APPENDIX A: WRITTEN PUBLIC COMMENTS

1. Bennett Lavenstein, M.D.—Childhood Neurology Society (CNS)

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3. Jill Fisch—Parent & National Director of Education and Awareness, Save the Babies Through Screening Foundation

4. Micki Gartzke—Parent & Director of Education and Awareness, Hunter's Hope Foundation

5. John Adams, Parent & President/Chief Executive Officer, Elivery Solutions, Inc.

6. Peter Sybinsky, Ph.D.—Chief Executive Officer, Association of Maternal and Child Health Programs (AMCHP)

7. Scott Grosse, Ph.D.—Health Economist, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC)

8. Jerry Vockley, M.D., Ph.D.—President, Society for Inborn Metabolic Disorders (SIMD)

9. Frances P. Downes, Dr.P.H.—Board Member, Association of Public Health Laboratories (APHL)

10. Jennifer Sullivan, M.S., C.G.C.—National Society of Genetic Counselors, Inc. (NSGC)

11. Philip R. Vaughn, M.D., M.B.A.—Vice President, Newborn Screening, Pediatrix Medical Group, Inc.

12. Carol Greene, M.D.—Clinical Geneticist, University of Maryland and Membership Chair, Society for Inborn Metabolic Disorders (SIMD)

13. Marilyn C. Jones, M.D.—President, American College of Medical Genetics (ACMG)

1. Bennett Lavenstein, M.D.
Childhood Neurology Society (CNS)
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children
April 21, 2005

I'm Bennett Lavenstein. I'm a pediatric neurologist here in Washington at Children's Hospital. In the interest of disclosure, I should tell you that I've had the pleasure of working with Dr. Rinaldo, and we've had some patients together over the years. It's been certainly educational for me.

We, I guess, have the distinct situation in looking at this list of being involved with 28 of these 29 disorders. I think the only one that we don't readily see on a daily or weekly or monthly basis is cystic fibrosis, speaking as a neurologist per se. But from the standpoint of the Child Neurology Society, we certainly want to make the following statement and position, and that is that we certainly support national minimum standards for newborn screening for the specified genetic disorders, and for some disorders timely intervention for affected infants can certainly assure significant reduction in mortality and morbidity, and in all cases secondary prevention through genetic counseling can be offered and can be particularly efficacious.

I think that federal oversight is necessary in order for all newborns to have equal access to identification and interventions for these disorders, and in addition a combination of adequate federal and state funding should be allocated to initiate and sustain statewide programs and limit the long-term effects of these disorders.

Key elements to a successful newborn screening program I think include parent and health care provider education, and these programs should include parental notification and consent, timely screening and testing prior to birthing facility or hospital discharge, post-discharge follow-up, resources for appropriate referrals, accurate systems for data collection, policies to ensure patient confidentiality, and access to interventions and treatments. In the event that state or federal policies institute some degree of mandatory testing, these requirements should not interfere with parents' rights to be informed of any and all procedures involving their newborns. So mechanisms should be in place that are appropriate and address parents' options.

Mandatory testing, counseling and follow-up requirements must be fully supported by designated federal funds, we believe, since the U.S. health care system currently either does not support such services in totality or perhaps does so somewhat inadequately.

As we know, every state has newborn screening. It's one of the largest prevention programs in the country. But certainly there's variability amongst the states, and uniformity is a sought goal. A number of organizations obviously have played a major role in supporting this movement, and some 29 disorders which are on your list have been identified. I don't think the national minimum standards will solve all of the ethical dilemmas or the cost concerns surrounding the current patchwork system where each state has different requirements for newborn testing. However, creating national minimum uniform standards using evidence-based practice will ensure that all infants have early access to screening and treatment.

I think with regard to neurologic diseases, I can tell you that last week the American Academy of Neurology clearly moved forward with multiple new genes being described for many neurologic diseases. Now they're trying to figure out which proteins they code for, which diseases they impact upon, and certainly it is a marriage of clinical experience, expertise and evidence-based medicine to bring all these things together to make it work, because in some conditions if we wait just for evidence-based medicine, it will take 10 years to figure out the impact of that disease. But thank you for the opportunity to participate. It's a marvelous conference.

2. Jana Monaco

Parent & Board Member, Organic Acidemia Foundation

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

April 21, 2005

Good afternoon! I am pleased to have the opportunity to once again speak on behalf of Expanded Newborn Screening. As the parent of a child with Isovaleric Acidemia who fell victim to the lack of comprehensive newborn screening and suffered life long brain damage, along another child who is living a normal life with the same disorder because of early screening, I come with a strong passion to see the goals of the ACMG report attained and implemented. It is enlightening to see how this report is helping to move states forward with newborn screening. Having attended these meetings since last June and reviewed the report, I can only offer my full support along with fellow parents to help this report become a national standard for newborn screening. We are so excited to not feel alone in or efforts and commend you for providing states with a wake up call to Expanded Newborn Screening.

Since the last meeting, I am proud to announce that Virginia passed a bill to expand our newborn screening program to 30 disorders beginning March 2006. The ACMG report influenced this process. They have also included language to allow the addition of other disorders when deemed necessary. They are now in the process implementing the necessary changes to carry out the bill. I have also been invited to be a state representative for our New York-Mid-Atlantic Regional Collaborative. I am honored to participate in such a capacity as I highly value the importance of parent presence and input. After all, we are the ones that manage and care for children with these disorders. We are at the mercy of all of the professionals whether the policies and guidelines are effective or not.

Our regional collaborative had its first meeting this past weekend. I was one of two parents on the committee with another parent, in attendance. I am not a physician, health department worker counselor or technician. However, as the parent of two affected children including one with multiple health issues, I wear many hats myself like my peers. I can honestly say that I have mixed feelings about the meeting and I only speak from a parent's perspective. The meeting included a general overview of the regional and national status and a discussion of the six objectives dealing with laboratory and procedures, education and follow up. There was a great deal of input from the committee and although there were numerous suggestions to achieving the objectives like telehealth systems, legislative advocates, and enhanced educational programs, there was a significant degree of barriers and problems expressed by the various committee members that hinder achieving these objectives. Concerns included problems with back up labs for emergencies and the fact that labs do not all operate under the same policies. The issue of reimbursement and fees was also expressed.

Lab space and the fact that all labs are not able to accommodate the MS/MS equipment according to the manufacturer's guidelines was yet another issue. Of course, staffing is always an issue whether it is technicians or clinicians and how reimbursement is going to be handled. As a parent, I had my own concerns which included the lack of knowledge within the medical community on these disorders and the lack of communication within our medical home. Guidelines or legislation for insurance company is another problem. We like numerous other families do not have coverage for metabolic medications because a form of them can be found in health food stores although they are not appropriate for our children's medical needs. There is great disparity with formula coverage. Many insurance providers do not recognize it as medical

food and hence do not cover it leaving families to bare a great financial burden. Virginia's new legislation does not include formula coverage. This is an issue that needs to be addressed by the Advisory Committee. These are just a few of the barriers that were discussed at the meeting. However, I can highlight that regardless of the issues, it all came back to the need for improved training, education and technology whether it was in the technical or clinical setting. Of course, this raised the issue of reimbursement. There was unremitting concern about where the funding would come from. As a parent, I was not completely confident that the regional committee had an overall good understanding of how the report was going to assist the development of the newborn screening programs. I feel as though the committee is supportive of the changes for the most part and will continue to work at the objectives, but has great concerns as to how to initiate the necessary changes and what kind of guidelines and assistance they will receive from the federal government.

I am confident that you will address these issues and help reduce the disparity that exists. I could not emphasize enough the value of parents. We are a very resourceful group of individuals and have the advantage of open communication with one another. We already educate, advocate, assist and translate. For us, there is a personal stake at hand. We are motivated by the wellbeing of our affected children and providing them with the best medical care possible. Our advocating efforts are not determined by financial gains or determined by monetary parameters or fall into a set methodology, but rather prevention of potential tragedies that we all know occur.
I wish to comment on a few item expressed earlier. I can attest that parents want to know what they are dealing with. They would rather avoid the long dragged out diagnostic odysseys that affect the entire family creating immense strain. It is much easier to learn a diagnosis early and incorporate it into life…cure or no cure, management or no management. Parents are also interested in trials and data bases. Parents with children affected with Methylmalonic Acidemia are knocking the doors down to get into the research program over at NIH. We are currently doing a gene analysis on Stephen. We know the disorder of IVA but are interested in helping to better understand the disorder and its mutations.

Thank you for your continued efforts and for the realization that it is important to have a standard to help move forward with Newborn Screening.

3. Jill Fisch
Parent & National Director of Education and Awareness.
Save Babies Through Screening Foundation
Statement to the Advisory Committee on Heritable Disorders
and Genetic Diseases in Newborns and Children
April 21, 2005

Thank you for the opportunity to address the committee again today. I also want to express my sincere thanks and gratitude to the committee for their continued efforts and great successes I have seen over the last several months. The lives of many children have been saved and others will have a better quality of life because of your work.

My name is Jill Fisch. I am the National Director of Education and Awareness for the Save Babies Through Screening Foundation. I am addressing the committee as a parent of two children affected with SCADD. I am sure most of you will remember the diagnostic odyssey my family endured while looking for a diagnosis for my youngest child Matthew, who is now 4 years old. This odyssey took us all over the country over a two year period. Matthew did not benefit from early detection as New York was not screening for his disorder at the time. This is why I am here today and will continue to be committed to all children and newborn screening until all children in all states are treated equally and fairly.

Since New York's expansion of newborn screening took place in the Fall, there have been two confirmed SCADD cases in the state. This shows that the system is working. As a member of the FOD Support Group, I have seen an increase in children who have received the benefit of early detection from newborn screening. The combined efforts of parents and the anticipated recommendations from this committee have caused many states to expand their newborn screening programs, however other states are not at that point. States such as West Virginia and Arkansas are two of several who have yet to move forward on expansion. Hopefully, these other states will expand in anticipation of the Secretary accepting this committee's recommendations.

However, it appears as though there is a serious situation regarding the expansion of newborn screening in Texas. House Bill 790 was been presented to the Public Health committee and is due to be forwarded to the entire House for voting the week of April 18th, if passed, 19 disorders would be added to the panel. Unfortunately, Pediatrix Screening and others worked with two representatives from San Antonio to create House Bill 3325. I was told that it was created to undermine House Bill 790. Sponsored by Carlos Uresti and Jose Menendez, this bill discards the recommendations of the ACMG report and the March of Dimes and asks for a panel to be convened in order to decide what Texas should screen for. It would take two more years before expanded screening to be passed in Texas. Advocates in Texas feel that this bill was written by Pediatrix solely for the purpose of delaying the passing of House Bill 790 so that Pediatrix would get an opportunity to perform newborn screening services in that state. I do understand that Pediatrix is a business, however I am concerned that such pressure can be exerted from an outside source that could cause great harm to the children of Texas. Everyone involved needs to work together to address these issues, instead of working against each other.

