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

Summary of 21th Meeting
May 13-14, 2010
Washington, DC

21st Meeting of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children

The Secretary's Advisory Committee on Heritable Disorders in Newborns and Children was convened for its 21st meeting at 8:30 a.m. on Thursday, May 13, 2010, at the Renaissance Washington, DC Dupont Circle Hotel in Washington, DC. The meeting was adjourned at 2:40 p.m. on Friday, May 14, 2010. In accordance with the provisions of Public Law 92-463, the meeting was open for public comments.

Committee Members Present

Rebecca H. Buckley, M.D.
J. Buren Sidbury Professor of Pediatrics
Duke University Medical Center
Box 2898
363 Jones Building
Durham, NC 27110

Bruce Nedrow (Ned) Calonge, M.D., M.P.H.
Chief Medical Officer and State Epidemiologist
Colorado Department of Public Health and Environment
4300 Cherry Creek Drive South
Denver, CO 80246-1530

Kwaku Ohene-Frempong, M.D.
Professor of Pediatrics-University of Pennsylvania School of Medicine
Director-Emeritus, Sickle Cell Center
Division of Hematology
The Children's Hospital of Philadelphia
University of Pennsylvania School of Medicine
34th Street & Civic Center
Philadelphia, PA 19104

R. Rodney Howell, M.D.
(Committee Chairperson)
Professor, Department of Pediatrics (D820)
Leonard M. Miller School of Medicine
University of Miami
P.O. Box 016820
Miami, FL 33101

Jana Monaco
3175 Ironhorse Drive
Woodbridge, VA 22192

Piero Rinaldo, M.D., Ph.D.
Professor of Laboratory Medicine
T. Denny Sanford Professor of Pediatrics
Vice-Chair of Academic Affairs and Intramural Practice
Department of Laboratory Medicine and Pathology
Mayo Clinic College of Medicine
200 First Street, Southwest
Rochester, MN 55905

Michael Skeels, Ph.D., M.P.H.
Director Oregon State Public Health Laboratory
3150 NW 229th Avenue, Suite 100
Hillsboro, OR 97124

Tracy L. Trotter, M.D., F.A.A.P.
Senior Partner
Pediatric and Adolescent Medicine
San Ramon Valley Primary Care Medical Group
200 Porter Drive, Suite 300
San Ramon, CA 94583

Gerard Vockley, M.D., Ph.D.
University of Pittsburgh
Professor of Pediatrics, School of Medicine
Professor of Human Genetics
Graduate School of Public Health
Chief of Medical Genetics
Children's Hospital of Pittsburgh of UPMC
3705 Fifth Avenue
Pittsburgh, PA 15213

Ex-Officio Members Present

Coleen Boyle, Ph.D., M.S.
Centers for Disease Control and Prevention
Director, Division of Birth Defects and Developmental Disabilities
National Center on Birth Defects and Developmental Disabilities
1600 Clifton Road, Mailstop E86
Atlanta, GA 30333

Denise Dougherty, Ph.D.
Agency for Healthcare Research and Quality
Senior Advisor, Child Health and Quality Improvement
540 Gaither Road
Rockville, MD 20850

Alan E. Guttmacher, M.D.
National Institutes of Health
Acting Director
Eunice Kennedy Shriver National Institute of Child Health and Human Development
31 Center Drive, Room 2A03
Mail Stop Code 2425
Bethesda, MD 20892-2425

Kellie B. Kelm, Ph.D.
Food and Drug Administration
Scientific Reviewer/Biologist
Division of Chemistry and Toxicology Devices
Office of *In Vitro* Diagnostic Devices Evaluation and Safety
10903 New Hampshire Avenue
WO66, Room 5625
Silver Spring, MD 20993-001

Peter C. van Dyck, M.D., M.P.H., M.S.
Health Resources and Services Administration
Associate Administrator
Maternal and Child Health Bureau
Parklawn Building
5600 Fishers Lane, Room 18-05
Rockville, MD 20857

Executive Secretary

Michele A. Lloyd-Puryear, M.D., Ph.D.
Health Resources and Services Administration
Chief, Genetic Services Branch
Maternal and Child Health Bureau
Parklawn Building
5600 Fishers Lane, Room 18A-19
Rockville, MD 20857

Organization Representatives Present

American Academy of Family Physicians
Frederick M. Chen, M.D., M.P.H., FAAFP
Department of Family Medicine
University of Washington
4311 11th Avenue, NE, Suite 210
Seattle , WA 98195-4982

American Academy of Pediatrics
Timothy A. Geleske, M.D., FAAP
North Arlington Pediatrics
1430 North Arlington Heights Road
Arlington Heights, IL 60004-4830

American College of Medical Genetics
Michael S. Watson, Ph.D., FACMG
Executive Director
American College of Medical Genetics
9650 Rockville Pike
Bethesda, MD 20814-3998

American College of Obstetricians & Gynecologists
Thomas Musci, M.D.
San Francisco Perinatal Association
One Daniel Burnham Court, Suite 230C
San Francisco, CA 94109

Association of Public Health Laboratories
Jane Getchell, Dr. PH.
Director
Delaware Public Health Laboratory
30 Sunnyside Road
Smyrna, DE 19977-1707

Association of State & Territorial Health Officials
Christopher Kus, M.D., M.P.H.
Associate Medical Director
Division of Family Health
New York State Department of Health
Corning Tower, Room 2162
Albany, NY 12237

Child Neurology Society
Bennett Lavenstein, M.D.
Child Neurology Society
Neurology Department
Children's National Medical Center
111 Michigan Avenue, N.W.
Washington , DC 20010

Department of Defense
Mary J. H. Willis, M.D., Ph.D.
NSPS YG-2
Department of Pediatrics
Naval Medical Center
34800 Bob Wilson Drive
San Diego, CA 92134

Genetic Alliance
Sharon F. Terry, M.A.
President and Chief Executive Officer
Genetic Alliance
4301 Connecticut Avenue, N.W., Suite 404
Washington, DC 20008-2304

March of Dimes
Alan R. Fleischman, M.D.
Senior Vice President and Medical Director
March of Dimes
1275 Mamaroneck Avenue
White Plains, NY 10605

Society for Inherited Metabolic Disorders
Barbara K. Burton, M.D.
President
Society for Inherited Metabolic Disorders
Children's Memorial Hospital
Division of Genetics and Metabolism
2300 Children's Plaza, Mail Code 59
Chicago, IL 60614

Table of Contents

Thursday, May 13, 2010

I. Welcome and Committee Business

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

- The Committee welcomed Dr. Jeff Botkin and Dr. Joseph Bocchini, who will join the Committee, pending processing of their Special Government Employee forms. Dr. Piero Rinaldo will be leaving the Committee, and the other members are grateful for his service. He will continue to work with the Committee in an advisory role. This will be Dr. Tom Musci's last Committee meeting because his term with the American College of Obstetricians and Gynecologists (ACOG), which he represents, has ended. ACOG has appointed Dr. Allen Hogge as its new representative to the Committee.
- **MOTION # 1 PASSED: "The Advisory Committee approves the minutes of its 20th meeting held on January 21-22, 2010". Dr. Alan Guttmacher moved the motion and it was seconded by Dr. Gerard Vockley. The motion was approved unanimously with 13 YES votes. One member was ABSENT-Dougherty.**
- The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group requested that the Committee participate in a survey. If members participate, they will be participating as individuals and not as Committee members.
- The Committee's recommendations on Krabbe disease, learning collaboratives in genetics and primary care, and resources to increase public awareness of newborn screening were approved by Secretary Sebelius. The Secretary's response to the Committee's recommendations on Severe Combined Immunodeficiency Disorders (SCID) and the Recommended Uniform Panel is pending.
- The ACLU, March of Dimes and other organizations have provided comments on the draft document regarding the use and retention of newborn screening dried blood spots, which was posted in the Federal Register.
- Dr. Guttmacher, NIH/ NICHD, gave an update on NIH's activities for implementing SCID pilot screening. NICHD has negotiated a contract extension with Health Research Inc. in New York to look at residual blood spots to discern the feasibility and evidence for new technologies to screen for SCIDs.
    - Upcoming grants include: (1) Natural History of Disorders Identifiable by Newborn Screening R01 and (2) Novel Technologies in Newborn Screening PAR.

- The Committee congratulated Dr. Michele Lloyd-Puryear on receiving the George Cunningham Visionary Award in Newborn Screening. She was cited for involving families and advocates in her work to promote newborn screening.

II. Carrier Screening

a. Report on Briefing Paper from the Sickle-Cell Disease Carrier Screening Workgroup

Kwaku Ohene-Frempong, M.D.
Committee Member
Professor of Pediatrics - University of Pennsylvania School of Medicine
Director-Emeritus, Sickle Cell Center
Division of Hematology
The Children's Hospital of Philadelphia
University of Pennsylvania School of Medicine

- The Committee heard from Dr. Kwaku Ohene-Frempong, the chair of the Sickle Cell Workgroup, about screening policies for sickle-cell disease among college athletes. This workgroup was set up because the National Collegiate Athletic Association (NCAA) has been making policies and recommendations concerning this disease. The Sickle Cell Workgroup is preparing a formal briefing paper that will cover what is known about the topic from research. The briefing will also address the impact of screening for the disease on affected populations as well as on community service providers and public health departments that may be called on to perform these screenings. Much of the available research is based on sickle-cell trait (SCT) newborn screening rather than screening in the college-age population.
- Dr. Ohene-Frempong described how newborn screening for SCT started in the 1970s and how today there are various policies for disclosing and reporting the diagnosis. In 2007, the National Athletic Trainers' Association released a consensus statement to raise awareness of SCT. In 2009, as part of a lawsuit settlement, NCAA recommended that institutions test student-athletes to determine their SCT status. In April 2010, NCAA adopted a SCT carrier status policy to take affect starting with the 2010-2011 academic year. The policy states that Division I student athletes must be tested for sickle cell trait or show proof of a prior test or sign a waiver releasing an institution from liability if they decline to be tested. There has been a lot of media attention on these recommendations.
- The Sickle Cell Workgroup is working on recommendations for universal safety precautions for all athletes, consent and privacy protections, establishment of nondiscrimination protections, and research and evaluation needs. All athletes should be taught about and engage in universal precautions (similar to the practices used with military training) because within high level sports there is a tendency to encourage

athletes to ignore physical symptoms and push themselves beyond a healthy physical limit. If an athlete collapses, he or she should be treated regardless of SCT status. Screening should be voluntary. The Committee should work with Sickle Cell Disease Association of America to develop guidelines and resources for screening athletes that protect their privacy.

- Finally, the Sickle Cell Workgroup believes that CDC should work to develop a registry of sudden death events. Dr. Coleen Boyle suggested that the proposed registry should include severe but nonfatal as well as fatal events. NIH should conduct research to understand the link between SCT and sudden death events. Dr. R. Rodney Howell believes that there is a need for input from professional medical associations and stakeholder groups, which could take place at the NHLBI meeting to frame a research agenda in June.

- Dr. Ohene-Frempong explained that NCAA did not address any levels other than Division 1, because those student-athletes have the longest training periods. They did mention the importance of educating the coaches about universal precautions. Dr. Lanetta Jordan, the chief medical officer of the Sickle Cell Disease Association of America elaborated on the NCAA rules, which State that if an athlete is identified as having SCT, the athlete will not be denied participation but will have a different training program. If the athlete is being recruited for professional sports, the professional teams may request a detailed medical record; having the SCT label may lead to the athlete not being recruited. It is known that SCT carriers can perform at the same levels as other athletes. Since coaches are supposed to practice universal precautions for everyone without differentiation of treatment, many student-athletes would prefer not to know their sickle cell status; especially since they would run a risk of negative labeling that could keep them out of professional sports. This type of labeling and discrimination is exactly the scenario the Committee seeks to avoid in the newborn screening programs.

- The Sickle Cell Workgroup found that most institutions are opting for the least expensive test, which does not give any details about hemoglobin and mutation. Dr. Michael Skeels commented that the newborn period may not be the best time to screen potential athletes if they are going to need the information when they are 16, 17, or 18 years old and entering professional sports. The families may be aware that the child has SCT, but the piece of paper with that information may not be retained long-term. Dr. Ned Calonge noted that, in Colorado, there is a project to archive NBS information in a permanent database (e.g., the birth certificate database). Dr. Skeels also noted that some State newborn screening programs have been approached about screening college athletes.

- Dr. Ohene-Frempong explained that the recent focus on student-athletes is due to a lawsuit against the NCAA filed by the family of an athlete with SCT who died. Therefore, legal liability is the driving force behind the new NCAA policies rather than a concern for health. The Committee discussed the Sickle Cell Workgroup's recommendations and found them to be very broad because they are preliminary. Dr.

