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

Summary of Fifth Meeting
July 21-22, 2005
Washington, DC

The Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children was convened for its fifth meeting at 9:05 a.m. on Thursday, July 21, 2005, in the Rotunda Ballroom at the Ronald Reagan Building and International Trade Center in Washington, D.C. The meeting was adjourned at 2:50 p.m. on Friday, July 22, 2005. In accordance with the provisions of Public

Law 92-463, the meeting was open for public comments from 1 p.m. to 2:00 p.m. on Friday, July 22, 2005.

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Executive Secretary

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Liaison Members Present:

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I. WELCOME, OPENING REMARKS

Rodney Howell, M.D.
Chair, Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
Professor of Pediatrics
University of Miami School of Medicine

Steven Smith
Senior Advisor to HRSA Administrator Betty James Duke, Ph.D.
Health Resources and Services Administration (HRSA)
U.S. Department of Health and Human Services (HHS)

Dr. Howell welcomed everyone to the fifth meeting of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children and introduced Mr. Steven Smith, who was speaking in place of HRSA Administrator Dr. Betty Duke, who was unable to be present. at the meeting. Mr. Smith, he noted, is a senior advisor to Dr. Duke and assists in all aspects of the agency's management, including budget oversight, policy development and program administration. From 1980 to 2001, he worked at the Administration for Children and Families.

Mr. Smith brought greetings from Dr. Duke and thanked the Committee for providing a great public service to DHHS and the Nation. He expressed particular thanks to Dr. Howell for serving as chair and Dr. van Dyck and Dr. Lloyd-Puryear, who have kept Dr. Duke and the Secretary of Health and Human Services well informed about what the Committee has been doing.

He noted that HHS has more than 200 advisory committees, and HRSA alone has 16 advisory committees. The Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children is one of the preeminent committees. HRSA needs the experience, good judgment, and advice of the Committee. Newborn screening is an area where science has advanced, and public policy has to keep up with it.

Mr. Smith said he said he knew the Committee would be considering public comments on the American College of Medical Genetics (ACMG) report, *Newborn Screening: Toward a Uniform Screening Panel and System*. HRSA looks forward to the Committee's review of the comments and to advising us. HRSA hopes the Committee's recommendations help HRSA (1) improve access to services, especially to the underserved, the most vulnerable populations; (2) ensure that services are high quality (science); and (3) make services culturally competent (e.g., health literacy considered in giving information to parents who have to make treatment decisions).

Dr. Howell thanked Mr. Smith and noted that there was a busy agenda for the 2-day meeting, so questions from the audience would be permitted only during the official public comment period:

- **Update and Committee discussion of the ACMG report on newborn screening**. Dr. van Dyck would begin with an update on the status of the ACMG report *Newborn Screening: Toward a Uniform Screening Panel and System.* The Secretary of Health and Human Services is awaiting the Committee's comments and recommendations on the ACMG report so the Committee would be spending a considerable amount of time on that.

- **Update on the status of the states with respect to newborn screening by** Dr. Bradford Therrell, Director of the National Newborn Screening and Genetic Resource Center (NNSGRC).
- **Presentations on the role of evidence and other factors in public policy decision-making.** As a follow-up to the Committee's earlier discussions about the role of evidence and other factors in decision-making, several outside experts would make presentations related to this topic.
- **Presentation by the American College of Obstetricians and Gynecologists (ACOG) on newborn screening.**
- **Discussion of the Committee's three subcommittees' charges.** The Committee would discuss the charges of the Education & Training Subcommittee, the Follow-up & Treatment Subcommittee, and the Laboratory Standards & Procedures Subcommittee. Dr. Howell noted the Committee would defer further discussion of the subcommittees' charges until after the presentations on the decision-making process.
- **Subcommittee meetings and reports.** Concurrent meetings of the Committee's three subcommittees would be held on Friday, July 22, 2005, and would be open to public participation. Subsequently, the subcommittees would report on their plans and activities to date.
- **Public comments**. Members of the public would be given an opportunity to make statements to the Committee.

Approval of Minutes. Dr. Howell said the first item of business was the approval of the minutes from the previous meeting of the Committee held April 21-22, 2005. Dr. Boyle moved to approve the minutes, and the Committee unanimously voted to approve them.

Committee Correspondence. Dr. Howell drew Committee members' attention to two letters in the materials they received prior to the meeting. One was a letter he recently sent to HHS Secretary Michael Leavitt on behalf of the Committee. The Committee had not yet reviewed the final report at its January 13-14, 2005 meeting, Dr. Howell's letter said, but had unanimously recommended the following with respect to the disposition of the draft ACMG report: (1) that the final ACMG report to HRSA be sent to the Secretary of Health and Human Services under Chairman Howell's signature on behalf of the Committee; (2) that the final ACMG report be released into the public domain as soon as possible for review and comment; (3) that the Committee review, report, and make comments on the report as a Committee during the public comment period; and (4) that the Committee provide advice to the Secretary on the public comments received by the Secretary.

Dr. Howell also drew attention to a letter written to him by Dr. Howse, President, March of Dimes on July 8, 2005. Her letter raised questions about the proposed charges for the Laboratory Standards & Procedures Subcommittee. Dr. Howse said that she did not think that decisions about adding new conditions to the uniform panel should reside in any specific subcommittee. Dr. Howell asked Dr. Brower to briefly discuss proposed modifications to the charge of the Laboratory Standards & Procedures Subcommittee she chairs. Dr. Brower did this. Dr. Howell postponed further discussion of subcommittee charges until the afternoon of the first day of the meeting.

II. COMMITTEE BUSINESS—THE ACMG NEWBORN SCREENING REPORT AND PUBLIC COMMENTS

A. Update on the Status of the ACMG Report

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

Dr. van Dyck reported on the status of the ACMG report *Newborn Screening: Toward a Uniform Screening Panel and System.* In all, there were 187 public comments, including 155 submitted by the May 8, 2005, deadline and 32 submitted after the deadline. As the Committee had requested in April, Dr. Lloyd-Puryear sent each Committee member a set of the public comments, along with an alphabetized list of the individuals and organizations who commented on the report, about 6 weeks ago, so that Committee members would be able to review the comments and discuss them at this meeting.

The U.S. Department of Health and Human Services (HHS) has begun its internal review of the ACMG report and public comments with Federal agencies that are affected or have programmatic responsibilities related to newborn screening. HRSA, the agency with primary responsibility, will take all the information it has gathered related to newborn screening and will review that information and send its recommendations to the Secretary. The plan is to move as expeditiously as possible, but the time frame will be months. The mechanism, by which the recommendation to the Secretary will emerge, Dr. van Dyck explained, is still being worked out, but HRSA will probably draft a report, and then have Federal agencies comment. HRSA will share the outcome with the Committee once it has HHS clearance.

B. Committee Discussion of the ACMG Report and Public Comments

Rodney Howell, M.D.
Chair, Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
Professor of Pediatrics
University of Miami School of Medicine

Dr. Howell said he thought the public comments on the ACMG newborn screening report were extremely thoughtful. The vast majority said the report was very good too; some were focused on newborn screening for immunodeficiency etc; and a small number of comments were not supportive. Dr. Howell said he believed it would be helpful to discuss the issues raised in the comments that seem to call for Committee action to improve the process of making recommendations related to newborn screening. Committee members agreed that this was a good approach. Dr. Boyle added that perhaps the Committee should also consider which issues might be specific to the Committee's three subcommittees.

Issues Raised in Public Comments on the ACMG Report That Call for Committee Action to Improve the Process. Dr. Howell then proposed the following as a preliminary list of areas that he thought the Committee should take on as its task to move the report forward and asked Committee members for their comments:

1. The need to consider newborn screening for immunodeficiency disorders
2. Cutting edge technologies for newborn screening—their development and validation, method of implementation, etc.
3. The need for a broad approach to long-term follow-up, data collection and analysis, methods of diagnostic confirmation and presumptive tests
4. How to get findings from newborn screening back to the medical home and how to facilitate affected individuals back into adult care
5. The need to develop much better treatment for disorders identified via newborn screening
6. The need to evaluate health systems and perform outcomes research to ensure better functioning of the newborn screening system and related health systems
7. The need to educate families, professionals, and the public about newborn screening and related issues
8. The need for new and better screening technologies to include timing of screening; spectrum of diseases; ethical, legal and social issues; privacy issues; the sharing of patient data; other areas, storing of samples, etc.
9. Public policy decision-making related to newborn screening

Dr. Howell asked Committee members for comments on the following recommendations that the Committee might make:

- 10. There should be a uniform panel of newborn screening tests that all states should do. Having variation among state screening programs is scientifically unsound, as well as deadly for babies of families in certain states.
- 11. States must retain strong oversight over newborn screening programs. Newborn screening is a public health issue, and regardless of whether the screening is done commercially or in a state lab, states must have oversight over screening programs to make sure that they are consistent.
- 12. There should be a national quality assurance program for newborn screening.

Dr. Telfair recommended adding the following two items to Dr. Howell's list:

13. Access to health care—the need to look at health systems in terms of access from the consumer's perspective

14. Literacy—the need to translate information into an understandable way for the general public

Dr. Dougherty stated another item: 15. Issues raised by the state health departments or the Association of State and Territorial Health Officials (ASTHO) and the labs about financing for screening and cost-effectiveness analysis.

Dr. Howell noted that copies of recent, *ASTHO Issue Report, Financing State Newborn Screening Systems in an Era of Change,* had been distributed to Committee members. Dr. Becker said he did not think that state officials felt the report was compelling enough to be considered a blueprint for national policy—and he suggested that Committee needs to engage state health officials as important partners in advancing newborn screening and the adoption of the uniform panel.

Dr. Edwards suggested assigning each of the 15 or so topics in the list of proposed topics to one of the Committee's subcommittees, to a working group, or to the Advisory Committee as a whole. Dr. Howell said he thought working through the list would be an agenda item for years but agreed that the Committee might assign topics to subcommittees.

Inviting a Nonvoting Representative of ASTHO to Participate in the Deliberations of the Committee. Dr. Becker suggested that perhaps the Committee should consider ASTHO Executive Director Dr. George Hardy's request in September 2004 that a state public health policy level person be added to the Committee. Dr. van Dyck noted the Committee's charter specifies how many members are allowed, and the Committee membership is full right now. People can propose additional Committee members when people turn over, but decisions about who becomes a member rest with the Secretary of Health and Human Services.

Dr. Howell asked Dr. van Dyck to comment on how the Committee might involve state health officials. Dr. van Dyck said there are at least two ways that state health officials might be involved: (1) Committee members could propose to Dr. Howell state health officers who would be appropriate to serve on the subcommittees; and (2) subcommittees could hear from state health officers in the deliberations of the Committee. In response to a question from Dr. Boyle about whether state health officials could be liaison members of the Committee, Dr. Lloyd-Puryear explained that state health officials could be "nonvoting representatives, appointed by specific organizations. They can be part of the Committee's deliberations and the organization must cover the representative's travel and other costs.

Several Committee members agreed that it made sense to ask ASTHO to send a nonvoting representative to the Committee. Dr. Rinaldo suggested that other organizations also might be invited to send a nonvoting representative. Dr. Alexander replied there might be others the Committee wants to invite, but that shouldn't interfere with the Committee's action on ASTHO. Dr. Howell agreed that state health departments are such a critical aspect of newborn screening that beginning with ASTHO seems like a good idea. Dr. Becker made the following motion, and the Committee passed it unanimously:

> ***MOTION #1: The Committee recommends that the Association of State and Territorial Health Officials (ASTHO) be invited to send a nonvoting representative to participate in the Committee's deliberations.***

Dr. Edwards suggested that each subcommittee consider other organizations that should have nonvoting representatives at the Committee and recommend them to the Committee. Dr. Howell agreed to this.

Drafting a Letter to the Secretary of Health and Human Services Regarding the ACMG Newborn Screening Report and Public Comments on the Report. Dr. van Dyck reminded the Committee that it still needs to send a letter to the Secretary in which it makes a formal statement about approving the ACMG report and commenting on the public comments on the report. Dr. Howell agreed and indicated that he would like to have the Committee discuss what points should

be in the letter to the Secretary so that a letter could be drafted by him and Dr. Lloyd-Puryear, then circulated to Committee members for their review.

Dr. Howell explained that his intention was to draft a letter saying the Committee had read all the public comments on the ACMG report, and having read them, would recommend that the Committee focus in several identified areas to respond to these comments and for future direction for the Committee. Dr. Telfair remarked that it would be helpful in putting the letter together to agree on the key content areas. Dr. Howell and other Committee members agreed.

Several Committee members made additional suggestions for the letter. Dr. Alexander stated that most of the public comments on the ACMG report were positive and clearly endorsed a uniform newborn screening panel that should be done in all states. The concerns raised in the public comments, he said, fell into two broad categories:

- *Concerns about the process for identifying conditions* to be included on the ACMG uniform newborn screening panel, given that there is limited evidence and the need to come to some kind of decision. Despite the criticisms of the process, most people did not quarrel with the outcome. The presentations to the Committee on making decisions with limited information will help the Committee be in a better position to respond to these criticisms.
- *Concerns about the consequences of implementing the uniform newborn screening panel.* One area of concern that needs to be addressed above and beyond what is in the ACMG report is the need to ensure that a process for doing follow-up (confirmation of diagnosis, counseling, and care) is in place before massively expanding newborn screening. Other areas of concern that need to be addressed pertain to physician preparation, parental education, and ensuring that funding is in place to provide equitable access to newborn screening.

Perhaps, Dr. Alexander suggested, the Committee could assure the Secretary that these issues need to be addressed above and beyond what is in the report and that the Committee intends to address them. Dr. Boyle agreed, stating that she thought that the Committee's letter to the Secretary should be fairly general and state that the Committee is using what it learned from the public comments to help it evaluate its decision-making processes and future agenda.

Dr. Becker replied that the Committee would probably move past the report before HHS completes its internal process, but as part of the process it must attend to a few routine activities, the public comments.

Mr. Robertson recommended that the Committee's letter advise the Secretary about how the Committee believes public comments related to things such as the issue of scientific validation and process affect the report, saying something like: "The Committee recognizes these issues, but we do not think it detracts from the core ACMG newborn screening report, so we still recommend the report." He reminded the Committee that the ACMG report was not its (the Committee's) report.

There was a long discussion of what the letter to the Secretary should say. Some Committee members agreed that most of the public comments on the ACMG report sent to HHS were favorable with respect to the report and supportive of a uniform newborn screening panel." Dr. Rinaldo said he thought most of the negative comments missed the point that the main focus of the ACMG expert panel was to articulate general principles and develop a uniform newborn screening panel. Dr. Hawkins and Dr. Becker agreed. Dr. Dougherty expressed some concerns

about the evidence base underlying the recommendations that the ACMG uniform panel be adopted by every state.

Dr. van Dyck agreed with Mr. Robertson, saying the Committee ought to consider how the public comments affect the Committee's overall opinion of the report and its recommendations. Dr. Rinaldo said that rather than looking at the comments one by one, the Committee should assess whether the criticisms change the core conclusions about the uniform panel. Dr. Brower suggested that the letter say that the public comments do not change the 29 conditions and secondary conditions based on these comments, but do change how we act in the future. Dr. Dougherty agreed - the letter could say that the Committee has heard these concerns and has taken several steps to improve things (e.g., inviting a representative from ASTHO and whatever the Committee decides to do following the presentations on making policy decisions when evidence is meager).

Dr. Howell agreed to this plan. He noted, however, that the letter should say that the Committee is going to support the ACMG report and will be working on some of the concerns raised in the public comments in its future work.

Dr. van Dyck emphasized that the Committee had to make some recommendation to enable Dr. Lloyd-Puryear and HRSA staff to draft the letter and distribute it to the Committee for further input. He added that the letter should highlight no more than five or six issues. There were several suggestions about what these issues should be. Dr. Becker said he thought that the Committee's list of subcommittees identified the primary issues. Dr. Edwards suggested highlighting as one point issues not addressed in the ACMG report. The Committee then made a list of these areas, which included the following:

- Concerns about the methodology used by the expert panel (to be listed first)
- Management issues: partnering with the medical home, transitioning into adult care, new and better treatments
- Financing issues, including the cost of newborn screening expansion and treatment
- Cutting-edge technologies: their development, validation, and implementation of new technologies and new applications of existing technologies and new areas of clinical utilization
- Approach to long-term follow-up and data collection and analysis
- Methods of diagnosis and confirmation of presumptive diagnosis
- Need for evaluation of health systems and outcomes research, improvement of newborn screening and related health care systems
- Education for families, professionals, and the general public
- Research: better and new screening technologies, incidence and spectrum of diseases, ethical and legal issues
- Privacy issues: sharing of patient data, consent and refusal, storage of samples, etc.
- State policy-setting processes
- Quality assurance
- Public health oversight

- Whether the newborn screening will be mandated or just be a recommendation

Dr. Robertson recommended that the Committee say that the public comments do not take away from the report's central findings or recommendations. Dr. Howell agreed. Dr. Van Dyke said that during lunch, the staff would make a separate list of the issues raised by Dr. Howell

Dr. Howell said the Committee would return to discuss its letter to the Secretary of Health and Human Services about the ACMG report and public comments on the report after it had heard the presentations from experts on the role of evidence and other factors in decision-making.

