

**Advisory Committee on Heritable Disorders and  
Genetic Diseases in Newborns and Children  
Second Meeting**

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**September 22 & 23, 2004**

The Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children was convened for its second meeting at 9:00 A.M. on September 22, 2004, and was adjourned at 3:00 P.M. on September 23, 2004 at the Jurys Hotel, Washington, D.C.

In accordance with the provisions of Public Law 92-463, the meeting was open to the public from 1 P.M. to 2:00 P.M., September 23, 2004.

**Committee members present:**

R. Rodney Howell  
Chair

Duane Alexander\*\*

William Becker

Amy Brower

Peter Coggins

James W. Collins\*

Denise Dougherty\*\*

Gregory Hawkins

Piero Rinaldo

Derek Robertson

Coleen Boyle\*\*

Peter van Dyck\*\*

\* Liaison Members

\*\* Ex Officio

**Staff of the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children attending was:**

Dr. Michele Lloyd-Puryear, Executive Secretary

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## Welcome and Introductions

After **Dr. R. Rodney Howell, Committee Chairperson and Professor of Pediatrics at the University of Miami**, called the meeting to order, **Dennis Williams, Ph.D., M.A., Deputy Administrator, Health Resources and Services Administration (HRSA)**, welcomed Committee members and thanked attendees for attending the second meeting of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. Dr. Williams also thanked Dr. Howell for serving as chairperson, and Peter van Dyck, M.D., M.P.H., M.S., Associate Administrator of the Maternal and Child Health Bureau (MCHB), HRSA, for serving as the HRSA representative for this Committee.

Dr. Williams noted that Federal maternal and child health experts have been involved in newborn screening for many years. Their involvement began when Robert Guthrie devised a practical system for the collection and transportation of blood samples and the screening test for phenylketonuria (PKU). Federal maternal and child health experts supported the field trial for the PKU test, which eventually involved 400,000 infants in 29 States. Soon after the field trial, State laws that mandate newborn screening provided the foundation for HRSA's current genetics program. However, recent advances in technology and the development of individual State laws have resulted in a patchwork of standards for newborn screening. Dr. Williams stated that all children deserve the same basic standard of care no matter what state they are born in. He highlighted the importance, especially to parents, of equity not just in screening, but also in the service infrastructure that supports the screening program. While the Federal government cannot impose standards on States, this Committee will advise the Department of Health and Human Services (HHS) on the appropriate guidelines to issue that States should follow to improve their newborn screening programs. Dr. Williams acknowledged the challenge is to find a balance between costs and the need to perform comprehensive screening on all newborns. Ethics and privacy issues also need to be considered in developing the guidelines.

Dr. Williams asked the Committee to analyze the American College of Medical Genetics report, "Newborn Screening: Toward a Uniform Screening Panel and System," and advise the Secretary of

HHS on the acceptance and implementation of the recommendations. Dr. Williams concluded by emphasizing that newborn screening is a high priority for HRSA. He looks forward to receiving the Committee's advice.

The Committee unanimously approved the minutes from the first meeting held on June 7-8, 2004. Dr. Howell also introduced Committee members who were not in attendance at the first meeting—James Collins, M.D., M.P.H., Denise Dougherty, Ph.D., and Derek Robertson, J.D., M.B.A.

### **American College of Medical Genetics' Report to HRSA/MCHB Newborn Screening: Toward a Uniform Screening Panel and System**

**Michael Watson, Ph.D., Executive Director of the American College of Medical Genetics (ACMG)**, discussed the decision making process used in developing recommendations for a standard newborn screening panel as part of this draft ACMG report that was produced for HRSA. The Committee was given the draft report prior to the meeting in order to review it and to enable the Committee to discuss the report and its recommendations at this Committee meeting. However, while the Committee has been able to review the report, public distribution will occur when HHS prints and distributes the final ACMG report.

Dr. Watson began by noting that in the two years since work on the report began, there have been many changes in States' newborn screening programs. Many States have increased the number of mandated conditions in their States, and there is more variation in the types of conditions that are mandated. Dr. Watson noted the difficulty in counting the number of conditions screened for in a State. Disorders included in a newborn screening panel are not always mandated by the States. In some cases, legislatures have mandated screening of newborns for certain disorders, but the tests have not yet been implemented. In yet other cases, States are conducting pilot tests on a subset of their newborn population.

Newborn screening in the United States is not universal, nor is it fairly distributed. There are only three conditions for which there is universal screening in the United States: PKU, congenital hypothyroidism, and galactosemia. Dr. Watson noted that given the variation among States,

supplemental newborn screening is primarily left to consumer initiative at the present time. One of the goals of the ACMG project is to promote standardization in newborn screening across the country by encouraging newborn screening programs to become aligned and uniform in their screening.

There is enormous variability in how decisions are made about what should be screened, and what evidence is evaluated in making those decisions. This variability has tremendous implications for analytical quality, interpretation of results, and collection of outcome data. Dr. Watson noted that very little outcome data is being collected at this time. However, to make informed decisions about newborn screening panels, it is necessary to begin collecting outcome data.

Dr. Watson reviewed the goals of the HRSA ACMG project. The primary goals were to develop a uniform panel of conditions and to develop a decision-making tool for use in newborn screening program expansion or contraction, including the development of criteria for newborn screening. States could use the criteria to assess individual conditions and determine their appropriateness for newborn screening. Secondary goals included enabling program evaluation to ensure realization of program outcomes, and examining the value of a national process for quality assurance and oversight. Dr. Watson focused his discussion on the first two goals.

Dr. Watson reviewed the process of producing the current draft report, including the extensive input received from experts from around the world. Representatives of programs, consumers and interest groups provided their comments and input for the report. Extensive reviews of the literature have also been conducted. Two work groups were organized under the project; one workgroup developed recommendations regarding the uniform panel and criteria that would determine the appropriateness of a condition for screening, and another workgroup has been examining diagnosis and follow-up issues of those newborns identified in screening programs. In addition, external review groups have reviewed materials, as they have been produced. A written draft report to HRSA has been delivered in the last several weeks.

The overarching principles of the project were developed through an understanding of what is important to each stakeholder in newborn screening. The principles include:

- Universal newborn screening is an essential public health responsibility that is critical to improve the health outcomes of affected children
- Newborn screening policy development should be driven by what is in the best interest of the affected newborn with consideration of the interests of unaffected newborns, families, health professionals, and the public
- Newborn screening is more than testing. It is a coordinated and comprehensive system consisting of education, screening, follow-up, diagnosis, management and program evaluation
- The medical home and the public and private components of the screening programs should be in close communication to ensure confirmation and the appropriate follow-up and care of identified individuals
- Evaluation and recommendation of conditions appropriate for newborn screening should be based on scientific evidence and expert opinion
- To be included in a newborn screening program, a condition should meet the following criteria: the condition is identifiable at a phase in which it would not ordinarily be recognized clinically; there is an available test with appropriate sensitivity and specificity; and there are demonstrated benefits of early intervention and timely identification
- The primary targets of newborn screening should be conditions that meet the criteria listed above. The newborn screening program should also report any other result of clinical significance
- There should be centralized data collection for longitudinal assessment of disease-specific screening programs
- Total quality management should be applied to newborn screening programs
- Newborn screening specimens are valuable health resources. Every program should have a policy to ensure confidential storage and appropriate use
- Public awareness coupled with professional and family education and training are significant program responsibilities that must be part of the complete newborn screening system

The next step in the project was deciding what conditions to evaluate. Dr. Watson discussed the issues surrounding accurate and uniform counting of conditions included in States' newborn screening panels. Variation in State programs extends to how conditions are counted; it can be based on the phenotype of the condition, established groups of conditions, primary markers (which may

relate to several different conditions), test response to treatment, or number of loci linked to a common phenotype. Complicating factors include clinical, biochemical, and molecular complexity of the conditions under consideration, constant progress in the understanding of conditions' natural history and etiology, implementation of multiplex platforms that allow the simultaneous detection of numerous biochemical markers, and gaps in the level of clinical knowledge among stakeholders involved with, or advocating for, the decision to pursue increasingly greater numbers of conditions.

Out of the 5000 genetic diseases listed on OMIM (Online Mendelian Inheritance in Man), case-by-case choices were made to strike the best possible compromise between established practices, expert opinions, and scientific evidence. In the end 84 conditions were selected for full evaluation. Lacking the expertise to address infectious diseases, the ACMG working group left infectious diseases out of the group of conditions to be evaluated. However, Dr. Watson indicated this Committee may need to discuss how to address the inclusion of infectious diseases in a newborn screening panel.

Conditions chosen for evaluation included endocrine disorders, hematologic disorders, inborn errors of metabolism among other conditions. Only 18 of the 84 conditions chosen for evaluation are currently screened for in 50% or greater of newborns in the United States.

Dr. Watson discussed possible approaches to standardization and uniformity, including assessment of the scientific evidence in the literature. The available literature was reviewed for information pertaining to incidence, natural history, screening test, diagnosis, quality, treatment of the condition, and other associated issues. For example, with regard to incidence, the best information available is from newborn screening programs. This data approximates general population data. Since many of the conditions included in a newborn screening panel are rare, standard errors in incidence estimates are large unless data covers the general population. In addition, many of the conditions have multiple genetic etiologies. Depending on how the condition is defined, those incidences can be broken out into the individual etiologies of the conditions, thereby making the issue more complex. Onset of condition is also important, since the goal of screening is to intervene and make a difference in the newborn's outcomes, but onset poorly captures non-penetrant cases. The burden of the condition is also an important criterion, with the evaluation of conditions biased toward more severe conditions for which the most significant difference could be made.

In addition, the screening test itself can raise issues. The gold standards by which one establishes a diagnosis have evolved rapidly the mapping of the human genome. Dr. Watson noted that functional tests, used to indicate that an individual is expressing a condition, could be more useful than genotypic tests (as generally used in newborn screening), which can only indicate whether an individual has the marker for the disease. Both may be valuable to newborn screening, depending on what information is desired. In addition, screening tests have evolved from singleton tests to algorithms and second-tier testing. Diagnosis is also increasing in complexity, with permutations of genes (synergistic heterozygotes) resulting in combinations of disorders. Many disorders, including extremely rare disorders, require similar treatment, which allows the project team to extend its view to a much broader group of patients with biochemically related diseases for which the treatment is quite similar.

The quality of the evidence is also an issue; natural history studies are becoming increasingly difficult as a result of ongoing intervention. Dr. Watson noted that there is a very limited national, organized data collection effort that would allow us to collect the kind of information needed to evaluate these kinds of criteria. In addition, some data collection is now proprietary. Given the rarity of some of the conditions that are screened and treated, there have been reduced pre-market data requirements, and more post-market surveillance. Such practices may become a model for collecting data on patients.

Dr. Watson discussed the review of the scientific literature. The literature for each condition varies in quality and magnitude. Project staff conducted a systematic review of all sources, including clinical evidence, cost/economic evidence and modeling, reference lists (Medline, PubMed), books, Health Technology Assessment Reports, the Internet, professional guidelines, and epidemiological studies. The literature was evaluated for study design, inclusion of subjects and outcomes, and effectiveness of treatment. The project team relied heavily on the Health Technology Assessment Reports produced by the National Screening Committee in the UK, which has done extensive reviews of the literature and the science behind a large number of the conditions screened in newborn screening programs. Limitations of the reports include the use of unwarranted assumptions and the use of the “self-evident evidence paradox” that states that if an intervention is truly effective, no one will study it.

The workgroup was charged with defining the criteria by which to assess the conditions. The group sought input from a variety of stakeholders, including providers of laboratory and clinical services and consumers, and consulted the literature, to create definitions and scores for each of the criteria developed to assess both the evidence and expert opinions. Criteria defined the condition, the test and the treatment:

- Incidence of condition
- Identifiable condition at birth
- Burden of the disease
- Test availability
- Test characteristics
- Availability of treatment
- Cost of treatment
- Efficacy of treatment
- Early intervention
- Early identification
- Mortality prevention
- Diagnostic confirmation
- Acute management
- Simplicity of therapy

There were 292 responses to the surveys sent out to assess the conditions chosen for evaluation. There were gaps in the geographic distribution of the respondents, but respondents represented a wide array of stakeholders. Respondents were asked to score particular conditions based on the criteria presented, and also were asked to evaluate whether each criteria was appropriately weighted. As a result of that input, changes were made to the definitions, language, and weights of some of the criteria. For example, importance to the newborn as well as availability of multiplex testing was given more weight because of its importance to public health.

Conditions were sorted based on their scores, whether or not a highly sensitive specific test, validated in the general population, was available for the condition and the level of evidence in the literature supporting the various criteria listed above. Dr. Watson reviewed the conditions that were ultimately included in the recommended uniform panel. Twelve conditions on the core panel are currently screened for in 50% of newborns in the United States. There are nine organic acidurias, five fatty acid oxidation disorders, six aminoacidurias, four hematological disorders, and six defined as other, for a total of thirty conditions.