Alan Fleischman recommended changing the language to "universal safe training guidelines" rather than "universal precautions" because the latter term has other medical meanings. Dr. Ohene-Frempong explained that because the workgroup is working with an athletics group, rather than a disease advocacy or professional medical group, coming up with recommendations is much more complicated. In the end, the Committee reached consensus that the Sickle Cell Workgroup was on the right track but did not take a formal vote on the recommendations.

b. Proposed Task Force on Carrier Screening

Sara Copeland, M.D.
Health Resources and Services Administration
Maternal and Child Health Bureau

- Dr. Sara Copeland presented on the status of carrier screening projects and the proposed task force's plan of action. The task force would look specifically at carriers of genetic mutations, which are primarily a reproductive issue. The carriers have autosomal recessive disorders, which means they are not at risk for developing a disease but are at risk of having an affected offspring. Some considerations for conducting carrier screening include the impact of the disorder on the health of the carrier or the offspring, the frequency of carriers in the population, and the availability and cost-effectiveness of valid screening methods. Once the carriers have been identified, knowledge about the potential impact of the trait as well as some options to treat the disease and manage the symptoms should be made available to them. Additionally, there are considerations about consent, privacy, stigmatization, and the benefit/harm of the carrier test relative to the anxiety it might cause. Finally, the proposed task force must consider the public health impact of carrier screening (e.g., will screening decrease the burden of disease in proportion to time, resources, and reimbursement) and its impact on clinical practice.
- There have been two prior large meetings on the topics – Genetic Carrier Screening: Moving Population Genetics from Theory to Practice (2006) and Population-Based Carrier Screening for Single Gene Disorders (2008).
- Key questions include
    - Who to screen: the entire population, people with specific ethnic backgrounds who might be affected, targeted individuals because they have a family history?
    - How to screen: genetic testing for sequencing, blood spot testing, downstream markers that might indicate a carrier status?
    - When to screen: newborns, children, at the age of consent (18 years old), people planning to get pregnant, people who are already pregnant?
    - What is the purpose: inform reproductive choices, health impacts, and other reasons? Will this information stay with individuals or will they need to be re-screened at a future point in time?

- Who ensures that the testing follows guidelines and that adequate counseling is available? Direct-to-consumer testing kits were recently made available at Walgreens, but they have now been pulled from market.
    - Dr. Copeland noted that one publication found that less than 50% of obstetricians in California offered CF prenatal screening. As the panel of diseases to screen for grows, so does the potential to screen based on ethnic backgrounds. The best example of targeted population screening is the Ashkenazi Jewish's community-based efforts to screen for Tay Sachs disease. Unfortunately, other targeted population screening efforts have lead to discrimination and stigmatization, as in the example of the U.S. Air Force policy on sickle-cell disease. Previous meetings concluded that the top considerations for carrier screening should be carrier frequency, disease burden, and the cost of screening. It appears that the best approach is to engage the communities of the targeted subpopulations, as in the Ashkenazi Jewish example.
- Who is targeted for screening and or counseling? The consensus from the previous meetings is that the community should drive which carrier screenings are offered to which individuals. Subpopulations should be targeted only when there is a specific scientific reason to do so.

- There are multiple complex tests to describe who is a carrier, and coming up with a recommendation on testing is very difficult. A great need for data to measure what is actually occurring exists. We need a way to better understand pre- and post-testing education—how to assess the appropriateness of the counseling and the competency of the primary health care providers in evaluating the results.
- The 2006 meeting concluded that there needs to be greater standardization of criteria for how to select tests, a better understanding of the burden and natural history of the conditions, and a means to assess the performance of tests and the reading of the laboratory reports. There was a suggestion to expand the model for carrier screening that began with the Jewish population and to go to grassroots and community-based organizations for other subpopulations. Mandatory screening can put certain populations at a disadvantage. Case law has set a precedent against genetic discrimination.
- Dr. Copeland explained that currently no active group at the national level is looking at carrier screening, so the Committee was asked to start a task force. It will be a joint working group that sorts through the opinions on whether and how carrier screening should be performed. She has completed a literature review and is waiting for the Sickle Cell Workgroup to finish its preliminary recommendations, which the proposed Carrier Screening Task Force will build upon. There is a list of people interested in being on the task force, and other interested persons should contact Dr. Copeland. They plan to hold a core group meeting via telephone and then develop writing groups based on broad topic areas.

- Dr. Fleischman recommended keeping the newborn carrier screening issue separate from the general issue of carrier screening at other stages, such as preconception.
- Dr. Brad Therrell noted that newborn screening programs report the results back to the physician or hospital and it is unknown what happens after that.
- Dr. Skeels noted that newborn screening programs operate at the discretion of State legislatures, which decide which screenings are or are not authorized. Most of the time, newborn screening programs are not authorized to look for asymptomatic carrier status. He also recommended that the task force look at the Clinical Laboratory Improvement Amendments to see if any of the licensing criteria apply to the direct-to-consumer testing kits.
- Dr. Therrell described Texas's mandate for SCT screening as part of newborn screening. The public health department informs parents by letter if SCT has been detected and advises the family to seek counseling.
- Dr. Rebecca Buckley asked if the task force would look at X-linked defects as well as autosomal defects, and Dr. Copeland responded affirmatively.
- Dr. Rinaldo recommended that the task force consider the type of tests that could be used for carrier screening. He noted that the granularity of the screening platforms, the costs, and the residual risk vary dramatically. Dr. Copeland responded that she thought this issue should be addressed by a writing group of the proposed task force.
- Dr. Vockley stated his concern that focusing on carrier screening could divert resources and attention away from newborn screening activities that could have bigger impacts on health outcomes.
- Dr. Howell suggested that the task force add some representatives from for-profit groups that offer wide-scale carrier screening with chip technologies.
- Dr. Christopher Kus asked if Dr. Copeland uncovered any guidelines in her literature that describe what to do when a carrier is identified through newborn screening. She responded negatively.
- Dr. Denise Dougherty is concerned about how the task force can conduct systematic evidence reviews with such a limited evidence base.
- Dr. Boyle wanted to ensure there was a joint effort and coordination between this task force and the Secretary's Advisory Committee on Genetics, Health and Society (SACGHS), and Dr. Copeland responded affirmatively.
- Dr. Ohene-Frempong observed that the United States, unlike other countries, does not have specific public health policies in place to prevent carrier diseases. For example, Cyprus wants to reduce the number of babies born with severe Beta-Thalassemia, so they strongly suggest carrier testing for people getting married. There seems to be an assumption that having information about one's carrier screening status enables the

individual to use it for reproductive planning purposes, but research has not been conducted to confirm this. There is an implicit assumption that carrier screening combined with non-directive counseling leads to the prevention of births of children with these disorders.

- Dr. Michael Watson expanded on Dr. Ohene-Frempong's remarks by stating his concern that the task force be certain of the accuracy for the particular markers for each disease and their predictive capabilities so that the potential carrier screening programs are delivering accurate predictions.
- Ms. Michelle Fox from the National Society of Genetic Counselors explained that ACOG's current recommendation for cystic fibrosis screening is that couples should be apprised of the availability of carrier screening but they should also understand that it is part of the newborn screening panel in many States.
- Dr. Skeels asked about the scope of the task force—whether it will address only disorders or will it address other types of clinically significant variants as well. Dr. Copeland responded that the purpose of the task force is to look at criteria for which disorders might be introduced to a panel, but they will not be establishing a panel of disorders to be screened for.
- Dr. Botkin observed that there are some large gaps in the literature on carrier screening and how clinicians respond to the information and work with the affected families. He suggested that the task force focus on the gaps in the literature regarding how people use carrier screening information to make reproductive decisions.
- Ms. Andrea Williams from the Children's Sickle Cell Foundation expressed concern about how a person with multiple ethnic backgrounds would receive targeted population screening. She also asked that the Committee address how newborns identified as SCT continue to retain information about their status as they enter their teenage and adult years. She believes there is a need for long-term follow-up initiatives for SCT to address the overall health needs of the child.
- The Committee chose not to vote on the task force charge at this time, as the Committee is waiting for input from SACGHS.

III. Newborn Screening: Systems, Information, and Technology Needs

a. Health Information Technology Workgroup Report

Sharon F. Terry, M.A.
President and CEO
Genetic Alliance

Alan E Zuckerman MD
Lister Hill National Center for Biomedical Communications
National Library of Medicine, National Institutes of Health, HHS

- During previous meetings, the Committee recommended the formation of a Health Information Technology Workgroup (HITWG). This workgroup has now been formed and has met twice to develop its charge and goals and to clarify its relationship to the existing subcommittees.
- Dr. Alan Zuckerman shared the proposed charge, "to advise the Advisory Committee and its subcommittees on opportunities to use health information technology, systems, and standards to facilitate the exchange and use of newborn screening information." The goals of the workgroup are
    - To bring forward recommendations, reports, and best practices for implementing systems and standards in newborn screening for the Committee to deliberate and, if approved, distribute to the appropriate agencies and programs;
    - To ensure that the products coming from the Committee and its associated subcommittees and workgroups are in line with the Secretary of Health and Human Services' current information technology standards; and
    - To bring forward recommendations on how to monitor the adoption and implementation of health information technology standards in newborn screening. We need to ensure the standards are being used and address some of the barriers to the adoption of those standards.
- The workgroup will meet three times a year, in conjunction with the Committee meeting, and will conduct most of its work by telephone. The proposed membership includes three liaison representatives from the three subcommittees, representatives from Federal partners such as CDC, CMS, and AHRQ, representatives from the State level, representatives from professional societies, and representatives from technology experts and vendors. The workgroup does not intend to duplicate the work of the subcommittees, but will work with the leadership on their health IT-related needs and will assist them in creating new vocabulary and coding guidance as new screening tests are introduced.
- Ms. Sharon Terry explained some of the current issues in health IT that may influence newborn screening. The first example is the growth in HL7 laboratory results messages to support electronic heath records (EHRs). CMS and AHRQ are developing standards for children under CHIP-RA, and CMS is developing quality measures for newborn screening that will link to EHR regulations. The Nationwide Health Information Network includes funding for State HIEs, to include newborn screening. The ARRA/ HITECH Act will bring increased attention to public health informatics and immunizations. As health IT roars ahead, the Committee should ensure that newborn screening remains part of the guidance.

- The HITWG introduced a proposal to monitor State use and compliance with the existing HRS/NLM-developed guidelines for coding, terminology, and electronic messaging in newborn screening. If the HL7 lab result messages become part of the certification for EHRs, it will serve as a means to get newborn screening results into the patient's lifetime EHR. This can contribute to building a medical home for children identified through newborn screening. The HITWG also wants to develop a detailed proposal to collect data on State activities to be presented at the September meeting. In addition, the workgroup would like to be charged with expanding the coding and technology to include screening for new conditions and for confirmatory testing. Finally, the workgroup would like to be involved in setting quality measures for newborn screening.
- The HITWG must move quickly because the regulations that will likely go into effect in 2013 will probably be formulated within the next 6-12 months.
- Dr. Thomas Musci recommended including representatives from the prenatal care provider community in the workgroup. Frequently, patients come back to the prenatal care provider for a postpartum visit, and the provider does not know that there was a positive screen on the newborn.
- Dr. Howell asked if the workgroup had adequate support to do all of the work they proposed. Dr. Zuckerman responded affirmatively, but Ms. Terry suspected the workgroup would need additional resources and she would do her best to steer resources towards it.
- Dr. Kus asked how the workgroup would monitor HL7 messaging, and Dr. Zuckerman responded that they would collect data through the National Newborn Screening System and other surveys.
- Dr. Nancy Green from Columbia University observed that in an HRSA-funded project, a survey of New York State primary care providers found that fewer than 30% of providers routinely check the newborn screening results even in a newborn clinic follow-up setting. She encouraged the workgroup to think about solutions to promote meaningful use of the results.
- Dr. Timothy Geleske remarked that AAP's Education in Quality Improvement for Pediatric Practice (EQUIPP) quality improvement program has a module to improve attention to newborn screening results.
- Dr. Roger Eaton recommended that the workgroup identify an individual with expertise in privacy regulations to consult with on improving communication and provider follow-up. Sharon Terry responded that her organization has a senior counsel with privacy expertise and that person will be linked into the work of the HITWG.
- The Committee was comfortable with the workgroup's charge but did not take a formal vote on it. Dr. Howell requested that the workgroup provide a report on HL7 monitoring and an update on their work at the September meeting.

b. Newborn Screening Translational Research Network and Long-Term Follow-up Datasets

Michael S. Watson, MS, PhD, FACMG
Executive Director
American College of Medical Genetics
American College of Medical Genetics Foundation

- Dr. Michael Watson from the American College of Medical Genetics spoke about the work of the Newborn Screening Translational Network (NBSTRN) to standardize datasets for long-term follow-up. This work was initiated because the evidence base on genetic disease is generally very limited and there is a great need to bring together information in order to understand better which genetic diseases may or may not be good candidates for newborn screening. The NBSTRN would like to facilitate the development of clinical histories of these diseases because many of the diseases are very rare and there is significant variation within the diseases themselves. In order to pull together a large enough dataset to understand the diseases and their subtypes, compatible data and data systems are needed.
- HRSA funded three LTFU priority projects of the Regional Genetics and Newborn Screening Collaboratives. The Massachusetts Newborn Screening program developed a State-based model, while Region 4 created a project to pull the information into databases and data warehouses that hold identifiable, de-identified, and anonymous data. The Southeast Regional Collaborative has been looking at dietary interventions and has been monitoring patient progress and follow-up.
- The Newborn Screening Translational Research Network has a contract to serve as a coordinating center to develop resources and infrastructure that supports long-term research and development, with the ultimate objective of providing an adequate evidence base to determine what should be included in newborn screening programs.
- Informatics underlies the infrastructure that they are developing and the NBSTRN is adopting the model from the NCI's cancer biomedical informatics grid, but building it from the bottom up in a modular way rather than from the top down.
- The regional collaboratives are beginning to work with individual States on the type and detail of information they collect at the point of care when patients are diagnosed and receive follow-up care. The group is looking at which aspects of information should be provided back to the States so they know the outcomes of patients identified through their programs. This information collected could act as an evaluation tool to assess the efficiency of a program and its ability to move patients through a system.
- The NBSTRN has established a standing committee with 12 workgroups, each working on different aspects of the development of the translational research network. There are

various IT options and designs, which are different from condition to condition, under consideration. The Clinical and Translational Science Award Network (CTSA) is taking the lead for some conditions. For other conditions, the regional collaboratives are taking the lead. There is a policy workgroup looking at the development of EHRs and the privacy issues associated with them. The LSD workgroup of the NBSTRN will be meeting at the end of June to develop pilot study protocols. One workgroup identified 88 data points that are acquired at the point of care that can inform outcomes and assessment. Most of the data points were of interest from an epidemiological perspective, public health perspective, patient care perspective, and a new knowledge generation perspective. At the Clinical Centers workgroup meeting, they found that 80% of the data points for each individual condition were in common across all conditions but 20% of the data points were disease specific.