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

Bradford Therrell, Ph.D.
Director
National Newborn Screening and Genetics Resource Center (NNSGRC)

Dr. Therrell gave an update on newborn screening activities in the states, referring to two handouts. The first of the handouts was a two-page "U.S. National Screening Status Report—Updated 7/12/05" (which indicates the status of each state in terms of screening for the core 29 conditions and the secondary conditions identified in the ACMG newborn screening report.

The second handout of maps and graphs presented by Dr. Therrell showed growth in the number of states screening for specific conditions from May 2004 to June 2005. Considering what is universally available, either by mandate or universal option, currently 6 is the lowest number of disorders screened by New Hampshire, although several other states are close to that number in their screening panel. Some states have screening for 10 to 19 disorders universally available. The lower numbers of screened conditions seem to be in the Mountain States and in the South. Two states have screening for 23 to 25 disorders universally available. Four more states screen for 26. Five more do 27. Thirteen more do 28. Nine other states do 29 disorders, but only 2 of them actually mandate all 29 conditions recommended by the ACMG expert group. In the maps and graphs, screening for MCADD (medium chain acyl-CoA dehydrogenase deficiency) is used as an indicator of 12-14 other disorders screened by tandem mass spectrometry (MS/MS).

A graph of the percentage of newborns screened for various conditions in the United States as of June 2005 indicated that the percentage of newborns screened for all 29 conditions in the ACMG uniform panel is at least 60 percent, with the exception of the percentage screened for cystic fibrosis (now 33 percent).

NNSGRC asked states whether they had changes in their newborn screening programs in the past 6 months they wanted to report. Dr. Therrell stated their responses:

- California began mandated screening for all 15 MS/MS conditions and CAH (congenital adrenal hyperplasia) on July 11, 2005. It does not screen for biotinidase or cystic fibrosis and also has no legislative mandate for hearing screening.
- Colorado has mandated the full scan of MS/MS disorders and expects the screening to be implemented in spring of 2006.
- Connecticut added 13 more MS/MS conditions in January 2005, so it currently screens for the full panel. This state also is screening for cystic fibrosis, but it is not mandated.

- On January 3, Georgia added MCADD, PKU (phenylketonuria), HCY (homocystinuria), MSUD (maple syrup urine disease), and (TYR) tyrosinema and changed over to MS/MS. In late June, the state changed its rules to say that a sample is valid after 24 hours instead of 48 hours. Georgia is one of five states still without a fee but is developing a fee structure.
- Iowa began screening for cystic fibrosis in mid-July; I It is now the second state to mandate all 29 conditions in the ACMG-recommended uniform panel. The lab has courier service and is operating 24/7. It uses its fees to support various services and expects an increase in 2006.
- Kentucky is adding disorders in a stepwise fashion. It mandated the addition of CAH, biotinidase, cystic fibrosis, and the full scan MS/MS in March 2005, is adding CH (congenital hyperthyroidism) in August, and MCADD in September. Kentucky has not yet mandated cystic fibrosis or (BIO) biotinidase deficiency.
- Michigan universally is piloting 11 additional conditions detected by MS/MS, so it has expanded its newborn screening panel to include 29 conditions as a pilot. It is working towards a fee increase to pay for the comprehensive program and services, and for cystic fibrosis.
- Minnesota has mandated screening newborns for cystic fibrosis, and anticipates start-up by Spring 2006. It is moving to a new laboratory facility in October 2005.
- Missouri added 20 disorders after a 5-month pilot of MS/MS plus BIO. In August, the $25 fee will increase to $50. The state's pilot of screening for BIO will begin late this year, and a cystic fibrosis pilot in 2006.
- Nebraska is one of 3 or 4 states that have a law which mandates screening without an option for dissent, and there have been challenges to that law, which the state continues to win. One lawsuit is over the right to dissent from newborn screening. The state supreme court recently ruled that the state has the right not to offer dissent. Another lawsuit filed in Federal court on grounds of religious discrimination has now been dropped. Nebraska expects to add screening for cystic fibrosis and CAH in January 2006. It is doing expanded screening by MS/MS as a free option, and 95 percent of the people are accepting that option.
- New Hampshire is the state with the least number of mandated disorders. An advisory committee recommended expanding the newborn screening panel to include disorders such as CAH, MCADD, BIO, Sickle Cell Disease and cystic fibrosis, but the state legislature did not approve it. A new law gives the commissioner and the advisory committee more power. If it is signed. the advisory committee will move forward and expand the program by next year.
- New Jersey currently does not mandate screening for 13 conditions detected through MS/MS but screens for them anyway as part of the differential diagnosis. It has a new law which requires that the state inform the parents about testing that is not mandated by the state and where the testing is available. The state has also changed its rules to say that a heel stick filter paper sample is valid after 24 hours instead of 48 hours.
- North Dakota is adding cystic fibrosis early in the fall and increasing its fee from $36 to $44. It follows the lead of Iowa NBS lab where the samples are sent
- Oklahoma added CAH and cystic fibrosis to its screening panel in February 2005.

- Rhode Island, though currently screening only for MCADD and amino acid disorders, is trying to expand to the 29 core conditions listed in the ACMG uniform panel by July 2006. They have an active program that looks at all newborns by day 6 to see who has been screened and who hasn't been, and then they track those babies without a screen to try to get them back in.
- South Dakota, which previously mandated screening for only three disorders, has expanded its rules to include a previously universal pilot for CAH, BIO, and Sickle Cell Disease and the MS/MS full scan. It sends MS samples to Texas, cystic fibrosis samples to Massachusetts, and a private laboratory provides the rest of the testing in-state.
- The Texas legislature finally has agreed to allow start-up funds for the expansion of newborn screening. The extent of the expansion will be determined in part by the fee structure. The current fee is $19.50 a sample, and they have authority to raise it to $36 a sample after they respond to a written review (October 2005) of its program by NNSGRC and perform an in-depth cost analysis by March 2006. When these conditions have been satisfied by the commissioner and the Texas Medical Association, Texas can expand the state's program, which is anticipated by October of 2006.
- Utah has begun a full scan MS/MS pilot using the local private laboratory, ARUP. It has a fee of $31, authority to go to $35, but will raise that figure to $65. Utah expects to be doing the full 29 conditions and secondary targets, CAH and BIO by January 2006. cystic fibrosis is not included.
- Virginia now screens for MCADD and the basic amino acid disorders, but is not screening for cystic fibrosis or doing expanded MS/MS. The Virginia Board of Health mandated screening to include the full ACMG uniform panel and the anticipated start is March 2006.
- Washington State's cystic fibrosis NBS advisory committee will recommend r cystic fibrosis to the Board of Health n October. .

Questions and Comments

Following Dr. Therrell's presentation, Committee members posed a number of questions. Dr. Edwards asked whether the changes in screening were occurring in response to the ACMG report or the March of Dimes recommendations or some other recommendations, or whether they just happened spontaneously even before the ACMG report was released. Dr. Therrell said that the ACMG report and the March of Dimes report card had definitely contributed. States were waiting for the ACMG report, which was released in March 2005. Dr. Rinaldo said he suspects that the acceleration began around 2002, when the ACMG/HRSA panel began to be developed.

Dr. Brower asked whether hearing screening, which is in a different database, should be brought into one central database. Dr. Therrell said that makes sense to him and that he had advocated for that. The problem is that the programs inside the state health department are often set up in two different silos, so the states report their hearing data to Centers for Disease Control and Prevention (CDC) and report their metabolic data to NNSGRC. Between 15 and 20 states actually collect their hearing data on the newborn screening metabolic form. Dr. Howell added that a per similar issue might arise in the case of congenital heart disease or Wilson's disease, where the time frame is not in the usual 24 to 48 hours.

Mr. Robertson asked about what the District of Columbia was doing. Dr. Therrell reported that it was screening for 10 disorders. D.C. has a contract with a private laboratory which offers expanded testing through the hospitals, so the testing is sort of at the option of the parents. . Dr.

Therrell said that he had heard that physicians may not know that their states do certain tests. Dr. Howell closed the session by commenting that the Education & Training Subcommittee has as much or more work to do with professionals as with the public.

IV. THE ROLE OF EVIDENCE AND OTHER FACTORS IN DECISIONMAKING

Dr. Howell opened this session by welcoming three speakers invited to give presentations to the Committee about various aspects of the question of how to make decisions on the basis of evidence and other factors—particularly when evidence is limited, as it is in the case of newborn screening because of the rarity of the conditions.

A. Evidence, Politics, and Technological Change

Bhaven Sampat, M.D.
International Center for Health Outcomes and Innovation Research (INCHOIR)
Columbia University

Dr. Sampat gave a presentation on the interplay between evidence and politics in managing technological change in medicine. His presentation was based on work done by his colleagues at Columbia University, Annetine C. Gelijns, Ph.D., and Alan J. Moskowitz, M.D. According to Dr. Sampat, industrialized nations are facing many challenges that stem from the remarkable medical progress over the past 50 years or so. Managing innovation is a formidable task. Decisions to adopt innovations are always made in context of considerable uncertainty about indications, populations, risks, effectiveness, and those sorts of things. Costly new technologies raise important economic questions and also trigger questions about whether a particular technology is the best way to spend our scarce health care dollars, although better empirical evidence about the costs and consequences of medical technologies can make policy decisions sharper and better grounded, translating analysis into policy is itself a highly difficult process. Three under examined challenges make transforming evidence into policy difficult:

- **Challenges inherent in the dynamics of technological change**. Many areas of medicine are characterized by extremely high rates of innovation. Furthermore, after new technologies are introduced into practice, the medical profession shapes and expands their application, as the case of CABG illustrates. Only 4 percent of patients who were treated with CABG today would have met the eligibility criteria of the trials that determined the surgery's initial value. Even cost-saving technologies can increase expenditures if they expand the size of target market. In addition, totally new and often unexpected indications of use are sometimes found, as in the case of alpha blockers. First introduced for hypertension, alpha blockers were found 20 years later to be an important agent in the treatment of benign prostate hyperplasia. The dynamics of technological change makes the questions and evidence base change, a situation that argue for ongoing assessments. Randomized clinical trials (RCTs) conducted in specialized centers with well-defined populations are used to permit hypothesis testing, but even if well conducted, RCTs have limits (e.g., short time horizon, questions about generalizability, costly to conduct). Consequently, regulatory decisions are made in a context of uncertainty—a situation that argues for post marketing studies with observational studies and practical RCTs. Funding for post marketing studies is limited, though, so considerable uncertainty will always remain about the value of many evolving technologies.

- **Challenges in using analytical policy tools.** Although regulatory decisions rely heavily on quantitative data, the acceptability of particular risk-benefit tradeoffs depends on value judgments. To illustrate, the heart failure drug Flosequinan was approved because it improves quality of life, but later was withdrawn because it was found to reduce survival; yet when the issue was presented to heart failure patients with very debilitating disease, 40 percent responded that they would accept a slightly higher risk of death to achieve a better quality of life. Similar issues arise in budgetary and reimbursement decisions where payers and advisory bodies, such as the advisory committees for Medicare and Medicaid, struggle with making tradeoffs between costs and benefits. These decisions increasingly are grounded in what's known as cost-effectiveness analysis—a technique for comparing the relative value of various clinical strategies typically in terms of quality-adjusted life years (QALYs) or the cost of an intervention per quality-adjusted life year saved. Cost-effectiveness analyses can encourage purchase of good value for money, but there are variations in how the evidence is operationalized (e.g., should cost-effectiveness ratios be used as strict thresholds or not?), as well as other challenges associated with the use of this technique (e.g., such analyses may not take into account whether the technology is established or emerging and whether the cost-effectiveness ratio is static or evolving).
- **The challenge of inherently political factors,** especially those dealing with the preferences of stakeholders, helps shape the translation of evidence into policy decisions. Even if there is enough evidence to do cost-effectiveness analyses, policymakers still must wrestle with conflicts of values and interests. Cost-effectiveness analyses, for example, may be insensitive to such important qualitative considerations, such as equity and distributive justice. For this reason, it is important that policymakers consider how to integrate qualitative considerations (e.g., the preferences of stakeholders) into priority-setting.

In sum, Dr. Sampat said, the difficulties in translating evidence into policy manifest themselves in a range of ways, including in the evolving applications of technologies, questions about the interpretation and extrapolation of evidence, and a wide variety of value judgments. He and his colleagues believe that these uncertainties and questions about the evidence base argue for a continued evaluation of technologies both in the pre- and post marketing settings. They also believe that the existence of a variety of value judgments also raises the question of institutional innovation, in particular the question of how policymakers, and society, should integrate myriad stakeholders into priority-setting.

Questions & Comments

Dr. Howell noted that in discussions of screening newborns for rare diseases, one of the issues that has surfaced is that such diseases are rare by definition, but once they are defined and once a treatment is available, all persons who appear with that are immediately treated. Thus, the need for developing a system for following all these children as a "post marketing" type strategy is going to be a very critical issue, because we are going to be learning more about the conditions over time.

B. Making Policy When Evidence Is Meager and in Dispute

David Atkins, M.D., M.P.H.
Chief Medical Officer, Center for Outcomes and Evidence
Agency for Healthcare Research and Quality (AHRQ)

Dr. Atkins gave an overview of systematic, evidence-based methods to evaluate screening, referring to a January 2005 *Health Affairs* article that he co-authored, "Making Policy When the Evidence is in Dispute." Dr. Atkins noted that that he had spent several years working as an internist and clinical epidemiologist with the U.S. Preventive Services Task Force, which wrestled with a lot of difficult screening questions in the midst of some heated political controversies. Policymakers often lack ideal evidence at the time they must make a decision, he said, but most debates about screening reflect differences in perspective, a values, political issues and resources rather than disagreement over evidence. According to Dr. Atkins, the requirements of an effective screening test are the following: (1) the condition has important health consequences; (2) the condition can be detected in the presymptomatic period; (3) there is an acceptable screening test with adequate sensitivity and specificity; (4) early intervention is more effective than treatment at the time of symptoms; and (5) the benefits of early detection outweigh any harms. But the real debate is how much benefit there would be and whether there are there any downside consequences of a screening policy, and how would you weigh those benefits and the downstream consequences to say whether screening is worth doing on a universal basis.

Public policymakers must integrate considerations of evidence, values, and resources in order to make a good decision, as a Muir Gray's figure with three intersecting circles labeled Evidence, Values, and Resources suggests. Noting that many public policy debates are manifestations of conflicting perspectives and values as much as disagreements over the evidence, Dr. Atkins recommended the policymakers systematically ask the following questions to help disentangle embedded issues of values, evidence, and resources:

1. **What is the outcome I value most?** Debates over evidence may reflect disagreement over the importance of different outcomes. In the case of prostate cancer screening, we screen because we think that screening will detect prostate cancer earlier, but we're really trying to reduce deaths from prostate cancer or the morbidity from advanced prostate cancer. There are other consequences of such screening (e.g., false positives and negatives, inconvenience), as well as adverse effects of treatment (e.g., impotence, incontinence, death, overtreatment). Different people will value these outcomes differently.
2. **How good is the evidence that the intervention can improve important outcomes**? One step in a systematic review of the evidence is looking at quality of evidence. A systematic review of the evidence is conducted to distinguish what is known from what is not known and thereby to facilitate decision-making. According to Dr. Atkins, such a review is especially useful when the evidence is poor because it allows you to separate good studies from bad ones. One misperception is that evidence-based methods are overly reliant on RCTs and thus set an untenable standard for evidence. The U.S. Preventive Services Task Force, which sets an admittedly high bar for evidence, made recommendations that were based on other types of evidence; it just scrutinized that evidence a little more closely. There is no one formula for what makes a good study; the formula varies with the topic. The highest quality literature within a body of published literature consists of the studies you can be most confident are giving a correct and unbiased answer. A systematic review of the evidence does not have to be quantitative or

exhaustive. A systematic review of the evidence should be explicit—in other words, to make the methods used explicit; avoid bias; distinguish intermediate from clinical outcomes; search systematically for relevant studies; consistently evaluate the quality of individual studies; and use transparent reasoning, reproducible results.

3. **How good is the evidence that the intervention will work in the real world?** This is another important question that is often overlooked in policy debates. Carefully controlled research studies often overstate the benefits of the intervention as it works out in real practice (what epidemiologists would call external validity). The reason they overstate the benefits is that the harms may be minimized because they are conducted in a carefully controlled setting where all the patients are getting the best tests. In the real world (e.g., in an overworked state screening program or an overworked pediatrician's office), things may be quite different (e.g., patients lost to follow-up, incorrect diagnostic tests, inappropriate interventions offered after screening). How applicable are the findings in this carefully controlled study to the question you really want to know, which is should we be doing this in the general population?
4. **How do potential benefits compare with the possible harms and costs of the intervention?** One of the biggest challenges once you have some evidence about how an intervention can work under ideal settings and some guesses about how well it's likely to work in the real world is deciding whether the potential benefits are large enough to justify the possible harms and costs (e.g., noneconomic costs, things like opportunity costs or diversion of resources). What is the real-world implication of telling every state to use a uniform newborn screening panel? How big are the benefits? What are the potential harms?
5. **What constitutes "good enough" evidence for a policy decision?** When people are debating about policy issues when the evidence is poor, they often are just saying they have different thresholds for that term "good enough." People's thresholds for what constitutes "good enough" evidence depend on what they value. Some people would rather act now even though there is not much evidence, whereas other people would rather not act until they are sure about what is going to happen.
6. **What other considerations are relevant?** The final question to consider is what other considerations are relevant. These include concerns of equity, cost, and feasibility.