Twenty-five additional conditions were identified as report-only. The presence of these report-only conditions is generally detected during screening for one of the conditions in the core panel, due to

the nature of the test. However, the report-only conditions may not be treatable or may be a condition for which the natural history has not been established because of the rarity of the condition. Dr. Watson suggested that the report-only conditions might not warrant the State investment needed for long-term tracking, because the meaning of that information is unknown. However, such information is valuable for the families and their providers. Dr. Watson emphasized again the number of conditions on the uniform panel and report-only category depends on how these conditions are counted. It may be necessary to reconsider report-only conditions, as well as those conditions for which no test currently exists, based on new screening methods, new treatments, and the evolving knowledge of the natural history.

Dr. Watson reviewed the evaluation flowchart that was used to confirm the survey findings by applying the evidence from the literature. Dr. Watson noted that the scores alone did not result in the recommendation to the uniform panel that is proposed. In arriving at their recommendations, they also considered responses to the survey and applied decision nodes from the evaluation flow chart. For example, sorting also occurred based on test availability, treatment availability and necessity, a known natural history, and whether all detected patients are affected.

Survey scores were also correlated and compared with existing evidence in the literature through the development of fact sheets on individual conditions. The levels of evidence guidelines of the American Academy of Pediatrics (AAP) were used to create the condition fact sheets. The fact sheets also contain information about the condition, such as the name, type of disorder, whether there is variation in ethnicity of individuals affected with the condition; what kind of screening method is used; what is its newborn screening status in the United States, and an indication of the magnitude of the existing literature for the condition based upon the number of PubMed references as of August 2004. The fact sheets also contain information on the gene or genes that are involved, the locus or loci involved, the survey score information, and costs. Dr. Watson noted that the cost estimates were variable, since most respondents did not understand the full costs of screening and treatment.

Dr. Watson reviewed the prospective evaluation tool that was developed. The project team made the survey tool more general so that States and programs can apply this tool to collect information. However, he cautioned, “some science does not need to be redone,” and that the review of scientific

literature of conditions might be something best done centrally, rather than have fifty programs convening the same experts to discuss the evidence. This centrally collected scientific evidence could then be supplied to the programs so the experts can use it to make decisions about what to include in their panel.

After going through the process of scoring conditions, applying the evaluation flow chart, and validating their results with the literature, the expert group devised a set of recommendations:

- Mandate screening for all core panel conditions
- Mandate reporting of any clinically significant conditions identified while screening for core conditions
- Maximize use of multiplex technologies and “second tier” tests
- Recognize that the range of benefits from newborn screening go beyond the infant’s mortality and morbidity
- Recognize the whole spectrum of benefits to families and society derived from early identification
- Advocate for outcome and effectiveness data collection

Dr. Watson concluded by outlining next steps. There are a number of ongoing projects that will improve the effectiveness of newborn screening programs, including a project to develop confirmatory algorithms for positive screens, and the development of “action sheets” for primary care providers, outlining appropriate responses to positive screens, including timelines and referral resources. In addition, HRSA recently funded regional newborn screening collaboratives, to help shift newborn screening activity to the local community level. Ongoing review of the evidence in the literature is critical to improving knowledge of both the conditions themselves and the outcomes from treatment, and possible financing mechanisms. In addition, Dr. Watson pointed out that an important to remember that moral and value judgements cannot be quantified by the literature. And both enter into the decision-making process.

Committee members discussed Dr. Watson’s presentation and the ACMG report. Due to the mechanisms used to disseminate the survey (e.g., listservs), Dr. Watson was unable to estimate how many individuals were asked to respond. Dr. Watson clarified the point that literature review

findings were inserted into the scoring process early on. Sensitivity and specificity, while useful pieces of information, were not included on the fact sheets since the data was not available. The most useful data came from newborn screening programs, but due to lack of uniformity and standardization in setting cut-offs and test characteristics, there is inconsistency, making the aggregation of State data difficult. For this reason, it is possible to estimate analytical validity, but not clinical validity.

Dr. Watson responded to questions about whether the scoring process was somehow “backward” —augmenting expert opinion with scientific evidence rather than vice versa. He noted that most of the conditions evaluated were so rare as to not have a large enough population from which to draw conclusions based on the scientific literature alone. For this reason, Dr. Watson suggested that a system of long-term tracking of newborns diagnosed with rare diseases is needed to enhance our knowledge base on health outcomes, the clinical course of disease, effective treatments, etc.. Such studies would increase our knowledge base and would support decisions regarding inclusion in/removal from a newborn screening panel. The National Institutes of Health’s rare disease centers might be instrumental in gathering this data, but it will most likely need to be a multi-agency effort.

Several suggestions were made to improve the strength and clarity of the report. Committee members noted that it is difficult to determine the extent to which the report presents an evidence-based review. It was suggested that the evidence used in producing the report be more transparent, perhaps through a re-worked methods section, so that those reading the report can make either the same or different conclusions based on the evidence presented. It was suggested that the fact sheets clearly identify gaps in the evidence base in the literature, and also they should not limit the literature provided on a fact sheet to twenty references. It was also suggested that the report clearly state the systematic process used to arrive at its conclusions to give it the proper strength, and that an epidemiologist also review all the fact sheets. A section in the report outlining the limitations of the conclusions drawn was also suggested.

Committee members discussed the nature of the recommendations they might make at this time. Dr. van Dyck noted that there might be two different “levels” of recommendations from the Committee—those that aim to improve the quality of the ACMG report, and others that address the

more “public” face of the report. The latter would deal with the conditions included in the mandated newborn screening panel.

This was followed by a Committee discussion on the evolution of inclusion criteria for State newborn screening panels. States traditionally kept a tight adherence to a certain set of criteria, including incidence, test availability, and treatment efficacy. At times these criteria have been codified into State legislative law. However, these criteria have slowly evolved to become less stringent. Knowledge of incidence has been supplanted by knowledge of whether the test would identify a condition before the phenotype presents. The concept of efficacious treatment has been replaced by whether there are benefits of early intervention, etc. There has been a transition from reliance on rigorous criteria to the examination of the best available evidence in the literature.

It was pointed out that if this Committee does not recommend a core panel to get States moving in the direction of uniformity in newborn screening panels, private companies may continue to offer screening, but may not offer all the newborn screening program components necessary for a complete newborn screening system. Committee members noted that the report provides a gap analysis so that the right data can be collected in order to continue adding tests to newborn screening panels.

A brief public commentary period focused on the ACMG report. Dr. George Cunningham, director of California’s newborn screening program and a member of the ACMG working group, noted that the working group also addressed quality assurance, and efficiency and effectiveness of the program and system as a whole. Dr. Cunningham also noted that the issue for policymakers is when is there enough evidence to support action? Dr. Cunningham stated the ACMG working group believes this report presents enough evidence to make the core panel recommendation. According to Dr. Cunningham, the scores have confidence intervals that are sometimes very wide, and both the scoring system and the validity of the sample is debatable. However, the resulting report identifies all the factors that must be considered when making a decision, and provides a protocol that can be used by States to do their own individual assessment. These concerns should not prevent HHS from making preliminary recommendations; however, Dr. Cunningham cautioned the Committee to be clear about the definition of “mandate” and its implications.

Dr. Harry Hannon noted that there are two or three disorders included in the “absolute” core panel of thirty conditions that are discussed in the text of the report where some difference in opinion existed as to their inclusion. Dr. Hannon requested that the tables should be “stand alone” documents, and properly note any issues regarding the conditions listed. In addition, an audience member asked the Committee to encourage States to conduct pilots of tests, for emerging diseases such as SCID.

## **Use of MS-MS by State Newborn Screening Programs**

**Brad Therrell, Ph.D., Director, National Newborn Screening and Genetics Resource Center,** reviewed the state of the States with regard to newborn screening, the use of tandem mass spectrometry (MS/MS), and the barriers to implementation of both traditional and MS/MS screening tests in State newborn screening programs. Dr. Therrell first reviewed how decisions regarding newborn screening are made. Ultimately, the State legislature controls the decision-making process; every State has a law mandating screening, sometimes specifying disorders and laboratories. Some legislatures pass on newborn screening decision-making responsibility to State Health Officers, State Boards of Health, and advisory committees. Decisions about newborn screening are influenced by the interests of the various stakeholders, as well as the costs and benefits associated with screening and the scientific evidence of such screening. According to Dr. Therrell, eight programs mandate two tests, all but two programs have standing advisory committees, and fees exist in all but five programs. Fees range from \$10 to \$139.33. However, Dr. Therrell noted that fees may not cover all costs of a program, nor do they always cover the same elements across States.

Dr. Therrell illustrated the variety of different models of laboratory services employed by States and the effects that these arrangements have on the number of conditions included in States’ newborn screening panels. For example, the northwest region, which includes Alaska, Oregon, Idaho, and Nevada, contracts with the State laboratory in Oregon for their newborn screening panel. Oregon’s newborn screening laboratory discontinued performing customized panels for each State in the region, thereby driving States to either adopt their panel or find another laboratory. Some States have contracts with other public or private labs to handle all of their screening, while others contract out only certain disorders or supplemental testing services. In other areas, the State has contracts with more than one laboratory, and in others the State does not allow other laboratories to perform

newborn screening in their State-only the State public health laboratory may perform newborn screening.

Dr. Therrell reviewed the status of MS/MS in State newborn screening programs. Some States have mandated testing, while others are conducting pilot tests or optional testing. Some States that have not been able to justify the cost of MS/MS equipment, given the size of their population, have opted to send their samples to other State laboratories. Thirty-one States mandate more than 8 disorders be screened by MS/MS (although more conditions may be offered to parents for their newborn but screening for the conditions is not mandated). Some States name the disorders to be screened, others indicate “all disorders that can be detected by MS/MS,” and others simply give a number of disorders to be screened. Some States, when listing conditions to be screened, add the caveat, “subject to available funding” in their regulations.

All data regarding incidence is reported voluntarily by the States; most States report data, but they run several years behind. Dr. Therrell noted that they are currently creating an online system for State data input, as cases are identified.

Barriers to implementing traditional screening were identified in a telephone survey of those States not testing for certain disorders. Barriers to screening include:

- Financial concerns
  - ◆ Lack of cost effectiveness data to support decisions, especially with lower incidence disorders (1 in 60,000 incidence was breakpoint for many States regarding whether or not to screen)
  - ◆ Data management—involves fixing computer systems, which can be costly
  - ◆ Authority to increase fees—may require approaching board of health; this option may not be acceptable in fiscally conservative States
  - ◆ Authority to utilize funds from fees, which may not necessarily be directed back into the newborn screening program
  
- Personnel concerns
  - ◆ Hiring freezes

- ◆ Finding qualified personnel without being able to offer competitive salaries
- Follow-up issues
  - ◆ Cut-off determinations
  - ◆ Lack of sub specialists such as clinical geneticists
- Advocacy confusion (deciding which test is more important)
  - ◆ Internal “politicking” for certain disorders
  - ◆ External (disease-specific groups)
- Privatization

Dr. Therrell reviewed the barriers to expanding newborn screening using MS/MS, as reported by States (regardless of whether they currently have MS/MS available). When asked what criteria their State used when determining what new disorders to add to their program, most respondents rated benefits of early intervention as the most important criteria, followed by screening test sensitivity and specificity, knowledge about the burden of the disease if untreated, costs of screening and diagnosis (short- and long-term), and incidence of the disorder in the population. Respondents listed these criteria regardless of whether their State currently used MS/MS.

When asked about issues that impacted the ability to expand newborn screening to include MS/MS, States that do not currently have MS/MS available stated that funding limitations are the most important barriers, followed by acquiring support within the organization, and then acquiring support from advocacy/parent groups. States currently using MS/MS had slightly different responses, indicating that the required advisory board recommendation was a barrier to implementation. When asked which criteria have been the most challenging to address in the context of MS/MS, most States responded that the short-term cost of screening and diagnosis is the most difficult, followed by knowledge of the burden of disease if untreated (for States not currently utilizing MS/MS) and long-term cost of follow-up (for States currently using MS/MS). Other criteria include access to diagnostic services for referred cases, and access to treatment and clinical management services after diagnosis.

Laboratory issues that presented difficulties in implementing MS/MS included the high costs of equipment and supplies, the availability of trained staff, development of appropriate cut-offs for the population, and delays in obtaining/availability of equipment and supplies. Issues related to follow-up that presented difficulties included accepted protocols or guidelines for diagnostic workups, availability/access to appropriate follow-up centers and specialists, resources and staff for adequate long-term tracking, and lack of a systematic approach to data collection.

Dr. Therrell concluded by noting that State newborn screening programs perform only limited research, given their focus on providing services. Exceptions to this include State laboratories that are affiliated with medical schools or larger programs with the resources to perform research. States with laboratories performing research include California, Iowa, Massachusetts, New York, North Carolina, and Wisconsin.

Dr. Therrell responded to Committee members' questions, explaining that even with the number of States currently using MS/MS technology, he does not believe there is enough capacity to handle all States' screening needs. Committee members discussed how to determine whether an MS/MS machine is utilized to capacity, highlighting the myriad factors that would go into the calculation, including cost, downtime, staff expertise and other factors.