- The NBSTRN is also looking at new technologies for newborn screening. The Mayo Clinic has been looking at competing technologies for newborn screening for lysosomal disorders. The NBSTRN has been working with them to compare the technologies against each other in a uniform way and to identify the technologies that are the most appropriate and applicable to newborn screening.
- The NBSTRN is also working on language standardization in LOINC and SNOMED so that the data is compatible with HL7. At the individual State level, States are interested in being the holders of follow-up data for patients identified through newborn screening. It is likely there will be a hybrid model for where data is held primarily held or shared from a primary source. No State will have enough information to aggregate individual data for outcomes in the same way it could be done with national and international aggregated data.
- Dr. Boyle asked if the pilot studies were virtual or involved actual data. Dr. Watson responded that once the datasets are defined and the tools are in place, they will be collecting actual data. Dr. Boyle also asked if there will be a consent process for enrolling children and families into the network. Dr. Watson responded that the patient consent process will take place at the point of diagnosis when the provider offers them the opportunity to have their data captured.
- Dr. Jeffrey Botkin asked about how the clinical nodes will work down the road as they conduct comparative effectiveness research. Dr. Watson responded that patients will probably end up in an academic medical center environment; however, the intention is that diagnosis and follow-up care is the primary objective, with research as a secondary goal.
- Dr. Buckley asked if the NBSTRN was involved in the Primary Immune Deficiency Treatment Consortium since their goals are similar to this project, and Dr. Watson responded affirmatively. They are trying to engage them and to talk to as many potential collaborators as possible.

c. Assessment of Newborn Screening Clearinghouse's Meeting—Information and Data Collection for Newborn Screening: A National Approach

Sharon F. Terry, M.A.
President and CEO
Genetic Alliance

- HRSA established a newborn screening clearinghouse to contain current data and quality indicators to measure the performance of newborn screening programs in such areas as false positive rates and other quality indicators determined by the Committee.
- The legislation requires that the Committee report on long-term case management outcomes; minimum standards and related policies and procedures used by State newborn screening programs; standardization of definitions and names of disorders; quality assurance, oversight, and evaluation of State newborn screening programs; identification of the causes and public health impacts of the risk factors of heritable disorders and testing results; and confirmatory testing and verification of positive results. HRSA has already begun to assess the current National Newborn Screening Information System that is housed at the Newborn Screening and Genetic Resource Center.
- Ms. Terry, the principle director for the National Newborn Screening Clearinghouse, reported on a meeting that was held as part of an Association of Public Health Laboratories (APHL) meeting to discuss data issues mentioned in the legislation. The meeting agenda was set by HRSA, APHL, NLM, and the Genetic Alliance. Roughly 130 people attended the meeting, mostly APHL members, who were from the State newborn screening program and regional collaboratives. This is the beginning of a year-long process to collect information from various stakeholders on the needs of a data system for the nation. The goal was to listen to the State programs, and find some easy solutions that already exist that could be implemented in newborn screening. The agencies also wanted to tell APHL members about external activities in data collection, storage, and use. Essentially, it was a town hall meeting.
- APHL members brought up concerns regarding if the indicators currently collected by the NNSIS are suitable for the emergence for health IT. One such concern was the lack of consensus, in some cases, on the definition of disease. In some States the default is whichever definition a local specialist uses. If there are common definitions, there needs to be a coding and terminology guide, designated as either mandatory or voluntary. Also, there are some fears that clinical activities will occur for the sake of the standard. Members also wanted to know how States will be compared. The newborn screening system is currently split between HRSA and CDC, with little coordination. There are also fears that States will put money into developing special projects such as HL7 but will have to start all over again once national policies change again.

- Instead of filling in the same pieces of information over and over, State programs would prefer multiple "hoses" coming from one data entry. There was also concern that information might be examined in multiple, contradictory ways, leading to contradictory conclusions. In addition, there was concern that State newborn screening programs might expand workloads beyond their current capacity. Finally, members were wary of creating a "shame- on-you" data collection system, although it would be helpful to have reports available by State, disease, or screen so that some comparisons could be made.
- There were some vendors present at the meeting who said that it is possible to push data to a collection center without onerous manual labor. Vendors have been involved in a dynamic way in expanding hearing screening. There is also a need to compare what the States are already tracking for their own needs and what is being tracked for the NNSIS, so that there is not a need to report the information to two separate systems. In terms of data standardization, there needs to be a forum to allow States to discuss units of measurement, seasonal variations, etc. The members suggested gathering all of the available data to determine how messy it is. They encourage States and vendors to create their own programs with interoperability, rather than creating 51 separate programs. Currently, there is no AARA funding available for newborn screening, and there needs to be more advocacy for it. Newborn screening programs could learn from infectious disease systems. The agencies would like to position newborn screening as example of health IT in action.
- Dr. Jane Getchell asked what the ultimate vision was for newborn screening health IT. Ms. Terry explained that there are already many disparate systems in place so the vision is to get those systems to talk to each other, which will require some strong leadership from groups such as this Committee.
- Dr. Tracy Trotter reminded the group that less than 20% of private physician offices have EHRs, so there is a long way to go before all of the integration systems discussed can be rolled out.
- Dr. Buckley brought up the issue of informed consent for health IT programs. Ms. Terry replied that many people, including the American Society of Human Genomics are currently thinking about the impact of health information technologies on informed consent.
- Ms. Terry observed that the nation's health information technology organizations are not paying sufficient attention to newborn screening, which means that it is up to the Committee to play a leadership role in gaining the necessary attention.

d. Survey of State Newborn Screening Programs

Amy Brower, Ph.D.
Project Manager, NCC-LTFU
American College of Medical Genetics

- Dr. Amy Brower observed that health IT is poised to affect our lives. The purpose of the Survey of State Newborn Screening Programs was to hear from State newborn screening programs about how their information has been collected over the past two decades, primarily through the NNSIS, and to plan for the future expansion of this type of national information system. The survey was drafted and reviewed by a team of stakeholders and representatives from HRSA, NICHD, Genetic Alliance, NNSGRC, CDC, APHL, ACMG representatives from both of the coordinating centers, and selected newborn screening programs. It is a broad survey that assesses what program users think of the current system. All the respondents were current users (two from each State and territory). If the State uses a commercial lab, the survey went to the lab as well. Two-thirds of the respondents work in newborn screening or short-term follow-up. In general, they communicate screening results to primary care physicians (80%) but only 8% communicate all results to parents. The majority of respondents use the telephone or fax to communicate results. To communicate the confirmatory diagnosis, 50% communicate it to the primary care physician and 50% communicated it to the specialist or subspecialist. Given the more urgent nature of communicating the confirmatory diagnosis, respondents reported greater electronic (email) sharing of results.
- Almost all of the respondents use NNSIS, with the majority using it as time permits and one- third using it on a daily basis. One-third of respondents report spending less than 10 hours per month on NNSIS. Respondents estimated that they spent $0-$3,600 per year entering data. Fifty percent of respondents reported accessing the Web site monthly. In terms of utilizing information on the Web site, 84% sought information on the number of diagnosed cases, and 71% wanted information on the amount of the newborn screening fee. Many are currently using data for program evaluation or development, and 50% conduct internal or external comparisons of their State to another State. Sixty-four percent think NNSIS is useful, while 12% think it is not useful. Seventy-six percent of respondents have their own database that they use as the primary tool for entering case definitions and newborn screening results.
- In terms of NNSIS expansion, respondents would like to see maternal data and be able to edit individual cases. In particular, they would like greater analytical capability so that they can ask questions about their own data and compare outcomes, overlay their results with national standards, determine future program needs, and assess their cases on a real time basis. They also want to do automatic downloads and uploads and embrace HL7 data exchange.
- The majority of laboratories have their own algorithm to identify true positive cases analytically in the laboratory. Approximately 50% of respondents said that they do not have the ability to confirm demographic information. Approximately 40% of respondents did not have the ability to do long-term follow-up, 37% could do it for some conditions, but only 17% could do it for all conditions. Long-term follow-up is not currently a focus but it might increase in the future. Forty-eight percent of respondents were able to

confirm that they did not miss any cases, while 45% were not able to confirm, and 8% did not know.

- When performing second screens, all respondents had a method for linking the screens together. The major link takes place through a method that was developed in their laboratory. In the majority of cases 54% of respondents have an electronic link between newborn screening and hearing data. This is the beginning of linkages between different newborn programs.
- All of the questions concerning the expansion of health IT received answers related to resources such as funding, staffing, or access to data to link follow-up.
- While 52% of respondents did not have concerns about information sharing, 44% did have concerns, which were all related to privacy. If the privacy issues could be addressed, more respondents would be willing to share. Sixty percent had concerns about NNSIS expansion but all of these concerns were related to privacy.
- The State programs would like to take the survey and expand it to State genetic coordinators and other people involved with health IT to get a broad view of NNSIS and information needs.

IV. Report on Second Screen Study

Jelili Ojodu, M.P.H.
Senior Program Manager for Newborn Screening and Genetics
Association of Public Health Laboratories

- Jelili Ojodu, the manager of the Newborn Screening and Genetics Program at APHL, presented a report on the Second screen study. Twenty-two-point-four percent of newborns receive the presumed benefit of a routine second screen. The literature suggests that cases of congenital hypothyroidism and adrenal hyperplasia that are missed on the first screen are detected on a second screening. Most newborn screening programs, however, do not support a routine second screening.
- APHL supports second screenings and has initiated a study as part of the harmonization of State laboratory practices. Approximately 22% of States conduct two mandated screens. The first screening takes place 24-48 hours after birth and the second screening takes place 2 weeks after birth. The scientific evidence behind the two screenings dates back to La Frankie (1985), with subsequent work from Doyle (1995) and a 2006 case for doing two screenings for endocrine disorders. The study includes all States that currently mandate two screenings, three states that conduct second screenings on over 85% of their population, and three additional States that represent the control group. The study had two parts, a retrospective part that goes back 5 years (2002-2007) and the prospective study. Because the study coordinators were not able to get CDC IRB approval, they had to go through each State's IRB process.

- The goal was to determine if additional cases of CH and CAH are captured by the practice of routine second screening. They also wanted to see if there were any biochemical or laboratory- based practices that cause non-detected cases in the first screening. Is the second screening effective in detecting treatable cases and preventing negative outcomes? They also wanted to look at the cost effectiveness of doing a second screening because it effectively doubles the cost of the panel. Finally, they wanted to look at the best way to answer and evaluate laboratory and medical results collected from the second screening. Using a lab form, each newborn that was picked up on first or second screen had a set of variables gathered into a secure electronic Web site, accessible only by participating States that input anonymized data. Each State had different cutoff values. In addition to collecting the laboratory information, the study also collected medical information (e.g., hypothyroidism type, neonatal history, CAH type). It takes the States personnel between 45-60 minutes to enter each patient into the system.
- The States with two screenings are Delaware and States concentrated in west/southwest. The participating States that screen between 85-90% of newborns a second time are Washington, Alabama, and Maryland. The control States are Wisconsin and Massachusetts; IRB approval for California is in process so it can also serve as a control State. Mr. Ojodu is seeking guidance from this Committee on gaining IRB approval. In order to lower the data collection burden on States, they were able to use CDC funding to provide $50/ hour for entering data but even with the funding, Colorado was not able to participate.
- Dr. Harry Hannon presented the results from the team-analyzed database, even though the data were not yet completely clean. The total cases found by year are represented in a graph, which shows that they vary a bit from year to year. The goal is to complete data collection for all of the States with IRB approval. Once the database is cleaned, they will compare the total number of cases from the first and second screenings. They will analyze and interpret the data and report back to each participating State so they can give feedback before it goes to the greater screening community. Finally, they would like to submit an article to a peer-reviewed journal.
- Dr. Howell asked about the timeline, and Dr. Hannon responded that they would like to have the study complete within a year.
- Dr. Skeels observed that some States require second samples if the baby had an early discharge, so the actual number of babies receiving second screenings may be higher than 22%. Dr. Hannon responded that the data from control States show that second samples are collected in approximately 10-12% of births.
- Dr. Michael Watson asked if the variability in the cutoffs had any relationship to the detection in the second screening, and Dr. Hannon replied that they had not yet conducted the analysis but they plan to do so.

