborn screening process. The results of this project will be used to develop models for improving newborn screening in the context of the medical home. The focus will be on developing communication strategies or system design that will minimize harm from false positives. The team starts with the presumption that there is substantial benefit from newborn screening and that any harms need to be minimized.

Quantitative study: public awareness and parental attitudes toward newborn screening. Ms. Terry explained that for the quantitative assessment of the public's awareness of issues inherent in newborn screening and the changes of parental attitudes and responses with increased education about this form of screening, the Genetic Alliance is partnering with the Genetics and Public Policy Center. During the course of the 3-year project, the plans are as follows:

- *Year 1:* The project team will prepare an annotated bibliography. It has already presented to the National Council of State Legislatures so that we can begin to educate the States about this project. The team will do a gap analysis and work to develop a survey instrument and consumer education models.

- *Year 2:* The project team will do a survey through a company called Knowledge Networks. A Newborn Screening Conference will be held to allow the broader community to participate.

- *Year 3:* The project team will create models for intervention for exchanging information related to newborn screening with parents and addressing the public awareness. It will develop a one-page checklist for primary care providers to use at the time of a positive screen and submit papers for peer-reviewed publications.

Two Other Newborn Screening Studies. Natasha Bonhomme, who is managing all of the Genetic Alliance's newborn screening projects, reported on the Genetic Alliance's two other HRSA-funded newborn screening projects.

Iowa Family Population Project. This project, headed by Kimberly Piper and Janet Williams, is focusing on populations who usually do not participate in the newborn screening system and trying to understand barriers to participation, and looking at systems that could help include these populations.

- *Year 1:* The project team will have health care providers, including members of AAP, ACOG, as well as members of the College of Chiropractic Medicine. They will be engaged to see how they and their patients can be better included in the newborn screening system.
- *Year 2:* The project team will convene an information and education committee to develop appropriate educational materials, as well as a communication plan specifically looking at how to include these populations that usually do not participate in newborn screening. In addition, the project team will convene a working group of parents from the American Indian, Amish, Sudanese communities, as well as parents of adopted newborns.
- *Year 3:* The project team will evaluate the distributed materials.

Newborn Screening Financial, Ethical, Legal, and Social Issues Project. This project is headed up by Sylvia Au in Hawaii and is being done in collaboration with the Western States Regional Collabortive, and the evaluation will be done by the RAND Corporation. The project team will conduct interviews with parents who have gone through false positive screens for congenital adrenal hyperplasia and congenital hypothyroidism, as well as with parents who have had uneventful newborn screens. Also, parents and future parents of newborns will be surveyed to evaluate materials to see exactly what those parents who have gone through in the newborn screening process, as well as those who really haven't even entered that.

Questions & Comments

Dr. Howell noted that a lot has been written about false positives, but it is usually not clear who did the counseling about the tests and the mechanism, so the results published are meaningless. Ms. Terry agreed. Dr. Kahn stated that family physicians were not included in Iowa study and that perhaps their omission was an oversight. Ms. Penny Kyler from HRSA said family physicians are included and they are also doing a project on hearing.

XII. HHS SECRETARY'S PERSONALIZED HEALTHCARE INITIATIVE

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. Gregory Downing reported to the Advisory Committee on the goals of the Personalized Healthcare (PHC) Initiative, a component of the HHS Secretary's high-priority initiative to expand the use of health information technology and electronic health records; about the activities of the PHC Workgroup formed under the auspices of the American Health Information Community (AHIC); and about the PHC Workgroup's plans to form a newborn screening subgroup.

HHS Secretary's PHC Initiative. The HHS Secretary's PHC Initiative has two goals:

- *Goal #1:* Link clinical and genomic information to support personalized health care.
    - Establish an interoperable public/private data partnership of networks to deliver information on individual medical outcomes and linking findings to genetic laboratory tests.
    - Establish a common pathway for data integration through electronic personalized health records.
- *Goal #2*: Support the appropriate use of genetic information.
    - Protect individuals from genetic discrimination.
    - Encourage policies and practices that provide sufficient protection to consumers that genetic test information is used only for their medical benefit.
    - Provide oversight of genetic testing to assure analytical and clinical validity.
    - Standardize across policies to federally funded databases of genetic information.