Dr. Therrell further elaborated on the advantages and disadvantages of regional collaboratives for newborn screening. He contrasted the northwest regional collaborative, which performs the same panel on all States' specimens in the region, with the New England collaborative (where testing is performed in Massachusetts). The New England collaborative may be less cost efficient due to the customization of the panel for each State in the collaborative. Dr. Therrell noted that geographic boundaries and distances do not appear to affect the formation of collaboratives, but rather price seems to be the driving force. States shop for price, and often choose to send their specimens to the laboratory at which they get the "best deal." Dr. Therrell also commented that Pediatrix, a private laboratory, has developed good models with some States. For Dr. Therrell, the concept of follow-up centers may be increasingly important as States that do not have big populations continue to add disorders to their panels and need specialists to follow-up with newborns who have positive screens for rare conditions.

Committee members also discussed whether parents are increasingly using private laboratories to obtain supplemental screening beyond the screening that their State offers. Pediatrix, Baylor, and Mayo Clinic all offer supplemental screening. Dr. Therrell noted that it might be possible to get data on the use of private supplemental screening by parents. Committee members briefly discussed whether there are differences in quality or other measures between public and private laboratories. Dr. Therrell stated that while all laboratories are certified through the Centers for Disease Control and Prevention (CDC) quality assurance program, State public health programs include follow-up, whereas private laboratories offer lab services only. It was noted that there is no data right now on differences in terms of efficiency, performance, downtime, rates of false positives, and other related measures between labs.

## **State Policy and Finance Framework for Newborn Screening Programs: Case Studies of Select States**

**Kay Johnson, M.P.H., M.Ed.**, began by thanking HRSA and Association of State and Territorial Health Officials (ASTHO) for supporting this report on the financing mechanisms employed by State newborn screening programs, as described in case studies of seven States: California, Mississippi, Minnesota, Maryland, New York, Oklahoma, and Oregon. The study sought to examine how States are handling State budget shortfalls, consumer demand for more tests, rapid technology changes, and pressures to privatize. Ms. Johnson noted that States are managing change constantly, and HHS has the opportunity to provide the States with the tools and information they need to continue to effectively respond to new demands. The study also sought to determine why change is happening in the way that it is.

Newborn screening did not start as a legislated or mandated public health activity; rather it was mandated as a result of parent advocacy for policy change. Similar advocacy and policy development continues today. Due to their authority, public health agencies are best positioned to perform the range of services, including follow-up, necessary for newborn screening on a population-wide basis.

The State policy framework that resulted from the Task Force on Newborn Screening has several characteristics, including:

- Focus on the system, not just a test
- Set policies for adequate funding
- Involve professionals and consumers
- Adopt mandates and privacy protections
- Establish new criteria for adding tests
- Set program guidelines (e.g., quality)

According to the task force, there should be adequate financing for screening, short-term follow-up, and diagnosis; comprehensive care and treatment for all individuals with conditions identified by newborn screening; and quality assurance and evaluation. The task force outlined two principles regarding financing of newborn screening systems: first that core funding for newborn screening programs should come from fees sufficient to finance testing, short-term follow-up, and diagnosis, and second that other public health dollars should be used as necessary; and the funds should be coordinated and blended for treatment. The task force report talked specifically about ways to finance treatment and the role of government in doing so. It highlighted opportunities for States to coordinate public resources, including Medicaid, State Child Health Insurance Program (SCHIP), and Title V Maternal and Child Health block grant funds, in order to ensure that families that can't afford treatment have access to it regardless of their ability to pay. Specifically, there are opportunities in Medicaid managed care contracts to require coverage of services related to newborn screening, and to require that managed care organizations ensure access to specialty providers, as necessary. For the health insurance plans they regulate, States can mandate coverage of services.

Ms. Johnson briefly reviewed the Federal and State policies related to financing for newborn screening, including Health Insurance Portability and Accountability Act (HIPAA), Americans with Disabilities Act (ADA), Individuals with Disabilities Education Act (IDEA) entitlements, Medicaid/EPSTD child health coverage, State newborn screening mandates, insurance benefit mandates, and SCHIP benefits.

Ms. Johnson noted that while the source of newborn screening funds is shifting, the majority of funds come from fees collected by the programs. However, nationwide newborn screening is not always funded by fees nor are the program components fully funded by fees. Five States and the District of Columbia do not collect fees. For States that do collect fees, such charges often only cover test and lab costs, and may not support the expansion of new technology and equipment. In addition, economic pressures may limit fee increases in the future. At least two thirds of newborn screening funding comes from private sources, but other sources of newborn screening funding include MCHB block grant funds and Medicaid dollars, which most often finance follow-up and treatment. In addition, fees are not always covered by insurance and Medicaid, and even when they are covered, Medicaid reimbursements are often below cost.

States included in the case study sample were chosen to represent a variety of approaches to newborn screening. States varied in geographic distribution, in the number and type of tests performed, whether they have undergone recent expansion or innovation, in the use of public vs. private labs, whether they use fees or blended funding, and in their approaches to follow-up. The sample also included one regional lab model. All programs, with the exception of New York, which does not collect a fee, saw a fee increase during the 1997-2004 period reviewed. Core funding for screening, short-term follow-up and diagnosis is drawn mostly from fees, with additional funds from the MCHB block grant, Medicaid, and the State. Ms. Johnson reviewed each State's financing approach, as well as challenges encountered when adding tests, which illustrate the unique character of each State, reflecting differences in public health infrastructure; legislative commitment and authority; conditions included; laboratory set-up; follow-up activities; and financing. The case studies indicate that States are focusing on the system, not just on testing; expanding the number of conditions/tests; investing in state-of-the-art testing; financing more follow-up; engaging parents and advisory committees; and negotiating quality and privacy issues. From the State perspective, factors driving change include the recommendations of the National AAP Newborn Screening Task Force, advocacy by parents and professionals, arguments for equality across States, HRSA efforts to increase State capacity, and advances in science and technology. At the federal level, a climate for change has been created as a result of genetics planning and program integration grants, demonstration projects, the development of regional collaboratives, and other initiatives, combined with action and advocacy by parents and health professionals, private laboratories and health professionals.

Ms. Johnson concluded by enumerating some factors that may affect the future of newborn screening. She stated that while adding MS/MS capacity in a lab may be simple to accomplish, the fiscal, ethical, and system of care decisions that accompany it are more difficult. In addition, introducing profit into newborn screening has changed its landscape, and has brought up the question of what might happen if a private lab were to take the funding for, but not the full responsibility of newborn screening, which traditionally has been part of the public health role. The political climate is against increasing health care costs, which could lead to unfunded mandates or lack of action. In this case fiscal constraints may drive policy rather than vice versa.

### **Newborn Screening in New York—“How it Works”**

**Kenneth Pass, Ph.D., Director, New York State Newborn Screening Program,** discussed how newborn screening and particularly its financing, work in New York State. The State of New York finances newborn screening through a mix of State dollars, MCH Title V dollars, and various grant funds that are occasionally provided. There are three methods in New York to go about changing the newborn screening panel: through legislative action, at the request of the Department of Health; through regulation, as directed by the commissioner; and as an edict, with the creation of a budget line-item by the legislature. Dr. Pass reviewed the evolution of the screening panel in New York, starting with PKU in 1965, and ending with the latest additions of cystic fibrosis (CF), congenital adrenal hyperplasia (CAH), and medium chain acyl CoA dehydrogenase deficiency (MCADD) in 2002.

After the addition of MCADD, discussion focused on including all disorders that can be detected by MS/MS. Dr. Pass noted that once MS/MS is in place, expansion of the panel is simple for a laboratory, but more resources are needed for follow-up, including sub-specialists to care for newborns who screen positive. The inclusion of one additional disorder on a panel could almost double the workload of metabolic sub-specialists. Sub-specialists’ concerns however, do not center on the increased workload, but rather the poor reimbursement for the services they provide.

Based on his experience with newborn screening in New York, Dr. Pass offered several observations on newborn screening. First, he noted the need for an advisory committee. Decisions

regarding a newborn screening panel are too much for one individual to manage. In addition, in order to expand screening, proactive support of the health commissioner and/or lab director is needed, as is active support from the State legislature. Advocacy by parent groups can influence such legislative support. Barriers to change include the continuing evolution of technology and the question of whether should, rather than can, we screen; staffing levels; and the absence of support groups from the clinical or lay community for certain disorders.

## **Expanded Newborn Screening: The Mississippi State Department of Health Experience**

**Daniel Bender, M.H.S., Maternal and Child Health Director, Mississippi Department of Health**, began by thanking HRSA for their support of newborn screening throughout the years. Mississippi's newborn screening program began in the early 1980's with support from HRSA's SPRANS grants for statewide newborn screening of PKU and congenital hypothyroidism (CH). A law was passed mandating statewide newborn screening for PKU and CH. A newborn screening fee was instituted, charging each hospital \$2.50 for each newborn. Mississippi has tried to combine funds from the newborn screening fee for lab costs, with MCH funds to finance the equally, if not more important, follow-up costs. In the late 1980's and 1990's, newborn screening education began for each delivering hospital and health department. Given that the State has only one tertiary medical center, Mississippi instituted genetics satellite clinics throughout the State as the panel of disorders grew. Some clinics specialize in sickle cell given that 48% of deliveries in the State are non-white. While the State has an advisory committee, each disorder added to the panel was vetted through the State legislature.

Mr. Bender described the evolution of the testing panel. The first law passed in 2000 instructed physicians to provide information on all available supplemental testing, but physicians felt that this allowed no formal tracking mechanism. A second law then stated that the advisory committee will advise the board of health, which will then instruct the health officer on decisions regarding the newborn screening panel. In 2000, a two and a half year old male child, Ben Haygood, died of MCADD in a small northern Mississippi town. This tragic event brought a push for more expanded screening utilizing MS/MS technology. The Tennessee laboratory, which had handled Mississippi's specimens for over twenty years, was unable to provide MS/MS screening, so Mississippi had to

look elsewhere for that service. Mississippi sought advice from other States on how to bid for expanded MS/MS screening services. Mr. Bender noted that it is important to know what you are asking for and what you want when evaluating options regarding laboratory services, and not to “bite off more than you can chew.” The State opted to contract with a private company for its laboratory services. The State opted not to have the private company do the follow-up although the company had offered to do so. The State has comprehensive relationships with their physicians, and therefore has the ability to find screened positive children and bring them in for follow-up. Mr. Bender credits those relationships with the successful transition from screening for five disorders to screening at present for forty disorders. With the increase in the panel, the fee increased from \$35 to \$70, most of which is used for follow-up services. Now fees cover almost all costs related to newborn screening, and the State uses some tobacco funds to place nurses in the school systems for follow-up.

After Mr. Bender’s presentation, Dr. Michele Puryear was asked to describe HRSA’s regional collaboratives for genetic services. HRSA divided the country into regions based on birth rate, and funded seven regional collaboratives and one cooperative agreement for a national coordinating center. The reasons for the initiative include many of the issues discussed today and at the last meeting, including the inadequate distribution of genetic services. The collaboratives are focused on providing the necessary expertise to States and address specific capacity issues across States.

### **Office of Technology Assessment’s (OTA) Newborn Screening Study: Relevance to Today’s Issues?**

**Judith Wagner, Ph.D., Scholar in Residence, Institute of Medicine, and Julia Ostrowsky, B.Sc., M.Sc. National Center for Food Protection and Defense, University of Minnesota,** presented the Committee with a review of the Office of Technology Assessment’s (OTA) 1988 report on the most cost-effective measures for infants and children, published as a chapter in “Healthy Children: Investing in the Future.” As part of the report requested by Congress, OTA studied early prenatal care, newborn screening, well-child care, accidental injuries, and child maltreatment. Dr. Wagner’s goal is to demonstrate the relevance of this study, now 18 years old, to the issues before the Committee today.

The report had several findings with regard to newborn screening. First, OTA found that the USA and Canada are the only developed countries without a national screening program. Second, there is a lack of a coordinated network of newborn screening services in some areas that may reduce the overall effectiveness of newborn screening. Lastly, OTA reported that expanding newborn screening strategies to include additional diseases (homocystinuria (HCY), galactosemia (GAL), maple syrup urine disease (MSUD) beyond PKU and CH, and/or to take a second specimen, would save more newborns from death and disability, but the incremental costs per case found would be high.

There are several limitations of OTA's cost effectiveness analysis. The outcome measures used (cases detected per 100,000 infants screened) are outmoded. If done today, the outcome measures of interest would be years of healthy life lost, or a measure of quality-adjusted life-years. These measures would be more applicable given the rarity of many of the diseases detected through newborn screening, and would have resulted in lower estimated costs per unit of effectiveness. However, Dr. Wagner noted that agreement on the appropriate outcome measures might never be reached. The OTA study also used a discount rate on future costs of 7%, which is higher than today's standard of 3%. It is unclear what effect this change might have had on the results; it may have reduced the cost of screening, but also it may have reduced the cost of treating the condition. At the time of the report, the data was limited on outcomes of the disease and of screening. The screening technologies evaluated for the report are now also outmoded. Dr. Wagner noted that these limitations demonstrate that the cost effectiveness of an intervention depends greatly on the way one values the alternatives.