To illustrate the application of this framework, Dr. Atkins used the example of universal newborn hearing screening, which he said was a difficult and controversial issue for the U.S. Preventive Services Task Force. At the time the U.S. Preventive Services Task Force looked at universal newborn hearing screening, it was clear from the evidence that you can detect hearing problems earlier by screening and those children with hearing problems should get into treatment earlier. In the case of newborn screening, one question that arose is what is the comparison? The benefits of universal screening were smaller if that strategy was compared to a strategy of screening high-risk infants. Also, the Task Force was concerned that the real world benefits were diminished by problems in follow-up testing and referral. Another consideration was that states often lack resources for follow-up. People's perceptions of the benefits of screening also differed. The task force cared primarily about language improvement, but parents valued the screening because it gave them information and allowed for social interventions.

What were the other considerations? Some people said screening should not be done unless resources for follow-up were available. Other people said the only way to get the resources was to start with the screening to show how big the problem is. Resource decisions are made at the state level, and states are financially strapped, so questions arose about how the recommendations were

going to play out in the real world: Was there going to be lots of screening and then no follow-up or would the resources for follow-up become available? The equity concern was another issue—there is something fundamentally troubling about the fact that what state you're born in seems to affect what you're screened for.

Dr. Atkins concluded by summarizing his key points as follows:

- Explicit approaches to evaluating evidence are useful, especially when the evidence is imperfect.
- It is helpful to clarify what you know at present and what you'd like to know to separate the issue of whether the parties involved are arguing about the evidence or arguing about issues of values and resources. Disputes often reflect legitimate differences in the perspectives of the different parties
- When considering whether the evidence is "good enough," Dr. Atkins said, it is helpful to consider the following: (1) the risks of waiting for better evidence (e.g., missed opportunities to help affected infants); (2) the risks of acting too soon (e.g., divert resources to ineffective intervention, possible harms); and (3) how good the probability of having better information in the near future is. Potential solutions to uncertainty included shared decision-making (although this is difficult in newborn screening); conditional coverage (e.g., lung volume reduction surgery for emphysema); individualized state polices (although such polices challenge notions of equity: and staged implementation.

Questions & Comments

Dr. Howell noted that the Committee's subcommittees would be considering what conditions to add to the uniform newborn screening panel recommended by the ACMG newborn screening report, and the first thing they will have to consider is how to examine evidence. He asked Dr. Atkins to comment on how in a systematic review of the evidence one gets around the problem of bias when experts are reviewing the evidence. Dr. Atkins replied that the critical thing is to be explicit ahead of time about what characteristics you are going to consider when deciding which studies are good quality studies. One way to do this is to have inclusion/exclusion criteria. AHRQ involves people with methodological expertise who are not invested in the outcome as experts, but it is also important to involve people who know the science.

Dr. Becker asked whether the Committee should do a retrospective, external methodological review of the ACMG report or just move forward and keep the methodological limitations in mind for the future as it considers the process for adding or modifying panels in the future. Dr. Atkins replied that this is a hard value decision. The Committee could say that the controversy is over a subset of these conditions, so we had better go back and take a closer and more systematic look at those conditions. The danger in just moving ahead, he said, is that the once you make a recommendation for 29 conditions in the uniform panel it is hard to drop 5 of those. Another option, if the Committee decides that it is better to move ahead, might be to set some clear say that although we are moving ahead, we do not know everything and would like to collect data on **"X"** from the states. That approach might make it easier to modify and add or remove conditions from the uniform panel if necessary.

C. Incorporating Evidence-Based Expert Opinion Into the Decision-making Process

John J. McCormick, M.D.
Deputy Director, Office of Orphan Products Development
Food and Drug Administration (FDA)

Dr. McCormick said that when people talk about "evidence-based expert opinion," he believes they are really talking about using experts in lieu of data. The questions are: How do we do that? And at what point do we give up on data and go to experts? Dr. McCormick offered the following tips and questions to bear in mind:

- **Data always trumps opinion.** The watchword at the FDA always is that data always trumps opinion, and I think that's not a bad sort of philosophy to have. The only difficulty with that is where do you get the data and how do you get the data?
- **Why is there no data?** The reason for a lack of data is frequently a lack of time and money.
- **Is the perfect the enemy of the good?** Academics and government sometimes spend so much time trying to make something just perfect, just right, that they never get around to doing it. It might be nice to have perfect data done in a double-blind randomized controlled trial (RCT), but if there is no RCT, we may be better off with the next best thing.
- **Risk/benefit.** Going to expert opinion as opposed to gathering data is a decision to give up on one form of evidence and go after another. The vast majority of decisions in medicine need to be and are done on a risk/benefit analysis. Most of us ask: What would the result be of a bad decision? But the one question that we need to ask a lot more is: What are the consequences of a bad decision, or more important the consequences of no decision?
- **Evaluate the expert.** When you go to an expert, you should evaluate what the expert knows and whether what he knows fits into where you want to go. You also need to know whether the person is intellectually honest enough to say, "I'm wrong," when he has strong beliefs and limited data. Some are expert because of exposure to data. Others are experts based on strong beliefs—and those you have to weed out. When FDA's Office of Orphan Products Development uses experts to determine the size of a population for an orphan drug for some of the rarer diseases for which data are not available, it accepts the opinion of 3 experts and requires its experts (1) to have no financial stake in the drug company; and (2) to indicate to FDA how they arrived at their decision. A couple of other things to evaluate are whether the expert has knowledge in an area that's similar to the problem you are dealing in and how generalizable is the information he has.
- **Why this conclusion?** Never take an expert opinion without asking the expert to provide a detailed analysis of the process used to come to his conclusions or recommendations. The ability to follow the expert's thought process is very important. Even if you don't have the knowledge the expert has, you can still see how the person arrived at particular conclusions.
- **Expert opinion/your decision.** Remember that it is the expert's opinion but your decision. Don't feel obligated to use expert opinion even when you ask for it. Your analysis of how the expert came to particular conclusions or recommendations is just as important as the conclusion.
- **Very few decisions are irreversible**. If you make decision that is troubling, the reasonable thing to do is specify a plan for obtaining additional information or follow-up data. In the case of newborn screening, you might want to see what the rate is of people with various

genetic diseases that you're turning up with these screens. Is it really worth it? If you are worried about pulling something back, you can sunset it. Vaccine recommendations change all the time, because the evidence that is available changes. Dr. McCormick said that his office has made a lot of mistakes making a decision on an imperfect set of data—and it doesn't have a hard time admitting them anymore. When evidence becomes clear, just say that you've done the wrong thing and will therefore try something else, hopefully with a better set of data this time.

V. COMMITTEE BUSINESS—THE PROCESS FOR MODIFYING THE UNIFORM NEWBORN SCREENING PANEL AND SUBCOMMITTEES' CHARGES

Rodney Howell, M.D.
Chair, Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
Professor of Pediatrics
University of Miami School of Medicine

Following a break, the Committee returned to discuss the following topics: (1) the process for modifying the uniform newborn screening panel recommended in the ACMG report *Newborn Screening: Toward a Uniform Screening Panel and System;* and (2) the charges of the three subcommittees established in January 2005—the Education & Training Subcommittee chaired by Dr. Howse, the Follow-up & Treatment Subcommittee chaired by Dr. Boyle, and Laboratory Standards & Procedures Subcommittee chaired by Dr. Brower.

A. Process for Modifying the ACMG Uniform Newborn Screening Panel

The first topic addressed by the Committee was the process for modifying the conditions in the uniform newborn screening panel recommended in the ACMG newborn screening report. Dr. Howell noted that for several conditions, there is recently defined, published or updated information about therapies that have been either very effective or partially effective, and newborn screening tests are in pilot phases in small groups, some states, etc.

Dr. Brower said what she heard during the earlier presentations on the role of evidence and other factors in decision-making earlier in the day was the importance of specifying parameters for assessing evidence ahead of time. Dr. Brower suggested having her Laboratory Standards & Procedures Subcommittee and the Follow-up & Treatment Subcommittee chaired Dr. Boyle identify the parameters they will use to evaluate evidence not only for the expansion of the uniform panel but also for evaluating follow-up data for the continued inclusion of the 29 and the secondary tests on the current panel, then submit these parameters for consideration by the full Advisory Committee.

Dr. Boyle replied that she had not envisioned her Follow-up & Treatment Subcommittee's having an explicit role in modifying the uniform newborn screening panel. She said the lesson she drew, both from Dr. Atkins' presentation and a suggestion from one or more of the ACMG report reviewers from the public comments was that one approach in going forward with the 29 conditions was to do more pilot testing, was *continued evaluation* as the expansion of newborn screening moves forward.

Dr. Howell agreed with Dr. Boyle, noting that although newborn screening has been around for many years, there really has not been a systematic mechanism for continued evaluations He added that one can make a very strong point for following up on some of the conditions that have been around a long time, as with phenylketonuria: We still don't really understand why there's such variability in outcomes of therapies and so forth. He said the notion of post marketing surveillance has been introduced for these children—and to have a system in place that would follow all these children scattered around the country, and resources to do that, would be a fairly big deal. He noted that Dr. Dougherty had raised the issue with him of the importance of having the Committee recommend that funding be made available, because simply telling states what they ought to do with respect to newborn screening and follow-up is not going to make things happen if the funds are not there.

Need for a Broadly Focused Group to Make Recommendations Regarding the Uniform Newborn Screening Panel. Dr. Edwards explained that the genesis of Dr. Howse's letter about the charge of the Laboratory Standards & Procedures Subcommittee was a telephone conference call among members of the Education & Training Subcommittee chaired by Dr. Howse. The members thought that some group beyond the Laboratory Standards & Procedures Subcommittee would have to be involved in scientifically evaluating the responses on the 29 conditions and looking at new tests—especially if the idea was to have a dynamic process of evaluation for new conditions and existing conditions in the uniform newborn screening panel. Possibly, Dr. Edwards said, the role of the Laboratory Standards & Procedures Subcommittee's role would be to oversee that entity.

Dr. Howell stated that he thought there was general agreement on the need to establish a group to make recommendations regarding modifications to the uniform newborn screening panel that would be much more broadly focused than the Laboratory Standards & Procedures Subcommittee. Dr. Brower replied that the members of her Laboratory Standards & Procedures Subcommittee concur that the full Committee, rather than the subcommittee, owns the evaluation and expansion of the uniform panel recommended in the ACMG newborn screening report. What the Laboratory Standards & Procedures Subcommittee believes it might do, however, is begin forming one or more working groups with the expertise needed to look at new screening panels using an approach that is agreed upon by the full Committee. The Laboratory Standards & Procedures Subcommittee could provide the structure and a draft agenda and proposal for moving the working group forward. Then the full Committee could evaluate what the subcommittee had proposed.

The Criteria and Process for Evaluating Old and New Conditions in the ACMG Uniform Newborn Screening Panel in the Future. Dr. Dougherty suggested a twofold approach to modifying the uniform panel going forward: (1) having some kind of group, working with the experts in evaluation research, to develop the criteria and a process for reviewing conditions for inclusion in the uniform newborn panel that would subsequently be approved by the Committee; and (2) applying the criteria to evaluate old and new conditions in the uniform newborn screening panel.

Dr. Rinaldo stated that the 19 criteria used in the ACMG newborn screening report could be used as the first step of an algorithm that determines whether conditions should be considered and evaluated for inclusion in newborn screening. This template could be modified to benefit from the feedback received via public comments and expertise on decision-making. In Dr. Rinaldo's view, the role of the working group Dr. Brower was proposing would be not to do all the work but to define the rules of engagement. Dr. Rinaldo said he thought that advocates—experts, people with vested interests, members of the public, and nonprofessional support groups—should be told that

if they believe they can make a case for certain conditions to be added to the uniform panel, they will be expected to provide specific things. There would be a review process to see if it's really the right time or the information is still not adequate.

Dr. Becker agreed that the template for the criteria for evaluations of conditions in the ACMG report—or some modification of that template on a couple of conditions—should be used as a starting point. He said he and Dr. Rinaldo thought that testing the new template, perhaps at the Committee's October 2005 meeting, would be a good idea. This approach would allow the full Committee to evaluate the criteria and process for reviewing conditions for inclusion in the uniform newborn panel, as Dr. Howse has requested. The Committee would be free to modify the template. Dr. Dougherty commented that questions in the survey (e.g., cost of the test, cost of treatment – is the treatment effective?) that were not in the algorithm. Dr. Howell and others replied that those items were included in the survey score.

Mr. Robertson said that if the Committee moved forward in this way, it would be ignoring some of the criticisms of the ACMG report, including criticisms of the survey. He recommended that the Committee look at the criticisms of the report and couple those with what the Committee had heard during the presentations on decision-making earlier in the day to develop a new approach to reviewing conditions for inclusion in the uniform newborn panel going forward.

Dr. Becker agreed with Mr. Robertson and said that combining information provided to the Committee on how to assimilate policy decisions when the evidence isn't randomized clinical trials (RCTs) and applying that information with the tool that was developed in the ACMG report could get the Committee to the point Mr. Robertson suggested.

Dr. Edwards said that one of the lessons of the presentations on decision-making was that the process of evaluating conditions for the newborn screening panel has to be dynamic. The process should permit the reassessment of data about old or already included conditions, especially when they are very rare conditions.

Asking Evaluation Experts for Advice on How to Modify the Process for Modifying the Uniform Newborn Screening Panel in the Future. Dr. Dougherty recommended that the Committee give the ACMG newborn screening report to Dr. Atkins and the other experts who had given presentations on decision-making earlier in the day and ask them about how to modify the process for selecting conditions for inclusion in the uniform newborn screening panel to make the process more evidence based. She said she thought the right questions were asked in the ACMG report but the approach was not reproducible.

Dr. Rinaldo and Dr. Becker supported Dr. Dougherty's idea. Dr. Rinaldo emphasized that the Committee should not ask the experts to look back to assess the validity of what was found in the ACMG report; rather it should ask them to look at the algorithm used in the ACMG report and give suggestions about how to improve it for the future. Dr. Howell said he agreed that it would be a good idea to have Dr. Atkins and other experts look at the ACMG report with a view toward improving the process for selecting conditions for the uniform newborn screening panel in the future.

Inviting an Expert to Discuss How the Advisory Committee on Immunization Practices (ACIP) Operates. Dr. Alexander noted that the ACIP's system for reexamining the timing of current immunizations and adding new vaccines into the armamentarium, and gathering additional data on existing ones seems to have many similarities to the process for adding and reevaluating conditions in the newborn screening panel and work fairly well. Thus, he

recommended that the Committee request a presentation from the ACIP at its next meeting. The Committee could provide some specific questions it would like the ACIP to address—for example, just what the ACIP does, what its procedures are, how it decides what to look at, what criteria it uses for considering new vaccines, revisiting old ones, etc. Dr. Edwards said that this was an excellent idea, because the ACIP seems to have a dynamic process that would be instructive for evaluating conditions for inclusion in a newborn screening panel.

Dr. Howell said that when the Advisory Committee on Heritable Disorders in Newborns and Children was structured, the idea was that the Committee could operate with subcommittees and working groups such as those used by the ACIP. He agreed that inviting a representative from ACIP to the Committee's October meeting was a good idea.

Discussion of the Public Comments on the ACMG Newborn Screening Report. Mr. Robertson asked whether the Committee was going to return to its discussion of the public comments on the ACMG report and address specific criticisms about the survey tool, about the report, etc. Dr. Howell assured him that the Committee would discuss the letter to the Secretary of Health and Human Services the following day and that the points that he had teased out earlier that day were generated by issues that were raised in public comments.

Asking Evaluation Experts for Advice to Review the ACMG Newborn Screening Report to Modify the Process for Modifying the Uniform Newborn Screening Panel in the Future. Dr. Boyle said that she was having a hard time trying to resolve the differences between the framework for the ACMG report that Dr. Rinaldo talked about and Dr. Atkins talk earlier in the day. She said perhaps Dr. Dougherty's suggestion of asking the experts in evaluation research to look at the framework that was used in the ACMG report might help her, or just moving the evaluation of old and new conditions in the uniform newborn screening panel into a more systematic process or a more transparent process. But she said she had a hard time thinking through actually what the Committee would do in taking that framework from the ACMG report. She said she was not arguing about the criteria; she was arguing more about how the evaluation was done—via a survey of experts. Dr. Boyle said that she thought what the Committee was going to do was to start with the evidence that was available, and then evolve from there and try to use the evidence around the criteria, but in a very systematic and transparent way, starting with the first thing, are there available tests? What does that mean? Define what that means. Maybe that's part of a nomination process that people have to go through to actually nominate new conditions for the panel.