- Dr. Getchell remarked that her program receives pressure to eliminate the routine second screen due to economic issues. In addition, regarding changing the cutoffs, it takes time to validate a new process, so any recommended changes will take time to implement.
- Dr. Therrell noted that States that do two screenings often have two different sets of cutoffs, but they only report one of those cutoffs to CDC. In addition, the lack of agreement on definitions is going to be a big issue for the analysis. Mr. Ojodu agreed that case definitions are extremely important. Initially, they did not factor resources into the study but once they went to the States, it was clear that there was a lack of resources to enter data.
- Dr. Rinaldo believes that congenital hypothyroidism will show a benefit from the second screening; however, for CH the results may be complicated by the fact that at least seven States use a second tier test. With California as a control, the control group will be too diverse.
- Dr. Botkin asked what specific concerns the IRBs had about approving the study—protecting human subject or resources. Mr. Ojodu responded that the IRBs expressed concerns about both.
- Dr. Hannon observed that the second screening is a great quality assurance program, but it is also an expensive quality assurance program.

V. Newborn Screening Contingency Plan

Coleen Boyle, Ph.D., M.S.
Centers for Disease Control and Prevention
Director, Division of Birth Defects and Developmental Disabilities
National Center on Birth Defects and Developmental Disabilities

- Dr. Boyle presented on the National Screening Contingency Plan that has been finalized and being submitted for the Committee's approval. It has eight objectives to be used as the basis for the plan.
- It is an operational plan rather than a strategic plan and gets very detailed on the who, where, what, why, when, and how of disaster planning. A workshop was held in September 2008 that included participants from State public health programs, State public health preparedness programs, clinical subject matter experts, and CDC experts. The scope of newborn screening ranges from the collection and transport of specimens to the education of families about newborn screening and follow-up. The plan was vetted and approved by HRSA. It is being submitted to the Committee for endorsement, then will go to Dr. Friedan for final signoff and be posted on the CDC Web site to share with appropriate partners. In addition, they intend to add language to the CDC Office of Preparedness and Emergency Response requirements so that there is some enforcement.

They want it to be part of State emergency planning work with exercises developed around it.

- Dr. Watson observed that there is currently a lack of preparedness because there is not an existing system that one can use for a preparedness plan.
- Dr. Getchell asked if contingency planning will become a performance measure under the PHEP grants, and Dr. Boyle responded affirmatively.
- **MOTION # 2 PASSED: "The Advisory Committee will send the contingency plan forward to the secretary". Dr. Trotter moved the motion and it was seconded by Dr. Buckley. The motion was approved unanimously. One member ABSTAINED- Dougherty.**

Friday, May 14, 2010

VI. Day 2 Welcome and Contingency Plan update

- Dr. Michelle Lloyd-Puryear drafted a formal response to the contingency plan that the Committee reviewed yesterday.
- **MOTION # 3 PASSED: "In order to establish a comprehensive national all-hazards approach to newborn screening incident response, the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children approves the CONPLAN and recommends that the secretary of HHS coordinate newborn screening emergency preparedness activities as defined in the CONPLAN within HHS's national response framework." Gerard Vockley moved to approve the statement and the motion was seconded by Dr. Buckley. The statement was approved unanimously with 11 YES votes. Three members were ABSENT- Dougherty, Ohene-Frempong, and van Dyck**

VII. Subcommittee Reports

a. Subcommittee on Laboratory Standards and Procedures

Gerard Vockley, M.D., Ph.D.
University of Pittsburgh
Professor of Pediatrics, School of Medicine
Professor of Human Genetics
Graduate School of Public Health
Chief of Medical Genetics
Children's Hospital of Pittsburgh of UPMC

- Dr. Vockley reported on the Laboratory Standards and Procedures Subcommittee meeting that took place the previous afternoon.

- The subcommittee heard a presentation from Georgeanne Arnold who proposed using existing newborn screening databases to mine prospectively information on outcomes for common disorders of Fatty Acid Oxidation (FAOD). This proposal is different from other efforts in that she is ready to start working now to assess the utility of the appropriateness of data that is currently collected. The Laboratory Standards and Procedures Subcommittee endorsed her proposal.
- The subcommittee heard a review of the parameters in second-tier screening and the statistical significance of those parameters. The discussion touched on the balance between sensitivity, specificity, and formal mechanisms for weighing the costs and benefits of a sequential screen.
- The subcommittee also discussed newborn screening quality assurance measures. They talked about the existing quality assurance systems with a look towards standardizing pre- and post-analytical practices for the newborn screening system from the collection of samples to the reporting of results and patient following-up. The subcommittee discussed the need to transition from asking how many tests can be performed to how well the current tests are performed.
- Ken Pass presented on his work with a new technology, the Luminex platform, which could improve the detection of antigen-based disorders.
- There was a proposal to develop a network of specialization of newborn screening laboratories for each region. As a larger panel of screenings is developed for newborn screening, it may make sense to have some regional laboratories specialize in certain tests, rather than to have every laboratory offer every test.
- The subcommittee is waiting for a complete report on a project from the Mayo Laboratory that compares competing platforms for identifying lysosomal storage diseases from newborn screening blood spots.

- Dr. R. Rodney Howell asked about the logistics of developing a regional specialization network. Dr. Vockley responded that each laboratory would have to figure out which tests it is interested in specializing in and suggested surveying some individual labs regarding which tests they are proficient in already or would like to become proficient.

b. Subcommittee on Education and Training

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

- Dr. Trotter reported on the Education and Training Subcommittee meeting that took place the previous afternoon. Many attendees from a wide variety of backgrounds, such as consumers, clinicians, and parents, attended.
    - Natasha Bonhomme, Program Manager, Newborn Screening Clearinghouse Project, gave an overview of all the work the clearinghouse has accomplished in

its first year. The beta Web site is now active. The concept is to create a clearinghouse so all information is in one place and all stakeholders have access to the latest information. Currently, there are over 2,000 links that might be helpful to someone looking for information on newborn screening.

- Joe McInerney, NCGPEG Executive Director, gave an update on the interactive, computer-based Family History for Prenatal Provider Project. It will undergo clinical testing and evaluation in the next few months.
- Sharon Terry briefed the subcommittee on SACHDNC's new Health IT Workgroup and its interface with education and training. The group agrees that health IT has to satisfy a practical need of the primary care physician in coordinating care plans for complex patients or else it will simply be one more thing physicians do not have time for.
- Deborah Heine reported on parental attitudes regarding newborn screening from the Consumer Task Force for a Genetic Alliance Cooperative Agreement. There was a good discussion with the parents in attendance, and the subcommittee hopes to continue to have an ongoing dialog with them.
- Kathy Camp gave an update on the activities of the Secretary's Advisory Committee on Genetics, Health and Society, and representatives of primary care organizations, AAP, AAFP, ACOG, updated the subcommittee on their activities. Dr. Tracy Trotter observed that, in recent years, newborn screening has received more awareness and attention.

- Dr. Trotter announced a new HRSA contract with the Genetics in Primary Care Institute for a project to pair primary care physicians with medical geneticists for a period of one year to increase the use of genetics in the physician's practice. The contract will have an advisory board and will be required to report back to this Committee. Some subcommittee members will sit on the Board.

- Dr. Christopher Kus asked how many physician-geneticist pairings were planned. Dr. Kyler replied that the contract does not necessarily require a geneticist; it could be a genetic counselor or other genetic specialist. The money is probably sufficient to fund 25 pairs across the country.

- Dr. Howell asked about efforts to increase public awareness of newborn screening. Dr. Trotter replied that he believes the most important objective should be to ensure that prenatal (OB-GYN) and primary care providers are more knowledgeable about newborn screening, since they will be the ambassadors to the general public.

- Dr. Coleen Boyle explained that at one point the Committee considered putting together a formal consumer campaign about the benefits of newborn screening. Ms. Monaco remarked that the major difficulty is obtaining the funding for a national campaign (estimated $2-$10 million). Dr. Howell suggested that the Committee should consider the national campaign issue further and brainstorm ways to obtain the funding. Dr. Kyler noted that HRSA has funded four qualitative and quantitative projects to examine

parental attitudes regarding newborn screening carrier testing across the country. The results could help guide the content and approach of a public awareness campaign. Ms. Williams remarked that the public health system also needs to prepare primary care physicians for the onslaught of patient questions that may arise due to a national awareness campaign.

c. Subcommittee on Follow-up and Treatment

Coleen Boyle, Ph.D., M.S.
Centers for Disease Control and Prevention
Director, Division of Birth Defects and Developmental Disabilities
National Center on Birth Defects and Developmental Disabilities

- Dr. Boyle reported on the Follow-up and Treatment Subcommittee meeting that took place the previous afternoon, May 13. The meeting was very productive with enthusiastic members in attendance. The subcommittee received updates on all of its ongoing activities and held a strategic planning session.
    - Long-term follow-up has been a primary focus for this subcommittee. Subcommittee members have now drafted a white paper on overarching questions and how to measure the success of long-term follow-up, including a matrix, a crosswalk between the objectives of long-term follow-up and the principal systems engaged in long-term follow-up.
    - Prior to this meeting, on May 2 some subcommittee members and other experts met with staff of the National Committee for Quality Assurance (NCQA) to discuss the overarching questions and develop quality measures to support them. The progress with NCQA will continue. Dr. Boyle thanked HRSA for providing support to NCQA to help the subcommittee develop this high-level framework to address long-term follow-up.
    - The subcommittee discussed the survey on medical foods, which was conducted in three regions, Southeast, Mid-west, and New-York Mid-Atlantic. The purpose of the survey is to understand better the real cost to families of providing medical foods, taking into account reimbursement issues. The analysis of the results is ongoing, and the intent is to present the survey to the Committee at the September 2010 meeting
    - A brainstorming session on the challenges and barriers to short-term follow-up generated the idea of using the birth certificate as an anchor to do ongoing quality control and quality assurance to make certain that newborn screening is taking place. Brad Therrell is drafting a white paper to lay out the issues from a state and national perspective. There are some privacy concerns, but there is also the potential to come up with useful recommendations. A paper will be ready to share with the Committee in advance of the September meeting.

- The subcommittee discussed potential collaboration with the Committee's new Health IT Workgroup and its crossover with the newborn screening birth certificate linkage, quality measures, medical home care coordination, Health IT could also play a role in contingency planning for families.
- The subcommittee held a strategic planning session since there are several new subcommittee members. The subcommittee is making progress on some of the long-term follow-up issues. The members reviewed and reaffirmed the subcommittee Charge. The subcommittee could move forward in the area of IT and in health insurance reform and welcomed ideas from the Committee. Dr. Georgeanne Arnold presented two issues to the subcommittee: (1) developing practice models for conditions for which there is not sufficient guidance; and (2) developing the infrastructure to get more timely data for outcome studies. The subcommittee endorsed both ideas as important for the Committee to consider in more depth; but the Committee did not endorse either process.
- Dr. Howell asked if the Committee can expect more recommendations on medical foods. Dr. Boyle replied that the subcommittee does not currently have a good understanding of what the survey analysis revealed. Hopefully, there will be a better sense of the information at the September presentation. Dr. Howell observed that there is currently some legislation pending on medical foods.

- Dr. Lloyd-Puryear urged the subcommittee chairs to review the Newborn Screening Saves Lives Act, as the subcommittees should provide leadership reviewing and addressing several areas of the legislation that the Committee must report on. Dr. Howell also asked that HRSA staff review the legislation and provide directives to answer in the Committee's report.

- Ms. Christine Brown, National PKU Alliance, commented that her organization is currently working with other organizations to secure 100 co-sponsors of the Medical Foods Equity Act in the House of Representatives by end of June. In addition, the National PKU Alliance wants to ensure that as HHS creates regulations around health care reform that medical foods are included as essential health benefits. It wants to ensure that people with metabolic diseases are eligible for the high-risk pool in terms of being able to access insurance; that metabolic disease are included in the high-risk pool. Dr. Boyle suggested that the Committee draft a letter to Secretary Sebelius to provide input on the inclusion of medical foods in the regulations currently being drafted.