I am open to hearing both sides and would hope, as a parent, that somehow this can be resolved to everyone's satisfaction. Pediatrix does run a great lab and I do feel some states would benefit from their services. If Texas is looking to build a new lab, hire and train new personnel—babies will not be getting comprehensive screening in just a few months. We all know this takes time. Texas should contract with an outside lab to screen babies supplementally until their state lab is ready to handle everything. They are not doing any out sourcing and they have Baylor right in

their own backyard. In the meantime, there needs to be concern for the affected children who will be born in the meantime. However as I said we all need to work together. I would appreciate any insight on this issue that can be given to me by the committee.

I am very excited to see the new research and test development taking place. New York is running a pilot program for lysosomal storage disorders and other tests are being developed which will save the lives of our children. How will the committee review new tests and technologies? I am very interested in learning what the committee's plans are in this regard. We are already seeing great progress with HRSA's commitment to newborn screening through the committee's recommendations strengthened by the success to date of the National Newborn Screening Coordinating Center and Regional Collaboratives.

As you know, SCADD is one of the disorders on the secondary panel in the ACMG report. I have not seen a natural history study done for SCADD which is one of the criteria in order to be added to the core panel. If these studies are not done, how can the committee help to get these studies implemented? My family is participating in the collection of data needed for a natural history study under Dr. Vockley as we have three affected generations in my immediate family. I am happy to share this data with the committee as it becomes available. When there is more data collection and sharing of this data, we can track treatment and its efficacy. As we all know the need for research and test development is imperative. I am looking forward to seeing the methodologies recommended by this committee for reviewing these tests and technologies and in turn, the benefit it will bring to the children. How will this be structured by the committee? How will these new tests and technologies be reviewed? How will translational research be recommended and evaluated?

I am concerned about the follow up of children once they are picked up by the newborn screen. These children need to be followed by different specialists, nutritionists and therapists. We need to develop collaborative partnerships between primary care providers, genetic and/or specialty care providers and health insurers to ensure continuity of medical care for children identified with disease by the newborn screening programs, within the medical home, which is an objective of HRSA and the NY-Mid Atlantic Consortium for Genetic and Newborn Screening Services. This is an issue that I will be following closely. I feel this needs to include children who did not benefit from early detection. How will the children be followed especially in a state like New York, where the metabolic centers do not have the proper funding? There needs to be a follow up system in place to assure that no child falls through the cracks and every child gets what they need. Drawing on my own experiences as a parent of a child who was not diagnosed through newborn screening, I feel very strongly that there be a follow up system in place for these children as well. With a national database where information could be entered and tracked regardless of whether or not diagnosis came as a result of newborn screening, we would have a much clearer picture of how well the children are being treated.

There is a situation in Missouri that has been brought to my attention. The Missouri Senate and House of Representatives have voted to accept the Governor's budget recommendations and the budget will now go back to the Governor who will determine which cuts will be incorporated into the Missouri budget 2005-2006. With these budget cuts, the Governor is looking to close the Outreach Clinics immediately. The funding provides salary support for Genetic Counselors who can not bill their time, as well as transportation to Outreach Clinics. Without the proper funding, the numbers of families served each year will be substantially decreased. In addition, genetic counseling and follow up for families throughout Missouri will no longer be provided. How can this be addressed by the committee?

I also would like to state for the record my concern over the ethicists who have been very vocal in the past few months in speaking out against newborn screening. I do feel that everyone is entitled to give their opinions freely, however I would hope that their concerns would be based on valid and current information. Newborn screening saves lives. I do not think that is a fact that can be disputed.

As a parent and committed advocate for newborn screening, I feel it is imperative to have parents serve on the HRSA sub committees. We have lived and breathed this every day and have much to offer. This is a very special role that the sub committees need. Public involvement is crucial. The value of our input is unmatchable. Parents have played an important role at both federal and state levels. There needs to be assurance by this committee that parents will be included in these sub committees. We have shown and will continue to show our dedication and support of this committee.

Thank you for the opportunity to share my thoughts today. I look forward to hearing answers to my many questions as the committee moves forward. It is my great hope that we can all work together to better the lives of our children.

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4. Micki Gartzke
Parent & Director of Education and Awareness, Hunter's Hope Foundation
Statement to the HHS Advisory Committee
on Heritable Disorders and Genetic Diseases in Newborns and Children
April 21, 2005

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 to address the committee once again. Your work over the past several months have already helped to not only improve the quality of children's lives, it has also helped to save the lives of many children. For this you all have my deepest gratitude!

My name is Micki Gartzke. I continue to be committed to the expansion of newborn screening. I am greatly committed to the value of, and the great need for education on newborn screening for professionals and families alike so that children receive the greatest access to equitably distributed newborn screening. This would ensure all children's right to an equal start to a healthy life. As a mom who has lost a child to lack of early detection, my commitment began the day I was told , "Your daughter has a fatal illness and the average life expectancy is 16 mos." She was 10 mos. old at that time.

A brief moment to refresh why I am here… my daughter died of Krabbe disease, a Lysosomal Storage disorder. Our family endured a 6 month diagnostic odyssey only to have it end with that fatal prognosis, and a but… like," but if we had known earlier, there is a therapy now out there, but it is too late now. These are words no parent should hear, especially when they are holding their 10- month old baby in their arms and the baby is smiling at them. Just thinking about that brings a momentary flashback to the moment I learned that my daughter would soon die. I was told this on August 7, 1997, my birthday. I knew at that moment that I would be committed to doing anything and everything in my power to prevent this from happening to other families. I know I do not need to tell you this. Yet, it is important for it to be said! As the Director of Education and Awareness for Hunter's Hope Foundation, my professional role has provided an excellent avenue to best achieve this personal commitment.

I am enthused and excited by the changes I have seen in newborn screening lately. It seems as if a ground swell has taken place in some states because of actions this Committee has taken. Each month there have encouraging changes in different states now expanding their newborn screening programs.

A good example that comes to mind is KY. KY recently had its NBS Bill passed and the Legislation signed by the Governor with the funding already set aside. This expansion is due to begin this July and will increase screening from only 4 diseases to... *tests for heritable disorders including, but not limited to, phenylketonuria (PKU), sickle cell disease, congenital hypothyroidism, [and] galactosemia, medium-chain acyl-CoA dehydrogenase deficiency (MCAD), very long-chain acyl-CoA deficiency (VLCAD), short-chain acyl-CoA dehydrogenase deficiency (SCAD), maple syrup urine disease (MSUD), congenital adrenal hyperplasia (CAH), biotinidase disorder, and cystic fibrosis (CF), 3-methylcrotonyl-CoA carboxylase deficiency (3MCC), 3-OH 3-CH3 glutaric aciduria (HMG), argininosuccinic acidemia (ASA), beta-ketothiolase deficiency (BKT), carnitine uptake defect (CUD), citrullinemia (CIT), glutaric acidemia type I (GA I), Hb S/beta-thalassemia (Hb S/Th), Hb S/C disease (Hb S/C), homocystinuria (HCY), isovaleric acidemia (IVA), long-chain L-3-OH acyl-CoA dehydrogenase deficiency (LCAD), methylmalonic acidemia (Cbl A,B), methylmalonic acidemia mutase*

deficiency (MUT), multiple carboxylase deficiency (MCD), propionic acidemia (PA), trifunctional protein deficiency (TFP), and tyrosinemia type I (TYR I).

KY's Newborn Screening Act also includes language for adding additional diseases in the future, based on the recommendations of this committee. The language is as follows, "*The listing of tests for heritable disorders may be revised to include conditions as deemed appropriate by the cabinet based on the recommendations of the American College of Medical Genetics.*"

KY has seen that it is in the best interest of the state and its children to make this commitment to expand NBS. This state's progress is an example of combined efforts of doctors, legislators, industry, professional groups and a shining example of the important role parents play in this process. I was closely involved in every aspect of this process, this shows how change can happen with strong collaborative efforts and parental support.

States that have not yet expanded, such as Arkansas, Oklahoma, and New Mexico, amongst others, need guidance and assistance from this Committee as the struggles for education, infrastructure, development, follow-up and training continue alongside the ever-steady funding issues. Too many states not yet proactive and it is my hope is that all states will follow this Committee's recommendations.

It is exciting to see the research and test development taking place for many different diseases. The Lysosomal Storage Diseases NBS Pilot in NY State is currently underway. This Pilot program is also an excellent example of the teamwork that is truly needed to accomplish such visionary goals. State, industry, research and advocacy groups are working collaboratively to achieve this common goal of newborn screening for this first round of LSDs. The addition of new screening tests to the core panel in the future will save even more babies lives.

The need for more ongoing research and test development will and must continue! Complementing that is the need for ongoing methodology for reviewing tests and technologies. I have many questions regarding these subjects. How will the Committee structure this? How will it review these new tests and technologies? How will it recommend and evaluate translational research? HRSA's commitment to newborn screening is already yielding great success through this Committee's recommendations, the Regional Collaboratives, and the NNBSGRC.

Follow-up of diagnosed children is vital, as is access to the variety of medical professionals and services they need so they will continue to thrive.. Today I saw the State budget in Missouri put in jeopardy a key point of delivery of services. What additional educational efforts and methodologies will be used to accomplish this effectively.

I am concerned about the ethicists who continue to speak against newborn screening, especially those whose media contacts have been responsible for large articles in national newspapers. I have met with a couple of ethicists and while I believe they express great interest in the children and they have the right to fully express their opinions, I hope that they base these concerns not only on valid information with citable sources, but on current information as well. We all know newborn screening saves lives!

A Dartmouth Medical School telephone survey of 500 people was published in USA Today. The survey showed that 66% of people ages 40 and older say they would be willing to be tested for an incurable cancer, thus showing their desire for Early detection. I can't help but wonder if a similar poll were done about the early detection of newborn screening if the same 2/3 majority would express a similar desire for early detection?

Education still remains the key component. We need better systems for educating medical schools, health professionals and families about newborn screening. The future health professionals in our country need to be educated on the diseases that will be detectable through newborn screening. This will help to expand the number of specialists we need to help treat the children.