Dr. Dougherty said that what she had been suggesting was to have the evaluation experts indicate to the Committee how the criteria might be addressed in a more systematic and rigorous way in future deliberations about modifying the uniform newborn screening panel. She said she wasn't sure about the timing of the process, whether the Committee should hear from the ACIP first or do the two things in parallel. Dr. Howell replied that he prefer to do both things at the same time rather than to stagger them.

Dr. Alexander stated that he thought that the survey of scientific experts that was used for the ACMG newborn screening report had served its purpose. The survey was the best that could be done under the circumstances to test expert opinion, and he would not quibble with the results or want to revisit the survey. A survey of the experts would not be the best approach to use in the future. The improved approach the Committee is talking about putting in place will be used not only to look at proposed additions to the screening armamentarium but also periodically to revisit the existing ones as well—get data, ask for more data to be collected, make sure that there are no

problems cropping up that need to be addressed. Dr. Alexander said that he would be comfortable with such a mechanism as long as there is an adequate oversight.

Dr. Dougherty said that she was not proposing reconfiguring the survey, just addressing the evidence. Dr. Howell said the Committee would consider that and added that another important issue the Committee members should also bear in mind was that it would need to have a mechanism for continuing input of the public and parents about newborn screening tests.

Dr. Rinaldo stated that he agreed with Dr. Alexander. The process for the ACMG report was really driven by the fact that there were 84 conditions that had to be considered at the same time. He thought it would be interesting to compare the outcome of what happened the first time with what happened the next time if a different process was used.

Dr. Howell concluded the discussion by saying the Committee would seek the opinion of evaluation experts about the ACMG report and move ahead with developing a process for modifying the uniform newborn screening panel in the future.

Comments on the Advisory Committee on Immunization Practices (ACIP) by Dr. Alan Hinman. Dr. Howell noted that one of the former leaders of the ACIP, Dr. Alan Hinman, was in the audience and asked him to make a few comments about the organization. Dr. Hinman introduced himself by saying that he had worked with the Centers for Disease Control and Prevention (CDC) for many years and for 10 years was in charge of the immunization program; he was at one time executive secretary of the ACIP.

The situations faced by the ACIP and the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children are not identical, but there are some nice parallels. According to Dr. Hinman, the ACIP started out about 40 years ago as a committee of 15 members who reviewed all the evidence and wrote all the recommendations about immunization practices themselves. Although the ACIP has become increasingly interested in explicit evidence-based approaches, 40 years ago there were a limited number of vaccines, and the evidence was fairly good. The Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children is coming into a much more complex situation. Dr. Hinman stated that currently much of the content work at the ACIP is done by staff, predominantly staff from CDC, but also people from the National Institutes of Health. A considerable amount of staff work goes into researching the issues, and drafting statements with members of the ACIP who form subcommittees or workgroups around particular topics. A recent statement on meningococcal conjugate vaccine, for example, was drafted by a workgroup consisting of members of the ACIP, other people who had expertise, representatives of the manufacturers, as well as CDC staff. It was then was reviewed and approved by the ACIP. The Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children does not have that level of staff support, and it is going to be very difficult for a committee that meets four times a year to resolve the issues being raised. Dr. Hinman suggested that subcommittees, workgroups, and other people would be needed to help resolve a lot of the methodological and content issues the Committee was addressing.

How the Committee Will Review Evidence Related to the Uniform Newborn Screening Panel. Dr. Howell returned to the topic of the decision-making process for the Committee, but asked Committee members to hold off with their comments on the subcommittees until later. He clarified that the subject was how the Committee would examine evidence. Among the general ideas, he noted, were that the Committee would look at evidence in a systematic way. There would be a series of questions to be asked prospectively about each of the issues.

Dr. Telfair stated that when the Committee considers what kind of evidence and the scope of evidence it wants to look at, it should broaden the evidence to include data related to programmatic implementation and issues, and consumer data. The full Committee, and particularly the Follow-up & Treatment Subcommittee, should also consider service data as evidence.

Dr. Howell asked whether anyone on the Committee was interested in pursuing issues related to cost/benefit analysis in any depth when considering whether to add additional tests to the uniform panel in the future. Dr. Dougherty said whether the Committee had decided to proceed with the process of asking evaluation experts such as Dr. Atkins to review the process, including the criteria, the weights, the method for collecting data used in the ACMG report and give some advice about how that could be improved for the future, in which case the experts might be asked to look at cost-effectiveness.

Dr. Howell said that he thought the Committee had agreed to ask Dr. Atkins and the other evaluation experts who had given presentations earlier to do this and to suggest improvements to the Advisory Committee. When asked, Dr. Atkins confirmed that he was willing to do review the process and suggest improvements at the Committee's October 2005 meeting. Dr. Howell assured Committee members that Dr. Atkins' reassessment would be to inform the process of making decisions about the uniform newborn screening panel in the future. He also said the Committee would get back to the letter to the Secretary of Health and Human Services about its comments on the ACMG report and public comments on the report on the following day.

Deciding Where Responsibility for Defining the Uniform Newborn Panel Should Rest. Dr. Howell then asked whether anyone else had anything more to say about the Committee's decision-making process. Mr. Robertson asked whether the issue rose in the July 8, 2005, letter from Dr. Howse in which she suggested assigning the responsibility of defining the uniform panel to a working group of the full Committee or a new subcommittee had been resolved.

Dr. Howell said that the topic had been discussed on the conference calls a good bit, and noted that Dr. Brower had discussed it when she talked about the Laboratory Standards & Procedures Subcommittee's charge earlier in the day. Although the Committee would be discussing the subcommittees' charges later in the meeting, Dr. Howell said, it might not come to a final conclusion on this until after it had obtained more information (e.g., about the ACIP model). Noting that the addition or removal of a condition from the uniform panel is of interest to the full Committee, Dr. Howell assured everyone although the process of adding or removing conditions from the ACMG-recommended uniform newborn screening panel might begin in a subcommittee, the final decision would not reside in any subcommittee.

Process for Nominating Conditions to Be Considered for Inclusion in the Uniform Newborn Screening Panel. Dr. Hawkins raised the issue of what process would be used for a person to request that a new test be evaluated or come to the Committee to be evaluated for inclusion in the uniform newborn screening panel? Who will make that request? Does that come from the Committee? Does it come from an individual? Does it come from a group?

Dr. Howell said that this issue had not been discussed and asked for Committee members' thoughts. Dr. Rinaldo said that he envisioned HRSA running the process of almost a call for applications. HRSA should develop the process for anyone who thinks a condition should be considered and then inform the public and the various professional organizations about the process. He added that he thought it would be great to try to start the process of considering conditions at the Committee's October 2005 meeting.

Dr. van Dyck said he thought recommendations should arise from several sources—get letters, have a public comment period to raise an issue, or the Committee may want to create a mechanism. Dr. Boyle said she sits on a committee (not a Federal committee) that evaluates reproductive hazards at the NIEHS, National Institute of Environmental Health Sciences, and anyone can nominate a particular chemical, drug, or exposure they consider might be a potential reproductive hazard. They can do this via email and just bring up that you're concerned about X, Y, and Z. Then a committee workgroup does a preliminary evaluation of the evidence, submits it to the committee, and the committee decides if a more formal evaluation is deemed necessary.

Dr. Rinaldo, noting that since the Committee would hopefully be getting an idea of improvements to the ACMG algorithm and criteria at its October meeting, suggested the possibility of posting a notice in the Federal Register that there would be an opportunity in the public comment period for people to nominate conditions for further review.

Dr. Coggins commented that whether a test or treatment is available changes all the time, so perhaps the Committee should have a standing agenda to review the tests that were identified but not adopted to see if a test or treatment is now available. . Dr. Howell said he thought this was a good idea, adding that tests for some conditions have been developed since the ACMG report was put together.

Dr. Howell also said that he thought the sense of the Committee was that it would take information or nominations of conditions from anybody who sends it from anywhere with no restrictions. He asked whether HRSA could put a notice in the Federal Register, and Dr. Lloyd-Puryear said yes.

Dr. van Dyck and other Committee members said they thought announcing anything in the Federal Register before there was a Committee-approved process in place to evaluate conditions was premature. They recommended that the Committee wait until it had approved and voted on a process. Dr. Rinaldo suggested developing a simple application form with questions about the availability of the test and the treatment. Dr. Dougherty said such a form should not be too burdensome to parents. Dr. Howell said he thought the form should ask two basic things: (1) Is there a reliable laboratory test available? – then have a reference; 2) Is there treatment available? – then have reference? It was agreed that Dr. Michelle Lloyd-Puryear would work with Dr. Becker and Dr. Rinaldo to develop a nomination form, which the Committee would review at the October meeting.

B. Proposed Charges for the Committee's Three Subcommittees

The materials handed out to Committee members in advance of the meetings included proposed charges for each of the Committee's three subcommittees established in January 2005—the Education & Training Subcommittee, the Follow-up & Treatment Subcommittee, and the Laboratory Standards & Procedures Subcommittee.

Charge of the Education & Training Subcommittee. In Dr. Howse's absence, Dr. Edwards presented the charge of the Education & Training Subcommittee to the Committee. Dr. Boyle asked what was meant by gaps" in the second bullet. Was the subcommittee talking about what Dr. Terry Davis said about there being a lot of materials available, but in terms of literacy level and from a health communication and education standpoint, are lacking. Dr. Edwards said yes, and Dr. Hawkins suggested changing the word "gaps" to "deficiencies," and Dr. Edwards agreed to this.

PROPOSED CHARGES FOR SUBCOMMITTEES—JULY 2005

A. EDUCATION & TRAINING SUBCOMMITTEE

Chair: Dr. Howse

Members: Dr. Edwards, Dr. Becker, and Dr. Hawkins

Proposed Subcommittee Charge (in briefing book July 2005)

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

Changes following Committee discussion:

- second bullet: change "gaps" to "deficiencies"

Charge of the Follow-up & Treatment Subcommittee. Dr. Boyle presented the charge of the Follow-up & Treatment Subcommittee. Dr. Brower, noting that this subcommittee is probably going to be evaluating whether or not there are treatments and whether treatments work sooner than they are published, asked if there was some way that subcommittee could share this information with other Committee members? She also asked if there was any plan in the subcommittee to start to foster clinical research in head-to-head trials of different treatments. Dr. Boyle said the subcommittee had not yet given much thought to treatment-related issues. Dr. Therrell confirmed that the subcommittee would have a fair amount of data on follow-up programs from the states and from a couple of HRSA-funded research projects.

PROPOSED CHARGES FOR SUBCOMMITTEES—JULY 2005

B. FOLLOW-UP & TREATMENT SUBCOMMITTEE

Chair: Dr. Boyle

Members: Dr. van Dyck, Dr. Dougherty, Mr. Robertson, and Dr. Telfair

Proposed Subcommittee Charge (in briefing book July 2005)

- Engage in a multistep process that
  - identifies barriers to short- and long-term follow-up of newborn screening (NBS) results specific to the challenges in integration of health care systems, financing of services and information technology
  - develops recommendations for overcoming identified barriers in order to improve short- and long-term follow-up of NBS results
  - recommends mechanisms for establishing accountability for NBS follow-up guidelines

Changes following Committee discussion:

- first bullet: change to "short- and long-term follow-up and treatment"
- second bullet: change to "and information systems"

Charge of the Laboratory Standards & Procedures Subcommittee. Dr. Brower explained that the Laboratory Standards & Procedures Subcommittee's charge was really about defining and implementing a mechanism for the periodic review and assessment of the conditions included in the uniform panel, the infrastructure services needed for effective and efficient screening of the conditions included in the uniform panel, and the laboratory procedures utilized for effective and efficient testing of the conditions included in the uniform panel.

PROPOSED CHARGES FOR SUBCOMMITTEES—JULY 2005

C. LABORATORY STANDARDS & PROCEDURES SUBCOMMITTEE

Chair: Dr. Brower

Members: Dr. Alexander, Dr. Coggins, and Dr. Rinaldo

Proposed Subcommittee Charge (in briefing book July 2005)

- Define and implement mechanisms for the periodic review and assessment of
  - The conditions included in the uniform newborn screening (NBS) panel
  - infrastructure services needed for effective and efficient screening of the conditions included in the uniform NBS panel
  - Laboratory procedures utilized for effective and efficient testing of the conditions included in the uniform panel
- Define and implement mechanisms for the periodic review and assessment of conditions included in the uniform NBS panel
  - Identify the criteria to be used by the Committee in recommending inclusion of a new condition in the uniform panel, and define the type of evidence that the subcommittee will utilize in making decisions
  - Establish ad hoc working groups comprised of people with the necessary expertise to evaluate tests, technologies, and benefits to the individual and society
  - Complete timely reviews
  - Provide assessment(s) to the Advisory Committee for consideration
- Define and implement mechanisms for the periodic review and assessment of infrastructure services needed for effective and efficient screening of the conditions included in the uniform NBS panel
  - Examples: sample collection, sample transport, result reporting to physicians and families, and referral for a confirmation of diagnosis and counseling
  - Establish a working group comprised of people with the necessary expertise to evaluate infrastructure services
  - Complete timely reviews
  - Provide assessment(s) to the Advisory Committee for consideration
- Define and implement mechanisms for the periodic review and assessment of laboratory procedures utilized for effective and efficient testing of the conditions included in the uniform panel
  - Establish a working group comprised of people with the necessary expertise to evaluate laboratory procedures, including nomenclature, testing strategies, cutoff values, reporting requirements, performance metrics, and case definitions
  - Complete timely reviews
  - Provide assessment(s) to the Advisory Committee for consideration

Changes following Committee discussion:

- *See text below and in Section VII.*

Several Committee members raised questions about the second component of the subcommittee's charge—"Define and implement mechanisms for the periodic review and assessment of conditions included in the uniform newborn screening panel." Dr. Telfair asked two questions: (1) Who will set the agenda in terms of what gets covered and what are the key questions to be answered?; and (2) Who would be the liaison for the working group if it is going to be made almost exclusively of those not on the Laboratory Standards & Procedures Subcommittee?

Dr. Becker said he thought that additional consideration was needed to determine exactly what process the Committee was going to use for the continuous assessment and the addition or modification to the uniform newborn screening panel—i.e., would this be a charge of one of the subcommittees or a workgroup, would the Laboratory Standards & Procedures Subcommittee provide structure, or would there be a process like the Advisory Committee on Immunization Practices (ACIP) centered around the full Advisory Committee Dr. Dougherty said she thought it would be a good idea to defer making a decision on that component of the Laboratory Standards & Procedures Subcommittee's charge until after the Committee had heard the ACIP presentation at its October meeting.

VI. AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS (ACOG)—NEWBORN SCREENING GUIDELINES

Anthony Gregg, M.D.
Director of Maternal Fetal Medicine
Medical Director, Genetics
University of South Carolina School of Medicine

Dr. Gregg, appearing on behalf of ACOG's Committee on Genetics, began his presentation by noting that ACOG is a group unified by its commitment to the health care of women. ACOG has between 40,000 and 50,000 members: including national and international fellows, physicians who are board certified in the field of obstetrics and/or gynecology; junior fellows, ABOG in approved residency training programs in obstetrics and gynecology; associate members, physicians recognized for their provision of valuable services in obstetrics/gynecology who have not gone through an approved residency training; educational affiliates who hold non-M.D. degrees and are active in some facet of ob/gyn); and medical students.

ACOG's four primary missions are: (1) to serve as a strong advocate for quality health care for women; (2) to maintain the highest standards of clinical practice and continuing education for its members; (3) to promote patient education and stimulate patient understanding of and involvement in medical care; and (4) to increase the awareness among the members of the college and the public on the changing issues that face women's health care.

ACOG has numerous committees, one of which is the ACOG Committee on Genetics. ACOG's Committee on Genetics, which has existed for several years, considers all aspects of genetics as it relates to reproduction, and develops appropriate recommendations regarding clinical management, education, and research issues. It has a formal liaison with other groups such as the American Academy of Pediatrics (AAP), the American College of Medical Genetics (ACMG), and the Teratology Society. It interacts with the Center for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH), as well as other Federal agencies, as needed.

The Committee on Genetics develops written opinions on newly emerging or rapidly changing issues in the field and responds to matters referred by other ACOG committees and groups. An ACOG committee opinions represents the committee's assessment of emerging issues in obstetrics and gynecologic practice and are reviewed regularly for accuracy. ACOG opinions are strictly guidelines. ACOG does not make policy statements or seek to establish the standard of care

The ACOG Committee on Genetics' first Opinion, issued in October 2003, was on newborn screening. That opinion, ACOG Committee Opinion No. 287, recognizes that newborn screening dates to the '60s with technology such as tandem mass spectrometry (MS/MS) and that the expansion of newborn screening programs must be considered. ACOG believes that when adopting national and statewide newborn screening policies, it is important to seek maximum sensitivity and specificity. There is a tradeoff between the false negative and false positive rates, so confirmatory testing is required.