To achieve the first goal, a PHC Workgroup was established as one of several AHIC workgroups. AHIC is a public-private collaborative that sets priorities and oversees and/or endorses health information technology standards, certification, the National Health Information Network, and policies on a national level. It is supported through the Office of the National Coordinator for Health Information Technology within HHS. AHIC and the PHC Workgroup (as well as other AHIC workgroups) are Federal Advisory Committee Act (FACA)–driven committees and their activities are in the public domain.

Charges of the PHC Workgroup. 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.

PHC Workgroup's Activities. The PHC Workgroup makes recommendations to AHIC. To develop these recommendations, the PHC Workgroup first receives background testimony. It then determines whether further work should be done in a particular area. If more work is needed, a subgroup of the PHC Workgroup is formed to perform additional research and draft initial recommendations. The subgroup is constituted with workgroup members, senior advisors, and additional resources from communities of interest to the specific area of recommendations. It does not follow FACA requirements. The co-chairs of the subgroup present their recommendations to the PHC Workgroup for comment and discussion. Once the PHC Workgroup reaches a consensus on the recommendations, a letter containing the recommendations is drafted to the chair of AHIC, and the recommendations are presented at one of the AHIC meetings for full prioritization and approval before going into the standards development process.

In focusing on what was needed to support the vision of a consumer-centric system in which clinicians customize diagnostic, treatment, and management plans, the PHC Workgroup identified four perspectives as being important to the vision (consumer, clinician, researcher, health plan, and

payer), as well as four priority areas across these: genetic/genomic tests; family health history; confidentiality, privacy, and security; and clinical decision support.

The PHC Workgroup has made recommendations to AHIC to develop a PHC use case addressing genetic/genomic tests and family health history, and those recommendations have been accepted by AHIC. The PHC Workgroup will discuss confidentiality, privacy, and security, as well as clinical decision support, this Fall.

PHC Workgroup's Activities Related to Newborn Screening. Newborn screening was raised as an important category of genetic/genomic tests during the spring 2007 visioning and priorities-setting sessions of the PHC Workgroup. Members of the PHC Workgroup held informational discussions about newborn screening throughout the summer with the Federal agencies that are involved in this, as well nongovernmental entities that are active in newborn screening

The topic of fostering information sharing for newborn screening was first introduced for detailed discussion at the PHC Workgroup meeting of Aug. 17, 2007. Dr. Mike Watson from the American College of Medical Genetics (ACMG) and Dr. Marie Mann from HRSA gave outstanding presentations on the topic and convinced the PHC Workgroup to establish a Newborn Screening Subgroup.

The overarching goals for the PHC Workgroup with respect to fostering information sharing related to newborn screening are (1) to identify, develop, and encourage adoption of appropriate standards for instrument manufacturers and public health laboratories, and electronic health record vendors, to facilitate the interoperable exchange of newborn laboratory test results (including genetic, metabolic, and hearing screens); and (2) to ensure timely communications between the State public health laboratories and newborn nurseries doing screening and immediate followup and the primary health care professionals and specialists who are involved in the diagnosis, treatment, and management of these infants.

Newborn metabolic screens have different information needs than other genetic tests (e.g., the ordering provider is often different from the primary care provider; there is a need for followup and confirmatory testing; some positive screen results may require emergency intervention upon result reporting). Ultimately the interface with family history is going to be quite important for many of these conditions. Without the use of health information technology, gathering enough information to evaluate the natural history and evidence-based treatment protocols will not be possible. At the same time, there are many issues related to the privacy and security of health information technology. A report by RTI identified the aspects of newborn screens as having some important criteria and need for further study.