Public involvement in Committee matters is a must – especially parents who have lived through the lack of early detection and access to treatment. The parents who have had the misfortune to experience the diagnostic odyssey and ensuing challenges of lifelong disabilities and or premature death have real world experience and first hand knowledge that needs to be recognized, heard and considered in moving forward from this point. Our experience and knowledge is invaluable. We are representatives of the market. I cannot emphasize enough my next point, and I will not rest until there is assurance by the Committee that parents will be included on the subcommittees! Parents deserve a role since they are the ones affected.

I know you will make the right choice on this, just as you have done on many other matters. I am confident that this Committee values the needs of the children above all else!

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5. John Adams
Parent & President/Chief Executive Officer, Elivery Solutions, Inc.
Statement to the Advisory Committee on Heritable Disorders
and Genetic Diseases in Newborns and Children
April 21, 2005

I am a PKU dad. Thanks to Bob Guthrie and a lot of other people who fought the battles for newborn screening in the 1960s. I'm happy to be able to share with you the fact that my son, who is 18, graduates from high school this year and has been admitted, hopefully, to the University of Toronto for this fall.

I got reengaged in this issue a couple of years ago when there was a bit of a crisis in our PKU community in Ontario, my home province, because there was a threat to the funding for the Adult Program for Medical Foods and Formulae. That's still not completely resolved, but some very capable people in Canada taught me some lessons, saying John, if you're going to engage in that issue, we've got to let you know about some other issues, some other gaps in the system of newborn screening. It tears my heart out as a parent who has a newborn screening success story to know that there are babies in many jurisdictions, not just America, who are dying or being damaged needlessly.

I have to tell you, I'm a proud Canadian, Torontonian and Ontarian, but I do believe in evidence-based decision-making, and I want to give you a little bit of an international perspective here today. Perhaps I'm the only one who is adding that flavor here today.

In Ontario, it's sad to report that we screen newborns for three conditions: PKU, congenital hypothyroidism, and hearing. Compared to any of the American jurisdictions, that is substandard. There is none of your jurisdictions today that are screening for as few as that. Ontario is not alone. We only have one province, Saskatchewan, that is screening for 29 conditions using tandem mass to a relatively fulsome extent.

I also have to report to you that our federal government is AWOL on the question of newborn screening. I also, in one of life's ironies, have to report that the doc who delivered my PKU newborn-screened son is now the Minister of State for Public Health for Canada. She owes newborn screening something, and I intend to collect that debt. Dr. Caroline Bennett.

My sense in reading all of the 324 pages of the report was that it was a snapshot of the state of the art, the best available evidence, not yet perfected. I also have to report to you that the inherited errors of metabolism professional community in Ontario and in Canada are at their wits' end with frustration at trying to move the agenda forward and have, as a group, all resigned from the Province of Ontario's Advisory Committee on Newborn Screening out of sheer bloody frustration.

I'm delighted to be able to participate in this open forum today. The Ontario government's Advisory Committee on Genetics is meeting today behind closed doors. They do not publish their meetings. They do not publish minutes. They do not take public presentations. So I'm here to salute you for the openness of the American way of doing business.

Now, I say that because not everyone outside of America thinks that the American model is the way to go. You may have noticed that.

But I want to say to those people that in my case, my evidence is if some good Canadians and other people hadn't listened to the Bob Guthries of the world, my son would have been condemned to a lifetime of profound mental retardation. So it's important to listen to the right Americans.

Now, as recently as yesterday, I had a meeting with the cabinet minister in the Province of Ontario in his office about the deficit in newborn screening in our jurisdiction, and one of his assistants, a very bright person, raised in a premeeting, well, what about the lack of consensus? So I'm here to tell you that my counter to that point was I put down on the table the 324-page report of the American College of Medical Genetics and said I do believe there is a new threshold of consensus, including a consensus identifying when there is a lack of consensus in certain situations.

You have already performed yeoman service for us in being able to address that, and I want to say thank you as a Canadian for the American taxpayers' investment in a number of things, including the National Newborn Screening and Genetics Resource Center, which is a wonderful source of information for people like me. So thank you so much.

I do have a suggestion or two. I hope as you move forward that you do not focus exclusively in your decision-making on what's best for America but you also have some regard for the role model in this field that you are performing for people in other jurisdictions.

I also would make the suggestion that the report correctly identifies the growing problem of the lack of person power in terms of the deep talents that are required increasingly in this field. You might want to give some consideration to having HRSA support the development of smart systems so that we can, with authoring systems, try to capture the deep knowledge that is involved in the craniums of some of the people around this table and other experts and getting it into a more accessible format so that high levels of service can be rendered to children and adults in need without requiring the scarce knowledge, the scarce supply of that deep knowledge. We have to find a way to democratize and push down into the system the ability to put the intelligence and best practice available at the hands of a clinician when there's a child or an adult who is in a period of crisis. I have a few ideas about that I will explore offline.

Thank you very much for this opportunity. I love this committee. I love this report.

6. Peter Sybinsky, Ph.D.
Chief Executive Officer, Association of Maternal and Child Health Programs
Statement to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
April 21, 2005

April 12, 2005

Michele Lloyd-Puryear, MD, PhD
Maternal and Child Health Bureau
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Dear Dr. Puryear:

The Association of Maternal and Child Health Programs (AMCHP) commends the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children for their hard work addressing the important issue of newborn genetic and metabolic screening. The American College of Medical Genetics (ACMG) report, *Newborn Screening: Toward a Uniform Screening Panel and System*, recently released by the Maternal and Child Health Bureau, is an exceptional example of compiling expert opinion and evidence-based research to form national recommendations.

AMCHP represents state public health leaders who promote the health of America's families. Our members come from the highest levels of state government and include directors of maternal and child health programs, directors of programs for children with special health care needs, adolescent health coordinators, other public health leaders and parents. These programs are funded in part by the Maternal and Child Health Services Block Grant, Title V of the Social Security Act of 1935, which is the only federal program devoted to improving the health of all women, children, youth and families. AMCHP members serve over 1 million children with special health care needs, many identified by the newborn screening programs they administer. Although state newborn screening programs vary among states, most Title V programs ensure follow-up and access to health services for children.

AMCHP applauds the comprehensive approach to evaluating the 84 conditions, recognizing the need for a public health system that includes policies and standard but also allows for some flexibility, and addressing newborn screening system components in addition to laboratory testing. However, state Title V programs have concerns regarding information that was not addressed in the report.

The findings outlined in the ACMG report have a considerable impact on the follow-up requirements of state MCH programs. Due to the broad obligations of state Title V programs, AMCHP believes the report inadequately discusses the extensive state responsibility for providing follow-up. In addition, the report does not provide a definition of follow-up to guide future state efforts. The report neglects to acknowledge the significant commitment and financial responsibility of newborn screening programs to ensure access to re-screening, specialty care and long-term tracking and monitoring of children and their families. State newborn screening programs consist of numerous agencies and professionals including, but not solely laboratories. State Title V programs hold the ultimate responsibility for meeting state mandates for assuring screening, re-screening, notification, access to medical and developmental specialists, and long-term tracking of children with metabolic or genetic disorders. The Secretary's Advisory Committee should carefully review the implications of the uniform panel on follow-up and develop national recommendations to provide the needed assistance to meet the demand equally across states.

State newborn screening programs continue to build the basic infrastructure for a complete system, including adequately trained professionals to provide screening and follow-up, data systems to track the progress of children, and educational materials for professionals and families. However, states are building a system with limited financial support that is inadequate to meet current demands. The report however, remains silent on financing of the uniform panel. The addition of new technologies, testing requirements, reporting requirements and follow-up services adds to programs' financial strains. The Secretary's Advisory Committee should develop, with the assistance of state programs, recommendations to provide adequate funding to meet the ACMG recommendations. The recommendations should consider new funding options for states and propose changes to other financing structures that pay for newborn screening systems.

Finally, the ACMG report provides an evidence–based structure for how their recommendations were developed that may provide state programs the needed information to change their newborn screening systems. However, the report recommended but did not provide guidance for an ongoing federal system for evaluating new conditions or new technologies as they become available. The Secretary's Advisory Committee should develop a procedure for nationally adopting additional conditions to the uniform panel.

Once again, AMCHP supports the intent of the Secretary's Advisory Committee and much of the information provided by ACMG. This helpful report was needed and will provide a foundation for states to consider as they examine their newborn screening systems. As the Secretary's Advisory Committee moves forward, AMCHP would welcome the opportunity to designate a representative to provide the Committee a state MCH program perspective.

If you have questions or would like more information, please do not hesitate to contact Meg Booth at AMCHP at (202) 775-0436 or mbooth@amchp.org.

Sincerely,

Jeffrey Lobas, MD, MPA
President

7. Scott Grosse, Ph.D.
Health Economist, National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention (CDC)
Statement to the Advisory Committee on Heritable Disorders
and Genetic Diseases in Newborns and Children
April 21, 2005

Scott Grosse, PhD
Centers for Disease Control and Prevention
Atlanta, Georgia

Remarks for public comment session, Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children, April 21, 2005

I am a health economist with the National Center on Birth Defects and Developmental Disabilities at CDC and work with Coleen Boyle on newborn screening issues. I would like to respond to the question that Piero Rinaldo asked earlier about specific objections to the ACMG report. CDC has a number of specific objections, and I will give just a couple of examples. We are concerned that certain statements in the fact sheets may be inaccurate or misleading. Our focus is on the more common disorders, not the relatively rare ones for which data are lacking. In particular, we have concerns with the fact sheets for congenital adrenal hyperplasia (CAH), cystic fibrosis (CF), hearing loss, hemoglobin SC disease, and medium chain co-A dehydrogenase (MCAD) deficiency. I will mention just some of the issues with the CAH fact sheet. First, the fact sheet states with regard to presence of the phenotype that "Males are usually undetected". In fact, newborn screening programs such as the one in Texas report that the majority of males with classic CAH are detected on the basis of symptoms prior to the reporting of newborn screening results, as documented in a 1998 article by Brad Therrell and colleagues. Second, the fact sheet states that 9% of children with CAH die without screening and early intervention. No original study is cited to support that estimate. A review of the epidemiologic literature on CAH conducted at CDC found that the reported death rate in unscreened CAH cohorts ranges from 2% to 9%. The 2% estimate comes from a historical Swedish study by Thilen and colleagues (1990). Two other studies, that involved smaller cohorts, found no deaths in unscreened cohorts with CAH despite careful case ascertainment. The fact sheet does not reflect the range of evidence in the scientific literature.

8. Jerry Vockley, M.D., Ph.D., President
Society for Inborn Metabolic Disorders (SIMD) Statement to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
April 21, 2005

Thank you, Mr. Chairman, for the opportunity to speak, and thank you to the Committee for your efforts on behalf of those with inborn errors of metabolism and other genetic disorders.