The Committee on Genetics' Opinion goes on to recognize that in the absence of constitutional or Federal mandate for newborn screening, state statutes or regulations determine specifics related to newborn screening. Two states require parental consent for screening. Tests are specific depending on the state. The fees and the sources for the fees in these cases vary across states. The document recognizes that systems must be in place for adequate communication and treatment, and that these things do cost money. Technology is driving change, but the costs may prevent families from universal access to technological advances being considered. ACOG is also concerned that newborn screening with MS/MS may result in the identification of disease for which there are no effective treatments and that the identification of more disease entities will result in the need for greater follow-up, resulting in added cost without benefit.

Dr. Gregg noted that the ACOG Committee on Genetics' Opinion on newborn screening states that obstetricians should be engaged educating pregnant women about newborn screening. ACOG believes that educating health care providers about newborn screening is critical and that there is an education loop with information about newborn screening flowing between care providers, pregnant women, non-pregnant women, and families with affected children.

An important question, Dr. Gregg said, is when women should receive education about newborn screening. Each of the points at which education might be provided has advantages and disadvantages: (1) gynecologic care (recurrent, early age, but remote from time information might be necessary); (2) preconception counseling (patients are motivated and attentive, but few are present for preconception counseling); (3) early or late pregnancy (patients are motivated and attentive but often have distractions); (4) postpartum (patients motivated and attentive, but may be a vulnerable population for consent and often have distractions).

Dr. Gregg went on to discuss the ACMG report *Newborn Screening: Toward a Uniform Screening Panel and System.* ACOG believes that a major omission in the ACMG report was its failure to include obstetrician representation on the expert panel. Furthermore, ACOG is uncertain that obstetrician representation was integral in the survey of health care providers and consumers related to the importance of various features of the data collection instrument. Finally, ACOG notes that although five major areas were to be considered by the ACMG report, only one of these—the uniform newborn screening panel—was discussed extensively; the remaining four areas were discussed with much less vigor and focus. ACOG does believe, however, that the uniform panel in our opinion was very well thought out and extremely well done. The fact sheets in the report could be used as a rapid resource for obstetricians faced with specific questions posed by patients.

Near the end of his presentation, Dr. Gregg highlighted the overlap between the American Board of Obstetricians and Gynecologists and the American Board of Medical Genetics. He noted that many of the specific areas of education required by the American Board of Medical Genetics to receive certification in clinical genetics relate to issues being addressed by the Advisory Committee. In 2002, the American Board of Obstetricians and Gynecologists had about 33,000 active Diplomats, and 4 percent of them were certified as maternal/fetal medicine sub-specialists. That same year, the American Board of Medical Genetics had certified a little more than 1,000 people with clinical genetics certificates and 10 percent were people who were also obstetrician/gynecologists. Dr. Gregg said that since all generalist obstetricians consult with maternal/fetal medicine specialists when there are complicated pregnancies or genetic issues, it might be relevant to begin some of the training related to newborn screening among maternal/fetal medicine specialists.

Finally, Dr. Gregg showed Committee members a monograph entitled "Preconception and Prenatal Carrier Screening for Cystic Fibrosis," jointly put together and distributed by ACOG and the ACMG in October of 2001. He said he believed that this monograph could serve as a prototype for the education of care providers.

Questions & Comments

Dr. Howell asked Dr. Gregg what the current policy and practice is in the obstetrics community with regard to educating mothers about newborn screening. Dr. Gregg said he believes that most obstetricians are very busy in their day-to-day practices and don't spend much time educating mothers about newborn screening. On the other hand, he said he believes there is room for change.

Dr. Rinaldo asked Dr. Gregg whether the ACOG Committee on Genetics had given any thought to acceptable parameters for newborn screening sensitivity and specificity. Dr. Gregg said he did not think statistical measures were specified but that it was important that such measures be specified. Rinaldo also challenged Dr. Gregg's comment about adding costs without benefit and promised to send Dr. Gregg references, including a publication from Dr. James Filiano at Dartmouth. Finally, Dr. Rinaldo said he hoped the ACOG Committee on Genetics would do an opinion on the critical relationship with certain covert metabolic disorders in pregnant women caused by fact the fetus has a disease (e.g., between 15 and 20 percent of cases of acute fatty liver in pregnancy are caused by the fact the fetus has LCHAD deficiency).

Dr. Becker asked how the Advisory Committee might best engage ACOG to join in a partnership to get obstetricians/gynecologists more engaged in education of pregnant women about newborn screening. Dr. Gregg recommended that the Committee send a letter inviting ACOG to send a liaison person to the Committee.

Dr. Alexander asked whether the time of first and second trimester serum analyte screening (perhaps when results are delivered) might offer an opportunity to obstetricians to educate pregnant women about newborn screening. Dr. Gregg said he agreed that the times obstetricians are discussing the nature of serum analyte screening, the nature of first trimester screening using ultrasound markers, first or second trimester anatomy ultrasounds, would be opportune times to bring up newborn screening. This is what he envisions should take place.

Dr. Lloyd Puryear, noting that ACOG was pilot testing newborn screening parent brochures and educational materials for discussing newborn screening with parents, asked how the pilot testing had gone. Dr. Gregg said that they are in ACOG's executive committee waiting for final approval to be disseminated.

Dr. Howell underscored the importance of the educating pregnant women about the complete newborn screening panel recommended in the ACMG report before they give birth, especially in states with very meager screening programs. In some states, if parents have not planned ahead and ordered the materials, it will be very difficult for them to get the full panel of tests done. Dr. Robertson said he agreed that it is good to tell parents that once their baby is born it will be tested but added that parents might not remember much about what they are told at the time of ultrasounds. Dr. Gregg, noting that there are multiple time points and various levels of interest when pregnant women present He did not think there is one specific point when women should be educated about newborn screening that is right for all women

Dr. van Dyck asked whether ACOG had given any thought to recommending prenatal discussion of newborn screening at some point during the pregnancy as part of the written content of prenatal care, Dr. Gregg said that prompts exist for things such as glucose screening and ultrasound at a certain time and that adding another prompt to electronic or handwritten medical records to make sure people are doing what they need to do with respect to newborn screening would not be difficult. Dr. Gregg said he was not sure what the mechanisms for adding such prompts would be, but he guessed that multiple ACOG committees would have to be involved.

VII. COMMITTEE BUSINESS—SUBCOMMITTEE REPORTS

The Education & Training Subcommittee, the Follow-up & Treatment Subcommittee, and the Laboratory Standards & Procedures Subcommittee of the Advisory Committee held meetings that were open to the public from 9 a.m. to 11 a.m. on Friday, July 22, 2005. On Friday afternoon, the subcommittee chairs provided reports to the full Committee.

A. Education & Training Subcommittee Report

Acting Chair
Stephen Edwards, M.D., F.A.A.P.
American Academy of Pediatrics

Members:
William Becker, D.O., M.P.H., Ohio Department of Health
Gregory Hawkins, Ph.D., Wake Forest University School of Medicine

In Dr. Howse's absence, Dr. Edwards chaired the July 22, 2005, meeting of the Education and Subcommittee and therefore gave a report on that meeting. He noted that the subcommittee had had a productive session, with about 20 people other than the subcommittee members attending and contributing to the discussion. Much of the meeting was devoted to a series of presentations.

The first presentations to the subcommittee were from three professional organizations about their activities related to educating the public and health care providers about newborn screening:

- American College of Obstetricians and Gynecologists (ACOG)—Beth Steele and Anthony Gregg, M.D., ACOG Committee on Genetics
- American Academy of Pediatrics (AAP)—Amy Brin, Manager, Screening Programs, AAP Division of Children with Special Needs
- American Academy of Family Physicians (AAFP)—Norman Kahn, Jr., Vice President for Science and Education

All three organizations reported having a subcontract with HRSA's Maternal and Child Health Bureau to distribute educational materials for parents and professionals developed by Dr. Terry Davis and her colleagues. They also reported on their other educational activities. AAFP will be doing focus groups on who received their materials to learn about the impact of the program.

Following the ACOG, AAP, and AAFP presentations, several potential problems in educational efforts related to newborn screening were discussed. One point made was that it will take a good amount of time and multiple iterations to get the message about newborn screening imprinted on physicians—in fact, the most discouraging thing said was that it takes 10-12 years to get physicians fully incorporating new materials into their practices. For optimum communication with parents, the obstetrical community will have to be involved in educational efforts related to newborn screening. ACOG's Dr. Gregg stated that there are several opportunities for interactions with pregnant women but noted that many people do not present to an obstetrician until they are 22 weeks pregnant (nearly the third trimester). He also noted that unless physicians really buy in to newborn screening, they will not incorporate it into their practices on a regular basis.

In another presentation, Dr. Becker focused on what has been going on at the state level with respect to educating the public, physicians, and others about newborn screening. Almost every state has a brochure on newborn screening, but a recurring theme was that educating people about newborn screening will require multiple venues and times. Dr. Becker suggested that slide sets be developed to put on the Web sites of different medical organizations to help educate physicians about newborn screening.

In the next presentation, Ms. Gilian Engelson reported on a recent meeting hosted by the National Institute of Child Health and Human Development (NICHD) at which representatives of several Federal agencies met to discuss what they are doing in newborn screening education. The Education & Training Subcommittee had not been dealing with this group previously but sees this group as an important resource. The final topic discussed at the meeting, Dr. Edwards reported, was expanding the membership of the Education & Training Subcommittee. In a teleconference with Dr. Howse, July 1, 2005, current subcommittee members identified potential membership slots—ACOG; AAFP; the nursing association; a parent, and the public. ; birthing classes; screening program staff; and health birthing centers; screening program staff; health educators; a metabolic sub-specialist; ASTHO; the International Society of Nurses, and the National Conference of State Legislators. It also wanted someone from HHS. Although the subcommittee cannot accommodate all the suggestions for new members, it hopes to make a decision about new members via a conference call in the near future.

Questions & Comments

Dr. Howell noted that the education of non-English-speaking people—particularly Hispanic, a large and growing population—was another group that the Education & Training Subcommittee ought to consider in its deliberations. He said that adding people to the subcommittee would be important.

B. Follow-up & Treatment Subcommittee Report

Chair:
Colleen Boyle, Ph.D., M.S.
Associate Director, Science and Public Health Team
National Center of Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention (CDC)

Members:
Peter van Dyck, M.D., M.P.H., M.S., Health Resources and Services Administration
Denise Dougherty, Ph.D., Agency for Healthcare Research and Quality
Derek Robertson, J.D., M.B.A., Powers, Pyles, Sutter & Vervill, PC
Joseph Telfair, Dr.P.H., M.S.W., M.P.H., Secretary's Advisory Committee on Genetics, Health, and Society

Dr. Boyle reported that the Follow-up & Treatment Subcommittee had found its rhythm and was meeting regularly and starting to move forward. She said that on the basis of the morning's discussion and other input she had received at this meeting, she wanted to modify the subcommittee's charge slightly from the charge in the briefing book for the meeting and make it very explicit.

Revised Followup & Treatment Subcommittee Charge

- Engage in a multistep process that
  - identifies barriers to short- and long-term followup and treatment of newborn screening results specific to the challenges in integration of health care systems, financing of services and information technology systems
  - develops recommendations for overcoming identified barriers in order to improve short- and long-term followup of newborn screening results
  - recommends mechanisms for establishing accountability for newborns screening followup guidelines

In the first bullet, the words "and treatment" have been inserted to make it explicit that the subcommittee is covering treatment as well as the actual event of follow-up. In addition, she changes the word information technology in that bullet to "information systems: to enlarge it beyond just information technology-related issues.

Dr. Boyle also noted there were several telephone discussions about adding expertise to the subcommittee, and the Follow-up & Treatment Subcommittee extended invitations to six individuals; the first four already accepted:

- Jill Fisch-Levy, the director of Educational Awareness at the Save Babies Through Screening Foundation
- Brad Therrell, the director of the National Newborn Screening and Genetic Resource Center (NNSGRC), who updates the Committee on the status of the states every meeting and has a direct line to all of the state newborn screening programs

- Javier Aceves, a primary care physician from New Mexico who is representing the medical home perspective.
- Carol Green, who is from the University of Maryland School of Medicine, and representing the perspective of a metabolic specialist.
- Julie Miller, who oversees the Nebraska newborn screening program
- George Cunningham, the Chief of the Genetic Diseases Branch in California Department of Health

In addition, the subcommittee has identified some consultants or types of expertise that will be considered as needed such as, child neurology, maternal and child health directors.

The Follow-up & Treatment Subcommittee has begun to address its first charge and has had numerous discussions trying to get a sense of the state of knowledge of and identifying barriers in health care systems, financing, and information systems. Dr. Therrell has told the subcommittee about Dr. Tim Hoff, at SUNY in Albany, who has done a survey of newborn screening programs about long-term follow-up. The subcommittee expects to draw from and extend this work in a subsequent survey that Dr. Therrell and Dr. Hoff will be doing that will enable the subcommittee to poll programs about barriers in health care systems, financing, and information systems. Also, there will be a session at the Association of Public Health Laboratories (APHL) meeting in Fall 2006, Dr. Boyle and Dr. Therrell hope to conduct some type of qualitative research related to newborn screening followup done by subcommittee and to get information from experts attending the meeting.

Finally, the Follow-up & Treatment Subcommittee has identified priority areas, work groups, and assigned people to take the initial lead in these areas:

- **Health care systems barriers to follow-up and treatment.** Dr. Dougherty is taking the lead to identify the status of knowledge to try to develop a statement and guidelines around the barriers to short- and long-term follow-up and treatment and how to overcome those health care system barriers.
- **Financing barriers to follow-up and treatment.** Dr. van Dyck and Dr. Therrell will look at financing issues. The subcommittee has discussed the possibility of bringing speakers to the Committee's October 2005 meeting to present on Medicaid and private insurance at the state level and at a higher level perspective. Dr. Boyle said they will discuss this further and then get back to Dr. Lloyd-Puryear about this.
- **Information systems barriers to follow-up and treatment.** Dr. Boyle is taking the lead. Dr. Alan Hinman, from the Public Health Informatics Institute, has been very helpful in this area.

Noting that the Follow-up & Treatment Subcommittee wants to highlight the parent and advocacy perspective, Dr. Boyle reported that Ms. Fisch-Levy and Mr. Robertson will work together to understand what has been done by the parent groups (e.g., the Genetic Alliance has done surveys of its clientele looking at specific barriers). In addition, Ms. Fisch-Levy is going to go through the public comments on the report ACMG report *Newborn Screening: Toward a Uniform Screening Panel and System* to see what barriers are relevant to the subcommittee's charge.

C. Laboratory Standards & Procedures Subcommittee Report

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

Members:
R. Rodney Howell, M.D., Chair, ACHDGDNC
Duane Alexander, M.D., National Institutes of Health
Peter Coggins, Ph.D., Perkin Elmer
Piero Rinaldo, M.D., Ph.D., Mayo Clinic

Dr. Brower reported that the Laboratory Standards & Procedures Subcommittee had had a great meeting. In addition to the four members of the subcommittee, participants included nine other people and two consultants who working with the subcommittee: Ms. Jana Monaco, who is a parent and a board member of the Organic Acidemia Association; and Dr. Harry Hannon, Chief of the Newborn Screening Branch, Division of Laboratory Sciences, Centers for Disease Control and Prevention (CDC).

One of the topics discussed at the meeting was the charge of the Laboratory Standards & Procedures Subcommittee. In light of the previous day's discussions of the evaluation of the expansion of the panel and the current panel, Dr. Brower said, the subcommittee wanted to clarify some of the issues related to its charge:

- The third and fourth components of the Laboratory Standards & Procedures Subcommittee's charge—to define and implement mechanisms for the periodic review of infrastructure and laboratory procedures, respectively—are to operate in the context of the effective and efficient testing of the conditions in the uniform newborn screening panel. The subcommittee wants to look at the core infrastructure that is available for the implementation of this panel and define those elements that are important in the core infrastructure. It also wants to look at metrics in the preanalytical, analytical, and post analytical phases of newborn screening. The subcommittee wants to clarify questions about the uniform newborn screening panel, which includes 29 primary screening targets and the 24 secondary targets. It also wants to identify whether there is confirmatory testing available for that current uniform panel. The subcommittee hopes to take advantage of and capitalize on efforts that are already ongoing—whether at the Association of Public Health Laboratories (APHL), through the regional collaboratives, or other groups—and build those into the goals of the subcommittee.
- The second component of the Laboratory Standards & Procedures Subcommittee's charge is to define and implement mechanisms for the periodic review of conditions included in the uniform newborn screening panel recommended in the ACMG report—including the appropriateness of the conditions in the current uniform panel and of new conditions that might be added to that panel. Dr. Brower reported that the subcommittee had come up with a rough draft of proposal for presentation to the Committee as a whole for discussion.