The PHC Workgroup is developing representation from a number of different communities in terms of providing input and testimony and ultimately developing recommendations. The next steps will be: 1) to form the Newborn Screening Subgroup with broad representation from the Federal agencies involved in health, InterMountain Healthcare, ACMG, public health laboratory organizations, academia, and advocacy communities; (2) to solicit widespread input on the development of recommendations from communities of interests; (3) to foster advances in standards development and implementation for specialty laboratory health information exchange; (4) to examine linking test results with clinical decision support tools; and (5) to leverage expertise and successes in AHIC recommendations and optimize use of resources.

Dr. Downing stated that he would like to establish a formal link between the PHC Workgroup and the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children.

The Advisory Committee could serve as a resource to the PHC Workgroup in developing recommendations, help disseminate materials, reach out to stakeholders, inform the PHC Workgroup of complimentary activities, and discuss potential pilot projects to demonstrate the utility of health information technology in the area of newborn screening.

Questions & Comments

Dr. Howell said that the Advisory Committee was extremely pleased that the PHC Workgroup and HHS Secretary have decided to integrate a lot of the newborn screening efforts into the PHC record. He said he was sure that all the members of the Advisory Committee and newborn screening community would be delighted to provide any help or information they could. Dr. Howell also noted that he would like to see the RTI report's comments about newborn screening. Dr. Downing replied that he would be happy to send him the relevant portion of the report.

Dr. Watson asked Dr. Downing to comment on the anticipated timeline for pilot projects. Dr. Downing replied that the first priority is defining the parameters of how information flows and where the standards needs are. Newborn screening is a bit of a hybrid between public health laboratories and primary care, and a use case may be needed. Once the problem list for the workgroup is identified, it will probably take 3 to 5 months for the first set of recommendations to come forward. The process for getting these recommendations prioritized and the standards development and aspects of certification into the vendor-based process will probably take about 14 months. Thus, the overall process from now to the endpoint of certification for vendors would be about 18 months. For the pilot projects, considerably more information will be needed (e.g., about what the current state of electronic information exchange is at state laboratories). Dr. Howell observed that some of the projects that come through the Advisory Committee might well be referred Dr. Downing as pilots projects.

Finally, Dr. Downing reported that the HHS Secretary would be releasing his Department-wide report on personalized health care shortly, and the report includes a very nice description of the Advisory Committee's work and how it contributes overall to improving the quality of care.

XIII. COMMITTEE BUSINESS

R. 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

Discussion of Materials Under TAB #17. Dr. Howell asked Advisory Committee members to discuss some materials included under TAB #17 of the materials in their notebooks: (1) an article by Katherine Harris and Kenneth Pass about the increased incidence of congenital hypothyroidism in New York State; (2) U.S. patents related to newborn screening; and (3) the current version of the Advisory Committee's standard operating procedures ("ACHDGDNC: Policies and Procedures for Operation and the Development of Recommendations for Screening Newborns and Children for Heritable Disorders and for the Heritable Disorders Program").

Article on increased incidence of congenital hypothyroidism. Dr. Brower reiterated that the Laboratory Standards & Procedures Subcommittee had briefly discussed the Harris and Pass article about the increased incidence of congenital hypothyroidism in New York State. Dr. Brad Therrell

would be convening a workgroup to work through the issues and to give the subcommittee an update at the January 2008 meeting. A report will be made to the full Advisory Committee at that time.

Information about patent issues in newborn screening. Dr. Howell explained that Dr. Harry Hannon had brought some patent infringement issues related to State newborn screening laboratories to the attention of the Advisory Committee. Apparently, some State Attorney Generals have advised their newborn screening laboratories that it would not be legal for them to provide data because of patent issues. Three U.S. patents have been involved: (1) a patent held by a group at the Pasteur Institute on the Connexion 26 gene involved in congenital screening for deafness; (2) a patent on the use of molecular hybridization and enzyme digestion that has to do with direct genetic analysis to detect sickle cell anemia; and (3) a patent on a method for interpreting tandem mass spectroscopy for the clinical diagnosis of genetic disorders [TAB #17 of materials distributed to Advisory Committee members]. Dr. Cary Harding, who works with the Oregon newborn screening program, explained that the problem the Attorney General raised in Oregon was not that the newborn screening program could not share data but that it could not share cutoff points because the cutoff points were patented.