The Society for Inherited Metabolic Disorders (SIMD) is dedicated to improving scientific and public understanding about inborn errors of metabolism, and to promoting advances in the identification and care of those affected by inborn errors of metabolism. Members of the SIMD are scientists, physicians, nutritionists, nurses and other health professionals working in patient care and in research, in the laboratory and in the clinic, in academia, in public health, in private medical systems and in the biotechnology industry.

SIMD members provide diagnostic and treatment services to individuals of all ages with inherited metabolic disease to minimize the risks of disability and death. SIMD members play a prominent role in the diagnostic follow-up and treatment of children detected by newborn screening with inborn errors of metabolism.

SUPPORT FOR THE ACMG REPORT

We first wish to state our unequivocal support for the ACMG report "Newborn Screening: Toward a Uniform Screening Panel and System." Members of the SIMD have been involved in this process, including as part of the expert panel. We have submitted a formal letter in support of the report as part of the public comment process, and we urge you to ask the Secretary to move forward expeditiously to implement the report.

INVOLVEMENT OF FRONT-LINE EXPERTS IN FOLLOW-UP AND TREATMENT

We also look forward to the work of this Committee's three important new Subcommittees, and offer the following comment. We recognize that members of the parent Committee serving on each of the Subcommittees are deeply committed to the welfare of children and to the smooth working of newborn screening as an important public health system. However, as those who routinely diagnose inborn errors of metabolism and provide life-long therapy for these disorders, we hope that the Subcommittees, especially the Treatment and Follow-up Subcommittee, will address the entire spectrum of issues critical to the lives of our patients and their families. While initial follow-up has traditionally fallen within the boundaries of a newborn screening program, it is clear that lifelong treatment with on-going involvement of

knowledgeable caregivers is needed to realize the benefits of the initial screening. This on-going treatment bridges newborn screening and the rest of the health care system. In addition, careful collection of long-term information on the outcome of children identified by newborn screening is needed as part of a continuous feedback system for quality monitoring and improvement. Optimal design and implementation of long-term treatment and follow-up systems will be best achieved only if expert providers of the long-term treatment and follow-up are involved from the beginning in system design.

Involvement of front-line experts is especially critical to properly address issues of diagnosis and management of variant forms of disease discovered by newborn screening. Any advance in medical screening and diagnosis leads to new discoveries about human health and disease, and has profound impact on health care and society. For example the introduction of MRI scans of the brain led initially to some instances of more invasive diagnostic evaluations for what we now recognize as normal variations. Screening for PKU is of course an unequivocal success story, yet we all should remember that it was only through newborn screening that we recognized the existence of the mild hyperphenylalaninemia variants and learned to properly treat them. We now know that this treatment needs to be tailored to each child to assure that we cause no harm. Through this and similar experiences with other diseases, members of the SIMD have accumulated the knowledge and perspective to understand and treat not only children with classic disease, but also those with variant forms. We are, for example, the experts who see children with life-threatening medical crises due to 3-methylcrotanyl carboxylase deficiency; but we also understand that the condition is usually benign.

We note therefore with some concern that no current member of the Follow-up and Treatment Subcommittee is an expert in the treatment of metabolic disorders detected by newborn screening. The clinicians and scientists of the SIMD can provide this expertise for inborn errors of metabolism, and urge you to include us as a significant partner in the activities of the Follow-up and Treatment Subcommittee. We will be the best resource to help design systems to avoid incorrect diagnosis, mislabeling of patients, and over-treatment or under-treatment. Our expertise – along with that of practitioners directly involved in the care of children with endocrine disorders and hemoglobinopathies – is needed to round out the subcommittee and assure good long-term outcomes for children identified through newborn screening.

NEED FOR ADEQUATE RESOURCES, INCLUDING FUNDING

Finally, as we mentioned at your last meeting, we continue to urge you to continue efforts to assure availability of adequate resources, including adequate funding and personnel for successful newborn screening and long-term follow-up and treatment.

Again we thank you for this opportunity to speak, and want to assure the Committee that the SIMD and its members are eager to help you in your efforts on behalf of the people we both serve.

9. Frances Pouch Downes, Dr.P.H.
Board Member, Association of Public Health Laboratories
Statement to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
April 22, 2005

The Association of Public Health Laboratories (APHL) represents public health laboratories in the 50 states and six territories, linking them with federal partners such as the Centers for Disease Control and Prevention (CDC) and Health Resources and Services Administration (HRSA), as well as county, local, and international laboratories. Public health laboratories have been responsible for newborn screening since the mid-1960's and currently conduct approximately 97% of all newborn screening tests in the US; in fact, all current public newborn screening programs operate through the auspices of a state public health department. In most states, the state public health laboratory performs the testing, while in others, a contract laboratory performs the testing, which may be another state laboratory or private laboratory.

APHL commends HRSA for its efforts to effect the production of this report on newborn screening, the American College of Medical Genetics (ACMG) for providing the organizational structure through which the report could be developed, and the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children for putting forth recommendations for state screening programs and identifying a core panel of conditions.

The state public health laboratory, as the home for most newborn screening programs in the United States, is aware of the details involved in providing a quality newborn screening system for its state. Each of these programs is state-initiated, state-supported and tailored to the needs and resources of that state, as indicated in this report. No program purposefully sets artificial limits on the content of its screening panel, its follow up procedures, data collection activities, or its system evaluation. While this report makes a strong case for uniformity across screening programs, the solutions offered may not be those within the control of the screening laboratory without federal legislation and funding. APHL supports standardization of test reports and the criteria used to classify a result as a “screen positive.” APHL further endorses the concept of classifying the conditions within a screening panel within categories, rather than listing each condition separately. Every newborn screening laboratory recognizes the benefits of multiplex testing. APHL believes a more thorough discussion of the multiplex technologies beyond tandem mass spectrometry would strengthen this report. The report emphasizes the current under-utilization of information technology, and APHL agrees that implementation or utilization of appropriate information technology to enhance programs should be pursued and is willing to assist the advisory committee in this area.

Laboratories have regulatory responsibilities for pre-analytic and post-analytic phases of testing. In the second section of the report, recommendations are put forward relating to aspects of the newborn screening system that lie beyond laboratory operations. Since in many cases these activities interlock with laboratory functions, APHL would like to provide input on these recommendations. Everyone is aware of the angst caused by false positive reports, and all programs work to reduce the number of such reports. However, from a laboratory perspective, a false negative report is worse. Given the suboptimal nature of the dried blood spot specimen provided on each newborn, the lack of medical history, and the need for swift testing and reporting, the goal of newborn screening programs is to optimize analyses to generate the fewest number of false positive reports, while minimizing the danger of generating a false negative report. This ongoing process in the laboratory is dependent upon full communication between the laboratory and the medical care providers. Stronger language on the need for this clinical feedback in the HRSA report would provide much needed support for laboratories trying to improve testing algorithms.

APHL recognizes the importance of collecting national data for evaluation of newborn screening programs. However, as with discussions on use of residual specimens, state laboratories need assurance that state-specific data are used only with their foreknowledge, consent, and proper acknowledgement by the user of the states' roles in collection of such data.

Newborn screening programs were established by each state to serve its own population. APHL agrees with the HRSA report statement that "States also must retain their significant roles and responsibilities. They have a clear authority with regard to oversight and evaluation, as well as enforcement." The report notes elsewhere that "there is also a potential expanded national role in oversight and enforcement, data collection, program evaluation, and the development of educational materials to support newborn screening." Screening laboratories would welcome national support for educational materials, both for parents and clinicians, as well as support for the external evaluation of their programs, as initiated by the Council of Regional Networks (CORN) organization and evidenced by the numerous states that participated. Current discussions regarding accreditation of public health agencies and licensure of laboratorians could result in enactment of federal legislation that could change the nature of the current Federal-State relationship, whereby a national oversight role in newborn screening might be possible at some time in the future. Today, guidance from the federal government on mechanisms by which newborn screening programs could perform an ongoing self assessment, guidance regarding mechanisms with which a condition can be evaluated for placement in a screening panel, guidance in making sure all components of the system are integrated and functioning properly, and provision of a national quality assurance program as is now operating at the Centers for Disease Control and Prevention (CDC) are all welcome support by these programs. APHL appreciates the need for national leadership but is not convinced that such leadership can be achieved by oversight and enforcement. As the organization representing the laboratories providing newborn screening in the states, APHL has a role to play in that leadership, especially in developing any further legislation and funding strategies.

Because of the potential implications of the report, there is a need for ample discussion of how public health laboratories and the entire newborn screening system can begin to implement the recommendations. We propose a wider vetting process for the recommendations from the report, perhaps in the form of a consensus conference or similar mechanism.

Finally, APHL thanks the authors of this report and is grateful for the opportunity to provide comments today. I would be happy to take any questions now.

April 14, 2005

Michele Lloyd-Puryear, MD, PhD
Maternal and Child Health Bureau
Health Resources and Services Administration
5600 Fishers Lane
Parklawn Building, 18A-19
Rockville, MD 20857

Dear Dr. Lloyd-Puryear:

As you know, the Association of Public Health Laboratories (APHL) represents public health laboratories in the 50 states and six territories, linking them with federal partners such as the Centers for Disease Control and Prevention (CDC) and Health Resources and Services Administration (HRSA), as well as county, local, and international laboratories. Public health laboratories have been responsible for newborn screening since the mid-1960's and currently conduct approximately 97% of all newborn screening tests in the US. All current public U.S. newborn screening programs operate through the auspices of a state public health department. In most states, the state public health laboratory performs the testing, while in others, a contract laboratory performs the testing, which may be another state laboratory or private laboratory.

APHL commends HRSA for its efforts to effect the production of this report on newborn screening in the US, the American College of Medical Genetics (ACMG) for providing the organizational structure through which the report could be developed, and the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children for putting forth recommendations for state screening programs and identifying a core panel of conditions. The report is thorough in its description of newborn screening, in its description of the goals of the contract placed by HRSA with ACMG, in its detailing of the process used to develop the recommended screening panel, and its recommendations drawn from the process. APHL would certainly agree that the five “barriers to an optimal newborn screening system” identified in the report present real obstacles that must be overcome in order to advance newborn screening practice in the US. The report is divided into two sections: the first on laboratory practice and screening panel content, and the second on other aspects of the newborn screening system. Our comments will follow this same structure.