VIII. **Evidence Review Workgroup Update**

James Perrin, M.D.
Chair, Evidence Review Workgroup
Professor of Pediatrics, Harvard Medical School
Director, MGH Center for Child and Adolescent Health Policy, Director, Division of General Pediatrics
Vice Chair for Research Mass General Hospital for Children

- Dr. Jim Perrin updated the Committee on the work of the Evidence Review Workgroup. The Evidence Review Workgroup was charged with understanding the incidence and prevalence of particular conditions, the natural history of these conditions (including when they show up clinically), and genotype-phenotype relationships of the conditions. They also looked at methods and accuracy of screening as well as the methods of diagnosing children who screen positive. Finally, they looked at the different methods of treatment to determine whether it is better to treat children as early as possible or to wait until the disease presents itself as well as the availability of those treatments.
- The most important aspect of this work is the level of certainty that is possible, i.e., whether sufficient evidence exists to recommend adding the condition to the screening panel.
    - The evidence for treating early infantile Pompe disease is strong, although there are some complications for children who are CRIM positive versus CRIM negative.
    - For SCID, the first challenge is in case definition. There is a lack of population screening, but more data is gradually becoming available. The evidence for early identification and treatment is good.
    - For Krabbe disease, the population screening data were inconclusive and there are some challenges about case definitions and early versus late onset of the disease. There are tremendous problems with false positives. The panel had questions about how well the test can identify children who could benefit from early treatment.
    - The natural history of children who screen positive for hemoglobin H and cyanotic congenital heart disease is not clear. Also, there is a lack of evidence that early identification of hemoglobin H can help with treatment.
- Population testing data are particularly critical for these rare diseases. To use population-based data to make decisions about screening and treatment, a large population is needed for effective screening and understanding the characteristics of the tests. In general, the evidence suggests that early treatment helps. Incidence and prevalence data can provide positive predictive values as well as sensitivity and specificity.
- Dr. Perrin reiterated that the Evidence Review Workgroup would like to hear feedback from the Committee on how to focus more uniformly evidence reviews to support the Committee's decision-making process.
- Dr. Ned Calonge recommended looking at evidence and methodology of more common diseases and applying them to more rare diseases. The Committee would like more specific recommendations about how to fill in the evidence gap. They also would like more information about how exactly the treatment will play out—it might extend a life but the long-term treatment outcomes are unknown because the therapies are new. What will be the life trajectory for that child? There may be issues with over-diagnosis because

of the spectrum of screen-detected disease versus clinically detected disease. We will have to take what we know and develop an entire spectrum of benefits, i.e., what are the trade-offs of waiting and detecting clinically. It is time to move beyond evidence alone and apply logical inferences as well as a more robust process for filling in the evidence gap. The Committee is also frustrated about inability to gather long-term follow-up data. Child-specific economic data is not available. Dr. Perrin responded that he shares the Committee's concerns and they are doing their best to address the evidence and data gaps.

- Dr. Michael Skeels asked if the evidence review groups could include more economic analysis to assist those translating the recommendations into practice. Having data about the cost of the laboratory work and follow-up and the costs avoided can help persuade elected officials to expand the screening panels. Dr. Perrin responded that they could expand the expert questions to include economic questions.
- Dr. Christopher Kus asked about the cost of false positives. Dr. Howell commented that once an entire population begins to be screened for a disease, the screening tests uncover other patients who would never have shown up clinically.
- Dr. Michael Watson asked about the availability of treatment because Medicaid does not pay across states. Perhaps health care reform could address the availability of cross-state coverage.
- Dr. Colleen Boyle replied that we do not have good evidence that is true for all conditions and treatments and their relative benefits and harms. She recommends empirical-based modeling to see what the impacts would be.
- Dr. Michelle Lloyd-Puryear suggested pulling together a working group composed of members of the Committee and other experts to develop evidence review processes and systematic decision-making approaches for rare diseases.
- Dr. Jana Monaco reiterated that the reality with rare diseases is that there will never be large enough numbers to provide the evidence, so the Committee must pull together the best recommendations possible versus waiting for perfect evidence.
- Dr. Piero Rinaldo asked if the workgroup could consider secondary targets for diagnostic conditions with the same biochemical monitors that are already on the panel as primary targets.
- Dr. Gerald Vockley cautioned the workgroup to balance the two extremes, i.e., identifying children who have a severe disease and who can benefit from early identification versus situations where early identification and treatment is harmful. In general, the only emotional appeal that researchers and clinicians have is on the beneficial extreme, not the other extreme.

- Dr. Christopher Kus pointed out that Medicaid programs do pay across state lines in some cases. Furthermore, the current health care reforms might be able to facilitate this better.
- Dr. Colleen Boyle observed that in the evidence review process there is both a publication bias and an expert bias against considering harms. She suggested developing sensitivity parameters to minimize this effect.
- Dr. Rodney Howell suggested setting up a workgroup to consider how to address better potential harms from identification and early treatment.

IX. Evidence Review Workgroup Report: Final Report on the Candidate Nomination Hemoglobin H

Alex Kemper, M.D., M.P.H., M.S.
Associate Professor
Department of Pediatrics
Duke University

- Dr. Alex Kemper presented the final report on the candidate nomination for hemoglobin H. Hemoglobin H is a type of alpha-thalassemia caused by deletions or non-deletional mutations of three out of the four alpha globin genes and causes adverse health outcomes such as anemia, hepatosplenomegaly, choletlithiasis, and growth retardation.
- Hemoglobin H is currently a secondary target, which means they are part of differential diagnosis of the core panel of condition and would or could be identified as part of core panel conditions. A survey by APHL revealed that eight states currently report hemoglobin Bart's.
- The workgroup first conducted a systematic literature review and then turned to a group of experts to uncover unpublished data. In the end, the workgroup identified 21 articles that met all of their criteria for abstraction. Most of the identified pieces of literature are case series for individuals who were identified clinically rather than through screening. For natural history, California reported that the birth prevalence for hemoglobin H was one in 15,000 for the period 1998-2000. According to a subsequent publication, the prevalence for deletional hemoglobin H was nine per 100,000, newborns and the prevalence for hemoglobin H mutation was 0.6 per 100,000 for the period 1998-2006.
- Most of the case series focus on the Asian and Mediterranean regions because hemoglobin H is more common there. In the California study, 78% of cases were deletional, while 23% of cases were non-deletional. The California study reveals that the positive predictive value for hemoglobin Bart's screen is very high. The children with non-deletional hemoglobin H tended to be diagnosed at younger ages and have higher rates of medical problems. Unfortunately there are no screen positive case series

available. There are also no economic studies available. In future years, the workgroup anticipates there will be more data available from Hawaii.

- The experts corroborated the literature findings for national history and the harms associated with hemoglobin H disease. There were no other data on the impact of pre- or early-symptomatic treatment, follow-up on screen positive individuals, or economic analysis.
- Evidence gaps trigger the following questions:
    - What proportion of children would benefit from condition-specific treatment? There is a lack of follow-up data on screen positive children.
    - What is the variation in prevalence across the United States?
    - Does early identification improve the health of identified children?
    - What is the threshold for moving a target from secondary status to one of the core targets?
    - In terms of infrastructure, what are the expectations for newborn screening laboratories, public health clinicians, and families if there is a move from secondary to a primary target?
- Dr. Watson clarified that hemoglobin H was not part of the secondary target but several states have chosen to make it part of their secondary targets. Dr. Piero Rinaldo corroborated Dr. Watson's comments.
- Dr. Michael Skeels clarified that in Hawaii, hemoglobin H is between a primary and secondary target. If the laboratory technician can visually see fast bands, they will perform HPLC. Hawaii is one of six states that are following through on all Barts.
- Dr. Kathy Hassell commented that the state laboratory for Colorado and Wyoming identifies 250-300 individuals with alpha-thalassemia per year. She would like to see some guidance from the Committee on how to treat patients who discover they have a genetic disease based on screening for something else.
- Dr. Vockley commented that he had not heard any compelling evidence to suggest that hemoglobin H belongs on the screening panel. There was no compelling clinical need presented. He wanted to see a clinical argument for testing (e.g., a child shows up very ill at age two, so the child needed to be diagnosed at the newborn period).
- Dr. Piero Rinaldo observed that the issues with hemoglobin H are similar to other diseases the Committee has considered previously. Hemoglobin H can be a late onset disease, which may present clinically between 0-73 years of age. He asked how many patients receive a splenectomy, at what age they receive them and whether or not they require transfusions afterwards. Dr. Alex Kemper responded that they could not find systematically developed literature.
- Ms. Victoria Odesina, from the Genetic Alliance, commented on the fact that consumer-based organizations do the majority of counseling for hemoglobin H and other diseases.

Therefore, the Committee needs to assist the consumer-based organizations in interpreting laboratory results and advising families.

- Dr. Elliot Vichinsky remarked that the only time hemoglobin H can be accurately diagnosed is in the newborn period because it is an unstable hemoglobin. Newborn screening provides the opportunity to diagnose and educate these patients before they are missed and adverse health effects occur.
- Dr. Alex Kemper agreed with Dr. Vichinsky's comment that diagnosing in the newborn period would enable early intervention to educate the family, inform their reproductive decisions, and teach them what to look for in infants (e.g., splenomegaly). There are also a large number of miscarriages due to maternal complications from hemoglobin H, and these patients would benefit from prenatal counseling
- Dr. Jane Getchell commented that it is very important to test the dried blood spot soon after collection due to the low stability of Bart's. Dr. Lorey disagreed.
- Dr. Skeels commented that people running screening programs, regardless of the recommendations of the Committee, face an ethical decision about deciding to ignore evidence that is right in front of them every time they perform IEF. It is a practical decision about having knowledge and deciding whether or not to share it. Including it in the panel would bring about better uniformity.
- Dr. Ned Calonge commented that he suspected that California and Hawaii would continue to test for hemoglobin H regardless of the recommendations of the Committee and add to the knowledge base. He does not believe it should be done for every child in every state because at some point in the future the evidence may reveal more information about the benefits and the harms.
- Dr. Fred Chen observed that primary care provider would find it helpful to hear from experts given the uncertainty about how to treat the disease.
- Mr. Jelili Ojodu and Dr. Brad Therrell sent out a survey to all states to get a more detailed view of current practice. So far, 30 states have completed the survey and of the 30 states completing the survey, eight states report on Hemoglobin H. It appears that there is wide variation from state to state regarding whether the hematologists even want the laboratories to report on Bart's. Dr. Therrell would like the Committee to recommend that laboratories report Bart's.
- Dr. Alex Kemper explained that there is a long-term follow-up paper pending but it was not available to the evidence review group. Dr. Rodney Howell believed that the paper would be helpful in expanding or modifying the recommendations and that it would be worthwhile to examine it prior to making a final decision. He recommended moving hemoglobin B to Category 3, but thought it is easier to put in the context of Category 4.

- **MOTION # 4 PASSED: "To not add hemoglobin B to the Recommended Uniform Screening Panel and to place it as Category 4 "Additional Evidence Needed". Gerard Vockley moved the motion and it was seconded by Dr. Trotter. The motion was approved unanimously with 11 YES votes. Three members were ABSENT- Dougherty, Ohene-Frempong, and van Dyck.**
- Dr. Watson recommended looking at all the non-isoallele hemoglobinopathies and bringing the recommendations forward at one point in time. Dr. Gerard Vockley agreed with the suggestion.
- Dr. Rebecca Buckley suggested that the Committee recommend that when hemoglobin B is identified in the course of screening, it be reported. Dr. Howell suggested that the Committee hold off on Dr. Buckley's suggestion until they have the results of the state survey.
- Dr. Michelle Lloyd-Puryear informed the Committee that HRSA, APHL and the National Newborn Screening and Genetic Resource Center are holding a workshop in California with state labs to look at hemoglobinopathies and Bart's and asked if the Committee could lay out issues in advance to be sure that they are covered in the agenda.
- Dr. Fred Lorey commented that hemoglobin H does not appear to be much different than many of the other Category 2 mass spec disorders. He believes it should be a secondary target.
- Dr. Eliot Vinchinsky commented that the panel is being naïve in understanding the patients' access to the health care delivery system. The majority of hemoglobinopathy patients are from poor Laotian families who do not have access to care and do not get prenatal care. Given the reality of health care for these families, the newborn period when providers can educate the families before the children get anemia or viral infections.

X. Response to Council on Bioethics' Report on Newborn Screening—Committee Discussion

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

- The President's Council on Bioethics Report on Newborn Screening has created a lot of discussion. Even though the group has been disbanded, the publication is in circulation and this Committee has significant concerns about it.
- Dr. Tracy Trotter reminded the Committee that the purpose of the report was to lay out the ethical principles that guide the practice of newborn screening in the United States.