Dr. Brower observed that the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) has recently been finalizing a position paper on patents that might be of interest. Dr. Howell asked HRSA to make sure that the paper was distributed to Advisory Committee members.

- ***DECISION #11****: HRSA will distribute the SACGHS position paper on patents to Advisory Committee members.*

Advisory Committee's standard operating procedures. Dr. Lloyd-Puryear explained that she had added a 4-year term limit for workgroup members to the Advisory Committee's standard operating procedures. She asked Advisory Committee members to make sure that the change was acceptable. She also asked subcommittee chairs to think about that and either reappoint their current members or ask for different subcommittee members. Dr. Dougherty requested clarification in the distinction between a working group and a subcommittee, noting that they have different appointment procedures. Dr. Lloyd-Puryear said she did not think that those changes were necessary, so long as the Advisory Committee was abiding by the Federal Advisory Committee Act (FACA). Subcommittees create their own procedures, and the Advisory Committee can decide whether a subcommittee comes under FACA or not.

Activities to Get Underway as Soon as Possible. Dr. Howell recapped some of the decisions made during the course of the present meeting about activities that were supposed to get underway *prior to* the Advisory Committee's meeting on Jan. 14-15, 2008:

- HRSA will move expeditiously to develop mechanisms for administrative review of nominations proposed for inclusion on the uniform newborn screening panel, so that HRSA can process the nominations for the two conditions already nominated (Krabbe disease and severe combined immune deficiency) and any other nominations that come in.
- Dr. Perrin and Dr. Green will submit a revised final document regarding the external Evidence-Based Review Group (ERG) and evidence-based review processes to HRSA as soon as possible. HRSA will distribute the document to Advisory Committee members and schedule a conference call with Committee members, so they can approve or modify the plan prior to the Advisory Committee's January 2008 meeting. Once the plan has been approved, HRSA will move expeditiously to establish the ERG.

- The Nomination Review and Prioritization workgroup of the Advisory Committee, which Dr. Howell created at this meeting, will get together to develop draft criteria for determining whether a nomination is ready for an evidence-based review and to make recommendations to the Advisory Committee about how to handle the prioritization of multiple nominations to the uniform newborn screening panel. Dr. Brower will chair the group, Dr. Piero Rinaldo and Dr. Howell will serve on the workgroup, and Dr. Nancy Green will serve as a formal consultant.
- Dr. Boyle and the Followup & Treatment Subcommittee will revise the white paper "Long-Term Followup After Diagnosis Resulting from Newborn Screening: Statement of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children" to reflect concerns identified by Advisory Committee members at this meeting. HRSA will distribute the revised paper via e-mail to Advisory Committee members so that they can review and comment on the paper. In addition, HRSA will organize a conference call with Advisory Committee members so that they can vote on whether to approve the revised paper.
- Dr. Hawkins and the Education & Training Subcommittee will submit the subcommittee's proposal for funding a study on newborn screening education in the context of the health care provider-patient relationship to HRSA, so that HRSA can circulate it via e-mail to Advisory Committee members. The new Workgroup on (Infant, Childhood, and Adolescent Genetics and Newborn Screening) Research, chaired by Dr. Watson, will then help the Advisory Committee determine how the study fits in with its other research priorities.
- The report of the Task Force on Oversight of Genetic Testing of the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) will be available for public comment in November. Dr. Brower encouraged Advisory Committee members to read it and comment on it during the fairly short public comment period.

Agenda Items Proposed for the Committee's January 2008 Meeting. Dr. Howell asked Advisory Committee members for suggestions for agenda items for the next meeting on Jan. 14-15, 2008:

1. Dr. Burton said she expects a flood of additional nominations of conditions to the uniform newborn screening panel by the January 2008 meeting and that people who submit those nominations are going to want know what that timeline for the consideration of their nominations is. For that reason, she suggested, a large amount of time at the January meeting should be devoted to figuring out how to process multiple nominations. Dr. Howell concurred, and the following was agreed to:
    - The Advisory Committee's newly appointed Nomination Review and Prioritization Subcommittee should therefore present recommendations regarding; (1) draft criteria for determining whether a nomination of a condition to the newborn screening panel is ready for an evidence-based review; and (2) how to handle the prioritization of multiple nominations.
    - Dr. Perrin and Dr. Green should give an update on the ERG and evidence-based review processes.
2. Dr. Kahn volunteered to help with presentations to the Advisory Committee on the movement toward a patient-centered medical home, the promise of practice-based research networks, and the incorporation of evidence-based treatment and quality improvement into practices. Dr. Howell stated that such presentations would be worthwhile.