How interventions are defined and what baseline program they are compared with influence both the findings and the usefulness of analysis. An intervention isn't simply whether one tests for a specific disease or not. The elements of a screening intervention include:

- The number of samples, timing relative to birth, and location of sample collection
- Diseases to be tested for
- Screening technologies to be used
- Laboratory procedures
- Confirmatory procedures
- Follow-up and treatment regimens

OTA chose as its baseline a one-specimen regime for PKU and congenital hypothyroidism, which was universal at the time. OTA compared this baseline with expanded alternatives involving second specimens, or additional tests on the first specimen, or combinations of additional tests on the first specimen and the second specimen, based on the current questions operative in the field. OTA found that all alternatives were costlier than the baseline. Using cost-effectiveness frontier mapping, OTA was able to identify two superior strategies. However, Dr. Wagner demonstrated that the strategies chosen as superior depend upon what is chosen as the baseline.

Dr. Wagner compared the OTA study with two recent cost-effectiveness studies. The first study was published in 2002, and was based on the Wisconsin newborn screening program. The baseline comparison used was no screening for MCADD, compared with MS/MS screening for MCADD as the alternative. The study found that there was a positive benefit of using MS/MS in screening in terms of cases and years of life lived, but it would also lead to additional costs, and therefore using MS/MS to screen for MCADD was not cost effective. Dr. Wagner contrasted this study with the Health Technology Assessment produced by the National Health Service in the United Kingdom. The baseline in this study was the existing PKU screening program. The first level of comparison was to change the technology used for screening (to MS/MS) and add one disorder—this was cost saving. Adding other diseases was also cost saving. The two studies contradict one another, but the critical difference is the choice of a baseline and how alternatives were aligned.

Julia Ostrowsky concluded the presentation by discussing the considerations for designing today's cost effectiveness analyses. Private sector labs pose a greater and more complex issue for cost effectiveness analyses. OTA examined costs and savings outside the public sector. It is important in today's newborn screening environment in order to consider the effects of the private sector lab on cost flow. Involvement of private labs present possible cost savings in capital investment in MS/MS equipment and specialized training of personnel for the State. However, private labs may also create possible loss of fees to the State. In addition, offering supplemental testing for an additional fee (to those who can afford it) poses equity issues to resolve.

A wider range of screening outcomes also complicates newborn screening cost effectiveness analyses. Analyses have to consider at least four types of outcomes: providing treatment to avoid

neonatal mortality or severe mental retardation; offering treatment that may reduce morbidity later in life; offering screening outcome information for family planning purposes only; and conducting screening for research purposes, with no immediate clinical benefit to affected infants or their families. In addition, a wider range of tests is available than when the OTA study was conducted, presenting a greater need for evaluating outcomes and effectiveness. Issues to consider include the impact of screening organization (e.g., regional systems, centralized labs, etc.), the effects of reducing disparities among States, and the potential role of Federal-State partnerships in financing and guiding implementation of national goals.

## **Cost Effectiveness Analysis of Newborn Screening**

**Stephen Downs, M.D., M.S., Associate Professor and Director, Children’s Health Services Research, Indiana University School of Medicine,** further discussed cost effectiveness analysis for newborn screening. Inborn errors of metabolism are a significant cause of mortality and morbidity, and new technologies, such as MS/MS, have enhanced our ability to detect them. However, the introduction of MS/MS and other developments have raised the question of cost effectiveness. Despite the fact that screening can reduce morbidity and mortality, the conditions detected are rare, and there are significant costs related to screening and follow-up.

Dr. Downs explained that the objective of their study was to determine, based on the range of newborn screening tests and technologies, the incremental costs and clinical effects of screening. It was also a preliminary effort, on a small budget, to “cross check” the findings of the ACMG report. The study involved “evaluating trade-offs,” to understand the total costs and effects of various screening tests, taking into account testing, treatment, and the disease-induced costs that might be avoided with appropriate screening, and to make the trade-offs in screening explicit.

The study first examined the costs and effects of individual screening tests, compared with a baseline of no tests. However, this study was of limited interest given that tests are not usually examined individually. The second aspect of the study compared MS/MS and a panel of individual tests. Dr. Downs used a decision tree for the analysis, with a branch associated with each cost and effects, which add up to a total cost for each screening test. The study attempted to examine all associated costs, including costs to society. The probability of each outcome was derived from the

literature, including efficacy and sensitivity of the test. The study also was able to derive from the literature the prevalence of disease, sensitivity and specificity of the tests, the costs of testing, the costs of treatment, disease outcomes, costs of disease outcomes, and the values associated with disease outcomes. Costs of testing, however, did not tease out fixed and incremental costs of adding tests.

Dr. Downs discussed the weaknesses in the data used. Weaknesses in the data include poor data on incremental costs of testing; the inclusion of indirect (productivity) costs of health outcomes (a panel on cost effectiveness in health did not recommend this); the use of mid-range cost estimates for MS/MS when the costs are variable; and the use of modest confirmatory/false positive costs. In addition, the rates of adverse outcomes from MCADD in the unscreened population are unknown; the prevalence of MCADD and PKU may be overestimated; and the risk of death from undetected CAH may be overestimated. However, Dr. Downs noted that screening using MS/MS still appears to be a “bargain,” even when using a “pessimistic” case model, which adjusts the data to account for the potential weaknesses mentioned.

Dr. Downs offered several conclusions from the study. First, he noted that screening for most inborn metabolic and endocrine disorders is cost saving or reasonably cost effective; exceptions may include CAH and GAL. Second, screening for GAL may be prohibitively expensive. Lastly, MS/MS appears to be cost saving or reasonably cost-effective, due to its ability to multiplex, its ability to replace other testing modalities, and its ability to detect MCADD. Dr. Downs enumerated the reasons why the analysis is preliminary and incomplete: the fixed and incremental costs of screening programs were not teased out; the risks of sequelae from undetected disease (MCADD, CAH) are uncertain; and costs to evaluate “secondary targets” detected by MS/MS and costs savings from avoiding diagnostic odysseys were not quantified. Dr. Downs noted that although the study used the societal perspective, the societal perspective is not part of the analysis. The Committee will need to grapple with this perspective. Newborn screening programs bear the costs of screening, but others incur the benefits of screening, such as insurance companies, educational programs, and families.

## **Cost Benefit Analysis of MS/MS in Newborn Screening in California**

**George Cunningham, M.D., M.P.H., Chief of the Genetic Disease Branch of the California Department of Health Services** presented a preliminary economic analysis, funded by HRSA, of a pilot program conducted in California to study how best to incorporate MS/MS into their existing newborn screening program. The pilot, funded by the State legislature, was conducted from January 2002 through June 2003, and in that time it detected 51 cases of the disorders being screened.

California's cost effectiveness analysis was based on practical policy decisions that the State agency must make. Given that the State already operates a newborn screening program, what are the incremental costs of adding MS/MS to the existing program? What are the incremental benefits? Dr. Cunningham emphasized that the data and estimates used are based on the actual California pilot program experience and the demographics of the State.

First, a classic cost-benefit analysis was conducted using conservative estimates—the annual costs of screening and treatment costs of individuals detected or missed. Estimates were based on the actual personnel needs for the comprehensive program, which includes educational materials, testing, interpretation reporting, the costs of paying for follow-up contracts, and for quality control for laboratory and clinical elements of the screening. The classic cost-benefit analysis resulted in additional annualized program estimated costs after start-up of \$10,782,405.

Benefits of the program were examined. The baseline was the cost of care avoided based on the distribution of the 83 cases, which they would expect to find if screening is done on the whole population, and reports in the literature of the natural history of the disorders. The study was concerned specifically with what it will cost California because this data is what their State policymakers are interested in examining. Total lifetimes costs, without MS/MS screening, were estimated at \$10,568,350; while total lifetime costs with screening were estimated at \$5,117,905, for a net benefit of \$5,450,445. Adding to that the economic value of lives saved, the total cost benefits are \$48,150,445. This results in a cost benefit ratio of \$4.46. Dr. Cunningham noted that given the controversy around assigning numeric values to human life, cost-effectiveness or cost utility analyses are usually favored over the cost-benefit design used in this study.

Committee members discussed the application of cost-effectiveness and cost-benefit analyses to the newborn screening issues before them. Much of the data used in these analyses is variable. For

example, detection rates could be made less conservative, the impact of false positives could be considered, the costs of equipment could be increased or decreased—all leading to different conclusions. However, Dr. Howell noted that all the presentations pointed toward the same general conclusion—that newborn screening is generally a cost-effective measure and a sound public health investment. It was also noted, however, that the overall conclusions from the presentations might not apply to all thirty conditions listed in the ACMG report. Committee members discussed the variability of false positive rates, costs of equipment, etc. among States. It was suggested that if all States worked toward a common goal—in setting acceptable false positive rates and in collaborating to obtain better prices of equipment—then much of the State-to-State variability could be resolved. It was also suggested that perhaps the Committee should accept the value of newborn screening and focus on how to improve the newborn screening programs in the country given the resources available, rather than debate the cost-effectiveness of the measure.

### **Public Comment Session**

George Hardy, Jr, MD, MPH, Executive Director, of the Association of State and Territorial Health Officials (ASTHO), public comments emphasized three key points: 1) the role of the state public health agency; 2) the need for an adequate support systems and 3) state representation on the advisory committee. State public health agencies have played a pivotal role in the administering of effective newborn screening programs across the nation. In the advent of new advances in service integration and national infrastructure, Dr. Hardy urged the Committee to recommend the necessary guidance and adequate funding to support a comprehensive system of care for newborns across then nation. In pursuit of this comprehensive system of care, Dr. Hardy noted the need to include additional perspectives from critical components of the states. Dr. Hardy's comments were concluded with acknowledgements (see Appendix A) and no further discussion.

Norman Kahn Jr, Vice President for Science and Education for the American Academy of Family Physicians (AAFP) brought his comments to the committee as the Project Director for the Genetics Primary Care Faculty Development Initiative. Dr Kahn introduced a promising new curriculum for the nations' primary care clinicians that is to be released in 2005 at the World Meeting of the Nation's Family Physicians. The web based curriculum will provide on-line support in the area of genomics, with a concentrated effort on newborn screening. Dr. Kahn explained that the new curriculum will serve a dual purpose as both and educational tool for clinicians and patients. Dr.

Kahn ended with appropriate acknowledgements (see Appendix A). Dr Boyle (CDC) followed up with a question concerning how to locate additional information on the module for newborn screening. Dr. Kahn's responded that the information will be available after April 2005 and the primary contact will be MCHB's Dr. Marie Mann.

Mr. Kharrazi, parent, from Alameda, CA, discussed the effects of delayed diagnosis on families affected by cystic fibrosis. Mr. Kharrazi, expressed his support of the new category of report only disorders, which are the result of recent technological advances and have provided wonderful health benefits far surpassing the previous techniques. With support from over 40 families Mr. Kharrazi detailed the serious and often irreversible damage that delayed CF diagnosis can have on the infant and subsequently their families. From quality of life to long – term guilt, the issues reap considerable damage on the infants, families, and society as a whole. With this noted Mr. Kharrazi, recommended the Committee seek funding to delve deeper into the cost benefit analysis of early diagnosis for not only the child but the family at large. Mr. Kharrazi closed with acknowledgements (see Appendix A) and no discussion followed.

Dr. Nancy Green, Medical Director of the March of Dimes, gave brief comments stating the March of Dimes support for the findings and recommendations in the report to be submitted to the Secretary. Dr. Green continued by reiterating the March of Dimes intentions to continue working toward improving the screening process, high quality follow-up and their commitment to public and professional education. Emphasizing the need to maintain this new coordinated system between the state and federal efforts for implementation and evaluation, as well as the ongoing application and validation of new technologies clinical applications, Dr. Green made note of HRSA's exemplary new regional projects. She concluded with a suggestion for the formation of four subcommittees to assist the advisory committee in moving forward newborn screening policy. The four committees were: new technologies and clinical applications; evaluation of identified affected children; quality assurance and control; and newborn screening education and training. Dr. Green integrated acknowledgements for a host of federal agencies. Her comments concluded without additional discussion.

Ms. Sharon Terry's, President and CEO for the Genetic Alliance, public comments focused on several important facets of the newborn screening paradigm. Ms. Terry explained how newborn

screening has brought decision making and lived experiences to a cross roads where consumers and affected individuals attempt to balance economic resources at the stake of young lives. Ms. Terry pointed to the key issues uncovered by the Genetic Alliance's Public Health Action Group. These concepts include lack of newborn screening awareness, inadequate community resources, advancing technologies but slow progressing legislation and policies. Strongly supporting the focus on the uniformed screening panel, Ms. Terry brought to the table specific recommendations for the advocacy community. These included proactive outreach, input from underserved and underrepresented communities, medical home resources, uniform newborn screening panel of at least thirty test across the states and increased resources and training for health professionals and communities alike. Ms Terry closed her discussion with a recommendation to support the panel as determined by the ACMG report but to include the advocacy's aforementioned recommendation as a larger more comprehensive package. The comments ended with no further questions.