The process starts with HRSA collating the preliminary information, digesting it, and providing it to the full Advisory Committee, and the full Advisory Committee has a critical role throughout this process:

- On the basis of a questionnaire or HRSA's work with outside groups, conditions would be nominated to be added to the uniform panel. The nomination forms would go to HRSA staff, which would do a preliminary evaluation of the information. If HRSA staff believes the condition meets a certain level of evidence and criteria, the condition would be presented to the full Advisory Committee.
- The full Advisory Committee would review the information from HRSA and make a decision either to approve and proceed or, if there was not sufficient information available, defer.
- If the full Advisory Committee decided to defer because there was not enough information, it would also specify what additional information is needed.
- If the full Advisory Committee decided to approve and proceed, two gatekeeping questions would be addressed: Is a test available? And is a treatment available? The Laboratory Procedures & Standards Subcommittee would evaluate the data on whether a test is available; and the Followup & Treatment Subcommittee would evaluate whether a benefit is available.
- If the condition passed the two subcommittees' evaluations, it would go to the full Advisory Committee for evaluation. If the full Advisory Committee approved, the chair of the full Advisory Committee could assign it to an ad hoc working group. The ad hoc working group would include a liaison member from the Laboratory Procedures & Standards Subcommittee and a liaison member from the Followup & Treatment Subcommittee.

Questions & Comments

Dr. Howell asked Committee members whether they were clear about what Dr. Brower's Laboratory Standards & Procedures Subcommittee was proposing. Dr. Howell commented that he thought the Laboratory Standards & Procedures Subcommittee had tried to respond to the concerns that were expressed by Committee members earlier. It was trying to figure out a way to evaluate the test, which is critical, the benefit or treatment, which is critical, and then vet it through the full Advisory Committee and have an ad hoc working group with a broad variety of expertise not only from the Laboratory Standards & Procedures and Followup & Treatment Subcommittees, but other groups that would be looking at it, and come back to the full Committee with a final recommendation.

Dr. Edwards asked whether the ad hoc working group that would make a recommendation would an ACIP-like organization. Dr. Alexander replied that it would be, and Dr. Edwards signaled his approval.

Dr. Dougherty observed that there seemed to be quite a few steps around identifying whether there is a test and treatment. Since she had thought one of the nominations of the conditions would be that somebody would say there is a test and a treatment, she wasn't sure what HRSA would be doing except assessing the validity of the claims in the nomination. Couldn't the full Advisory Committee do that, and then send the issue directly to the ad hoc working group? What

would the Laboratory Standards & Procedures Subcommittee and the Followup & Treatment Subcommittees be doing?

Dr. Howell replied that HRSA would be looking at the things generically but not making decisions about it. At Dr. Howell's request, Dr. Marie Mann elaborated on this point, saying that what HRSA staff would be doing would be minimal. The staff would be checking the submission to assess whether it met the minimum requirements If the staff thought there was adequate information, it would prepare a package for the full Advisory Committee. Then the full Committee would review the information and decide whether to proceed or not.

Dr. Dougherty said if HRSA just put the package together, the Laboratory Standards & Procedures Subcommittee and the Followup & Treatment Subcommittee would be left with a huge job unless they had criteria for the things that they were supposed to consider. Dr. Brower replied that the Laboratory Standards & Procedures Subcommittee would be seeking to answer the question: Is there any type of test available that is reliable? The question for the Followup & Treatment Subcommittee would be: Is there a benefit available? Each of these subcommittees would be asked to come up with its own standardized assessment for responding to these questions and for determining whether to recommend to the full Advisory Committee that these tests or benefits should go on to the ad hoc working group. Dr. Dougherty suggested that the Followup & Treatment Subcommittee ask a broader question: Is there a benefit available, and are there harms?

Dr. Dougherty asked what the ad hoc working group was supposed to do. Dr. Lloyd-Puryear explained that the ad hoc working group would have a broad representation that would reexamine the evidence to make sure the subcommittees got it right. The ad hoc working group also would examine the other important areas discussed in the ACMG report—burden of disease, cost, public advocacy, all those additional issues.

Dr. Dougherty suggested that perhaps the Committee could get some help from Dr. David Atkins and others about putting criteria together for the Laboratory Standards & Procedures Subcommittee and the Followup & Treatment Subcommittee and the ad hoc group, so that the Committee makes sure that all of these criteria fit together in those three intersecting circles of Evidence, Values, and Resources shown by Dr. Atkins in his earlier presentation. She said she was trying to make sure that there is an explicitness of the process and not just judgment of these groups. Dr. Becker said he agreed with Dr. Dougherty on this point.

Dr. Alexander noted that the process outlined by Dr. Brower is a modified screening process in itself. HRSA's role is mainly to assemble the data and pass it on without even a whole lot of comment for the Committee to see whether it meets the criteria for further consideration and pursuit. The whole Committee then decides if there is enough here to make it worth going further. It then refers the matter to the two subcommittees, which would do a further probe and decide whether there is sufficient evidence, benefit, and a quality test, and testing of the test to make it something that is ready for consideration for addition to the whole panel. If in their judgment it meets that, then they come back to the full Committee and say this is ready, it is worth the investment of time, dollars, and resource, for an ad hoc working group to be appointed to consider this and bring forward a recommendation to the whole committee as to whether this is ready for addition to the panel.

Dr. Coggins said that there should definitely be a set of criteria to judge everything against. He

also noted that the ad hoc working group would include standing members and other members determined by the condition under consideration. Dr. Howell commented that there had been considerable discussion about the explicit plans for the Laboratory Standards & Procedures Subcommittee, because that was the group that was looking at this. The other subcommittees and the ad hoc groups would need to have the same thing.

Dr. Becker requested that the Education & Training Subcommittee have a liaison to the ad hoc working group. Dr. Brower agreed that there should be a liaison for the Education & Training Committee.

Dr. Becker also noted that the entry point to the algorithm the submission of nominations, and the nomination forum and process for the submission of nominations still has to be worked out. He, Dr. Rinaldo, and Dr. Lloyd-Puryear will be working on this prior to the next meeting. Dr. Howell reiterated his desire to have the entry point be as broad as possible to encourage people to come into the fold, but also be certain that there is some moderate level of information at the beginning.

Dr. Dougherty said all of the plans and suggestions sounded great, and she thought perhaps the Committee should consider the issue of resources to get the analyses done. Dr. van Dyck said that the Committee and subcommittees would have to start and see what the resource requirements—money and personnel—were, but added that some resources are available.

Dr. Rinaldo asked whether the Followup & Treatment Subcommittee was amenable to the process that had been outlined thus far. Dr. Boyle, the chair of the subcommittee, said that she agreed with almost everything everybody had said—especially, Dr. Dougherty's comment about the need for the process to be transparent. Dr. Boyle said she thought that the approach outlined seemed like a good one, but the Committee would have to try it out and the process might evolve over time.

VIII. PUBLIC COMMENT SESSION

The following individuals made public statements. The written text of their statements appears in Appendix A.

1. Carol D. Berkowitz, M.D., F.A.A.P.
President
American Academy of Pediatrics (AAP) Executive Committee

Dr. Berkowitz, in a statement read by Amy Brin, Manager, Screening Programs, AAP Division of Children with Special Needs, noted that the AAP's Board of Directors had submitted comments on the ACMG report *Newborn Screening: Towards a Uniform Panel and System* at the beginning of May 2005. While endorsing the concept of expanded newborn screening, the AAP Board of Directors strongly maintain the need to establish a comprehensive follow-up system and the resources to support it. The AAP further offered the following points:

- **The role of the medical home in the followup system.** The 2000 AAP Newborn Screening Task Force report established the medical home necessity in successful short-term and long-term followup for identified newborns.
- **Physician liability.** Malpractice suits against pediatricians related to newborn screening

- **Education of pediatric professionals.** Because the ACMG report's recommendations are germane to all pediatric professionals, the AAP strongly suggests the development of a communication plan to notify and educate pediatric professionals about the ACMG report recommendations. AAP will use its resources to educate its 60,000 members.

Beginning in 2005, and through the support of partners such as HRSA's Maternal and Child Health Bureau and ACMG, the AAP will develop its first clinical report to outline the medical home's role in the newborn screening follow-up process. The report, which will be authored by a multidisciplinary group of experts in a wide range of pediatric domains, will delineate the primary care child health professional's role in quality care to identify newborns and children. The AAP looks forward to the opportunity to further partner with ACMG's National Coordinating Center for Regional Genetics and Newborn Screening Collaborative Groups to evaluate the implementation of this clinical report.

Following Dr. Berkowitz's statement, Dr. Boyle raised the possibility of discussing a liaison capacity for the AAP on the Advisory Committee. Dr. Edwards suggested that the Advisory Committee's Follow-up & Treatment Subcommittee consider an AAP representative. Dr. Howell, noting that it was invaluable to have the input of the AAP and its 60,000 members, indicated that the appropriate organization of formal input from the AAP was something the Committee would need to discuss.

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

Ms. Gartzke, noting that the top priority of the Hunter's Hope Foundation is universal and comprehensive newborn screening for all newborns, applauded the Committee's dedication, integrity, and hard work to make recommendations to expand newborn screening throughout the United States. Ms. Gartzke also approved of the Committee's three subcommittees and their openness. Underscoring the importance of education related to newborn screening, Ms. Gartzke, who lost a daughter to Krabbe disease in 2001, said that parental involvement on all levels of decision-making and advocacy are a major key to success. She also stated that that there must be a standard of care for newborn screening. She would like to see physicians—ob/gyns and pediatricians alike—mandated to provide information on newborn screening to expectant mothers in the prenatal period before the 35th week of pregnancy. Ms. Gartzke ended her statement by urging the Committee to keep up its good work.

3. Jana Monaco
Parent & Board Member
Organic Acidemia Association

Ms. Monaco said that the Organic Acidemia Association, whose mission is to provide information and support to families of children with inborn errors of metabolism and information to health professionals, supports the uniform panel recommended in the ACMG report *Newborn*

Screening: Towards a Uniform Panel and System. She reminded Committee members that the issue of newborns screening is near and dear to her heart, because she has two children afflicted with Isovaleric Acidemia, a son who suffered severe brain damage at age 3 ½ and a daughter age 2 ½- who is living a normal life with diet and medication because she was diagnosed early. Ms. Monaco said she and other parents hoped that the Committee would move forward with the process of recommending the ACMG report to the Secretary for his approval with the understanding that the identified issues of the report will be ongoing tasks to address and that as science and technology continue to change, so will the methodology of the process. The focus should be on progress rather that perfection. It would be beneficial to have the support of the ACMG report in assisting the remaining states in developing their screening programs and bring a sense of uniformity among states. She also noted that parents also believe that ob/gyns should initiate the discussion of newborn screening to help educate parents on these disorders during the prenatal period. Ms. Monaco thanked the Committee for its sensitivity to parents and stated that she viewed the opportunity to work with t Dr. Brower and her Laboratory Standards & Procedures Subcommittee as an honor. She urged the Committee to involve parents on all three of its subcommittees as a validation of the vital role parents play in addressing these issues.

4. Jill Fisch-Levy
Parent & National Director of Education and Awareness
Save the Babies Through Screening Foundation

Ms. Fisch-Levy thanked members of the Committee for their continued hard work and dedication regarding newborn screening and surrounding issues. She said it was wonderful to see some states expanding their newborn screening program in anticipation of the acceptance by the Secretary of Health and Human Services of the ACMG report *Newborn Screening: Towards a Uniform Panel and System*. On the other hand, New Hampshire and other states are still severely lagging behind, and there appears to be no movement in these states to expand Mississippi has the best screening panel in the nation, Ms. Fisch-Levy said, and extrapolating numbers from Mississippi suggests that 8,850 babies out of 4 million births in the United States would have a positive screen using the best panel currently available. Like other parents, Ms. Fisch-Levy stressed the need for parents to be involved in the decision-making process related to newborn screening. She said she was grateful for the opportunity to be a consultant to the Committee's Followup &Treatment Subcommittee and recommended that the Committee's Education and Training Subcommittee similarly involve Micki Gartzke in its work. Ms. Fisch-Levy reported that families in many states are still not being informed about supplemental screening. She stated that standards must be set. She recommended that the American College of Obstetricians and Gynecologists (ACOG) mandate that all pregnant women receive this life-saving information by the 35th week of pregnancy and that supplemental screening be ordered prior to delivery and be the standard of care. Supplemental screening should be a physician ordered test, and not left up to the subjective decision of the nurse. She hopes that AAP and ACOG will address whether the order should come from the pediatrician or the ob/gyn. Finally, in response to Dr. Gregg's statement during his presentation that if there is no treatment for a disorder, there is no benefit from screening for that disorder, Ms. Fisch-Levy asked: How can treatment be identified if children are not identified? Also, parents have a right to know what is wrong with their child.

5. Theresa Murry
Parent & Save the Babies Through Screening Volunteer

Ms. Murry, in a statement read by Jill Fisch-Levy, related the moving story of her daughter Michelle, who lived to be 20 years old, and then died mysteriously and suddenly in 1998 after a camping trip with friends. The only other time Michelle had been really sick was when she was 2 years old. She had spent a week in an intensive care unit in a comatose state then suddenly improved, but the doctors never figured out what she had. When Michelle became very ill after the camping trip, the doctors thought the problem might have been drugs or alcohol, though neither was detected in her system; she died within a few hours. The coroner ruled that Michelle "died of natural causes, cause unknown." Only because the doctor who treated Michelle in the emergency room kept running tests from samples at the medical examiner's office was it finally discovered MCADD (Medium Chain Acyl-CoA Dehydrogenase Deficiency)—a rare hereditary, fatty oxidation - disease caused by the lack of an enzyme needed to convert fat into energy—had caused Michelle's death. Ms. Murry recommended that every young person or an individual under 50 whose death is ruled "died of natural causes, cause unknown" be tested for metabolic disorders as a possible cause of death.

6. Alan R. Hinman, M.D., M.P.H.
Senior Public Health Scientist
Public Health Informatics Institute

Dr. Hinman, formerly with the Centers for Disease Control and Prevention (CDC), noted that he is now working with the Public Health Informatics Institute—a not-for-profit organization that has been working with HRSA's Maternal and Child Health Bureau for the last 5 years to integrate child health information systems. The basic premise of the institute, Dr. Hinman said, is that health and health services can be improved by the timely provision of accurate and comprehensive information. After citing statistics to illustrate the problem of apparent loss to follow-up rates in PKU and congenital hypothyroid cases of newborn screening results—and particularly a 50 percent loss to follow-up rate in hearing loss cases, Dr. Hinman said he was pleased that the Followup & Treatment Subcommittee chaired by Dr. Boyle was going to be addressing issues of information systems and bringing information to those who need to have it, and he urged that these issues be given priority.

Dr. Howell asked Dr. Hinman to bring the Committee up to date with the Federal initiative going on in electronic medical records. Dr. Hinman reported that there is a considerable amount of work on developing health information systems and health information networks nationwide. Much of this work pertains to the development of electronic medical records, but the primary emphasis is on electronic medical records for adults. The American Academy of Pediatrics (AAP) is trying to ensure that the special information needs of children are addressed as the Federal health information initiative goes forward. There is a pediatric steering group with representation from the National Association of Children's Hospitals and Related Institutions (NACHRI) and the other children's hospital organization, the Board of Pediatrics and the Academy that is meeting regularly and holding conversations with Dr. Brailer and with Dale Nordenberg from CDC who is on part-time detail to deal with child health issues in this arena.

IX. COMMITTEE BUSINESS—CALENDAR, NONVOTING

REPRESENTATIVES, LETTER TO HHS SECRETARY ABOUT THE ACMG REPORT

R. Rodney Howell, M.D.
Chair, Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
Professor of Pediatrics
University of Miami School of Medicine

As the final day of the meeting drew to a close, the Committee considered three topics: (1) the calendar for future Committee meetings; (2) the possibility of inviting professional organizations to send nonvoting representatives to the Committee; and (3) the content of the Committee's letter to the Secretary of Health and Human Services regarding the ACMG report *Newborn Screening: Toward a Uniform Screening Panel and System* and public comments sent to HHS about that report.

Calendar for Future Committee Meetings. Dr. Howell stated that the Committee's next meeting would be on October 20-21, 2005. The meeting dates tentatively set after that are January 19-20, 2006; May 24-25, 2006 (not 18-19th as shown on the calendar distributed to Committee members prior to the meeting); and Sept. 28-29, 2006. He said that Dr. Lloyd-Puryear had vetted those dates but that Committee members should let her know if they have a problem with any of them.

Inviting Professional Organizations to Send Nonvoting Representatives to the Committee. Dr. Lloyd-Puryear explained, in response to a question from Dr. Edwards, that the Committee's charter specifies that nonvoting representatives to the Committee are representatives from organizations such as the such as the American Academy of Family Practice (AAFP), the American Academy of Pediatrics (AAP), and the American College of Obstetricians and Gynecologists (ACOG) who participate in the deliberations of the Committee but are not permitted to vote. Such representatives are designated by the organizations they represent and are not subject to approval by the Secretary of Health and Human Services. Their travel and expenses must be paid for by their organization. (Dr. Edwards is a voting member of the Committee representing all health care workers in general, not an AAP representative to the Committee.)