3. Dr. Howell indicated that Dr. Susan Berry would be invited to give her scheduled presentation on the Inborn Errors of Metabolism Information System (IBEM-IS) of the Region 4 Genetics Collaborative at the January 2008 meeting.
4. Dr. Watson suggested that one agenda item at the January 2008 meeting be further discussion of issues related to screening for tyrosinemia. Dr. Howell agreed.
5. Ms. Sharon Terry suggested that the Advisory Committee devote time to or appoint a subgroup to engage in strategic thinking about the role and activities of the Committee in the future. Dr. Lloyd-Puryear suggested that the Committee first complete its work in developing the nomination and evaluation process for adding and removing conditions from the uniform newborn screening panel. Dr. Dougherty, observing that the process of revising the evidence reviews and evaluations will never end, said she thought it was possible to do both the evidence review and start the strategic planning. Dr. Howell said he agreed with Dr. Lloyd-Puryear.
6. Dr. Green suggested that the Advisory Committee, over the course of more than just one meeting, do some forward thinking about and develop recommendations to address issues related to performing research through State public health departments. On a related point, Dr. Boyle added that the Committee address the issue of informed consent and IRB-related issues for doing research and public health assurance work. Dr. Lloyd-Puryear suggested the possibility of a presentation from the HHS Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) or the HHS Office of Human Research Subjects Protection. Dr. Howell said he thought a presentation on these issues from the SACGHS on informed consent and IRB-related issues to the full Advisory Committee would be useful at the January 2008 meeting.
7. Dr. Watson, noting that Dr. Hannon had raised intellectual property questions from the perspective of public health laboratories, said that some intellectual property questions arise with respect to quality assurance diagnostic confirmation tests in the context of enforced exclusive licenses. He suggested that Dr. Jim Evans, the chair of the SACGHS Gene Patents Task Force, might be able to shed some light in this are. Dr. Howell agreed that it might be useful to have Dr. Evans give a presentation to the Advisory Committee.
8. Speaking from the audience, Ms. Julie Miller from Nebraska asked whether the issue of the monopolistic control of reagents or filter papers used in newborn screening was one that the Advisory Committee might address at some point. Dr. Harry Hannon, who has spoken about that with regard to filter papers, said the only thing to do is encourage other manufacturers of the product to submit and get approved for its use. The Centers for Disease Control and Prevention has been doing this. Dr. Alan Hinman added that the sole-source situation has affected vaccines, and the solution has been to develop stockpiles.

Calendar for the Advisory Committee's 2008 meetings. Dr. Howell asked Committee members to look at the calendar dates for upcoming meetings in 2008—Jan. 14-15th, May 15-16th, and Sept. 23-23rd—and indicate whether there were any problems with those dates. No one objected.

Finally, after asking whether there was any further business and getting no response, Dr. Howell adjourned the meeting at 1:58 p.m.

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

/s/ _____

R. Rodney Howell, M.D.
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

1. Micki Gartzke, Parent & Director of Education & Awareness, Hunter's Hope Foundation
2. Jill Levy-Fisch, Parent & President, Save Babies Through Screening Foundation

1. Micki Gartzke
Parent & Director of Education & Awareness
Hunter's Hope Foundation
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children
Sept. 17, 2007

Good afternoon, Mr. Chairman and ladies and gentlemen of the committee. Thank you again for the opportunity to provide public comments. As always, we are always very appreciative of this.