Mr. Dean Jerrehian, parent, speaking on behalf of the National Coalition for PKU Disorders, urged the speedy implementation of the American College of Medical Genetics recommendations. He encouraged the committee to move forward with the recommendation as precious lives are being lost daily and small steps toward a uniform system would prove most beneficial. Mr. Jerrehian took this time to point out concerns from the preceding discussions: creating a standard of care; the importance of a good follow-up program; and public versus private labs. Following closely with the stance taken by the National Coalition for PKU Disorders that newborn screening was the responsibility of parent advocates, the government and the medical community and ideally works as a private-public partnership, Mr. Jerrehian does not ask for the perfect screening program but a routine and comprehensive standard of care for all. He expressed the need for adequate follow-up among those tested as well as those not tested and finally Jerrehian took the stance that healthy competition will improve the validity of testing among private and public laboratories. Mr. Jerrehian closed with his thanks and acknowledgements to the committee for their efforts. There was no discussion following his comments.

Mrs. Jana Monaco, parent, speaking on behalf of the Organic Acidemia Association and Coalition for PKU and Allied Disorders, extended her regards to the committee for their attempts to make uniform screening a reality. Mrs. Monaco expressed pleasure in the supplemental screening information sent out to states. She recommended the committee accept the American College of

Medical Genetics recommendations for an expanded newborn screening program as is. Additionally, Ms. Monaco advocated for funding for the developmental metabolic sub-specialists throughout the country. Despite being a very small cohort, they have proven to be an integral part of follow-up and management and most notably deserve additional support. Ms. Monaco closed with her expressed gratitude for the support of the committee. Her comments were not followed by any further discussion.

Ms. Jill Fisch's, National Director of Education and Awareness, at the Save Babies through Screening Foundation (SBTS) comments focused on a number of topics. She began with thanks to the committee for acting swiftly to notify parents of supplemental screening options in the states. Ms. Fisch, expressed a number of recommendations that she wishes the committee consider. She asked for a plan to help low income families obtain supplemental screening through programs such as Healthy Start until access is available uniformly. Ms. Fisch also expressed the need to avoid the rigid thinking of testing only "treatable diseases" and to look to creating an inclusive standard of care that will provide ample data for future progression. Additionally, Ms. Fisch pointed out that this standard will help to clear up a number of issues across the states from counting analytes/markers to clinician apprehension. She closed with a recommendation for educational programs for the medical community that will impart the necessary knowledge to provide appropriate care for their patients. Ms. Fisch extended her thanks and her comments ended without further discussion.

Ms. Micki Gartzke, Director of Education and Awareness, at Hunter's Hope Foundation asked the committee to remember the focus of the meeting, the children and families. She centered her comments on two main topics, immediacy and solutions. She expressed thanks to the committee for their work on the issues of parental notification for supplemental screening options following the last committee meeting. She continued with a recommendation to make this process a state/congressional mandate to assure parental education on the availability of such tests. Ms. Gartzke cited innovation through regional networks, contracted public and private partnerships as the key to improving the overall quality and scope of newborn screening since states are facing limited resources and capacities. Thus, Ms. Gartzke, supported the recommendation to adopt of the American College of Medical Genetics report. She closed with thanks to the committee for their support and efforts. Ms. Gartzke's comments were not followed by additional discussion.

Dr. Karen Dixon, President, Parents of Children and Infants with Kernicterus, showed the committee a short video which focused on the value of screening for hyperbilirubinemia. Following the video, Dr. Dixon's comments were closed with no further discussion.

Dr. Michael Rock, Cystic Fibrosis Center Director, at the University of Wisconsin-Madison used his public comments to clarify some information for the committee from prior discussions. Dr. Rock expressed his gratitude for CF being included among the 30 disorders required for uniform screening. He chose to revisit and clarify the evidence for the following points cost analysis, nutritional benefits and cognitive benefits of CF screening. Additionally, he pointed to studies that support the success of newborn screening survival statistics that assert its success across the nation. Dr. Rock's comments concluded with no further questions.

Dr. Philip Vaughn, neonatologist, serving as an administrator at Pediatrix Medical Group, began his public comments with a brief overview of Pediatrix's mission and interest in newborn screening including hearing, genetics and metabolic diseases. Dr. Vaughn asserts Pediatrix's continued involvement in furthering the field of newborn screening through a variety of efforts. These included a host of private and public partnerships that support public health programs through outsourcing of lab testing, providing supplemental testing and licensing of tandem mass spec intellectual property. Dr. Vaughn affirms that Pediatrix's is working in conjunction with a number of agencies to promote the health and well being of infants. They are willing to participate in subcommittees and extend their support in this capacity as necessary. Dr. Vaughn's comments concluded without questions.

## **Discussion**

Dr. Howell opened the discussion for comment and questions about the ACMG report. Committee members first discussed the "report-only" category of disorders, since it may represent a paradigm shift from the way conditions are now reported and handled clinically. Dr. Watson explained that the "report-only" category stemmed from one of overarching principles of the project—that any clinically significant result should be reported out of the screening laboratory. For example, MSCHAD is a clinically significant condition, but its natural history is not known. What do you do with the information in the report-only category? It can be treated as a false positive, but it is

important that this information goes to the physician responsible in order to appropriately manage that patient. States would be able to collect the information, and decide whether to bring program resources to bear on that particular disorder. It was also suggested that a mechanism be developed to collect information on newborns who are not picked up through screening, but who are diagnosed outside of newborn screening programs with a report-only condition. The report-only category offers the opportunity to aggregate more information around some of the rarer conditions.

It was noted that only a handful of disorders in the report-only category are not included in the differential diagnosis of other disorders on the panel. Thus, the case cannot be made that these additional cases would detrimentally increase the case load of clinical centers involved in their diagnosis; the incidence of the secondary targets is very low.

### **Committee Business**

The main issue before the Committee was the consideration of the ACMG report. Dr. Howell indicated that the ACMG report could serve as a basis for Committee recommendations. A Committee member moved to accept the report and send it to the Secretary with written comments both from the Committee and the public. Before accepting this motion, Committee members discussed the report and possible recommendations, attempting to balance a careful review with an expeditious process, preferably before the next meeting. Dr. Howell clarified that the Committee is not responsible for modifying the HRSA/ACMG report, but rather for considering its recommendations and advising the Secretary on its contents. It is expected that the document will be available for public comment, and that all public comments will be made available to the Committee for review.

The Committee discussed the mechanisms by which it could begin to make recommendations to the Secretary immediately. Some Committee members expressed reservations in endorsing the report without having discussed it in detail or having obtained public comments on its contents. It was decided however, given the strong interest in forwarding the report to the Secretary as soon as possible, the Committee will accept and recommend the report and forward it to the Secretary immediately. There will then be a thirty day period in which electronic written comments from the public will be collected and the Committee will form its comments and recommendations and forward them to the Secretary with the appended public comments. The recommendations from the

Committee will include any reservations that Committee members may have about its methods or conclusions. A majority voted to accept this motion; two members abstained from voting.

Committee members discussed the remaining business matters before the Committee. Committee members asked that the agenda for the next meeting include a discussion of the ACMG report, a report on the regional collaborative centers newly funded by HRSA, a report on the rare disease centers initiative sponsored by the NIH Office of Rare Diseases, and a presentation on the new newborn screening online module from the American Academy of Family Practice. In addition, it was asked that the Committee receive more information related to the financing of newborn screening.

It was also suggested that the Committee discuss a work plan for the next year. The Executive Secretary will review the ACMG report and highlight all topics for potential further discussion. The Committee will decide as a group which topics to explore. Subcommittees will then be formed based on the topics chosen for discussion and the accompanying yearlong work plan. The schedule of meetings for the next year is Jan 20-21, 2005; April 21-22, 2005; July 21-22, 2005; and October 20-21, 2005. Dr. Howell thanked the members, speakers, and audience members for participating and concluded 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/ \_\_\_\_\_

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

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

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

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

## ***Appendix A: Written Public Comments***

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1. **Dean Jerrehian – Parent**
2. **Jana Monaco- Parent**
3. **March of Dimes-Jennifer Howse, Ph.D.**
4. **National Society of Genetic Counselors (NSGC)-Jennifer Sullivan**
5. **Matthew’s Mission Inc.-Jill Fisch**
6. **Richard Koch, M.D.  
USC School of Medicine**
7. **Martin Kharrazi — Parent**
8. **Hunter Hope Foundation-Micki Gartzke**
9. **Pediatrix Medical Group, Inc.-Philip Vaughn, M.D.**
10. **Genetic Alliance - Sharon F. Terry, M.A.**
11. **Association of Public Health Laboratories-Jelili Ojodu**
12. **American Academy of Family Physicians-Norman Kahn, M.D.**
13. **Stephen Edwards, M.D.  
Past President, American Academy of Pediatrics**
14. **Cystic Fibrosis Foundation-Michael Rock, M.D.**
15. **Association of State and Territorial Health Officials-George Hardy, M.D.**

**Comments of Dean Jerrehian as a Parent of a Child with a Metabolic Disorder and on  
Behalf of the National Coalition for PKU and Allied Disorders<sup>1</sup>  
September 22, 2004 ACHDGDNC Meeting**

I am incredibly lucky. I am the parent of an 11 year old boy, Matt, who has PKU. Matt has been treated by diet since he was a couple days old and is leading a perfectly normal life - going to school, playing with friends, riding his bike, playing ball. He is able to do all this because he was identified at birth by the Pennsylvania newborn screening program because Pennsylvania, like all states, screens for PKU. Pennsylvania screens for PKU because 40 years ago Dr. Robert Guthrie, along with parents, doctors and others, pressured Pennsylvania and other states into requiring a simple test for PKU. I submit these comments because I am lucky that someone was there for Matt to insist on PKU screening 40 years ago. I submit these comments to see if together we can try to change the luck of the kids born tomorrow.

According to the Maternal and Child Health Bureau web site, this Committee was created to “advise and guide the Secretary regarding the most appropriate application of universal newborn screening tests, technologies, policies, guidelines and programs for effectively reducing morbidity and mortality in newborns and children have or at risk for heritable disorders.” Thanks to the report of the American College of Medical Genetics as presented by Dr. Michael Watson,<sup>2</sup> we have conclusive evidence that the best way and perhaps *only* way to accomplish this goal today is to recommend all newborns are tested at birth for the disorders identified by the American College.

There is no question that it is nearly impossible to clinically identify the listed disorders pre-symptomatically and the first sign of trouble is most often serious, permanent injury or death. There is also no question that once identified by newborn screening, the listed disorders can be treated, virtually eliminated the most damaging consequences for these early identified children. Currently testing varies by state, making it a game of Russian Roulette for our children. In fact, there are thousands of children born every year with these “testable, treatable” disorders who will suffer severe and permanent injuries or die unless they are tested at birth. This leads to the inescapable conclusion that the recommended expanded newborn screening will prevent morbidity and mortality in these children.

Thus, we call for this Committee to immediately recommend that all newborns be tested for the disorders identified in the by the American College of Medical Genetics. While there may be some complicated issues that go along with recommending expanding newborn screening (a number of which will be discussed below), these issues do not change the fact that expanded newborn

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<sup>1</sup> The National Coalition for PKU and Allied Disorders is a nonprofit organization comprised of individuals, metabolic support groups and professionals directly involved with issues related to inborn errors of metabolism requiring low protein diet including, Phenylketonuria, Maple Syrup Urine Disease, Homocystinuria, the Organic Acidemias, the Urea Cycle Disorders, and Tyrosinemia. The National Coalition seeks to improve identification, treatment and management of PKU and the Allied Disorders and improve the lives of people with those disorders through advocacy, education, support, promotion and support of research, and services.

<sup>2</sup> Of course, the American College report is not the only evidence of the efficacy of expanding newborn screening. In addition to the experience of various states and private laboratories that have shown that this expanded screening works, a number of other articles on expanding newborn screening have appeared in the literature.

screening will save lives. Once this Committee acknowledges this by adopting the American College recommendations, the Secretary can provide guidelines on which disorders should be screened for to state legislatures, parents can use these recommendations to persuade states to do better for their children, doctors will know what is the best available care and babies all over the country will have an equal shot at leading healthy lives.