Dr. Edwards asked the Committee to consider the possibility of having liaison members to the Committee from organizations such as the AAFP, AAP, and ACOG. Dr. Alexander and several other Committee members indicated that they would support this idea.

Noting that pediatric nurse practitioners help care for children with disorders identified via newborns screening, Dr. Dougherty asked whether the National Association of Pediatric Nurse Practitioners (NAPNAP) or another nursing group should be asked to send a nonvoting representative to the Committee. Dr. Becker noted that NAPNAP is being considered for inclusion on the Education & Training Subcommittee. Dr. Rinaldo said that if the Committee wanted to include professionals with a defined role in newborn screening, then perhaps a representative of genetic counselors, who play a vital role in the follow-up of children with metabolic disorders, should be considered as a liaison to the Committee. Dr. Becker reported that genetic counselors were another group being considered for inclusion on the Education &

Training Subcommittee.

Dr. Howell said that if the Committee decided to add groups such as NAPNAP, it would be hard not to add groups such as the ACMG. Although nurse practitioners, genetic counselors, and the other genetic professionals, clearly play an important role, Dr. Howell said, his judgment was that the invitations for nonvoting representatives, at the onset, should be limited to the three very large independent groups that have a heavy involvement in newborn screening - AAFP, AAP, and ACOG.

Following the Committee's discussion, Dr. Edwards made the following motion, which was then voted on and unanimously approved by the Committee:

> ***MOTION #1: That the Advisory Committee invite the American Academy of Pediatrics, the American College of Obstetricians and Gynecologists, and the American Academy of Family Practice to send nonvoting representatives to the Committee.***

Dr. Telfair recommended that the Committee's subcommittees obtain the input of multidisciplinary providers who have a significant role in newborn screening by including such providers as members, representatives, or consultants. Noting that representatives get paid by their organizations, but consultants and members are paid for the HRSA's Maternal and Child Health Bureau, Dr. Lloyd Puryear reminded everyone to bear in mind the financial implications of inviting various people to participate. If representation and input from a particular organization is what Committee members want, they may be able to obtain it from an unpaid representative rather than a paid consultant. Dr. Howell agreed with her point.

Finally, Dr. Edwards asked a follow-up question: If the AAFP, AAP, and ACOG send nonvoting representatives to the Committee, could the Education & Training Committee adopt them and then still have its five or six other positions for subcommittee members? Dr. Howell replied, yes, that was correct.

Content of the Letter to the HHS Secretary Regarding the ACMG Newborn Screening Report and Public Comments. Dr. Howell next asked the Committee to discuss the content of the letter to be written to the Secretary of Health and Human Services about the Committee's comments on the ACMG report *Newborn Screening: Toward a Uniform Screening Panel and System* and public comments. A document presenting nine major points that would go into the letter was distributed to Committee members, and Dr. Howell said that an effort had been made in this document to capture the major points that had come out of the Committee's discussion the previous day.

Dr. Edwards moved that the Committee recommend the adoption of the statement.

> ***MOTION #1: That the Committee approve the content of the document that will be used by Dr. Howell to write a letter to the Secretary of Health and Human Services regarding the ACMG newborn screening report and public comments on the report.***

Following some discussion and minor revisions, the Committee unanimously approved this motion. The Committee agreed that the letter to the Secretary should include the following nine points (following a short introduction on the history and content of the ACMG report):

1. In September 2004, the Committee reviewed a draft of the ACMG report and voted to endorse and recommend the report and its findings and recommendations to the Secretary.
2. The Committee reviewed and discussed the report this past January and recommended its release to the public. The Committee also agreed to review the public comments and provide advice to the Secretary on those comments and the report.
3. The Committee has reviewed the public comments on the ACMG report sent to HHS and notes that the majority of them were favorable to the report and its findings. Almost all of the comments supported using a uniform panel in state newborn screening programs.
4. Upon review of the final report and the public comments to that report, the Committee is satisfied with the work of the ACMG expert panel, its methodology, its findings and its recommendations and again endorses the report and its recommendations
5. The Committee notes there were concerns about methodology used by the expert panel from some of the commentators. The Committee reviewed that methodology with experts and found the methodology satisfactory and concluded that the concerns about the methodology do not negate the findings of the ACMG expert panel. Furthermore, the Committee thinks that the report and its findings are based on the best methods available at this time.
6. Although the Committee is satisfied that the methodology represents a useful approach, the Committee recognizes that analysis and evaluation is a dynamic process. For that reason, the methodology used by this Committee for its own work in recommending test and technologies to be used in newborn screening will evolve over time.
7. The Committee notes there were some concerns about issues the ACMG expert panel did not address in detail, although the report did note their importance *[Committee members recommended reordering this list]:* assuring connection to the medical home, transitioning into adult care, and access to new and better treatments; committee process and infrastructure for future evaluation of new conditions and technologies—their development, validation, implementation, and clinical utilization; the policy-setting process for state newborn screening programs; laboratory standards and procedures; the infrastructure needed for followup, including long-term followup and data collection and analysis; conducting appropriate research, including health systems and outcomes research, research on screening technologies, incidence and spectrum of disease, and ethical/legal/social issues; promoting education for families, health professionals (including prenatal), and the general public with attention to cultural, literacy, and linguistic issues; addressing privacy issues such as the sharing of patient data, consent

and refusal, and storage of biosamples; and financing issues, including costs of care and cost of newborn screening expansion and the newborn screening system
.

8. The Committee has begun to examine these issues and will address them in future deliberations. *[To be expanded with detail about subcommittees if space of the two-page letter permits]*
9. Finally, the Committee unanimously and strongly recommends that the Secretary take appropriate action to facilitate adoption of the ACMG recommended screening panel by every state newborn screening panel.

The Committee opted not to add anything in the statement about the need for making additional resources available. The Committee unanimously voted to accept the modifications in the letter. Dr. Rinaldo thanked other Committee members for their working efforts to find a common ground on the letter. Dr. Howell said that he would try to get the final letter to the Secretary incorporating these points together as soon as possible.

Dr. Howell thanked the Committee and adjourned the meeting.

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

/s/ _____	/s/_____
R. Rodney Howell, M.D. ACHDGDNC, Chair	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. Carol D. Berkowitz, M.D., F.A.A.P.—President, American Academy of Pediatrics (AAP) Executive Committee (statement read by Amy Brin, Manager, Screening Programs AAP Division of Children with Special Needs)
2. Micki Gartzke—Parent & Director of Education and Awareness, Hunter's Hope Foundation
3. Jana Monaco—Parent & Board Member, Organic Acidemia Association
4. Jill Fisch—Parent & National Director of Education and Awareness, Save the Babies Through Screening Foundation
5. Theresa Murry—Parent & Save the Babies Through Screening Foundation Volunteer (statement read by Jill Fisch)
6. Alan R. Hinman, M.D., M.P.H., Senior Public Health Scientist, Public Health Informatics Institute

1. Carol D. Berkowitz, M.D., F.A.A.P.
President, American Academy of Pediatrics (AAP) Executive Committee
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children

July 22, 2005

July 21, 2005

Dear Chairman Howell,

The American Academy of Pediatrics' (AAP) Board of Directors greatly appreciates this opportunity to provide comment on the Health Service Resource Administration's commissioned report to the American College of Medical Genetics (ACMG), "Newborn Screening: Towards a Uniform Panel and System" to the US Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. As you know, our long-standing commitment to newborn screening has been manifested through our continued partnership with the Maternal Child Health Bureau (MCHB). Through the years, this partnership has helped improve the ability of pediatricians to care for newborns identified via the newborn screening process. We join HRSA/MCHB in acknowledging the many benefits newborn screening provides to the health of newborns and their families. Moreover, we salute HRSA/MCHB in their endeavors to unify state newborn screening programs in order to address the wide disparity that currently exists.

In accordance with the Federal Register's call for public review of the ACMG report, the AAP's Board of Directors submitted the following comments from our expert committees and sections at the beginning of May 2005.

While we endorse the concept of expanded newborn screening, we strongly maintain that a clearly defined follow-up system must be established to support its effects on pediatric practices. Through our endorsement of the ACMG report, we join fellow national partners (i.e. March of Dimes) in the understanding that this Advisory Committee is charged to make such implementation recommendations. We acknowledge that such a process must be a dynamic one, incorporating pragmatic structural changes in the operation of the state program, as well as evolving tests and treatments. We salute this Advisory Committee's construction of subcommittees to address the issues of follow-up, laboratory standards, and education, as well as the crosscutting issues of finance and technology, as it illustrates a deep commitment to attaining a quality, comprehensive newborn screening system.

We further offer the following points of emphasis:

- Follow-up system: The role of the medical home is essential to ensure a quality newborn screening process. The 2000 AAP Newborn Screening Task Force report established the medical home's necessity in successful short-term and long-term follow-up for identified newborns. As the expansion of newborn screening seems inevitable, we look forward to our continued partnership with other national leaders about how to support the medical home in this role.

  As mentioned previously, it is necessary for a defined, appropriate and comprehensive follow-up system to be implemented. While we acknowledge that such a charge was not part of the ACMG's expert panels' work scope, we do note the report's implications require identification of such a model. The integration of expanded newborn screening on our states' public health systems, laboratories, medical homes, specialists, and families demands that such a system, as well as the resources to support it be in place.

- Physician liability: Malpractice suits against pediatricians related to newborn screening have increased. The proposed system must ensure that results are reliably sent to the medical home and that information about the suspected disorder is included. An expert contact number should also be given. Liability for informing the medical home and family about the need for additional testing should reside with the state.

- Education of pediatric professionals: The fully operational newborn screening program is complex, and naturally encompasses a vast number of health care professionals. As the ACMG report's recommendations are germane to all pediatric professionals, we strongly suggest development of a communication plan to inform and educate these audiences on the ACMG report's recommendations. In turn, we pledge to utilize our resources to distill and disseminate such information to our 60,000 members. It is only through such coordinated efforts that we can engage the pediatric healthcare community to meet the needs of these newborns, their families, and communities.

Please note that in our May submission of comments to HRSA/MCHB, we also included some editorial considerations.

At this time, we'd also like to inform you of our immediate plans to engage in these areas of further definition, as described above. Beginning in 2005, and through the support of our partners HRSA/MCHB and ACMG, we will be developing our first clinical report to outline the medical home's role in the newborn screening follow-up process. The publication of this report will solidify our commitment to expanded newborn screening, and our acknowledgement that our members, as well as all pediatric child health professionals, need unambiguous clinical guidance to know their role in this expanded system.

Earlier this month, we established an expert, multi-disciplinary authoring body from the pediatric domains of primary care, genetics, neonatology, neurodevelopment, neurology, quality improvement and informatics to draft this operationalized clinical report targeted at the point of care. The report's scope will explicitly delineate the primary care child health professional's role in quality care to identified newborns and children; specifically defining their role in co-

managing the condition with a sub-specialist and the family. Moreover, the backbone of this clinical report will be an algorithm, which will provide explicit “marching orders” for electronic health records (EHRs) developers to note pediatric functionalities their health information technology must have in place in order to support the medical home’s provision of care. Whereas, by defining the content of this document to a granular level, its outcomes can naturally be incorporated into EHR standards developing organization’s, such as HL7, pediatric initiatives, as well as the Public Health Informatic Institutes' efforts (in which Dr. David Ross briefed you on at your January meeting.) As this Advisory Committee has, we recognize the role of information technology in the provision of quality care, and in doing so, must consider its implications in drafting our intellectual property for providers and the public.

It is our hope that this clinical report will assist in identifying clinical standards of care for these newborns and children. We look forward to the opportunity to further partner with ACMG’s National Coordinating Center for Regional Genetics and Newborn Screening Collaborative Groups to evaluate the implementation of this clinical report. We believe that through ongoing evaluation of such standards, the pediatric community can ascertain best practice models.

Once again, we applaud HRSA/MCHB’s leadership in commissioning the ACMG report, and its continued forethought regarding expanded newborn screening. As we both share in the mission of improving the quality of lives for all children and youth, we look forward to continued dialogue about how we can assist in enhancing this domain of care.

Respectfully submitted,

Carol D. Berkowitz, MD, FAAP
President

CDB/ab

2. Micki Gartzke
Parent & Director of Education and Awareness

Hunter's Hope Foundation
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children

July 22, 2005

Thank you, Dr. Howell, members of the committee, and HRSA for the opportunity to speak today. Your outstanding dedication and your ongoing work to make recommendations to further assist states to expand their newborn screening programs is invaluable. Comprehensive universal newborn screening utilizing a tool like a uniform panel needs to be a regular practice in the United States. The children not only need this benefit, they deserve it because they are our future. You're the ones that are going to get the job done.

My name is Micki Gartzke. I live in Shorewood, Wisconsin. I'm a Midwest girl. I'm the Director of Education and Awareness for the Hunter's Hope Foundation. Recently universal and comprehensive newborn screening for all children born in the United States has become our foundation's top initiative.

It started out because we knew that children born with Krabbe disease needed to be identified through newborn screening to receive access to the effective and lifesaving treatment of cord blood transplant for Krabbe disease, which I have copies of the *New England Journal of Medicine* recently published study if anybody would like a reprint copy. We moved on to help all of the other diseases gain access to newborn screening for the benefits it provides those diseases, their families and children, because we just know it's the right thing to do.

This month being the month of July, the very month our country achieved independence in 1776, I recently attended a reading of the Declaration of Independence as part of our community's annual 4th of July celebration. I found it most insightful that the Declaration of Independence speaks directly to universal newborn screening with the well known line, we hold these truths to be self-evident that all men are created equal.

Well, we may be created equal, but that equality stops right now at birth with the state's newborn screening's inequality. I think our public health programs are one of our country's greatest gifts to all of our citizens. Our first public health program, the state-based newborn screening, is not living up to the long held acknowledgment that we are all born equal.

Historically, this lack of equality in newborn screening has had too much subjectivity involved. But this is now changing, and it is because of you guys that this is changing. Your commitment to excellence in making recommendations, using the best available evidence and the best available expert opinion. You're using high level of integrity and far reaching strategies. Much progress has been made toward the creation of a uniform nationwide panel.

In 2001, the year I became aware and consequently involved on a daily basis with newborn screening, there were only four states testing for 20 disorders or more. Today there are 25 states at that level. So we went up 21 states in four years. There are 25 states that still need to step up.

It highlight is there is much to be done, but it shows the great progress.

Along with all the parents I have ever spoken to, and it is in the many, many, many thousands now, I believe this committee is the committee to get the job done. They can do it efficiently and effectively. The structure of this committee with its subcommittees and its decision-making process I think is doing an excellent job.

Your continued openness to identify concerns, address criticisms, and work toward effective solutions continually spotlight that the benefit to the children remains the number one priority. We see no need for additional committees to be set up to repeat or possibly slow down the progress of expansion of newborn screening across the United States. HRSA has done an excellent and judicious job working with experts like you in all relevant fields before and since the establishment of this committee.

The infrastructure, implementation, and education continue to be the avenues driving progress. Education being of the utmost importance, from parents to physicians, the entire spectrum of medical care providers, including students training to be physicians. Parents will provide the demand for the education and the materials, but as I learned this morning, the physician buy in needs to be the number one objective accomplished through education. We need the physicians to buy in on newborn screening, or it's not going to happen in the manner that we're all working so hard to achieve.

There is so much that can be done so that all can be better informed about the vital lifesaving importance of newborn screening. I believe parent involvement in all levels of decision-making and advocacy are a major key to success. Like the others, I'll tell you a little story about parents of children born with rare diseases.

We have faced many challenges unlike any other challenge. We are the experts in our children's care. We bring the information and the ideas to our physicians. They're not providing them to us in most cases. They are learning from us, and they are usually open to learn that information from us. That is helpful, because they know that that is what provides their patient the best care.

The parents have access to the experiences of other parents, what they have done with their children in the past, and that is how the care is really getting taken care of at this point. So these physicians at this point do not know how to treat these rare diseases, and when this happens, it is very much an eye opener for parents.

This is how parents become advocates, because of situations like this. They get in the big system, and the system can't help them, and they can't help their child. Mothers and children, that's a very special relationship, and fathers and children is a very special relationship, too.

But when something happens to your child and the system established to help you can't help you, that changes everything. The playing field is different. That's how parents become their child's advocate.

Last week I spent seven days at our annual scientific and family symposium. We had parents there, 44 families, and they spanned the socioeconomic spectrum. Not only was our commonality

our children's disease, but the other commonality was that we all had to get our children care. Nobody had access. Nobody's physician knew what to do. Everybody learned from each other and went back to their physicians and said, this is what this family did, this is what they tried, this is the drug they used, they are using a feeding tube now, they are doing this therapy, they are doing that therapy. That was the common thing we had. Young parents, old parents, some parents more educated than others.

We were there all together, and parent advocacy was our common thread. Our foundation pays to bring families to our symposium, families that would otherwise not be able to attend the event. We want no disparity amongst our families, because we know that all parents are important, and there is value in everyone's perspective across the entire spectrum of parents.

We don't underestimate parent commitments and skills. Parents are willing to bring their skills and knowledge to newborn screening. Parents whose children were not identified, even though there is currently a newborn screening available for that disease, have specific valuable knowledge and experience that is of great importance.