This morning I arrived full of enthusiasm, as I always do. I mean, I can't cheerlead enough for you guys. That's all I'll say. We're always looking forward to the progress that's being made by the work of everyone involved sitting at the table in the subcommittees because we know that the children and the families are desperately in need of an expanded newborn screening panel and all the benefits that that will bring.

This afternoon I find myself still enthusiastic, however a little bit tempered by some of this morning's discussions. As you know, we submitted the Krabbe nomination, which we were very excited and proud to do, and we're looking forward to helping these children as well as helping any children who might gain access to newborn screening by helping to forward the process in any way that we can, and we would like to continue helping in any way that we can. We appreciate all the work that you're doing in this area. Everybody is very hard working and busy, and Godspeed all the way around.

We are anxious about some of the process issues, and we hope that they will be resolved quickly.

I wanted to share regarding the Krabbe newborn screening, what's been happening in New York State. For those of you that received our nomination form, some of this information is on that nomination form. The New York State Newborn Screening Program began screening for Krabbe disease on August 7, 2006. Coincidentally, that was my birthday. They are using a two-tier approach consisting of tandem mass assay and DNA sequence analysis. To date, they have tested approximately 300,000 specimens. They have referred 37 infants for confirmatory enzyme analysis. Two infants have undergone a core blood transplant. A third infant is currently undergoing a neurological exam to characterize the disease. A fourth infant is thought to have a later-onset form of the disease and is being followed by their physician and a neurologist. There's additional information regarding their testing on your form.

I was encouraged to see the information about the Evidence Review Group and the processes that are being developed. I did have one thought on the draft template for the evidence review. Under the main Item 6, it said "main questions," and then listed there is the word "burden." I believe we would like to see a definition, if possible, of the word "burden" because this can take on many different meanings depending upon where you stand in this spectrum. I mean, is it the burden to the child? Is it the burden to the medical system, to the family, the burden of the treatment, or the financial burden? Because to a family, to use the word "burden" in conjunction with newborn screening, a child, whether they're sick or healthy, is never a burden to their family. So I was just hoping we could get a definition for that.

One additional concern I had is the limited perspective for the Evidence Review Group with just a single consumer. I know it's a very strong voice that is on the Evidence Review Group, but I'm hopeful that a broader approach might be considered to strengthen the consumer voice by potentially adding another consumer or two.

I am very hopeful that the process timeline that was discussed this morning for the Evidence Review Group will be able to come together quickly.

Finally, I hope that those whose diseases are currently found in the secondary panel will have opportunities to nominate these conditions to be reviewed for consideration to be added to the core panel. The children with these conditions need this type of support and help, and if there's anything we can do to help those who might be nominating, we would be grateful.

Thank you. Please continue with all your hard work because I know you all work very hard, and we appreciate everything. Godspeed.

2. Jill Levy-Fisch
Parent & President
Save Babies Through Screening Foundation
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children
Sept. 17, 2007

Good afternoon, everybody. Thank you for the opportunity, again, to provide public comments. In anticipation of this meeting, I was very much looking forward to hearing about the nomination form and process. My comments mirror Micki's in many ways, so I apologize for the redundancy, but based on what I heard this morning, the biggest concern I have regarding the nomination process is the obvious underrepresentation of consumers in the Evidence Review Group. The consumer perspective has to be broader than a single consumer. The process outlined by the Evidence Review Group looks satisfactory and we are hopeful that the issues discussed earlier today will receive swift resolution.

On the draft template of evidence reviews, a clear definition of "burden" is of the utmost importance, as leaving it as is leads to subjective interpretation and likely confusion on the part of the families. Also, as Micki said, families do not like to view their children, no matter what their conditions are, as burdens, and families may take exception to the use of this language.

I was excited to hear this morning that Krabbe disease has been nominated. Having had the privilege to spend time with transplanted children, I am hopeful this nomination will be approved expeditiously so that future affected children will have access to early identification and treatment so that they might have the quality of life of those I have met.

I would also like to close with asking the committee that the second tier of diseases, as Micki mentioned, be given the opportunity to be reviewed and moved to the core panel as there are children affected by these disorders and it's something that we do need to take into consideration.

Thank you for your time.