- In 1968, the World Health Organization laid out 10 criteria for including a condition in a population screening program (known as the Wilson-Jungner Criteria). The National Research Council aligned itself with these criteria in 1975. In 2005, the ACMG expert group that came up with the core panel currently in use reported that their policy would be driven by what was best for the infant. A benefit to research study was not a criterion by any of these groups at that time.
- Responding element by element to the council on bioethics report:
    - First Element: The Wilson-Jungner criteria should continue to have relevance. Dr. Trotter believes that the Committee would affirm this principle.
    - Second Element: Do not mandate anything that does not meet the Wilson-Jungner criteria. Dr. Trotter believes that there is a misunderstanding of how the Council looks at secondary disorders. Secondary conditions will arise incidentally or as a consequence if the laboratory is doing the core condition screening properly.
    - Third Element: Endorse the option for States to offer screening, on a voluntary basis, for conditions that do not meet the Wilson-Jungner criteria. Dr. Trotter noted that classical criteria continue to evolve and expand, as evidenced by the work of the NAS/NRC, the expert group, and the ongoing work of the SACHDNC committee. When conditions are deemed not meeting the criteria, there is a role for research to evaluate further disorders for possible inclusion.
    - Fourth Element: When a differential diagnosis entails detection (e.g., a secondary disorder that would not otherwise be a suitable candidate for the core panel) these results should not be transmitted to the child's physician or parents unless there was informed consent at the time of screening. In Dr. Trotter's opinion, it would be unfair and unreasonable to disregard these results for humanitarian reasons. From a reality process, it avoids a diagnostic odyssey, that for many of these metabolic conditions are especially arduous, very sad, and extremely expensive. Knowing this data may inform reproductive decision-making and provide early supportive intervention for the child and family. Clinical research studies may be available, and the family should have a right to know about it. Dr. Trotter noted that the council and committee agree that informed consent is not appropriate for core conditions, but is required for research studies. Dr. Trotter also noted that instituting informed consent for mandatory newborn screening would put the programs at risk.
    - Fifth Element: Urge a thorough continuing re-evaluation of the disorders now recommended for the core panel. In Dr. Trotter's opinion, it is reasonable to evaluate continually the core conditions, and the Committee is currently tasked with that responsibility.
    - Sixth Element: They reject the technological imperative (e.g., just because you have a multiplexed platform, you should do more testing). Dr. Trotter believes

that the Committee's current review process addresses the relevance of technology.

- Dr. Piero Rinaldo remarked that the greatest level of misunderstanding concerns two points: Element 4 should make a very explicit distinction between primary and secondary targets, which cannot be done on the basis on screening test alone. With regard to the technology element, the specific reference to MS/MS, only two or three of the 60 or so markers are unique to a secondary condition.
- Dr. Howell suggested that Dr. Rinaldo send Dr. Trotter an e-mail with the specific language to clarify the existing misconceptions surrounding the secondary panel.
- After circulating the final draft of the revised report to the authors, the Committee intends to submit this document to a yet to be determined professional publication (i.e., Genetics in Medicine).

XI. Lysosomal Storage Diseases—Report on State Screening Practices

Michael S. Watson, MS, PhD, FACMG
Executive Director
American College of Medical Genetics
American College of Medical Genetics Foundation

- Dr. Michael Watson reported on the Newborn Screening and Translational Research Network (NBSTRN) activities for lysosomal storage disease newborn screening. NBSTRN has two major areas of activity: (1) supporting pilot studies of severe combined immunodeficiency syndrome (SCID) and lysosomal storage disorders (LSDs); and (2) supporting the development of new technologies and tests, and comparative assessments of different platforms for the same newborn screening test.
- SACHDNC has looked at the nominated conditions, Pompe, Krabbe, Fabry, and Niemann-Pick disease. Those conditions were not recommended for newborn screening then. SACHDNC has not been asked to look at Gaucher disease.
- New York State has been screening for Krabbe disease for four years, and issues have arisen around the incidence of the condition. The state has legislation to expand screening to four additional LSDs listed above, as well as SCID. Illinois has mandated screening for the five LSDs starting in October /November 2010. Missouri has mandated the same five LSDs along with any others that become amenable for the availability of screening technology. Washington State is involved in an NICHD-funded pilot study to develop new tandem mass spec-based screening technologies. Perkin-Elmer laboratory is bringing forward a supplemental screening program for LSDs potentially in any part of the country.

- NBSTRN wants to be involved in defining the pilots and in determining whether or not the tools they are developing actually work effectively. Primary care provider networks need a lot of support in the form of ACT sheets and guidelines about what to do in response to a notification of a positive screen regardless of whether or not it is identified as a primary or secondary target. This includes working with expert groups throughout the United States and funded NIH activities, such as the Lysosomal Disease Network.
- There are some ongoing parallel activities by an international group that has recently finished drafting guidelines on the diagnosis and management of asymptomatic LSD patients.
- NBSTRN is also developing the diagnostic algorithms that are associated with the LSD conditions to provide guidance on how to work through the evaluation and laboratory diagnosis of the patients.
- There are at least four competing technologies under consideration for LSD newborn screening. Two different groups are looking at these technologies: Duke University and a partnership between Advanced Liquid Logic and the Mayo College of Medicine.
- The next step is the first substantive meeting planned for late June. This is subsequent to a meeting of experts at the American College if Medical Genetics meeting in Albuquerque. The group of diagnosis and management providers will have a coordinated approach in developing protocols for diagnosing and evaluating patients. They will be supplementing the work already being done around all conditions in newborn screening. The NBSTRN Web site will have project summaries, protocols associated with LSD pilot studies, and pilot study results. In addition, several states will be engaged to think about how pilot screening data might be brought into a platform such as the laboratory performance database in Region 4 to capture pilot data from multiple states collaboratively.
- Ms. Monaco asked if there is a central database to collect all of the data from the state pilot studies. Dr. Watson explained that there are several databases. Currently, a subcontract is being negotiated with the Region 4 Laboratory Performance Program. Other data systems will be reviewed.

XII. Evidence Review Workgroup – Future Directions

Alex Kemper, M.D., M.P.H., M.S.
Associate Professor
Department of Pediatrics
Duke University

- Dr. Alex Kemper solicited advice from the Committee for future directions for the Evidence Review Workgroup.

- It is very important but very difficult to assess harm such as false positives, difficulties in establishing diagnoses, carrier identification, identification of an adult-onset condition during the early neonatal period, or identification of an adult-onset condition with little prognostic information. To what degree should the availability of health services for diagnosis or treatment factor into weighing benefits and harms?
    - Getting the case definition correct at the beginning of the review is critical because it guides what the workgroup includes and excludes in its review.
    - An outside technical expert panel can be a good process for refining the evidence the workgroup is examining. The technical expert panel could be used for case definition as well.
    - There was a recent article in *Genetics in Medicine* that proposed four general domains to evaluate conditions: analytic validity, quality of data sources, study quality, and adequacy of evidence or strength of linkages in the chain of evidence.
- There are several approaches to reviewing evidence – United States Preventive Services Task Force (USPSTF), American Academy of Pediatrics (AAP), Agency for Healthcare Research and Quality (AHRQ) funded evidence-based practice centers (EPC), Institute of Medicine (IOM), Cochrane Review Process (CRP), and the Grading of Recommendations Assessment, Development, and Evaluation Working Group (GRADE).
- Dr. Kemper proposed having a technical expert panel (modified from EPC) to help guide the evidence abstraction process, thinking through the case definitions and the questions for the analytic framework, and being explicit ahead of time in the analytical framework about the potential benefits and harms for each condition. When the analytical framework and key questions are developed, they will post on a Web site for public comment to increase transparency of the decision process. Next the feedback can be reviewed with the Nominations Workgroup.
- Harms are often not recognized and reported in manuscripts due to publication bias. It is difficult to assess harms because of a lack of denominator information.
- Dr. Kemper also suggested developing a manual of procedures within the Evidence Review Workgroup or by another group to revisit the operating procedures.
- Modeling is very difficult because there is a lack of data but it is possible to build a model that is not trivial using the most pessimistic estimates and most optimistic estimates. There would be a learning process because the conditions are complicated.
- Dr. Fleischman commented that the conflict of interest that is inherent with using the experts that know the most about the disorders could be a potential problem. The Evidence Review Workgroup needs to maintain transparency and independence, and think through this kind of technical expert group. Dr. Kemper agreed and mentioned that this is a communication issue the workgroup has also been wrestling with.

- Dr. Ned Calonge concurred with the issues and suggested an advisory panel, rather than an expert panel. USPSTF, for example, has task force leads who serve that role; at least one Committee member could sign up to be on the advisory panel as the lead for a topic to help go through the decisions. The experts could be included through the public comment period. Another strategy is sharing the analytical framework, key questions, and work plan with the experts to get their comments on the evidence review without actually having them on the technical expert panel.
- Dr. Calonge also supported the idea of looking at the manuals of procedures for both EPC and USPSTF and then creating a franchisable model. .
- Dr. Jim Perrin commented that the workgroup needs to be clear with the experts that they are looking for information, rather than opinions.

XIII. Evidence Review Workgroup Report: Literature Review for Critical Cyanotic Congenital Heart Disease

Alex Kemper, M.D., M.P.H., M.S.
Associate Professor
Department of Pediatrics
Duke University

- Dr. Alex Kemper presented the workgroup's case definition for critical congenital cyanotic heart disease, the planned approach to evidence review, and the preliminary findings on the accuracy of pulse oximetry.
- Congenital heart disease covers the wide spectrum of structural heart defects that are present at birth. Critical congenital heart defects (CCHD) cause severe and life-threatening symptoms and require intervention within the first year of life. Critical congenital cyanotic heart defects (CCCHD) are CCHDs that are associated with hypoxemia. These lesions can cause significant morbidity and mortality and newborn screening with pulse oximetry has been examined in large studies. Early identification of CCCHD infants can improve health outcomes.
- The workgroup convened a technical expert panel of pediatric cardiologists to define which heart defects are potentially detectable by pulse oximetry and which defects meet the definition of CCCHD. The full final report will include all the evidence from the studies published on pulse oximetry screening (the systematic literature review of 11 studies that met the inclusion criteria), as well as communication with investigators and advocates. All of the studies (except two) reported the specificity above 99%. Sensitivity was more variable, ranging from 42% to 100%. Dr. Kemper believes that there should be a meta-analytic approach to data.
- The critical evidence that is still needed includes:

    - How much does pulse oximetry increase the number of cases identified in the newborn nursery beyond what would be picked up by prenatal ultrasound and clinical exams?
    - Does pre-symptomatic or early symptomatic intervention in newborns or infants with CCCHD improve health outcomes?
    - What are the economics surrounding newborn screenings?
    - What are the potential harms?
    - How available are diagnostic and treatment services?
    - How might this be influenced by telemedicine?

- Dr. Ned Calonge observed that the pulse oximetry test would affect a new group of stakeholders – hospitals – unlike a new blood spot test. The workgroup needs to reach out to incorporate hospitals and health care workers in obstetrical services facilities.

- Dr. Jane Getchell asked if the pulse oximetry screening would have a health department follow-up, similar to the hearing screening. Dr. Kus commented that there is a parallel to newborn hearing screening in that the system needs to get the information to the health department to track it. Unlike newborn hearing screening, the diagnostic testing would occur in the nursery presumably before the baby went home, as opposed to following-up with diagnostic hearing testing after discharge.

- Dr. Frederick Chen suggested adding to the report more information about the denominator (how many of the cases are actually picked up clinically?) Dr. Jane Getchell asked if pulse oximetry is a regulated and standardized test. Dr. Calonge replied that the devices are FDA-approved but there is no application standardization.

- Dr. Fleishman wondered about a scenario in which a baby screened positive in a small rural community hospital that has an ultrasound machine but no neonatal technicians. The child would then have to be transported elsewhere, which introduces increased potential for harm.

- Dr. Coleen Boyle suggested adding some confidence intervals on the estimates in the report because the numbers are small. She also commented that many state public health infrastructures house state birth defect detection surveillance programs that are charged with connecting families to services and monitoring. . Dr. Boyle will connect Dr. Kemper with CDC to provide surveillance numbers.

- Dr. Kus raised the critical issue of risk for false positives and whether this is relevant or not.

XIV. Letter to Secretary Sebelius about Medical Foods and Health Care Reform

- Dr. Lloyd-Puryear drafted a letter for the Committee's approval.

- The second bullet was changed to "Individuals with those conditions recommended by the committee are high risk, and HHS regulations should ensure that they can access coverage for necessary medical treatments over the course of their lifetime."
- After being approved by the Committee, the letter will have to go through the Office of General Counsel at HRSA for review.
- Dr. Coleen Boyle wanted to ensure that the wording did not limit medical foods to metabolic conditions only.
- Dr. Hassell commented that the wording "high risk" is included because individuals with metabolic conditions should be included in the high risk pool.
- Dr. Rodney Howell determined that the Committee was in consensus on the letter and that it can move to the Office of General Counsel without a vote.