With respect to the “complicated issues,” it is a good thing that Dr. Guthrie did not worry too much about such ancillary matters. If he did, newborn screening for PKU may never have gotten off the ground (it certainly did not satisfy the criteria put forward at times for adding a screening test) and there would be thousands of more people born with PKU in institutions rather than productive members of society. For example, we often hear that a disorder should not be screened for unless there are adequate follow-up procedures in place. I call this the “ostrich fallacy.” Not screening for a disorder (putting your head in the sand) does not mean children do not get the disorder. In fact, unless the child dies, a child born with a disorder that is not identified at birth is going to require much more follow-up care than a child identified by newborn screening. If the argument is who does or pays for the follow-up,<sup>3</sup> it is certainly better to screen the children and notify the parents before the child is injured even if no follow-up is available than have no screening and no follow-up. Not only will follow-up be substantially easier for a pre-symptomatic child, parents have an incredible knack for fending for their children (the Amish in Pennsylvania who shun modern conveniences like telephones and cars, happily help pay for sophisticated laboratory equipment for their local clinic to help treat their disproportionately large population of children with genetic disorders). Thus, please do not recommend waiting for a state to implement a particular follow-up procedure before implementing testing; that is not doing parents or children any favors.

There is also a disproportionate amount of discussion on cost effectiveness of a particular test. While I believe that the American College of Medical Genetics and a number of other reports show that the recommended screening is cost effective (especially when all tests are bundled), there should be no requirement that every public health program be cost effective. In fact, the vast majority of government programs are not cost effective - which is why they are government programs rather than handle by private industry.

With respect false positive and false negative concerns, newborn tests for additional disorders should be compared to other routine screening tests such as mammograms, PSA, and colonoscopy rather than a “gold standard” like PKU. In any event, when my son was born, we were first told he had PKU, then we were told (after follow-up testing) his initial test was a false positive, and then we were told “oops” the second test was a false negative. So as the father of a child who was both a false negative and a false positive, I would prefer being a false positive to a false negative any day. By not testing for a disorder you have guaranteed none will be detected - which is much worse than an occasional false positive.

When asked who should do the screening - a state lab or a private lab, most parents would say they do not care as long as it is done. I agree with this, but would like to point out that if the state is not going to do the screening, it should get out of the way and allow doctors and parents the option of sending blood work to a qualified private lab that will do the full array. In fact, the state,

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<sup>3</sup> In the long run, follow-up treatment should be covered by insurance as any other medical condition.

doctor and/or hospital should be required to inform parents of the availability of the expanded screening - especially where not such testing is not required by state law.<sup>4</sup> This comment also applies to Dr. Therrell's presentation regarding barriers to states expanding their screening programs. If the states cannot expand screening in a timely and competent way, the children born in that state should not be penalized. The state should either contract with one of the qualified private labs or the parents should be allowed to opt out and send blood to a private lab.

More controversial perhaps is who decides what level of care is to be provided to newborns - or what tests should be done now and in the future. Testing should be done because pediatricians know it is good care. In fact it should be the *standard of care*. Thus, responsibility to conduct this screening lies first and foremost with the doctors and hospitals to which we entrust our children. The National Coalition for PKU and Allied Disorders believes that newborn screening is the joint responsibility of parent advocates, the government and the medical community and ideally works as a public-private partnership. While public health departments are excellent at tasks such as tracking disorders and ensuring proper follow care is available, doctors and hospitals are often in the best position to rapidly utilize the newest technology. Parent advocates should serve as watchdogs and to inject a level of urgency and reality into the debate. If a doctor knows comprehensive newborn screening may prevent devastating injury to a newborn, she must provide - or at least inform the parents of the availability of - the test, regardless of whether the government has said she must. If doctors fail to do so, then the government must step in. This essentially creates a failsafe system which ensures children get the best care available no matter where they are born. This model has proven effective in Massachusetts where the state, not hospitals, has instituted comprehensive newborn screening and in Pennsylvania where 99% of hospitals have stepped into the void to provide this screening obviating the need for the state health department to act. With the exception of Pennsylvania, , doctors and hospitals have historically not taken initiative with respect to or had any interest in newborn screening. Recently a number of doctors and hospitals have realized that expanded newborn screening is simply good care and have, without any legislative mandate, begun screening for more disorders than required by law. Although progress has been slow, this can be blamed on a 40 year old culture of neglect. Legislation may be necessary now to get doctors and hospitals up to speed, but in the future they need to pay attention to advancements in newborn screening.<sup>5</sup> Doctors should never again cede control of the standard of care to the state. If doctors do sit on their hands, parents should be prepared to force them to improve our children's standard of care by any means necessary - be it education, lawsuits, legislation or anything else that will help our children.

In preparing my comments for this meeting, I realized that I first became aware of the opportunity to expand newborn screening in 1998 when I met Michael Metil, a child my son's age who was severely disabled because he was born with Glutaric Acidemia at a hospital that did not screen for that disorder. In 1999, I attended an American Academy of Pediatric conference on newborn screening in Washington. I happened to find my notes from my public comments at that meeting in which I proposed immediate screening for the disorders we are talking about today. Later that year I attended a NIH meeting in which I made the same plea. In 2000, the American Academy of Pediatrics noted the lack of national consistency and published a call for more study of newborn screening. At that time, the National Coalition for PKU and Allied Disorders issued a

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<sup>4</sup> If a doctor knows about this test, it would likely be an unethical failure to obtain full informed consent if the newborn's parents are not given the test as an option.

<sup>5</sup> There must be a mechanism implemented to add new disorders and an opportunity for parents to nominate a disorder for inclusion.

statement essentially saying the time for study is over and the time for action had arrive. While some states and hospitals have taken action, for the most part not much as changed. Since our call for action four years ago, approximately 5,000 children have been needlessly injured. I would hate to come back here in four years, or even four more months to find out no progress has been made.

While we applaud the work of the American College of Medical Genetics and this Committee, we believe now is not time for further study, but the time for leadership and action. Children in North Carolina, Massachusetts and a few other states are now getting state-of-the-art screening. This screening has been shown to work and work well, saving hundreds if not thousands of children from serious and needless injuries or death. There is no reason why children in the rest of the country do not deserve this same level of care.

Internationally renowned pediatrician and educator, Frank Oski, once said “What distinguishes . . . pediatricians . . . from physicians in other branches of medicine is our belief that prevention is the way to go. We don’t try to turn the clock back - we want to set the clock right to start with. We can prevent disease by taking advantage of the opportunity presented by having children and newborns in our practice.” Here we have the ideal opportunity to start kids off right. There is no time to dawdle. Every day three children are born in this great country who are being missed and will suffer devastating injuries or death because they happen to be born in the wrong place - at the wrong time. If they were born in Massachusetts instead of New York or in two years instead of this week, everything would have been different for that child and their family. These are real children whose parents might be at the next Committee meeting with another horror story to tell. So let’s get to it and save some lives. Requiring that parents of newborns be informed of the availability of expanded screening from private labs and recommending every newborn in every state be screened for the disorders identified by the American College of Medical Genetics would be a great place for this Committee to start.

## **PUBLIC COMMENTS**

Jana Monaco- Parent

Good afternoon. It is an honor and pleasure to be here once again to speak on behalf of the Organic Acidemia Association and Coalition for PKU and Allied Disorders and foremost, my Stephen. When we last met, I shared my story about Stephen and his unfortunate fate with Isovaleric Acidemia due to lack of Comprehensive Newborn Screening. I also spoke of the joys and triumphs of our daughter Caroline who just celebrated a happy and healthy 2<sup>nd</sup> birthday on Monday despite Isovaleric Acidemia thanks to early detection. Since the previous meeting in June, our life continues to depict its ability to change drastically when a child is undiagnosed early and suffers brain damage. Shortly after, I had the pleasure of attending the National Coalition for PKU and Allied Disorders Conference in Detroit with my children and meet many other affected families as well as several physicians and professionals dedicated to children and the field of genetics and metabolism. However, Stephen caught a strep infection from me the day after we returned. Unlike me, he was hospitalized and to our surprise, went into septic shock. Once again, I found myself on the fast track of medical intervention to save Stephen's life as his blood pressure plummeted. Dopamine was administered to stabilize his blood pressure as he was quickly transported from Inova Fairfax Hospital to the Children's National Medical Center's PICU, so that he could be closely managed by the metabolic team. With prompt attention and action from the medical staff of both facilities, Stephen responded to the "big gun" antibiotics as they call them, and remained in the hospital for ten days. We have now added \$48,000 to our infinite pile of medical statements. We have also recently discovered that one of his surgically corrected testicles has moved out of position and just last week had one of those prolonged bouts of hiccups that fortunately did not result in a hospital stay... just a few sleepless nights for me. It is all in a days work in the life of a home with a brain damaged child. It has been said that good things come out of bad situations. As a result of Stephen's recent hospitalization, I will have the privilege of speaking before the Northern Virginia Pediatric Society on Newborn Screening and Metabolic Disorders in November.

I wish to thank this Committee for the letter that went out regarding states to notify parents of the option for further testing. I understand that our parent testimonies played a significant role in the development of that document. It brought tears to my eyes to think that Stephen's ordeal made a difference. We must not be complacent and stop here. As we await the American College of Medical Genetics' recommendation for the expanded list of disorders to be screened for, I urge you to accept and approve it "as is." We parents want all thirty disorders with the hope of more to come in the future. Because of the great time, effort and research that went into compiling this list I ask you to move forward and get it published. We need not reinvent the wheel, for time is of essence, and the publication of this list is crucial for those of us needing the leverage on the state level. I will be speaking at the Genetic Alliance Advisory Committee Meeting in Richmond next month in support of NBS. I need this publication to back me up.

As you leave here, remember what I and many other parents go home to and know that you have a hand in preventing other families from living the life that we do.

Thank you again for your hard work and dedication in the quest to Expand Newborn Screening for all babies.

**National Society of Genetic Counselors**  
**Public Statement: September 23, 2004:**

Good afternoon. I am Jennifer Sullivan, representative for the National Society of Genetic Counselors (NSGC). As you are aware, the NSGC represents genetic counselors worldwide and is the leading voice, authority and advocate for the genetic counseling profession. Over the years, the NSGC membership has contributed significant experience and expertise in implementation and coordination of state wide genetic services and clinical follow-up of positive newborn screen results. The NSGC strongly concurs that the status of newborn screening is at a critical juncture for re-evaluation. This reassessment is especially urgent because of the inequalities that can develop between states with new technology. For example the current discrepant implementation of tandem mass spectrometry has lead to the inclusion of variable disorders between states. In the near future the availability of new treatments for genetic disease (i.e. enzyme replacement therapy for Pompe disease) will create a new disorders which would then become potential targets of newborn screening.

The NSGC endorses the regular and systematic review of newborn screening through a standardized mechanism. Regular review in such a manner will permit the natural inclusion of diseases as appropriate and effective. The NSGC also enthusiastically supports the rationale for and designation of the 30 “core disorders” for newborn screening recommended by the American College of Medical Genetics (ACMG). Further, we agree that the reporting of all abnormal newborn screening detected during the process of providing these “core disease” results would enhance overall medical knowledge and care. In turn, we support the call for comprehensive and timely reporting of screening statistics, short term follow up of screening results, and long term follow up of affected individuals. The NSGC agrees that such reporting will facilitate the generation of invaluable information to guide present and future newborn screening initiatives.

Our organization represents health care professionals closely affiliated with both the reporting of newborn screening results and the coordination of patient care and follow up through clinical appointments. Thus, the NSGC respectfully requests that in its recommendations this Committee also address the need for careful evaluation of each state’s resources to support the ACMG suggestions. Existent state systems which have already incorporated expanded newborn screening have experienced increased demands for clinical follow-up services on already limited resources. We know first-hand the burden that genetic disease places on families, particularly when newly diagnosed, and therefore, we request the evaluation of each state’s clinical genetics resources consider how these resources will need to expand along with the newborn screening program. Further, the NSGC suggests that discussion of funding issues for anticipated services on all levels of the newborn screening process be included in any final recommendations related to expansion of newborn screening services.

NSGC also requests that any Federal policy regarding newborn screening include the stipulation that appropriate newborn screening requires the provision of comprehensive genetic services incorporating biochemical geneticists, clinical medical geneticists, genetic counselors, and metabolic dieticians. As the experts in genetic conditions, we want to ensure that high risk infants and their families receive the highest quality of medical care, regardless of geographical location or ability to pay.

In conclusion, the National Society of Genetic Counselors enthusiastically supports the efforts of the Secretary’s Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and

Children to address the issue of newborn screening. NSGC respectfully asks that this Committee consider the points we have presented within the context of any recommendations the Committee makes regarding the possible development of federal policy around newborn screening services. The NSGC continues to be at your disposal and will be pleased to work with you as the Committee continues to consider these issues.

**Public Comments**  
**Advisory Committee on Heritable Disorders**  
**And Genetic Diseases in Newborns and Children**

Thank you for the opportunity to speak today. My name is Jill Fisch. I am the President of Matthew's Mission Inc., a not-for-profit corporation formed to create awareness about newborn screening and to promote SCAD research. I am also the National Director of Education and Awareness and a member of the Board of Directors of Save Babies Through Screening Foundation (SBTS).