Parents of children who have diseases for which a newborn screen may become available in the future also have invaluable knowledge and experience. As it is anticipated that in the future many more tests will be added to newborn screening panels, the assistance of these parents may prove to be even more vital moving forward from this point on.

Parents have played the key role in expansion. You've heard this before. Within the last year, we've had Virginia, New York, and Kentucky all moving forward, all with parent advocates playing key roles. Interestingly, I just heard that Mississippi, with it's top shelf screening program, had 22,618 births. Out of that number, they identified 50 children with positive screens. That's 1 out of 452 children. I'm not an epidemiologist, so I don't know how that translates across the country, but I just wonder with 4 million annual births, if you look at 1 out of 452 children, that means that maybe 8,850 children would screen positive using the most comprehensive panel available today. There are going to be more children that will be identified in the future as these panels grow larger.

The opportunity cost is too great not to find these children any longer. While it may be hard to quantify the benefits of newborn screening, children dying unnecessarily have too many far reaching impacts to American society at large and specifically for the families affected by the premature deaths. Time is of the essence. Children continue to be born, 11,000 of them a day. I can't help but wonder how many children each and every day are going unidentified only to endure an odyssey of disabilities and untimely deaths.

The resources for follow-up treatment studies, all aspects, there must be funding made available. There must be a standard of care. The stories continue to be told of the subjectivity of families being able to access the current supplemental newborn screening.

States that border defining access and subjectivity in hospitals from one shift to another are creating additional barriers. This is no way for medical care to be practiced in America.

My hope is that there is a mandate, policy, or something like that for OB/GYNs and/or pediatricians to provide information on newborn screening to expectant mothers before the 35th

week of pregnancy.

The discussion yesterday regarding the consequences of no decision I found particularly interesting. But you all are going in the right way, you are all right on track. I want you to all please keep working together as well as you have because you are moving forward, you keep expanding your subcommittees, and you build this newborn screening program into the great asset it can become. I know you can do it.

Additional resources will follow this. I guarantee you that parents are a big resource, and we will help. I want to thank you. Your focus on the children and on the families, your commitment to excellence, and your dedication to creating universal access to comprehensive newborn screening is not only life saving, but it is also helping to create an even better America. Thank you.

3. Jana Monaco
Parent & Board Member
Organic Acidemia Association
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children

July 22, 2005

Good afternoon! It is a privilege to represent the Organic Acidemia Association in support of a Universal Newborn Screening Program. The OAA's mission is to provide information and support to families of children with inborn errors of metabolism. It also provides information to health care professionals along with its families across the country and internationally. Our organization also has many parents that are busy like me advocating for newborn screening in their own states along with supporting various efforts to enhance the research and management of their specific disorders. Our latest development is that of an Isovaleric Acidemia Research Fund.

As you know, Universal Newborn Screening is near and dear to my heart because my 7 year old son Stephen was one of those missed diagnoses of Isovaleric Acidemia and suffered severe brain damage at age 3 ½ years old. My 2 ½ year old daughter Caroline is living the normal life with diet management and medication that he missed out on, because she was diagnosed early. They have inspired me to work with the state of Virginia to pass the recent legislation expanding the state's NBS program from 9 disorders to match that of the ACMG report and serve as a state representative for one of the regional collaborative work groups. I have also accepted the invitation to serve as a parent educator for the LEND or Leadership Education and Neurodevelopmental Disabilities Program at the Children's National Medical Center here in DC. I see the opportunity to work with Amy Brower and her subcommittee as quite an honor along with my other endeavors as they are a validation that parents play a vital role with these issues. I like many other parents do what I am doing, because of the first hand experience that comes with living with these disorders. For us, it is a vested interest and I hope that this committee will fully incorporate parents into the subcommittees.

In light of yesterday's discussions and presentations, I have to agree on behalf of our organization that Education, Follow up and Laboratory and Infrastructure are the key areas to be addressed. As the subcommittees identify their goals and objectives and working process, I am confident that many of the issues identified in the public comments will be resolved. In listening to the various issues that were identified in the public comment period, I must stress that these are not new to our organizations. We parents address these matters on a routine basis because they have a direct effect on our children's health. We even incorporate the issues in family metabolic conferences welcoming the experts to come and speak on the topics. The education process is ongoing within our parent organizations. The evidence related presentations truly proposed some critical concepts to think about. Evidence that NBS saves lives and prevents mental retardation and death does exist. The fact that it might not be tremendously high numbers is irrelevant and every child's life should count. Waiting for more or better evidence translates into more lost lives and brain damaged children because these disorders are very unforgiving when missed. Scientific validity for screening does exist and parents support it regardless of uncertainties. One of our families has two children with Ketone Utilization Disorder (KUD). Though the research shows that there are probably only 50 to 60 cases worldwide and would not be identified with newborn screening, the family fully supports Universal Newborn Screening. We have agreed that the OB/Gyns should initiate the discussion of newborn screening to help educate parents on these

disorders during the prenatal period like they do with the AFP Screening. Waiting till a baby is born to introduce this knowledge and the prospect of supplemental screening to expectant parents is too late. OB/Gyns need to be a part of the process.

In light of all of this, we feel that Dr. Watson and his staff used their expertise to fulfill the duties commissioned to them and produced a quality report of a Universal Newborn Screening Program. The methodology chosen was a very effective tool to reach people and obtain the data to complete the process. Certainly as the process of Universal Newborn Screening is implemented, the development of innovative means will continue in regards to how, when and who will include other disorders to the recommended panel. It is our hope that you will move forward with the process of recommending the report to the Secretary for his approval with the understanding that the identified issues with the report will be ongoing tasks to address and that as science and technology continue to change, so will the methodology of the process. The focus should be on progress rather that perfection. They should not hinder the advancement of the report. Expanded Newborn Screening is taking off state by state with or without this report. It would be beneficial to have the support of the ACMG report in assisting the remaining states in developing their screening programs and bring a sense of uniformity among states. You as a committee have devoted an incredible amount of time and commitment to the

development of this report for recommendation and have done a phenomenal job in addressing the various aspects of newborn screening. I appreciate the fact that you have remained sensitive to those of us tragically affected by these disorders amidst all of the technical data. The personal aspect of it all must never be forgotten.

On behalf of the Organic Acidemia Association, I thank you for your continued efforts to produce the report and implement Universal Newborn Screening. You will truly make a difference.

4. Jill Fisch
Parent & National Director of Education and Awareness
Save Babies Through Screening Foundation
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children

July 22, 2005

My Name is Jill Fisch. I am the National Director of Education and Awareness for the Save Babies Through Screening Foundation. I want to thank all committee members for their continued hard work and dedication regarding newborn screening and the surrounding issues.

It is wonderful to see that certain states are expanding their newborn screening programs in anticipation of the acceptance of the ACMG report by the Health and Human Services Secretary. However, as well all know, there are still states severely lagging behind and there appears to be no movement in these states to expand. The death or impairment of a child should not be determined by the state in which they are born. For example, I have been in contact with the New Hampshire newborn screening program. Their hands have been tied by the Legislators in that state. I was told that regardless of what happens regarding the standards set forth in the ACMG report, they may very well choose to ignore it and expand as they see fit. We need to be able to exert more pressure on these states as the lives of children are at stake. I would like to point out the benefits the children of Mississippi are receiving as the newborn screening panel they use is the best in the nation. In the past year, there were 22,618 births in Mississippi. Fifty children had a positive screen which gave them immediate access to diagnosis and treatment. According to these numbers 8,850 babies out of 4 million births in the United States would have a positive screen using the best panel currently available.

It is apparent that this committee is examining the decision making process and how it will move forward in this regard. It is of vital importance for the decision making process to be structured WITHIN this Advisory Committee. We do not want to have another committee set up, rather it would seem more practical for this committee to devise its OWN structure. This is a crucial time for newborn screening and this committee has shown a vast knowledge of the issues at hand as well as extreme fairness, integrity and a willingness to listen to the needs of families. Having attended all committee meetings thus far I have seen first hand the thought and time the committee has put forth by the vast array of experts consulted and expert presentations.

Parents are the experts in the patient-doctor relationship when children with rare diseases are involved. Parents bring the information to the physician to assist the physician in caring for the child. Because of the heightened level of advocacy, parents provide invaluable resources to health care issues such as newborn screening.

I would also like to stress the need for parent involvement in the decision making process as things move forward as well as all aspects of the subcommittee work. Some of the subcommittees have moved in this direction and I am grateful to have been asked to be a member of the Treatment and Follow-up subcommittee. The knowledge and experiences that parents bring to these issues is invaluable. The education subcommittee currently does not have parental involvement. It is my great hope that this will change in the very near future. The parent can be

one with a child with a condition currently screened for, as well as a parent of a child with a condition that may be screened for in the very near future, such as Micki Gartzke. Micki would be a wonderful asset to the education subcommittee and so many children and families would benefit from her knowledge, caring and commitment.

Families in many states are still not being informed about supplemental screening. By the 35th week of pregnancy, ACOG must mandate that all pregnant women receive this life saving information. It must be a standard of care.

Unfortunately, I have heard yet another story of a hospital refusing to perform the supplemental screening. This family purchased the Pediatrix kit and brought it to the hospital, at my suggestion. The parents were very anxious to have the supplemental testing done. The hospital, Lenox Hill in New York City, refused to perform the test citing poor lab quality and inaccurate results. We all know this not be the case. My thought on this issue would be for the supplemental screening to be ordered prior to delivery and be the standard of care. This crucial testing can not be left to the subjectivity of the nurse on duty. There was another family who was told by the nurse on duty that the hospital would not perform the supplemental screening, even though the parents had brought the kit with them. In this case, the family was able to get the testing done by the nurse who came on duty during the next shift change. Standards must be set.

As a result of hearing these stories and many others, my question would be should this order come from the pediatrician or the OB/GYN? If it is physician ordered test, the pressure would be taken off of the families and it would become the standard of care as it should be. I would appreciate if this issue could be addressed in an expeditious manner by the AAP and ACOG. I would also like to comment on the ACOG statement that the disorders screened for should have effective treatment. If the babies are not identified how can treatments be developed? Also, Parents have a right to know what is wrong with their child.

I continue to be grateful to have the opportunity to advocate for children born on this country and once again thank the committee for all being done to save the lives of children. I am also grateful for the committee's willingness to involve parents in the process as we provide insight to the lives of affected families like nobody else can.

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5. Teresa Murry
Parent & Save Babies Through Screening Volunteer
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children

July 22, 2005

My name is Theresa Murry, and I am a Save Babies Through Screening Foundation volunteer. My story is a bit different than those of newborns who are either diagnosed too late or misdiagnosed. My story is that of a young girl that lived to be 20 years old, and who died mysteriously and suddenly after a camping trip with friends.

My daughter Michelle had only been sick really only once in her life. That was when she was two years old. The doctors at Texas Children"s Hospital tested her for over 70 different diseases and possible illnesses, all tests which came back negative. After a week in intensive care in a comatose state, she suddenly improved. The doctors stated that "whatever she may have had" must have been "cured" and there wasn"t enough of whatever virus "it could have been" left to detect in the tests they were running. Her illness at that time was deemed a "fluke." For the next 18 years, she lived a very normal and very uneventful medical life.

At 20 years old, she went camping with friends. She climbed a mountain and came back to the campsite tired and not really willing to eat much, so she slept instead. A few hours later, she became very ill, and by morning, she still hadn"t eaten. Her friends thought she had contracted the flu. Her condition worsened to the point to where they took her to the emergency room, and she was then transported to Herman Hospital in Houston.

After many tests and several hours of waiting, they determined that she "needed to sleep it off," convinced that it was some type of drug use or alcohol, though neither had been detected in her system. She was moved from the emergency room to "observation," where she died within a few hours.

After 4 months, the Harris County medical examiner ruled her death as though she "died of natural causes, cause unknown." As her parent, I was told, "these things happen" and "sometimes people just die and we don"t know why." I cannot express the anger and hostility that took over my life and the frustration our family felt as we were treated as if we were "parents in denial" or that somehow Michelle had contributed to her own death.

Our answers came 14 months after she died from the doctor who treated her in the emergency room. He also didn"t understand how a perfectly healthy girl could die so quickly at 20. With our permission, he continued to have tests run from "samples" that had been kept at the medical examiner"s office.

Michelle had died of MCADD, a rare hereditary disease that is caused by the lack of an enzyme required to convert fat into energy. People with MCADD cannot fast for very long. Remember, she hadn"t eaten after climbing the mountain with her friends.

My point in telling this is that even though I strongly support the screening of newborn children, I feel it is only the first step.

Recently I read that a geneticist at a Louisiana Children”s Hospital told one mother who wanted these tests run on her children that she needn”t worry about it. She was told by the geneticist that there was no way her sons, the youngest of whom is two and a half, could have MCADD, because that disorder only affects babies.

As the mother of a dead 20-year-old, I can confirm that this is ridiculous. How many other parents have lost a child to a disorder that our professionals have not been able to diagnose simply because they didn”t know where to look or didn”t even look in the right place? I sometimes hear of young people who died after a sporting event, or sudden but brief illness, and wonder. I can confirm it doesn”t get much worse for it to be undetected by a coroner as well. Our society teaches us that they are our last hope for answers.

I feel that every death, especially that of a young person or individual under 50 that is ruled “died of natural causes, cause unknown” should be tested for metabolic disorders as a possible cause of death. Though I realize that in no way will it bring back a lost loved one, it will help to put the death in perspective. Without answers, there is a gaping wound that will not heal that includes anger, dismay, guilt, and confusion.

Thank you for the time,

Theresa Murry

6. Alan R. Hinman, M.D., M.P.H.
Senior Public Health Scientist
Public Health Informatics Institute
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children

July 22, 2005

I'm a former member of the CDC team. I retired nine years ago from CDC. I'm Alan Hinman with the Public Health Informatics Institute, which is a not-for-profit organization that has been working with the Maternal and Child Health Bureau for the last five years on trying to integrate child health information systems. Our basic premise is that health and health services can be improved by the timely provision of accurate and comprehensive information.

As an example, looking at the CORN report for 1999, of the 4 million and some PKU tests that were done, 3,494 were reported as not normal, as a result of which, 302 cases of PKU or clinically significant variants were detected, a rate of about 11 followups per case diagnosed. However, there were 154 persons with non-normal tests who were apparently lost to follow up. If you divide 154 by 11, that suggests there may have been 14 cases of PKU missed in 1999.

We don't know that that is the case, but that is what was known to the program people who reported the data. If you look similarly at tests for congenital hypothyroidism, there were 52,217 not normal tests, resulting in a diagnosis of congenital hypothyroidism in 1,550, a rate of about 32 followups per case diagnosed.

There were 1,371 non normals who were lost to follow up. Applying the same ratio of 32 followups per case, that suggests there might have been as many as 42 cases of congenital hypothyroidism missed in 1999. Again, we don't know that that's the case.

We also know from similar data which are reported on the number of days between birth and initiation of therapy for primary hypothyroidism for the cases for which there are reports, only 44 percent were known to have treatment initiated within 15 days, which is the recommended cutoff. You should be under therapy by 15 days.

Twenty-four percent were known to have had therapy initiated after 15 days, and for 32 percent it wasn't known to the people who were reporting to the CORN system. Again, we don't know when these children were put on therapy. What we know is that we don't know.

We also know that currently according to folks in the National Center for Birth Defects and Developmental Disabilities, the loss to followup rate for newborns with abnormal hearing screening is on the order of 40 to 50 percent nationwide. So I suggest that there is an information problem, and it has at least some potential for having serious clinical repercussions at the present time.

A study that the Genetics Services Bureau funded found that 4.5 percent of primary care pediatricians were not notified of screen positive results. The results were reported to tertiary care centers, to the hospitals, to somewhere, but not to the primary care pediatrician, and that 26 percent of the time, screen negative results were not reported to the primary care pediatrician. In

this case, no news is not necessarily good news, it's just no news.

Again, I suggest this is an information problem. I am pleased that the Followup Committee is going to be addressing issues of information systems and bringing information to those who need to have it, and urge that this be given priority.

I would say a couple of things about this. We talk about integrated health information systems. What we mean by that is that the information is presented to the user in an integrated fashion. It doesn't really address what the hardware and software is, but whoever is an authorized user has access to all the information available about the child. That may be a pediatrician, it may be a public health program, it may be a family member or parent if they are authorized to have access to this information.

Parents have talked about the fact that they are the purveyors of information about their children. That's because physicians don't have it. We put the information in a way that it can be given to the providers so that one can see at one's screen what is happening with a child.

If you think particularly in the hearing arena with a 50 percent loss to follow up, these are children who are being seen at 2 months, 4 months, and 6 months for immunizations. Wouldn't it be nice if the pediatrician who was giving the 2-month DPT had available on the screen in the computer the fact that this child had a failed hearing screen and not been followed up, or that an abnormal dried blood spot screen had not been followed up, or that it had been followed up and had been found that there was no problem.

So I just encourage continuing priority to be placed on developing information systems. Thank you