XV. Public Comments: General

- Ms. Anne Marie Saarinen, an advocate for increased research on critical congenital heart disease, thanked the Committee for conducting the literature review on pulse oximetry. She reminded the Committee that the studies suggest there could be a sevenfold increase in detection rates with this tool. She also urged attention to families living in rural areas.
- Ms. Olivia Eastley spoke on behalf of her daughter, Veronica, who died last summer due to undetected CCHD. As a newborn, the baby appeared to be perfectly healthy but at six weeks of age, she died suddenly without any apparent symptoms except difficulty feeding. Ms. Eastley urged the Committee vote to approve universal neonatal pulse oximetry.
- Ms. Vi Kennedy spoke on behalf of her daughter, Taryn, who died suddenly from cardio-respiratory arrest from CCCHD at 27 days of age. She explained that pulse oximetry is a simple, inexpensive, noninvasive test to detect asymptomatic congenital heart defects. Ms. Kennedy asked the Committee to support pulse oximetry screening as the standard of care within 24 hours of birth.
- Dr. Gerard Martin is the senior vice president for heart, lung, and kidney disease at Children's National Medical Center. The center has developed a toolkit for implementing pulse oximetry and has screened 7,000 babies in the last year. In total, there have been three false positives, one true positive, and two positives for other types of heart disease. They are now extending the toolkit to 11 hospitals in the Washington, DC, area and to hospitals in Kuwait and Qatar.
- Ms. Gina Cioffi from the Cooley's Anemia Foundation, urged the Committee to include hemoglobin H as a secondary panel. There is a new registry for surveillance of hemoglobinopathies through a cooperative program between CDC and NIH, and

newborn screening would generate data to get population-based evidence on outcomes from people with hemoglobinopathies.

- Ms. Catherine Crump from the ACLU spoke about privacy and autonomy with blood spots. They were concerned that the residual blood spot report did not include strong enough language that consent is necessary for the long-term storage and research use of blood spots. ACLU is not opposed to newborn screening or residual blood spots being used for research purposes; they just want to ensure that researchers obtain the necessary consent.
- Ms. Jennifer Weisman from the HHS Office of Civil Rights was called on to speak, but she was not present.

XVI. **Committee Discussion and Committee Business**

- Dr. Chris Kus suggested a more formal recommendation for the Sickle Cell Workgroup for carrier screening. Dr. Rodney Howell suggested sending a letter to Secretary Sebelius.
- **MOTION # 5 PASSED: The Committee will send a letter to Secretary Sebelius to say that the Committee is looking at the issue and has some concerns about the NCAA screening issue and is reviewing it. Specific language in the letter should include "The SACHDNC recommends not screening routinely for sickle-cell trait as a prerequisite for participation in Division I sports." Dr. Trotter moved the motion and it was seconded by Dr. Calonge. The motion was approved unanimously with 9 YES votes. Dr. Boyle ABSTAINED. Four members were ABSENT-Dougherty, Ohene-Frempong, Rinaldo and van Dyck.**
- Dr. Althea Grant, from the Division of Blood Disorders at CDC, urged the Committee to construct a statement that is more nuanced because athletes cannot just opt out of screening. Also, increasing the number of people who are aware of their sickle-cell trait status is a Healthy People 2020 developmental objective.
- **MOTION # 6 PASSED: To end the meeting. The motion was approved unanimously with 10 YES votes. Four members were ABSENT-Dougherty, Ohene-Frempong, Rinaldo and van Dyck.**
- The meeting was adjourned at 2:40 p.m.

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

/S/	/S/
R. Rodney Howell, M.D.	Michele A. Lloyd-Puryear, M.D., Ph.D.
SACHDNC, Chair	SACHDNC, Executive Secretary

The Committee at its next meeting will formally consider these minutes, and any corrections or notations will be incorporated in the minutes of that meeting.

XVII. APPENDIX A: Written Public Comments

COMMENTS ON CONGENITAL HEART DISEASE (CHD)

1. **Olivia Easley, Parent of a Baby Recently Born with CHD in Maryland Who Did Not Survive**
2. **Vi Kennedy, Bless Her Heart &Parent of a Baby Who Died From CHD**

OTHER COMMENTS

3. **Gina Cioffi, National Executive Director, Cooley's Anemia Foundation**
4. **Catherine Crump, Retention and Use of Residual Dried Blood Specimens after Newborn Screening, American Civil Liberties Union**
5. **Andrea Williams, Children's Sickle Cell Foundation, Inc.**

1. Olivia Easley

Parent of a Baby Recently Born with CHD in Maryland Who Did Not Survive Statement to the HHS Advisory Committee on Heritable Disorders in Newborns and Children

May 14, 2010

9702 Whitley Park Place
Bethesda, MD 20814
May 10, 2010

Re: Advisory Committee Meeting on Heritable Disorders in Newborns and Children, Screening for Critical Congenital Heart Disease

To Members of the Committee:

I am speaking today on behalf of my daughter, Veronica Jane Easley, who died suddenly and unexpectedly last summer of undetected critical cyanotic congenital heart disease. I believe that the data in support of neonatal pulse oximetry screening speak for themselves and I will not reiterate them. I am here to provide a face to the tragedy of missed diagnosis of critical congenital heart defects.

Veronica, my third child, was born on April 29, 2009, and was seemingly perfect. Her APGAR scores were 8 and 9, and she weighed 8 lbs 7 oz. According to her hospital discharge physical examination, she was "a perfectly healthy newborn baby girl." And at the time, there was no reason to think otherwise.

Except for experiencing newborn jaundice that resolved by 10 days, Veronica thrived during the first month of her life. She was eating well, her color was good, and she had gained one pound by her 4 week check up.

At six weeks of age, Veronica began to develop some difficulty feeding. She spit up more often, seemed uncomfortable while nursing, and vomited on two occasions. However, being a third time mom, none of those symptoms were particularly alarming. My older children both had reflux and were not the easiest babies to feed. I spoke with my pediatrician's office and was advised that perhaps Veronica was intolerant to something in my diet.

A couple of days later, when her feeding difficulty persisted despite modifications in my diet, I scheduled an appointment with her pediatrician. Sadly, we never made it to that office visit. The night before the appointment, on June 18, 2009, Veronica died suddenly at home. She was 7 weeks old.

An autopsy conducted the following day at the Maryland Medical Examiner's Office found that Veronica had died from a critical congenital heart defect – total anomalous pulmonary venous connection (TAPVC) with an atrial septal defect (ASD). All four pulmonary veins returned directly to her right atrium, and her heart was nearly four times the normal size.

I was beside myself. I had no idea she was critically ill – she never was cyanotic, her breathing was never labored, and she had been gaining weight appropriately. After she died, I read about the symptoms of heart failure in babies; she had only one – difficulty feeding. It never crossed my mind that this mild and non-specific symptom could have been a sign of a life-threatening anomaly.

When I was pregnant with Veronica, I had had perfect pre-natal care, including chorionic villous sampling and a 20-week ultrasound performed by a highly respected maternal fetal medicine specialist. I did not know, however, that pre-natal ultrasound misses more than two-thirds of major congenital heart defects.[1] I was also unaware of the fact that congenital heart disease is the most common birth defect and occurs in 1 in 125 live births.[2]

Veronica's heart was a ticking time bomb. The symptoms of heart failure in babies are too non-specific; heart disease is, therefore, ripe for a delay in diagnosis. Veronica's disease escaped detection by me, my husband, my extended family, my perinatologist, the newborn nursery nurses, and finally, by her own pediatricians.

A screening test like pulse oximetry was her only chance. I would give anything to turn back the clock and demand that that simple and inexpensive test be performed on my baby girl. Perhaps she might be alive today.

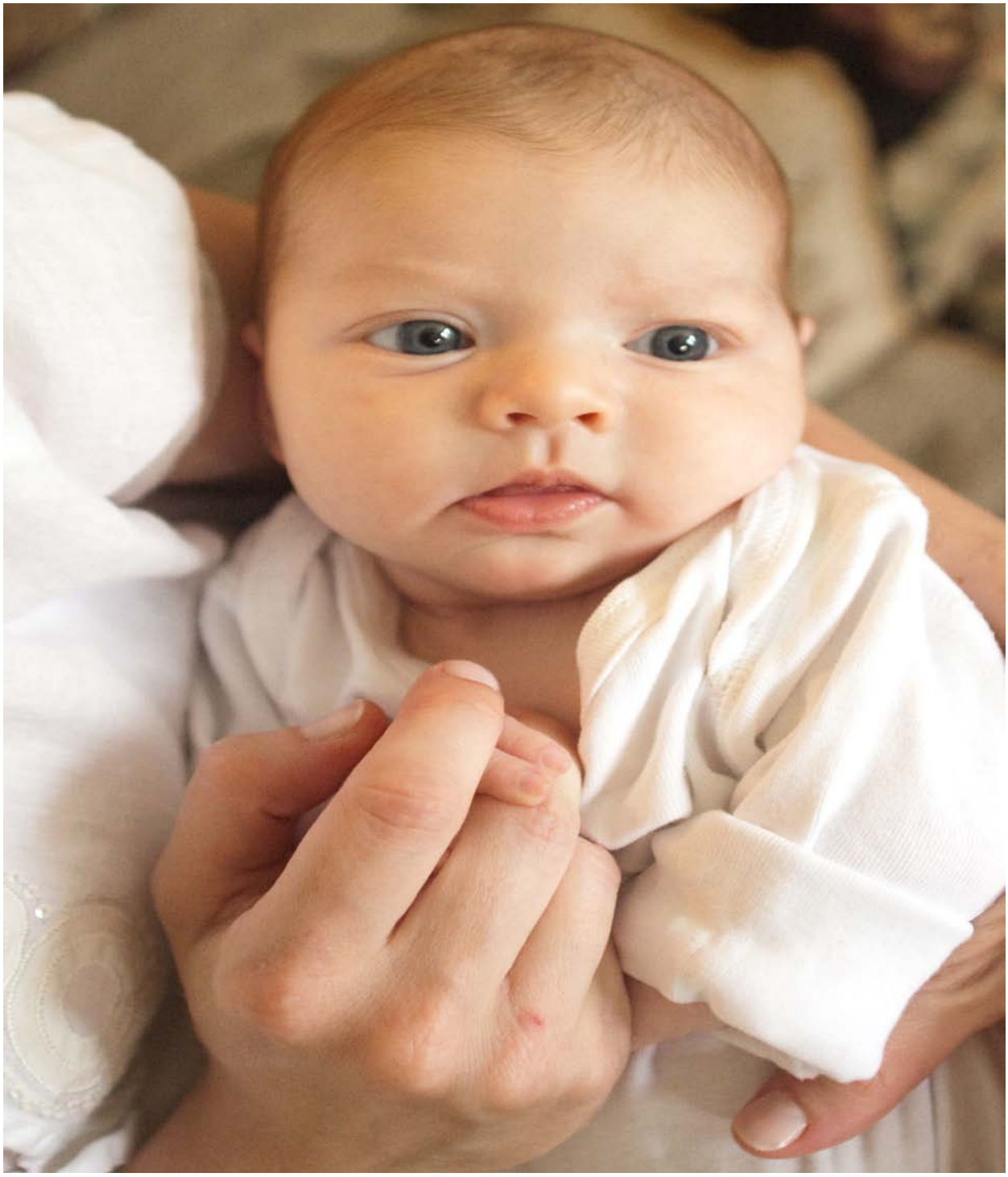
I hope you will vote to recommend universal newborn pulse oximetry screening and help to prevent other families from experiencing the tragedy that ours did.

Sincerely,

Olivia Johnson Easley, M.D.

---

[1] Friedberg MK, Silverman NH, Moon-Grady AJ, Tong E, Nourse J, Sorenson B, et. al. Prenatal Detection of Congenital Heart Disease. *J Pediatr.* 2009 July; 155 (1): 26-31.
[2] *Congenital Heart Defects.* Retrieved January 20, 2010, from the March of Dimes website: http://marchofdimes.com/professionals/14332_1212.asp



In memory of Veronica Jane Easley, 4/29/09 – 6/18/09
Photo taken on June 6, 2009

2. Vi Kennedy
Bless Her Heart & Parent of a Baby Who Died from CHD
Statement to the HHS Advisory Committee
on Heritable Disorders in Newborns and Children
May 14, 2010

A Devastating Loss Put to Action: Couple Advocates Heart Screening for Newborns

May 14, 2010

Good Afternoon.

To the Advisory Committee and Evidence Review Subcommittee:

Thank you for your time and allowing me to share my story with you. My name is Vi Kennedy and I am from Colleyville, TX; I am here with my husband and brother. I stand before you today as a registered nurse for 9 years, an advocate for CHD screening and most importantly a mother with a broken heart.

Our Story: Information that the case studies / autopsy reports don't include

I did not have a high-risk pregnancy and my husband and I did all that we could to prepare for our daughter's arrival. We took classes, conducted interviews, reviewed information with the Texas Medical Board and read Inspection Summaries from the Texas Department of Family and Protective Services to help us choose daycare options, and secured college funds for our daughter's future. Additionally, I changed jobs, followed the prenatal rules and performed all of the safety checks. Taryn was the 1st grandchild on both sides and the 1st great-great grandchild on my side. When Taryn was 27 days old, she suffered an unexpected cardio respiratory arrest at home and I had to perform CPR on her until EMS arrived. I remember the ambulance ride, and seeing my life fall apart right before my eyes.

Taryn was stabilized at a local emergency room, and then sent by air ambulance to Cook Children's hospital in Forth Worth, Texas. At this point, 1) SIDS 2) metabolic disorders 3) seizure disorder and 4) meningitis were all being ruled out. Later that same evening, the doctors pulled us aside and explained that Taryn had 2 CHDs (Total Anomalous Pulmonary Venous Return and an Atrial Septal Defect). The Pediatric Cardiologist explained to us that 1% of all babies are born with a CHD.