We are a family severely affected by SCAD. My father, two of my three children and I have all been diagnosed as having SCAD. My son Matthew was the first to be diagnosed, after two years of searching for answers as to why he failed to thrive and suffered from developmental delays.

There are a few issues I would like to discuss today. At the June Advisory Committee meeting, I spoke about Parental Notification of Supplemental Screening. It is imperative that Parental Notification be mandated across the country. This information must be given to families in the early stages of pregnancy, which would allow the family to weigh its options and make an informed decision. It is a known fact that people involved in newborn screening programs in various states have admitted to having supplemental screening performed on their children and grandchildren. It is quite unfortunate that the general public does not have the opportunity to obtain the same knowledge and give their babies the same healthy start.

We also need to have a plan under which low income families can obtain supplemental screening, possibly through the use of grant money or a voucher program. Perhaps this can be accomplished through the Healthy Start program. Until the states screen for all disorders, it cannot become an issue of only the rich being able to obtain supplemental NBS.

There has been much discussion regarding screening only for disorders considered to be treatable. If disorders are not screened based upon treatment availability, how will the medical community develop treatments for these disorders? There is substantial value in knowing. The use of the word 'treatable' is an issue due to the fact that in the 1960's the World Health Organization (WHO) decided that you can only screen for disorders that have known effective treatments. That was then, this is now. WHO's language should be updated to "screen for disorders for which there is substantial value in knowing." Genetic disorders can and do happen again. Regardless of treatability, parents need to know before they decide to attempt further pregnancies. While the death of a first child may not always be prevented, with comprehensive newborn screening, subsequent deaths can be prevented.

Kileen Hall, a board member of SBTS, and her husband lost their first child 28 hours after birth. Supplemental screening would not have saved him. The medical examiner concluded incorrectly that a heart defect was the cause of death. The couple had another son, who also died 28 hours after birth. The second death was preventable. Kileen and her husband suspected a connection between the two deaths. They found out their second child had VLCAD. They went back and had other testing performed on their first son. He also had VLCAD. Supplemental screening on Kileen's first son would have prevented the second death. Regardless of degree of treatability and evidence or lack of evidence to support such, supplemental NBS prevents or lessens serious consequences in many cases.

Some doctors and state officials are still saying that some of the disorders are so rare, it is not worth the expense of testing for them. It is as though a child with a very rare disorder is worth less than a child with a more common disorder. Remember, it is not disorders that are excluded, it is the children with these disorders who are excluded. The incremental cost for running the additional tests is insignificant. How many damaged or dead children do we need to document before we learn that early detection improves the quality of their lives? Let's screen them, find out who has what and collect data about interventions that are provided in a positive, proactive way.

We also need to address the manner in which states are counting disorders for which they screen. Many states are inflating their counts. There must be national standards set. The states should list the analytes/markers they are testing for as that must be a precise number and list separately the conditions to be considered in the differential diagnosis of an abnormal result for each of them, alone and in combination.

The last issue I would like to address is the resistance shown by members of the medical community when asked to perform supplemental NBS. I have had many cases brought to my attention where a family is prepared to have their child supplementally screened and have been talked out of it while still at the hospital. These families then had to seek the screening through their pediatricians. It would be quite tragic if a child suffered from a disorder and had serious complications while the family was trying to get the child screened. One pediatrician told a mother it is too time consuming to perform the test. There needs to be an educational program in place for the medical community so that they become informed and this does not happen. The best thing we can do is arm the doctors with proper knowledge so that they can provide the best care for their patients. When a parent is looking to have their child supplementally screened, they should be met with encouragement, not discouragement.

Thank you for the opportunity to share.

Jill Levy Fisch  
Founder and President of Matthew's Mission  
205 Delhi RD.  
Scarsdale, NY 10583  
914 588 1127

September 06, 2004

Dear Dr. Puryear:

I am delighted that you are accepting written comments in regard to the ACHDGDNC meeting on September 22-23. Naturally I am strongly in favor of expanding newborn screening to include tandem mass spectrometry. Obviously it should be on a national basis. My greatest concern is that there are no training programs which provide financial support for young physicians to enter the field of metabolism. Long ago, money was available to support fellowships in metabolism to learn the clinical skills necessary for good long-term outcome. At one time, NCH held annual meetings for clinic directors on development in this field. With newborn screening expansion, the need will be even greater. I hope that something can be done so that we will have a cadre of younger people entering the field.

Will you kindly put me on the mailing list to receive minutes of the Committee so I can keep up with progress in this field. I am pleased to report that Gov. Schwarzenegger has signed an expansion bill for California.

Richard Koch, M.D.  
Professor of Clinical Pediatrics  
USC School of Medicine

**Public Comments by Martin Kharrazi to the Advisory Committee on Heritable Disorders  
and Genetic Disease in Newborns and Children  
(September 23, 2004, Jurys Washington Hotel, Washington, DC)**

My name is Martin Kharrazi. I live in Alameda, California. My wife and I have five children. Our middle child has cystic fibrosis (CF). Our son was diagnosed 11 years ago on his third birthday. During his first three years of life, we struggled to learn of his diagnosis because at the time California did not have a newborn screening program that included CF, nor does it currently. Despite a five-day hospitalization for a respiratory infection at four months of age, poor growth even after dietary changes, foul smelling, runny and frequent stools, an insatiable appetite, chronic bronchitis and coughing, sleepless nights, and many other symptoms, we have discovered that our son's diagnostic odyssey is mild in comparison to other's. We cannot expect that our pediatric care providers can consistently make a CF diagnosis when far more common reasons exist for these signs and symptoms.

Dr. Watson and other speakers yesterday pointed out that the criteria for newborn screening are changing in the wake of recent technological advances, like tandem mass spectrometry and DNA analyses, and increasing public advocacy. A new category of "REPORT-ONLY" disorders has been created for those disorders picked up in the course of multiplex testing protocols. It appears that there is a perception by the Expert Panel that providing such information early in a child's life is important for families and their care providers and is in the best interest of the affected infant, even though demonstrated health benefits from early intervention have not been clearly established.

In support of this perception, I would like to provide the Committee with a summary of the impacts of delayed diagnosis on families, provided to me over the last year by over 40 families with CF after an e-mail request to a CF listserv. Families reported that a delayed diagnosis of CF comes with large irreversible negative impacts on the affected person's health and development, quality of life, longevity, compliance with medical regimens, self-image, family structure, and major life decisions. There were serious impacts on the relationships between family members. The stress around not knowing what was wrong damaged the family. Economic losses were common during the pre-diagnostic period. Parents developed strong views about incompetence in the medical care profession. Negative effects on families were compounded the later the diagnosis of CF was made. Trust in the medical system was lost, at a time when it could offer so much good.

Long-term parental guilt around not finding out sooner was difficult to avert altogether or remove later. Delayed diagnosis meant that opportunities were lost to make informed decisions about health care, employment, housing, insurance, reproduction, and other matters. Parents felt that appropriate steps could have been taken to prevent their child's now irreparable lung disease had they known sooner about the diagnosis.

A few parents who had a first child diagnosed on account of a second child being diagnosed early in life via newborn screening summed it up by saying that it is far better knowing the diagnosis rather than being tormented by not knowing it. It was extremely hard to plan for the future when it was unclear what was wrong with the undiagnosed child with CF. There was parental regret, anger and pity for the older CF child who was not able to benefit in the way the younger child could through prevention and focused CF medical care. This care is considered to be most effective for persons who present early without damaged lungs or nutritional deprivation.

As the Committee goes forward with making recommendations to the Secretary, it would be my hope that research funding becomes available to comprehensively measure and evaluate the costs, risks and benefits of an early diagnosis to not just the affected child, but to the broader family of affected children. This is an area in newborn screening research that has been largely neglected here in the United States. “REPORT-ONLY” disorders may offer a golden opportunity to evaluate the impact of providing information to families and physicians about disorders that do not yet have clear treatment benefits. The results of such work would help policy makers solidify the criteria for newborn screening, as the availability of tests for genetic disorders increases over time.

In closing, I would like to express my appreciation to those on the ACMG expert panel who have decided to include CF on the national core panel of disorders for newborn screening, a decision which is in line with recommendations to be coming out of the CDC and the CF Foundation later this Fall. Newborn screening is a necessary first step to the receipt of adequate medical care for CF and likely a countless number of other disorders.

Micki Gartzke Public Comments

9/21/04

Advisory Committee (on Heritable Disorders and Genetic Diseases in Newborns and Children Public Comments

Good afternoon, Mr. Chairman and members of the Advisory Committee (on Heritable Disorders and Genetic Diseases in Newborns and Children). Thank you for this opportunity and for your work on behalf of children and families in the United States. My name is Micki Gartzke; I am the Director of Education and Awareness for the Hunter's Hope Foundation. And just as Dr. Edwards did at the opening of his presentation at the last meeting of this Committee, I urge Committee members to remember that first and foremost you are dealing with children and families, not just diseases. I come to the newborn screening world from the perspective of a parent who has lost a child due to lack of early identification and consequently- lack of access to effective treatment. For this reason alone I am committed to help educate expectant parents of newborn screening, help children receive the greatest access to equitably distributed newborn screening and thus, their right to a healthy start in life. I am a childless mother- not by choice. It is not a role I relish. I will do whatever I can to prevent this unnecessary tragedy from happening to other parents

*(Jim Kelly, the Founder of Hunter's Hope and my colleague who presented public comments at the last "Committee meeting sends his regrets as he is unable to be here today due to scheduling conflict. He asked me to send along his compliments on your work to date and he looks forward to continued participation.)*

### **Immediacy and Solutions are my two main messages today!**

From a mom's perspective this is all about IMMEDIACY and the fact that there may not be enough money to throw at this, nor the time for the individual state health depts. to get up to speed on ALL aspects of newborn screening, keeping in mind the babies foremost, before many more thousands of children die or become permanently disabled, this concerns me greatly. Children continue to be born while waiting for programs to be tried and retried.

My kick-off comment is a great big thank-you to this Committee and HRSA for taking a leadership role in parental notification with your letter encouraging states to inform parents of supplemental screening. You are victorious in your pragmatism in this area and I believe there can be a significant impact in a relatively short time because of your immediate response to the comments you heard from parents as the last Committee meeting that parental notification needs to come first, above all else! This information must be given to families in the early stages of pregnancy, thereby allowing families to make informed decisions.

I say this because I continue to hear, why didn't I know about this... if someone would have only informed me, etc. These expectant parents have a right to make this choice, the states do not have the right to withhold this information.

Expectant parents truly need to be informed of this unwitting lottery their newborns are unnecessarily involved in. Why do I think this? It has been approximately two months since the HRSA letter of encouragement went out, a great first step, however, it may not have been the solution to the parental notification problem. I have not seen the states proactively pick up this ball and run with it. I, and a number of my professional and parent advocate newborn screening colleagues, have inquired to a number of relevant health officials regarding this letter and the ensuing parental notification issue. I wish I could report today that we feel positive about the states cumulative efforts in this area. Sadly, we do not. I will tell you, that I have heard State Newborn Screening officials tell me that they have informed their own families of supplemental newborn screening and ensured that their own families' newborns have received supplemental newborn screening, but have not been compelled to share this information with families in the states for which they have a duty to provide public health. I have concerns about this type of activity. I'm trying to understand how that is the right thing to do. You are the experts, help me understand why that type of leadership should be allowed to continue. I have seen budgets passed recently to upgrade newborn screening programs, that is great news, at the same time I see no funds appropriated for parental notification. Infrastructure and staff, yes, parental notification no, this is not good news! Because of this we recommend that this Committee either recommend that the States do parental notification or encourage Congress to require States to inform parents in writing of the potential for their children to receive additional newborn-screening tests that may not be required under state law. We must start by mandating that the hospitals educate parents on the availability of supplemental NBS tests. This parental notification must be meaningful and informed and require consent.

We think, like other professional societies and organizations, that Newborn screening should continue as a mandated state public health process, with ultimate responsibility for a successful program resting with the state public health department.

We believe it that innovation through regional newborn screening networks and contracted public - private partnerships is likely to be the key to improving the quality and scope of newborn screening programs, keeping the focus on the health of the newborns and efficient use of resources. State programs are under capacity and without funds for increasing competencies or capacity.

SOLUTIONS ARE AVAILABLE TODAY THROUGH PUBLIC PRIVATE PARTNERSHIPS e.g., Miss-Pediatrix Mayo-Minnesota; We all know what these models are, along with the models of regionalization of newborn screening programs and how they are already working. The solution seems so simple. Screening tests, technology, and treatments are all available today. We just need to use them. We need to fix our national NBS system so that currently available resources are used to give every child

the right to a healthy life.

#### Cost/Benefit

I recently read in the CA Senate Bill No. 1103 "According to the Centers for Disease Control and Prevention, the average lifetime cost of providing services to a person with moderate mental retardation is \$1,014,000. For every 20 additional cases identified through expanded screening, average lifetime cost savings could exceed \$20,000,000. \$20,000,000 savings on 20 lives, what is the savings on the 15,000-18,000 lives that I keep hearing about that are affected negatively on an annual basis. I am not a mathematician, but the number has got to be an enormous savings to our country!