The state public health laboratory, as the home for most newborn screening programs in the US, is aware of the details involved in providing a quality newborn screening system for its state. Each of these programs is state-initiated, state-supported and tailored to the needs and resources of that state. This is acknowledged in this report. No program purposefully sets artificial limits on the content of its screening

panel, its follow up procedures, data collection activities, or its system evaluation. However, when comparing programs, one quickly sees differences that in many cases may not be rectified regardless of proposed national guidelines. While this report makes a strong case for uniformity across screening programs, the solutions offered may not be those within the control of the screening laboratory without federal legislation and funding. Within most state governments, it is not possible for the laboratory to initiate legislative actions, nor even communicate with the legislative branch unless that branch requests information. Likewise, such constraints apply to "mandating reporting of all secondary target conditions" that can be identified through the use of tandem mass spectrometry. APHL does support standardization of test reports and the criteria used to classify a result as a "screen positive". APHL further endorses the concept of classifying the conditions within a screening panel within categories, rather than listing each condition separately, as done with hemoglobinopathies.

The recommendation that certain conditions be classified as "report only," with no follow up, is contrary to a basic tenet of newborn screening programs. Since the beginnings of newborn screening in the US, the screening laboratory has felt compelled to report all test results. With only five drops of blood and no medical history, it is the screening laboratory's obligation to report all laboratory test data to the primary care provider, who will determine its significance in context with all other medical findings for that child. This practice of complete reporting by newborn screening programs began with initiation of screening for phenylketonuria, when "presumptive positive" results were made a separate category from "referral level". Its most dramatic expression is in screening for hemoglobinopathies, in which carrier status is reported with full knowledge that a child does not have sickle cell disease and will have no sequelae from the findings.

Every newborn screening laboratory recognizes the benefits of multiplex testing. Dr. Robert Guthrie recognized its usefulness and attempted to develop a multiplex assay through modification of his bacteria inhibition assay (BIA) procedure that would detect phenylketonuria, maple syrup urine disease, and homocystinuria in a single agar plate. Tandem mass spectrometry is the dominant multiplex technology currently in use by newborn screening programs. However, it is not the only such technology, others being bead-based assays and DNA chip analysis, to name two. Although the report recommends use of multiplex technologies, tandem mass spectrometry is the only technology vigorously discussed. APHL believes a more thorough discussion of other technologies would strengthen this recommendation. APHL further notes that the report emphasizes the current underutilization of information technology. APHL agrees that any implementation or utilization of appropriate information technology that enhances programs should be pursued. APHL recommends that ACMG review the APHL report, "Requirements for Public Health Laboratory Information Systems" issued in September, 2003, regarding criteria for choosing an information system, as a potentially helpful reference for state newborn screening laboratories. In its currently operative "Strategic Plan 2002-2005," APHL recognizes the importance of laboratory quality ("Goal IV -Promote the development and use of quality laboratory practice in public health at the national and international level") and is working through its various committees to achieve this goal.

Newborn screening was initiated to prevent the inevitable loss of intellect in a child with phenylketonuria not receiving appropriate therapy. Therefore, APHL is uncomfortable with the recommendation that programs "consider that the range of benefits realized by newborn screening includes treatments that go beyond an infant's mortality and morbidity," thereby suggesting that a condition might be added to the screening panel solely for the benefit of the family. Certainly, all would agree that newborn screening is a genetic testing program and thus can uncover within a family unit a genetic condition unknown prior to screening. These programs also carry the additional burden that this genetic testing occurs, with few exceptions, without informed consent by, or knowledge of, the parents. State programs today understand this and deal with the reality of providing unknown and/or unwanted information to a new mother that can be valuable in the medical care for that child. APHL recommends caution when expanding tests

beyond those that directly benefit the newborn and endorses prioritization of the direct benefits to the baby tested. In section two, recommendations are put forward relating to aspects of the newborn screening system that lie beyond laboratory operations. It should be noted that laboratories have regulatory responsibilities for pre-analytic and post-analytic phases of testing. Since in many cases these activities interlock with laboratory functions, APHL would like to provide input on these recommendations. All programs are aware of the angst caused by false positive reports, and all programs work to reduce the number of such reports. However, from a laboratory perspective, a false negative report is worse. Given the suboptimal nature of the dried blood spot specimen provided on each newborn, the lack of medical history, and the need for swift testing and reporting, the goal of newborn screening programs is to optimize analyses to generate the fewest number of false positive reports, while minimizing the danger of generating a false negative report. This ongoing process in the laboratory is dependent upon full communication between the laboratory and the medical care providers. Stronger language on the need for this clinical feedback in the HRSA report would provide much needed support for laboratories trying to improve testing algorithms. Much of this effort to improve quality within the newborn screening system is outlined in the APHL position statement, *Quality Assurance in Newborn Screening* (enclosed).

Newborn screening programs were established by each state to serve its own population. APHL agrees with the HRSA report statement that “States also must retain their significant roles and responsibilities. They have a clear authority with regard to oversight and evaluation, as well as enforcement.” State screening laboratories understand this responsibility and integrate it into all aspects of their programs. However, the report notes elsewhere that “there is also a potential expanded national role in oversight and enforcement, data collection, program evaluation, and the development of educational materials to support newborn screening.” Screening laboratories would welcome national support for educational materials, both for parents and clinicians, as well as support for the external evaluation of their programs, as initiated by the Council of Regional Networks (CORN) organization and evidenced by the numerous states that participate. APHL acknowledges that current discussions regarding accreditation of public health agencies and licensure of laboratorians could result in enactment of federal legislation that could change the nature of the current Federal-State relationship whereby a national oversight role in newborn screening might be possible at some time in the future. Today, guidance from the federal government on mechanisms by which newborn screening programs could perform an ongoing self assessment, guidance regarding mechanisms with which a condition can be evaluated for placement in a screening panel, guidance in making sure all components of the system are integrated and functioning properly, and provision of a national quality assurance program as is now operating at the Centers for Disease Control and Prevention (CDC) are all welcome support by these programs. APHL appreciates the need for national leadership but is not convinced that such leadership can be achieved by oversight and enforcement. APHL believes it has a role to play in that leadership, especially in developing any further legislation and funding strategies.

APHL recognizes the importance of collecting national data for evaluation of newborn screening programs. However, as with discussions on use of residual specimens, state laboratories need assurance that state-specific data are used only with their foreknowledge, consent, and proper acknowledgement by the user of the states’ roles in collection of such data. APHL's Newborn Screening and Genetics in Public Health Committee has addressed many of the issues covered in the recommendations of section two: recognizing the importance of standardization of such matters as reporting formats, nomenclature of conditions in the screening panel among the laboratories, and standardized QA/QC programs, in addition to tasks necessary to implement new test methodologies, proper designation and action taken with invalid specimens, integrated data systems and electronic reporting of test results, organizing national meetings of all screening programs that include workshops on quality control in the laboratory and optimization of follow up practices, and engagement of the clinical community through advisory committees. Four APHL policy statements could provide guidance in many of the areas covered by this report (enclosed)*:*

Quality Assurance in the Newborn Screening Laboratory; *Parental Consent in Public Health Newborn Screening Programs*; *Residual Newborn Screening Specimens*; and, *The Role of the Private Laboratory Sector in Public Health Newborn Screening Programs*.

In conclusion, APHL thanks the authors of this report and is grateful for the opportunity to provide comments. Because of the potential implications of the report, there is a need for ample discussion of how public health laboratories and the entire newborn screening system can begin to implement the recommendations. We propose a wider vetting process for the recommendations from the report, perhaps in the form of a consensus conference. If you have questions or need further information, please contact Scott Becker, MS, APHL Executive Director, at sbecker@aphl.org, 202.822.5227 x225.

Sincerely,

Paul Kimsey, PhD
President

Enclosures:
APHL Position Statement/Policy Statement: Quality Assurance in the Newborn Screening Laboratory
APHL Position Statement/Policy Statement: Parental Consent in Public Health Newborn Screening Programs
APHL Position Statement/Policy Statement: Residual Newborn Screening Specimens
APHL Position Statement/Policy Statement: The Role of the Private Laboratory Sector in Public Health Newborn Screening Programs

Quality Assurance in the Newborn Screening Laboratory
APHL Position/Policy Statement

A. Statement of Position

The Association of Public Health Laboratories (APHL) recognizes and supports intense efforts to assure and sustain the highest quality of testing possible for newborn screening for public health programs. APHL continues to strongly support the quality assurance recommendations of the Task Force on Newborn Screening: A Blue Print for the Future (1). These recommendations are priority issues that need implementation as soon as possible by all states involved in any aspects of the newborn screening system. APHL strongly supports a sustained role for the APHL/CDC Newborn Screening Quality Assurance Program (NSQAP) and expansion of its services to include coverage for all disorders that are screened for by state screening systems. The organization recognized the NCCLS approved standard for collection of dried blood spots and supports its recommendation for collection of quality specimens (2).

B. Background Supporting Position

Newborn screening for detection of treatable, congenital or heritable diseases is a major public health responsibility. Effective laboratory testing of newborns using dried blood spot (DBS) specimens collected at birth, combined with follow-up diagnostic studies and treatment, helps prevent mental retardation and premature death. Quality assurance (QA) for newborn screening is a dynamic process of defining the quality of performance required for each step in the testing process (3). Quality control (QC) is the mechanism of monitoring the degree of adherence to defined criteria, taking corrective action when the system fails and documenting all of these events to convey the total quality of performance (3). Historically, QA has been perceived in clinical programs as synonymous with and only involving quality control of clinical laboratory testing. QA is widely recognized as much more than QC of laboratory testing, and indeed QA encompasses all parameters of the newborn screening system. Nowhere is this recognition more obvious than in the newborn screening systems. In these systems, the laboratory testing must work in harmony with all components from the specimen collection and birthing centers to the follow-up/counseling, diagnosis and treatment events. The information obtained by all these areas needs to be available to each participant in the system. The Clinical Laboratory Improvement Amendments of 1988 (CLIA'88) provides strong guidance and requirements for laboratories (4); in regard to laboratory facilities, personnel qualifications and competency, standard operating procedures, specimen collection, result reporting and review, quality control of tests, result turnaround times, assurance that clients are notified of all results especially in the case of abnormal values, and general effectiveness of the laboratory program. Newborn screening laboratories must achieve and maintain CLIA certification. The NSQAP operated at CDC and sponsored by the APHL provides proficiency testing (PT) and external quality control services for analytes measured in dried-blood spots by newborn screening laboratories. Successful participation in the NSQAP satisfies the CLIA requirements for PT (5). For tests for the few disorders not

covered by NSQAP, the laboratory must either implement a self-administered performance evaluation system and maintain appropriate records or, if available, participate in PT services for this disorder.

Nowhere is the importance of shared responsibilities in a laboratory QA system more obvious than in the newborn screening laboratory. These laboratories should monitor all core elements for their QA operations, including those elements that are shared and have overlapping responsibilities in the screening system. For each element, written criteria should be established for acceptable performance. Corrective actions and periodic audits should be performed and fully documented for all these activities. An overall flow chart for QA elements and QC actions should be developed based on the specimen pathway: pre-analytical, analytical, and post-analytical. In the pre-analytical category, the laboratory should monitor the quality of specimens received against set criteria, time from specimen collection to receipt by laboratory, assay kit lots, reagent lots, and instruments and their preventive maintenance. The analytical category includes monitoring results from calibrators, standards, and controls, comparing results from overlapping analysis of different reagent lots, monitoring results from the actual samples analyzed (particularly the population median), and establishing and periodically refining cutoff values for triggering follow-up action. For post-analytical category, the laboratory should monitor result reporting activities, presumptive positive results, unsatisfactory results, and confirmed positive results. Also post-analytical includes overall QA management, such as monitoring the time from receipt of specimen to start of treatment and the proportion of unsatisfactory specimens. Data systems including outcome data should be audited and documented. Policies for specimen retention and storage that comply with applicable laws and ethical standards should be documented and reviewed periodically. The identified elements are the minimal activities; other enhancements to the overall quality assurance effort should be considered and monitored for their effectiveness in contributions to high-quality operations.

C. References

1. Serving the Family From Birth to the Medical Home, A Report From the Newborn Screening. Task Force Convened in Washington, DC, May 10-11, 1999. Pediatrics 106:2000; 400-402.

2. Hannon WH, Boyle J, Davin B, Marsden A, McCabe ERB, Schwartz M, Scholl G, Therrell BL Jr, Wolfson M, Yoder F. Blood collection on filter paper for neonatal screening programs; approved standard-third edition. NCCLS document, LA4-A3. NCCLS, Wayne (PA) 1997;17:1-23.

3. Hannon WH, Henderson LO, Bell CJ. Newborn Screening Quality Assurance. In: Khoury M, Burke W, Thomson E, editors. Genetics and Public Health: Translating Advances in Human Genetics into Public Health Action. Oxford (UK): Oxford University Press. 2000:243-258.

4. Code of Federal Regulations, “Medicare, Medicaid, and CLIA Programs; Laboratory requirements relating to quality systems and certain personnel qualifications; Final Rule,” Federal Register (42CFR.493), January 2003.

5. Bell CJ, Hannon WH, Adams BW. Is the CLIA proficiency testing format appropriate for newborn screening? In Therrell BL Jr, Aldis BG, editors. Proceedings of the 11th National Neonatal Screening Symposium; 1995 Sept 12-16; Corpus Christi (TX). Washington (DC): ASTPHLD, 1996:1-2.

D. Implementation

APHL encourages the use of other quality assurance efforts, e.g., the periodic use of internal laboratory evaluations that utilize dried-blood spots prepared on the state's specimen collection card with submission of these blind-coded specimens to monitor the quality and effectiveness of the system, and other types of periodic quality audits of the laboratory testing system while maintaining documentation of these activities. Laboratories should take advantage of the onsite technical review team of the National Newborn Screening and Genetics Resource Center for a gap analysis and assessment of state newborn screening systems including all components to enhance the quality of performance.

As a participant in the Newborn Screening Task Force (1), the APHL Newborn Screening and Genetics in Public Health committee believes that it is necessary to further emphasize and, in some cases, expand the recommendations of this Task Force Report. APHL can articulate the state's public health processes and policies about newborn screening, and the inherent variability in the state's programs, to inform and shape national policy. APHL and the Newborn Screening and Genetics in Public Health Committee should continue to convey the position of the organization to other groups and the public that supports and documents the high-quality of newborn screening performed by state screening programs nationwide.

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Recommended by: APHL Newborn Screening and Genetics in Public Health Committee
Date Submitted: July, 2003
Date Approved by Board of Directors: January, 2005
Date Approved by Membership: Vote Underway
Sunset Date: January, 2010

APHL Position Statement/Policy Statement

Parental Consent in Public Health Newborn Screening Programs

A. Statement of Position

Explicit parental consent is not necessary for mandated public health newborn screening. This statement applies only where the panel of screened for conditions is limited to those of medical consequence which when detected in the newborn period can be treated so as to limit the medical consequences of the condition. The mandated screening program must also assure that the test assays employed have been fully analytically and clinically validated to standards established by the program, and that the clinical utility of the assay is known. Parental and provider education must be an integral part of the program even where documentation of consent is not required.

To the extent that state programs elect to utilize the process of documented informed consent to encourage and assure pre-test parental education they are to be encouraged and their experiences shared with all members. Any parental consent or dissent obtained should be clearly documented and maintained as part of the infant's newborn screening program record. Where programs elect to include new assays or conditions for which the above conditions cannot be met, explicit consent may be required under state statutes and policies and should be required in the spirit of informed participation in medical procedures of limited or unproven benefit. Any research use of newborn screening specimens must be done only with review of appropriate human research subjects' protection procedures.

B. Background/Data Supporting Position

The primary purpose of execution and documentation of a formal informed consent process in the conduct of medical procedures is to assure that the patient (or in the case of minors without the capacity to consent, the parent or legal guardian) has been informed of the relevant benefit and risk associated with the medical procedure. The information conveyed must include all "material information" so that an individual of reasonable mind could make an autonomous informed decision under similar circumstances. In the case of newborn screening the risk of adverse medical consequences associated with the collection of a few drops of blood by heel stick is small. The possible consequences of a false positive result are generally limited by referral for immediate follow-up and reassurance of the parents and other interested parties that no further medical consequences are anticipated. Where no specimen is submitted due to parental refusal to consent or elective dissent the possibility of missing the diagnosis of one or more of the conditions screened for by the program may be as high as 1/500 infants as indicated by the rate of referral for presumptive positive infants (as reported by the New York program). This figure depends on the state specific screening panel and population demographics. It has been suggested that this balancing of minimal risk of the test procedure and the significant medial consequences of a missed case could suggest "that the autonomy of the parent to make health care decisions for their minor children must give way to the state's role in protecting children from

harm."[1]

Currently only two states (Maryland and Wyoming) have elected to operate mandated public health newborn screening programs utilizing explicit consent. Most other states allow parental dissent on at least religious grounds. The experiences of Maryland and Wyoming, and the New York experience during the brief period of statutory consent requirement for HIV screening of the newborn specimen before this condition could be added to the mandatory unconsented program by legislative and regulatory amendment, suggest formal parental consent procedures can be incorporated into newborn screening programs. The recent experience in Massachusetts utilizing pilot programs to implement expansion of newborn screening and the inclusion of documented refusal of pilot screening additions suggest this alternative may also be feasible in limited circumstances. However, the practical implications of consent procedures for program costs in large scale universal screening programs of doing so has been the subject of much debate. The potential benefit of a better informed parent population may not warrant the potential expense.

The critical components of the newborn screening program which must be in place in order to support the absence of documented informed consent include:

- The mandatory screening panel includes only tests which have been fully analytically and clinically validated by standards established by the program,.
- The screening panel includes conditions only where early detection can be followed by interventions known to alleviate the severity of the condition. [2]
- The overall program includes mechanisms for appropriate health care provider education so that they are available to answer parental questions and concerns.
- The overall program includes mechanisms for parental education prior to testing, and as early in the pregnancy as possible.

C. References

Serving the Family from Birth to the Medical Home: Newborn Screening: A Blueprint for the Future, Report of the American Academy of Pediatrics Newborn Screening Task Force, 106 Pediatrics 389,409-410, 2000.

Genetic Testing and Screening in the Age of Genomic Medicine, the New York Task Force on Life and the Law, November 2000, pp 169.

(see footnotes)

D. Implementation

The APHL membership must convey this position of the public health laboratory community to state health agencies and health policy makers to assure that state newborn screening programs will be able to continue to operate under allowed dissent rather than mandated consent.

APHL, and specifically the Newborn Screening and Genetics in Public Health Committee, should continue to represent the position of the organization to other groups such as ASTHO, SACGT, ACMG, MOD, Hastings Center, CDC, CLIAC, etc.

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[1] Genetic Testing and Screening in the Age of Genomic Medicine, the New York Task Force on Life and the Law, November 2000, pp 169.

[2] Serving the Family from Birth to the Medical Home: Newborn Screening: A Blueprint for the Future, Report of the American Academy of Pediatrics Newborn Screening Task Force, 106 Pediatrics 389,409-410, 2000.

APHL should collect and maintain program educational materials and consent and dissent forms from all member state newborn screening programs and track any changes in program designs.

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Recommended by: APHL Newborn Screening and Genetics in Public Health Committee
Date Submitted: May, 2001
Date Approved by Board of Directors: January 19, 2002
Date Approved by Membership: June 5, 2002
Sunset Date: June 5, 2007

Residual Newborn Screening (NBS) Specimens
APHL Position/Policy Statement

A. Statement of Position

APHL supports the development of national consensus policies, procedures, and standards for retaining residual dried blood spot (DBS) specimens following NBS analysis. These policies and procedures must recognize existing federal regulations for clinical testing, state laws, professional guidelines, and ethical and legal precedents. The policies should also allow for introduction of new analytes and techniques into the NBS laboratory arena. To meet recognized laboratory quality assurance practices, DBS specimens must be retained for a time period and under conditions that permits analytical validation [1]. There may be other reasons to save DBS specimens, including test development, research, and forensic identification. To retain DBSs for such purposes requires clear guidelines that are incorporated into national consensus policies that state public health departments can follow in carrying out their authorized NBS programs.

B. Background

A survey of state NBS programs found large variations in policies regarding retention of specimens, extending from a few weeks to 21 years or longer [2]. In 1996, the Council of Regional Networks for Genetic Services (CORN) issued guidelines for the retention, storage, and use of DBSs following NBS analysis [3]. As this report noted, the length or retention of residual DBS specimens should be made on the basis of the stability of the analytes of interest, the potential use of the DBS specimens, and technical issues concerning proper storage and ease of retrieval. While methods for analyzing DNA from DBSs continue to improve and provide a mechanism for performing multiple molecular techniques from a single DBS, additional issues are raised concerning the availability of genetic information from these potential DNA banks.