Other published studies have also indicated the cost savings and effectiveness associated with expanded screening.

From the last minutes of this Committee's last meeting I read that the mission of HRSA's work is "to assure high-quality health care to underserved families and individuals nationwide, with the goal of moving towards 100-percent access to health care and zero health disparities for all Americans." As far as newborn screening goes I think the entire nation has been underserved and I commend this Committee and HRSA for moving forward to improve this vital national program. It is the very first health care we give our children, I can't help but wonder why this scope does not match the universal access of mandated immunization programs? From these same minutes I read that "Dr. Watson concluded his presentation by mentioning several issues to be addressed in the future, including that lysosomal disorder tests and treatments will soon be available." With tests and treatments in the pipeline for these disorders and others I look forward to the new guideline recommendations and am hopeful that they will be quickly be established and adopted as "standard of care" for newborn screening.

Again, I commend HRSA and Dr. Watson for his comprehensive project in this area, but in the two years that this valuable project has been ongoing, without mandated parental notification of supplemental screening, many thousands more children have been negatively affected.

State public health departments NEED TO USE ALL AVAILABLE RESOURCES, including private sector resources to screen infants at birth? I DO NOT UNDERSTAND HOW NOT DOING SO CAN BE IN THE BEST INTEREST OF PUBLIC HEALTH?

I know the Committee is going to continue to work hard and progress quickly on these issues and others. And I look forward to participating and helping however I can!

Thanks you for the opportunity to share my comments!

Micki Gartzke  
Director of Education and Awareness  
Hunter's Hope Foundation

Testimony for the Record on behalf of

**Pediatrix Medical Group, Inc.**

Submitted to the Advisory Committee on Heritable Disorders and Genetic Diseases in  
Newborns and Children

Dr. Rodney Howell, MD, Committee Chairperson

Submitted by:

Dr. Philip Vaughn  
on behalf of

Pediatrix Medical Group, Inc.  
1301 Concord Terrace  
Sunrise, Florida 33323

and

Pediatrix Screening, Inc.  
90 Emerson Lane  
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Before I begin my comments, I want to personally thank the members of the Committee and the other attendees for their attention to this important issue. I am Philip Vaughn, a board-certified Neonatologist currently serving in an administrative capacity at Pediatrix Screening.

Pediatrix Medical Group is the nation's largest healthcare company focused on physician services for neonatology, maternal-fetal medicine, and other pediatric subspecialty care. The company's roots lay in neonatology, but our commitment to the health of newborns allowed us to branch out into other related subspecialties and services.

Pediatrix Medical Group is composed of over 725 physicians in a national group practice. Our clinical practice cares for over 3,000 infants every day. Our Research and Education Department demonstrates our commitment to improving the lives of the infants we care for. Our research expertise includes data base management on nearly 1 million patient days per year. This data base now includes outcomes representing more than 4 million patient days. It is instrumental to retrospective research and prospective multi-centered clinical trials. Our educational outreach provides continuing physician and nursing education from across the nation and over 70 countries world wide through a web based educational system.

For the last decade we have been strong advocates of newborn hearing screening programs. Through our hearing screening programs over 250,000 infants per year are screened using automated brainstem response technologies. Identified patients are tracked through diagnostic and therapeutic care by our case managers in a case management system we developed and support.

With the addition of genetic and metabolic disease screening, Pediatrix Screening now tests more than 500,000 infants per year. The common theme is that early testing and intervention for hearing and metabolic disease is vital to ensuring the best possible patient outcomes. Newborn screening compliments our organization mission to ensure the healthiest possible start on life.

Recent communications from the Health Resources and Services Administration (HRSA) have expressed strong support for parents to be educated about additional newborn screening tests that are available for their baby—but not mandated. Other national organizations focused on the health of mothers and babies now publicly support comprehensive newborn screening and expanded efforts by private and public entities in this area to help improve the health of newborns through screening.

Expanding public-private screening partnerships is the logical means to serve the evolving needs of newborn screening programs nationwide. Pediatrix Screening proudly participates in several successful public-private partnerships that speak to our ability to tailor newborn screening programs to meet the needs of public health programs.

Our newborn screening services are readily available through a variety of channels and include a comprehensive spectrum of testing and follow-up services.

Elements of Successful Partnership Models include complete Outsourcing of Testing Services, Outsourcing of Tandem Mass Spectrometry, or Licensing of Tandem Mass Spectrometry Intellectual Property. All of these models are currently in use. Yesterday we heard about the Pennsylvania and Mississippi models of testing that involve outsourcing of laboratory testing. We are the private lab that performs testing for those programs. Pediatrix also licenses our interpretive algorithms to a number of laboratories providing newborn screening, including Mayo Medical Labs. Minnesota, in conjunction with Mayo now provides another model of public-private partnership that is improving the lives of newborns. Dr Rinaldo has indicated his concerns regarding unnecessary high false positive rates – rather with appropriate testing algorithms, such as those shared by Pediatrix Screening and Mayo, acceptable metrics can be established to ensure that excessive follow-up costs do not submarine efforts to expand screening. This model demonstrates partnership between Minnesota's Department of Health and a private lab, Mayo.

Finally, to fulfill the immediate testing need, Pediatrix offers our StepOne™ program. Pediatrix Screening offers informational brochures and supplemental testing services to individual parents, physicians and hospitals which can be obtained by phone, web, or by contract with health care providers and hospitals. This service is provided across the United States and can serve as an excellent method of delivering comprehensive testing.

The leadership teams at Pediatrix Medical Group and Pediatrix Screening are committed to support and collaborate with existing newborn screening programs. We are dedicated to improving the health of our newest generation.

Through our Research and Education Department we will continue to support opportunities for improved understanding of important newborn issues. This includes issues surrounding newborn screening where continued research is needed. The resources of our Research and Education Department stand ready to participate in this important task.

I would like to take a moment to clarify statements made earlier in this meeting. It has been our experience that private laboratories are not taking resources away from public health programs by performing testing. Most states do collect fees that cover testing, and some additional components of program administration (such as follow up). For those states that have chosen to outsource testing, some component of collected fees is used to perform testing, and other funds (whether part of fees, or separate appropriations) are used to fund the other program components. As such, screening programs that outsource testing retain funding for the remainder of the system. In fact, typically due to the efficiencies achieved in the laboratory component, funds are more

readily available for the other vital components of testing by outsourcing with the right partner.

Second, significant financial resources are being used in the care of diseases identifiable through screening today. As critical care medicine has improved, most children in crisis from these disorders are salvaged, but too frequently after irreversible damage. Life long disability care for these affected individuals ultimately is funded by some combination of public and, to a lesser degree, private payers. As such, funding programs conceptually should begin with an aggregation of funds used in treatment of affected infants, and funds used in current screening programs. With those funds properly accounted, we will then be able to allocate sufficient moneys to fund expanded screening with a focus on operational efficiency and objective outcome metrics (such as turn-around time, false positive rate, instrument up-time, etc....), follow-up care and case management, and ongoing research. Tax dollars ultimately are being used for these diseases, just inefficiently and after harm has been done. A more rational reallocation of funds currently used in the care of these disorders is required.

In closing, let me reiterate Pediatrix commitment to the health and wellness of the infants under our care. We look forward to supporting the continued evolution of expanded screening nationwide, and remain available to support the work of the Committee by our direct participation. We are pleased to be a member of the larger newborn screening community and eagerly anticipate the future of newborn screening.

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

Consumer Concerns about Newborn Screening

• Public Testimony •

Sharon F. Terry, MA  
President & CEO, Genetic Alliance

Thank you for the opportunity to make public comment today. Thank you also, for the work of your committee – for the vision and leadership of the Genetic Services Branch of MCHB/HRSA, and for the immense work of Mike Watson on the Uniform Screening Panel.

My name is Sharon Terry, I am the president and CEO of the Genetic Alliance – a coalition of 600 advocacy organizations representing over 14 million individuals affected by genetic conditions, both common and rare.

I sit in this position not as a professional but because:

I am the mother of two children affected by a genetic condition, and the founder of a small disease-specific advocacy organization.

The advocacy community has a great number of concerns regarding newborn screening. My brief comments will be both general and specific.

There are a number of premises that must be articulated when newborn screening is considered on the federal level. The first is overarching:

We are constrained by economic models developed within our crippled health care system – this conversation would be a different one in a nation with a more equitable alignment of resources.

Next, there are a series of basic premises for consumers:

- Parents want healthy babies – at any cost
- Often parents do not know that:
  - Their infants are being screened
  - Screening across states is variable
  - Attributes of tests such as sensitivity and specificity; analytical and clinical utility, and validity are variable
- In lived experience, the odds of being affected are either 0% or 100%
- Benefit analysis is not conducted from a medical model

**I would like to comment more fully on the last two points.**

**In lived experience: the odds of being affected are 0% or 100%**

In the moment that one receives a diagnosis, a line is crossed. One's worldview is quite different from the moment before the diagnosis. In the new experience, the discussion of odds – whether one or will or will not get a disease, becomes irrelevant and individuals have a poignant, though usually unconscious, understanding of public health perspectives verses personal health issues. The public generally assumes that odds apply to individuals. Consumers do not experience the

test, diagnosis, the day-to-day struggles, on a population level – it is completely personal. The affected family, individual, newborn uses their lived experience as the prism through which all life is assessed.

**Consumers do not engage in benefit/harms analysis using a medical model, nor do they consider just the affected child in their decision-making.**

In the minds of consumers, parents, decision-making about which tests should be part of a newborn screening panel is based on more than a narrow medical model. Families see benefit even in screening for conditions for which there is no treatment.

I recently asked our members about this issue. Here is an example of a reply from a mother who had two sons with Neimann-Pick Disease, that poignantly illustrates one reason why one might want to know about conditions for which there is no treatment – a criteria that in some systems is considered a hurdle.

*After the death of her youngest son, she had her older son tested: A year or two after Rick's diagnosis, when he was still apparently well, I asked him if he ever wished that he did not know that he had NPC, that he had never been tested. He said, "Oh no, Mom, now I know I am not stupid. I know there is a reason for some of the things I can't do". When we had thought that he had no obvious symptoms, Rick had been struggling to understand why he was not able to keep up with his peers, why there were some things that he could not do as well as he felt he should.*

Parents reported over and over to me that they need to know about genetic conditions in their family because they need to make informed decisions about lifestyle (for the family and the child), choosing caregivers and specialists, financial planning, choice of job, educational choice, finding a support group, securing insurance, aiding in building registries and participating in research.

**Thus the global context of decision-making and lived experience for parents includes more than what is traditionally considered in a medical model.**

*Now I turn to issues that are more specific:*

***The Genetic Alliance has a Public Health Action Team – an active group of people concerned about Newborn Screening and other public health issues. Parents and professionals engage in daily discussion about many of the problems and potential solutions. I would like to share a brief synopsis of the more frequently discussed concepts:***

1. It is a problem that there is inadequate understanding about NBS and the diseases associated with NBS. One part of the solution is the proactive work of parents & advocacy groups to raise the awareness of health professionals and the public.
2. It is a problem that many communities lack necessary information and resources. Using the proposed uniform screening panel is a welcome recommendation, but the implementation goes beyond the tests. Parents & advocacy organizations stand ready to be part of the solution to deliver the services that must accompany more robust screening.

3. It is a problem that technologies are advancing faster than policies, legislation and treatments. Advocates have, and will continue to promote effective public dialogue and decision-making.

4. It is a problem that consistent, uniform & continuous care is not available to all babies, all families, all Americans. The advocacy community initiates and sustains strong partnerships between parents, professionals & public.

Although your attention these two days is rightfully focused on the Uniform Screening Panel, I offer specific recommendations of the advocacy community for both the panel and the system. We request:

- **Proactive outreach to families and parents**
- **Input from underserved and underrepresented communities**
- **A uniform NBS panel of at least the recommended 30 tests, from state to state**
- **Resources for the Medical Home & for the necessary health professional education**
- **Health information accessible when and where it is needed**
- **National standards and INCREASED resources**

We ask this committee to recommend the Uniform Screening Panel as determined by ACMG report, to the Secretary. We also ask that you recommend the Panel not as a stand-alone entity, but as a part of a larger comprehensive package that would include the above requests – that would allow for:

- Resources to support the screening,
- Mechanisms for collecting data after testing, post market
- Systems that include resources beyond those usually included in the traditional medical model, including genetic counseling and services.

Finally, we are aware that there are many ‘elephants’ in the room – tensions between public and private labs, a lack of coordination among federal agencies, paternalistic and patronizing attitudes and even ‘special interest and ear-marking’ behavior among advocates. I am, in the face of all these potential obstacles, reminded of what an advocate for NBS said in a recent email discussion about the Genetic Services Branch of MCHB: “for their leader, it is all about the babies.”

In the name of all of us who have crossed the ‘affected’ line, I ask you to boldly, bravely, make it “all about the babies.” Thank you.