Currently, the Genetic Services Branch of the Maternal and Child Health Bureau, Health Resources and Services Administration, Department of Health and Human Services, in addition to supporting the National Newborn Screening and Genetics Resource Center, has funded two contracts to develop model policies and procedures for NBS programs (American College of Medical Genetics, UCLA Center for Society, the Individual and Genetics). Both organizations held conferences on these topics in late 2002 to consider the feasibility of establishing a multi-state or central DBS bank for the purpose of providing a resource for obtaining population-based data on prevalence of gene variants of public health significance, and the association of gene variants with disease and risk factors. At the meetings, consensus was not reached on these complex ethical, public education, and scientific issues.

Professional societies have also examined these issues[4]. Until such time that recognized national policies and procedures are in place, individual states will have to address a number of technical, legal, and ethical issues regarding retention of DBSs and other specimens for potential genetic, epidemiologic, research, test development, liability, or forensic purposes. As noted in the CORN report[2], these include: 1) the stability of analytes; 2) the length of time that specimens should be retained and for what purposes; 3) the requirement of legal consent; 4) a Human Subjects Review process; 5) the removal of identifiers; and 6) the ownership of the specimens.

As noted above, state programs retain DBS specimens for a number of reasons that include potential liability, investigative, developmental, or forensic purposes. The CORN report lists some reasons for discarding residual DBSs, such as lack of stability, cost, adequacy of storage conditions and space, ease of retrieval, lack of a quality assurance system to ensure integrity of stored specimens, and absence of informed consent. Clearly, guidelines are needed to provide the benefits of NBS and genetic testing to the population of the state, while protecting the rights of the individual[5].

C. References

1. Hannon WH, Baily CM, Bartoshesky LE, Davin B, Hoffman GL, King PP, Neier SS, Peter JA, Therrell BL. Blood collection of filter paper for newborn screening programs, approved standards – Fourth edition. National Committee for Clinical Laboratory Standards document LA4-A4. NCCLS, Wayne (PA) 2003; 23:1-40.

2. Newborn Screening Committee. National Newborn Screening Report (1991). New York: The Council of Regional Networks for Genetic Services (CORN), 1994.

3. Therrell BL, Hannon WH, Pass KA, et al. Guidelines for the Retention, Storage, and Use of Residual Dried Blood Spot Specimen after Newborn Screening Analysis: Statement of the Council; of Regional Networks for Genetic Services, Biochem Molec Med 57:116-124, 1996.

4. Newborn Screening Task Force. Serving the Family from Birth to the Medical Home. Newborn Screening: A Blueprint for the Future, Pediatrics 106:383-427,2000.

5. Phenylketonuria (PKU): Screening and Management. NIH Consensus Statement 2000 October 6-18; 17(3): 1-33.

D. Implementation

APHL should continue to work with federal and state agencies, professional societies, legislative bodies, and other health policymakers in developing consensus policies.

APHL should assist state programs in addressing technical, legal, and ethical issues regarding retention of DBSs for possible additional testing.

Each state should develop policies and procedures for retention and access to NBS specimens, in compliance with state laws and, if feasible, in compliance with national guidelines as consensus is achieved.

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Recommended by: APHL Newborn Screening and Genetics in Public Health Committee
Date Submitted: July, 2003
Date Approved by Board of Directors: January, 2005
Date Approved by Membership: Vote Underway
Sunset Date: January, 2010

APHL Position/Policy Statement

The Role of the Private Laboratory Sector in Public Health Newborn Screening Programs

A. Statement of Position

Screening of newborns for treatable congenital conditions is a quintessential public health program where the benefit of protecting the infant from harm invokes the states' powers to supersede even the parental right to control the healthcare provided to their children. The statutory or regulatory authority invoked in states to mandate such screening programs requires that the laboratory testing involved be carefully controlled by the state public health agencies responsible for these programs. Only through this regulatory power is the overall program controlled and participation compelled. The role of private sector laboratories in the provision of state public health newborn screening testing should be limited to contracturally prescribed arrangements. Private sector laboratories seeking to offer laboratory testing targeted at the newborn population should be prohibited from describing these services as public health services in the absence of such contractural arrangements. This is not to suggest that private sector laboratories cannot offer test modalities to the newborn population, but that such tests must be clearly described as being distinct from any public health mandated program and outside of the states responsibility for tracking and case management provisions.

B. Background/Data Supporting Position

Non-governmental laboratories flourish in the same sphere as public health laboratories, because private sector laboratories supplement but do not supplant public health laboratories "Some disagreement as to the proper spheres of activity is inevitable," and this has been a long standing issue (see the 1962 Newsletter of the New York State Department of Health.) The debate continues today. (see Hausler, et al.) Where the resources of the state public health system are required to assure testing, case follow-up tracking, and the provision of appropriate health care management of all infants detected as presumptively at risk for one of the specific conditions in the mandated screening panel, it is imperative that the state agency control the content and claims regarding newborn screening programs.

It is also the obligation of a state public health newborn screening laboratory to assure that the mandatory screening panel includes only tests which have been analytically and clinically validated to standards established by the program. The laboratory must provide the scientific basis for determining that the screening program includes in the mandatory screening panel only conditions for which early detection can be followed by interventions known to alleviate the severity of the condition. The laboratory expertise should also be involved to assure that the screening program includes mechanisms for parental education regarding the conditions to be screened, the assays to be used, the treatment options available, the state resources that can be accessed, and the outcomes anticipated. Such parental education should occur to assure parental notice prior to testing. This should be accomplished as early in the pregnancy as possible. The laboratory should also participate in monitoring compliance of all health care providers including the clinical laboratories performing confirmatory diagnostic testing and assure that corrective

actions are taken where deficiencies are identified. The laboratory should assist in developing mechanisms for appropriate health care provider education to assure that they understand the testing process, the conditions screened for and their individual roles in infant tracking, referral, or management and the development of policies to assure that the availability of appropriate providers to answer parental questions and concerns.

Participation of private sector laboratories in mandated newborn screening programs should be limited to contractural arrangement to assure their full compliance with all program requirements including method validation, quality assurance and quality control documentation, reporting, tracking, follow-up, and provider education and compliance monitoring. In the absence of such contractual arrangements, activities of private laboratories targeted to clinical testing in newborns must be clearly distinguished from testing performed by mandated public health newborn screening programs.

C. References

Task Force Report on The Public Health Laboratory -- A Critical National Resource, 29 January 1993, Members of Task Force

ASTPHLD
Dr George Anderson (MI), Dr Arthur DiSalvo (NV), Dr William Hausler, Chair (IA)
Consultants
Dr John Liddle (NCEH, CDC, USPHS), Dr Joseph McDade (CID, CDC, USPHS), Dr Eric Sampson (NCEH, CDC, USPHS)

Serving the Family from Birth to the Medical Home: Newborn Screening: A Blueprint for the Future, Report of the American Academy of Pediatrics Newborn Screening Task Force, 106 Pediatrics 389,409-410, 2000.

Health News, 39(10) pp12-19, 1962, Newsletter of the New York State Department of Health.

D. Implementation

APHL, and specifically the Newborn Screening and Genetics in Public Health Committee, should continue to convey the position of the organization to other groups such as ASTHO, SACGT, ACMG, MOD, Hastings Center, CDC, CLIAC, etc. This effort is intended to assure that state newborn screening programs will be able to continue to operate as public health agency programs to assure access to testing and treatment.

APHL should collect and maintain state program statutes, regulations and contracts for services related to performance of laboratory services for public health newborn screening programs.

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Recommended by: APHL Newborn Screening and Genetics in Public Health Committee
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Date Approved by Board of Directors: January 19, 2002
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10. Jennifer Sullivan, M.S., C.G.C.
National Society of Genetic Counselors, Inc. (NSGC)
Statement to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
April 22, 2005

national society
of genetic
counselors, inc.

nsgc

Public Statement: April 22, 2005

Good afternoon. I am Jennifer Sullivan, representing the National Society of Genetic Counselors (NSGC). The NSGC represents approximately 2000 genetic counselors worldwide and is the leading voice, authority and advocate for the genetic counseling profession.

For many years, the NSGC membership has contributed significant experience and expertise in the implementation and coordination of state wide genetic services and clinical follow-up of positive newborn screen results. The NSGC applauds this committee for spearheading the evaluation of the current newborn screening protocols in this country. This evaluation is especially important because of the service inequalities that can develop between states with the expansion of technology and knowledge.

The NSGC endorses the rationale for and designation of the core disorders for newborn screening as recommended by the American College of Medical Genetics (ACMG). Given the lack of long term follow up for many of the conditions endorsed by the screening recommendations, we commend the Committee dialogue yesterday regarding this aspect of newborn screening. We urge the Committee to consider that such evaluation include two important components: 1) a system for regular re-evaluation of the core panel of diseases for the addition or removal of diseases, as the depth and breadth of knowledge in newborn screening, genetics, and medicine in general expands; and 2) a mechanism by which researchers, state programs, and other interested parties can provide new data regarding a disorder or disease for possible inclusion in the revised core panel for newborn screening.

Further, the NSGC highly values the disclosure of all relevant medical information, and we agree that overall medical knowledge and care would be enhanced through the reporting of all abnormal newborn screening results for these core diseases, provided that adequate psychosocial and coping resources are also available. 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 collect critical information to guide present and future newborn screening initiatives.

Since the NSGC represents health care professionals closely affiliated with both the reporting of newborn screening results and the coordination of patient care and clinical follow-up, we respectfully requests that this committee recommend careful evaluation of each state's resources to support the clinical follow-up and necessary long-term monitoring of any national recommendation made in regards to standardization of newborn screening policies. State systems that have already expanded newborn screening have experienced increased demands for clinical follow-up services, stretching already limited resources. We

know first-hand the burden that genetic disease places on families, particularly with the initial diagnosis. It is critical that the evaluation of each state's clinical genetics resources include how these resources will need to expand along with the newborn screening program. Further, the NSGC recommends 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.

Finally, NSGC also requests that any recommendations regarding a national policy for newborn screening include the stipulation that newborn screening requires the provision of comprehensive medical services incorporating primary care providers, genetic professionals, dietary professionals, and other disease specific medical specialists. It is essential to ensure that the high-risk infants and their families that are identified in newborn screening programs receive high quality and standardized medical care, regardless of geographical location or ability to pay.

In conclusion, the NSGC 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. The NSGC encourages the Committee to recommend periodic evaluation of the national and state directives regarding newborn screening to ensure the availability, accessibility and efficacy of such programs and their adjunct follow up services. Committee guidance regarding such reassessment may help avoid situations such as we have presently, with rapid disparities between state programs. The NSGC continues to be at your disposal and will be pleased to work with you as the Committee continues to consider these issues.

11. Philip R. Vaughn, M.D., M.B.A.
Vice President, Newborn Screening
Pediatrix Medical Group, Inc.
Statement to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
April 22, 2005

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

Submitted by: Dr. Philip Vaughn
On behalf of: Pediatrix Medical Group, Inc.
1301 Concord Terrace
Sunrise, Florida 33323

Chairman Howell, members of the Committee, thank you for the opportunity to address you this morning. I am Philip Vaughn and I represent Pediatrix Screening.

On behalf of Pediatrix Screening I would like to congratulate the Committee on its work and accomplishments to date. Because of your efforts the nation has a standard benchmark for newborn screening in the form of the ACMG report. This report has served to standardize the nomenclature of important metabolic disease. By creating a consensus statement as to the scope of disorders that should be screened, it has provided significant guidance to program developers and offered the best hope for these disorders to be incorporated into routine testing.

The endorsement of the ACMG report by this committee has energized the national debate on expansion of newborn screening. More programs than ever before are now discussing not if they should expand their newborn screening program, but when and how.

Pediatrix will remain involved in this public debate to encourage adoption of the ACMG recommended disorders. Our message has been consistent. We will advocate for the most comprehensive, quality testing, preferably the ACMG Uniform plus Report Only Panels, to ensure that all infants receive this standard of care. We will advocate for prompt implementation of expanded screening and encourage parent notification to ensure that parents are aware of what is possible through testing to protect the health of their baby. We will also encourage cost-effectiveness in newborn screening. And we will look for constructive ways to become an active technology partner with program coordinators to ensure these goals are achieved.

Again, thank you for your continued efforts. By building awareness we will increase the access to expanded screening. For our part Pediatrix will work to ensure high quality, most comprehensive, cost-effective newborn screening is made available universally as soon as possible to protect the lives and health of our future generations. We look forward to continued participation in this process.

12. Carol Greene, M.D.
Clinical Geneticist, University of Maryland
and Membership Chair, Society for Inborn Metabolic Disorders (SIMD)
Statement to the Advisory Committee on Heritable Disorders
and Genetic Diseases in Newborns and Children
April 22, 2005

Thank you for your dedication, your excellent work and this chance to speak. I am Carol Greene, a clinical geneticist at the University of Maryland, with two comments. The first comment is offered as a private person, and the second is a follow-up to Dr. Vockley's statement yesterday for the Society for Inherited Metabolic Disorders (SIMD).

First: Earlier today, the committee discussed problems with HIPAA with respect to communication to and from Departments of Public Health. This is also an issue between the primary care physician and specialists. I'd like to refer the Committee to a JAMA April 13 article. Please note this article focuses on HIPAA; it doesn't deal with state law. For HIPAA, the review article discusses the inappropriate implementation and interpretation of HIPAA by many states and institutions. It points out that in some cases more clear guidelines are needed, but that in some cases there is inappropriate interpretation of HIPAA despite clear guidance from the HHS Office of Civil Rights, which is responsible to implement HIPAA. Specifically it is my understanding that:

- HIPAA explicitly exempts required public health reporting.
- HIPAA – and a clear HIPAA FAQ – explicitly states that no patient authorization is needed for a clinician to talk to another treating clinician about a patient.
- HIPAA explicitly states that a primary goal of HIPAA is to not interfere with quality health care.

The article's authors suggest clinicians (and I add public health professionals and families) can report to OCR any interference with patient care by actions required by (or attributed to) HIPAA, or at least ask OCR for clarification when needed. I submit – as a private person – that if we begin routinely to report to OCR when HIPAA is given as authority for actions that interfere with patient care, just as we would report HIPAA violations, behavior would change. This committee might want to hear from OCR.

Second: In the spirit of the formal SIMD comment yesterday, I appreciate the excellent report and discussion around the Treatment and Follow-up Subcommittee, but I note that the draft charge presented today for that Subcommittee does not anywhere include the word "treatment". Dr. Boyle certainly did raise, as part of discussion of the definition of "follow-up", the question of whether long-term follow-up might include issues of who is responsible for funding treatment, and the committee did briefly explore this question in its discussion. However, in an earlier presentation, Judi Tuerck offered what appears to be a clear definition of the term follow-up and of long-term and short-term follow-up, and that definition makes a clear distinction between "follow-up" and "treatment". That definition fits with or might explain why the Subcommittee is called the "Treatment AND Follow-up Subcommittee". I refer therefore back to the statement yesterday by SIMD and hope that the charge of this important subcommittee will explicitly address treatment. I am not suggesting a specific item for the "charge", and certainly I am not suggesting that the subcommittee should establish standards. I do, however, suggest that inclusion of the word "treatment" in the Subcommittee's charge would help to assure that the Subcommittee considers important treatment issues—including efforts to assure adequate resources for all patients to receive appropriate treatment.

13. Marilyn Jones, M.D.
President, American College of Medical Genetics (ACMG)
Statement to the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children
April 22, 2005

April 22, 2005

R. Rodney Howell, MD, Chair
Advisory Committee on Heritable Disorders and Genetics Diseases of Newborns and Children

Dear Dr. Howell and Members of the Advisory Committee,

Thank you for this opportunity to speak in strong support of the activity of this Advisory Committee as it moves forward the agenda of a national newborn screening program. As you are aware, the American College of Medical Genetics received a contract from the Maternal and Child Health Bureau (MCHB) of the Health Resources and Services Administration (HRSA) of the Department of Health and Human Services (HHS) to assess the scientific and clinical evidence related to the appropriateness of 78 conditions for newborn screening. This effort stemmed from the 1999 recommendation by the American Academy of Pediatrics (AAP) Newborn Screening Taskforce that HRSA should engage in a national process to develop and implement a system for newborn screening. The ACMG was pleased that the Steering Committee for the project included representatives from the leadership of the AAP, the March of Dimes, the Centers for Disease Control and Prevention, MCHB/HRSA, the Agency for Health Research Quality, and importantly the Genetic Alliance. The project was organized around several working groups, each comprised of members with extensive knowledge and experience in newborn screening. Twenty-four individuals whose expertise encompassed science, law, health policy, and ethics constituted the Expert Group charged with development of the framework for the project, evaluation of the materials from other group's activities, as well as the final recommendations for inclusion for screening. Several members of this group have been at the forefront of the diagnostic and follow-up side of newborn screening and have specific expertise in genetic conditions. Two additional specifically charged working groups included another 24 experts in various aspects of newborn screening focused on first the diagnostic and follow-up aspects of a national program and second the uniform criteria for screening and the core panel of conditions for which screening should be considered. In addition, nearly 75 acknowledged international experts in the individual diseases that were being assessed contributed their time and expertise to reviewing the evidence for or against screening. There were three opportunities for public comment during the Expert Group's deliberations. I review what is well known to this committee to emphasize the amount of thought and input that preceded the recommendation.

Throughout the course of the project, the Board of Directors of the American College of Medical Genetics was appraised of the project's activities. Since the leadership of the ACMG is representative of the breadth of clinical and laboratory activities in genetics, there are some, like myself, on the Board not directly and personally involved in newborn screening. This review, therefore, offered another opportunity for critique by educated but not invested parties. The Board received the final report in the summer of 2004. At the conclusion of the October 2004 meeting, all 17 members endorsed the report. The Board recognized that the complexities involved in evaluating and comparing the many conditions were considerable and that the issues raised by new technologies were significant. However, these considerations did not mitigate the fact that the 29 proposed conditions were often devastating, that the natural history was well enough understood, that the screening tests had strong enough performance characteristics, and that the conditions were treatable with significant benefit to the infants who were

identified by screening. Thus the Board felt this project should move forward. The Board recognized that other conditions may be appropriate for inclusion at a later date as technology changes, natural history is better understood, and treatments improve.

The Board appreciated the expressed concern that other clinically significant conditions could be identified by virtue of either the multiplex capacity of the testing or the biochemical interrelatedness of the conditions and their associated markers. The great majority of these secondary conditions are already identified in the clinical setting. The ACMG Board agreed that it is appropriate to acknowledge the secondary conditions that are identified while screening for the core conditions, even though the natural history and response to treatment may be less well understood. For this reason, the Board agreed that concurrent with screening systems be established for collecting information about outcomes of identified newborns such that this new knowledge informs future changes in newborn screening programs. This is a critical piece.

We have already seen how follow up after implementation of a screening program can improve and inform testing. In the cystic fibrosis carrier-screening program one of the original mutations included in the panel has been identified as a polymorphism and has been dropped from the recommended panel. This might have taken years to identify had efforts to evaluate outcomes not been part of the program. Since the US health care system is an obstacle to outcomes research, designing this component into the screening program is critical.

We expect that our report will set the stage for a number of initiatives that will define a stronger national role in newborn screening to ensure that the outcomes expected from a child identified in the screening programs are realized. To this end, we hope that the committee will establish an ongoing process by which conditions already included in newborn screening are reviewed and candidate conditions, for which both new screening tests and treatments become available, are considered for inclusion. The leadership and membership of the ACMG hope to contribute to this effort. As you are aware, the ACMG has ongoing projects directed toward the development of management guidelines for primary care providers that should outline what to do with screen positive infants referred to their practices; establishment of confirmatory algorithms for those identified in the screening programs addressing both the activities of the screening laboratories and the diagnostic service providers; and development of guidance documents as to how to minimize the referral of those infants who are false positives.

The ACMG is pleased to have been offered the opportunity to develop the National Coordinating Center (NCC) for Genetics and Newborn Screening Regional Collaborative Groups through a HRSA funded cooperative agreement. The Advisory Committee to the NCC recently held its first meeting and has recommended development of a national network of genetic and other specialty service providers involved in the diagnosis and follow-up of those identified in newborn screening as well as those identified at risk for or affected with all genetic disorders. Complementing this work will be related projects from our partners both to assess the genetic services that have been accessed by patients identified in newborn screening and evaluate capacity needs for genetic service providers that we already know to be of limited availability. A second set of projects is targeted at the development of the business case for genetic services through efforts to document the value that genetic service providers bring to health care. Further, there are projects that focus on the pilot testing of management guidelines (ACT sheets) through our primary care provider partners and a set of projects that focus on improving disease information that can improve the delivery of screening and diagnostic follow-up and the process of newborn screening decision-making.

Medical genetics is a rapidly moving field. Its integration into public health programs and newborn screening programs offers an opportunity to further our goals of improving the quality of life for affected individuals as well as disease prevention. It will only be through organized efforts to understand the

outcomes in these individuals and their families that we will be able to ensure safe and effective screening for the public. The American College of Medical Genetics is delighted to have had the opportunity to participate in this project, which, we believe, makes a significant contribution to the health of the country's newborns.

Sincerely,

Marilyn C. Jones, MD
President, ACMG