Taryn had jaundice and after being discharged from the hospital. By the time she was 27 days old she saw her pediatrician 3 times and saw the home health nurse 2 times. Taryn did not have a heart murmur; she passed her birth weight by 2 weeks and also grew an inch, reaching all the milestones of a health baby. She never experienced any difficulty breathing until her "event" which doctors believe was a pulmonary hypertensive crisis. By the time we found out, it was too late and she had suffered significant brain damage. Her health declined over the next 24 hours in the PICU and we, as parents were faced with most horrific news. Surgery was not an option by the time the doctors we are able to detect her heart defects. I read many books while I was pregnant and did what I could as a woman to have a healthy pregnancy and child, but nothing prepared me for what happened or for what was to come.

I realize that there were no guarantees of her survival if Taryn's heart defects were identified earlier and surgery could have been a possible option. To not be given a CHANCE of a better outcome is unfair and unacceptable. The lack of early detection is taking a **gamble** that one might find out later with only a minimal chance of *having a positive* outcome. Early intervention is key....you cannot fix the problem if you are not aware of the problem.

Key Information Points:

- Taryn's APGAR scores were 8 and 9, and Taryn's Newborn Nursery Medical records indicate "healthy baby" on multiple accounts.
- Taryn's autopsy results stated, "Total Anomalous Pulmonary Venous Return is a known cause of sudden unexpected infant death. In a small proportion of patients, prior symptoms may be either completely lacking or so subtle as to not raise the possibility of this diagnosis."
- According to the American Heart Association:
    - Congenital Heart Defects are the most common birth defect and are the #1 cause of death from birth defects during the 1st year of life.
    - Nearly twice as many children die congenital heart disease in the U.S. each year as from all forms of childhood cancers combined.
- In the study by the AAP, "Effectiveness of Pulse Oximetry Screening for Congenital Heart Disease in Asymptomatic Newborns" published in 2003 indicates, "This screening test is simple, noninvasive, and inexpensive and can be administered in conjunction with state mandated screening".
- The recent scientific statement by the AHA/AAP "Role of Pulse Oximetry in Examining Newborns for Congenital Heart Disease" states, "CCHD is not detected in some newborns until after their hospital discharge, which results in significant morbidity and occasional mortality. Furthermore, routine pulse oximetry performed on asymptomatic newborns after 24 hours of life, but

before hospital discharge, *may detect* CCHD. Routine pulse oximetry performed after 24 hours in hospitals that have on-site pediatric cardiovascular services incurs very low cost and risk of harm."

Our Actions:
I stand before you as an advocate for change. But my plea is just not words. I have taken action to ensure children born with these defects have a fighting chance

1. I have contacted 2 of the largest hospital systems in the Dallas / Fort Worth area and asked them to incorporate pulse ox screening after 24 hours of birth into their Care Path for Infants in Newborn Nursery.
2. I have contacted the AAP by sharing my story with Dr. Ann Stark (Chairperson of the COMMITTEE ON THE FETUS AND NEWBORN which has a current initiative: The Role of Pulse Oximetry in Newborn Screening for Neonatal Congenital Heart). I received a letter from a representative of the AAP. It basically said I am sorry for your loss. More research needs to be done. I was acknowledged but not heard.
3. I have been working with my regional March of Dimes representative (Director of Program Services, Regions 3 & 4).
4. I have reached out to the Texas DHHS; who referred me back to you.
5. I have reached out to the American Heart Association and they sent me a booklet about CHDs after my daughter died.
6. My husband and I formed a 501(c)(3) organization called Bless Her Heart(http://www.blessherheart.org) and I wrote a pamphlet for distribution. The pamphlet is available in English, Spanish and Vietnamese. I have reached out to the community to provide them with information so that they can make informed decisions along with their pediatricians.
7. We have worked with other organizations for CHD awareness and advocacy, such as Save Babies Through Screening Foundation
8. We have come here to ask you for your support require a pulse ox as a standard of care after 24 hours of birth; prior to being discharged from the hospital. The cost of this screening is minimal and has the potential to identify some CHDs.

Our Request: How This Committee Can Support or Be An Advocate for Children Like Taryn

- Advise the Secretary regarding the most appropriate application of universal newborn screening tests....such as pulse ox screening for infants prior to discharge from the newborn nursery.

"Raising Congenital Heart Defect awareness one pamphlet at a time"
Bless Her Heart Mail: PO Box 191, Colleyville, TX 76034
Email: info@blessherheart.org

- Develop policies, guidelines and standards for pulse ox screening to reduce morbidity and mortality in newborns with CCHD.

Closing: It's In Your Hands

- How much more information do you need?
- How many more years do you need to implement changes?
- How many babies have to die to make a difference?
- How many more families have to suffer the loss of a child due to lack of screening for the most common birth defect?

You have the power and authority to make changes which would have the greatest impact to screening babies for CHDs prior to leaving the hospital. We all do our best to make decisions based on the information that we have. Now that you have additional information, it's in your hands to do something about it.

Vi Nguyen-Kennedy, Bless Her Heart

"Raising Congenital Heart Defect awareness one pamphlet at a time"
Bless Her Heart Mail: PO Box 191, Colleyville, TX 76034
Email: info@blessherheart.org

3. Gina Cioffi
National Executive Director, Cooley's Anemia Foundation
Statement to the HHS Advisory Committee
on Heritable Disorders in Newborns and Children
May 14, 2010

Cooleys Anemia
FOUNDATION

The Cooley's Anemia Foundation strongly urges the Secretary's Advisory Committee to add a universal screening requirement for alpha thalassemia, a common hemoglobin disorder that causes Hemoglobin H disease, Hemoglobin H-Constant Spring and fatal hydrops fetalis syndrome.

We believe that populations likely to carry the alpha thalassemia traits (those from China, the Philippines, Thailand, Vietnam, Cambodia, Laos and other Asian countries, as well as people of African ancestry) are increasing and that this immigration trend will continue. As reported by the state of California, the overall prevalence of Hemoglobin H disease among all newborns in California is approximately 1 per 15,000. California of course has the gold standard for testing and reporting of genetic disorders and rightly should lead the call for this screening requirement. The timing for doing so will synergize efforts and funding made available through the CDC and NIH for their new RUSH program which seeks to report on registration and surveillance of hemoglobinopathies. With the support of this Committee, these efforts have a great potential for success. Without this endorsement, I think that the RUSH program will be significantly impaired in its ability to make an impact on the problems that our Foundation seeks to education about and address on behalf of this nation.

For sure, implementation of this recommendation will save lives. While we understand that there will be a cost to cash strapped states for follow-up to families, we believe that the benefit outweighs these costs and that the ability of states to check for these syndromes during their ordinary check of newborn syndromes makes it prudent to conduct theses tests immediately after birth. Waiting and and hoping to diagnose Hemoglobin H or Hemoglobin H-Constant Spring diseases later in life through DNA testing is much more expensive; more importantly, newborn screening can ensure that clinically significant problems are detected and treated or prevented.

Newborn screening can also have an even greater impact in the area of children with hydrops fetalis. Most alpha thalassemia trait carriers are unaware of their status; when a fetus is positive for hydrops fetalis, in utero blood transfusions are essential if the fetus is to have a chance to be born

alive. Children who are identified with alpha thalassemia trait through newborn screening will therefore have the advance knowledge necessary to ensure that appropriate tests are performed when they are adults and starting families; more immediately, parents who discover that their newborn child has alpha thalassemia trait or one of the hemoglobin H disease will know to check for the possibility of hydrops in utero in future pregnancies.

The Cooley's Anemia Foundation highly recommends implementation of universal newborn screening for alpha thalassemia trait and appreciates this opportunity to publicly state its support for this initiative.

Submitted By:

Gina Cioffi

Gina Cioffi

National Executive Director

May 2010

4. Catherine Crump
Retention and Use of Residual Dried Blood Specimens after Newborn Screening
American Civil Liberties Union
Statement to the HHS Advisory Committee on Heritable Disorders in Newborns and Children
May 14, 2010

WASHINGTON
LEGISLATIVE OFFICE

AMERICAN CIVIL LIBERTIES UNION

May 14, 2010

Advisory Committee on Heritable Disorders
in Newborns and Children
5600 Fishers Lane, Room 18A19
Rockville, Maryland 20857

Comments of the American Civil Liberties Union

Re: *The Retention and Use of Residual Dried Blood Spot Specimens after Newborn Screening*

AMERICAN CIVIL LIBERTIES UNION
WASHINGTON
LEGISLATIVE OFFICE
915 15th STREET, NW, 6TH FL
WASHINGTON, DC 20005
T/202.544.1681
F/202.546.0738
WWW.ACLU.ORG

LAURA W. MURPHY
DIRECTOR

NATIONAL OFFICE
125 BROAD STREET, 18TH FL.
NEW YORK, NY 10004-2400
T/212.549.2500

OFFICERS AND DIRECTORS
SUSAN N. HERMAN
PRESIDENT

ANTHONY D. ROMERO
EXECUTIVE DIRECTOR

ROBERT REMAR
TREASURER

The American Civil Liberties Union (ACLU) welcomes the opportunity to comment on the retention and use of dried blood spot specimens collected in the course of newborn screening for inherited disorders. The ACLU is a nationwide, non-partisan organization with more than 500,000 members dedicated to protecting the principles of liberty, freedom, and equality as set forth in the Bill of Rights to the United States Constitution. For almost ninety years, the ACLU has sought to preserve and strengthen privacy and self-determination in all aspects of American life.

Last month, the Advisory Committee on Heritable Disorders in Newborns and Children ("Advisory Committee") issued a draft set of recommendations to the Secretary of the U.S. Department of Health and Human Services in the form of a briefing paper entitled *Considerations and Recommendations for National Guidance Regarding the Retention and Use of Residual Dried Blood Spot Specimens after Newborn Screening*. The briefing paper contains praiseworthy suggestions for improving newborn screening programs.[1] However, the Advisory Committee falls short when it fails to recommend that states obtain express, informed consent to the retention of samples beyond the completion of newborn screening and to the subsequent use and dissemination of samples. Instead, the Advisory Committee ambiguously asserts that states "should consider whether consent or dissent from families is necessary for uses other than newborn screening and, if so, under what circumstances."[2] In other words, the Advisory

[1] The ACLU supports the Advisory Committee's recommendations that newborn screening programs develop strategies to educate health care providers and that both providers and state newborn screening programs themselves should take affirmative steps to ensure that families understand newborn screening, including possible future research uses of newborn blood samples. Briefing Paper at iv.
[2] Briefing Paper at iii.

Committee leaves the issue of informed consent to state-by-state experimentation, and accepts the possibility that consent may be dispensed with entirely.

The ACLU recognizes the importance of newborn screening. Even absent consent, we support screening for identifiable conditions which would result in substantial impairment of a child if not immediately detected and promptly treated, and for which there is available effective ameliorative therapy that is in fact offered to the child regardless of ability to pay. This is the rare circumstance in which the state's interest in protecting newborn health is so compelling that it trumps countervailing privacy and autonomy interests.

The ACLU believes that, in all other cases, informed consent is required. This includes retaining newborn blood spots after completion of the screen and research use of the samples by states and third parties. Proceeding with such uses in the absence of express, informed consent is not only improper, but also risks undermining the public trust and goodwill upon which newborn screening programs depend.

The Advisory Committee's Proposal Represents a Radical Departure from Traditional Practice.

Even in its original form, newborn screening was unusual because it is a population screening program subjecting virtually all of those born in the U.S. to the collection and analysis of their tissue. From its beginnings in the 1960s until recently, the exceptionally broad reach of this government-mandated intervention was justified and cabined by the seriousness and immediacy of the health concerns at issue.[3] In recent years, this has begun to change. States are increasingly using newborn blood samples for medical research, some of which is calculated to improve newborn screening, and some of which is completely unrelated to screening.

In short, the Advisory Committee has endorsed a fundamental transformation of newborn screening. The Committee seeks to convert a program developed for the benefit of the child whose blood is taken into one benefitting medical research. It would change the program from one in which the impact of the program is finite and known into one in which infants' blood may be used for a broad array of purposes, possibly including some not currently imagined, by unidentified people, for an undetermined length of time into the future.

The Retention and Use of Newborn Blood Samples Implicates Important Privacy and Self-Determination Interests.

The ACLU acknowledges that newborn blood samples are useful for medical research. Yet not everyone shares the Advisory Committee's opinion that the samples are a "public good." Indeed, some parents view the samples, which contain their newborn child's DNA, as deeply personal and private. Even some of those who are willing to donate their child's blood for research uses oppose a regime which requires them to relinquish all control over the future uses of the blood.

---

[3] President's Council on Bioethics, *The Changing Moral Focus of Newborn Screening* p. 2, 21 (Dec. 2008)(approving screening in cases where "the targeted condition is an important health problem, whose natural history is well-understood, and whose symptoms are amenable to early intervention and effective treatment.)

There are many reasons for these views. For some, they reflect deeply held religious beliefs. Other individuals legitimately fear discrimination because of their genetic profiles, for example because they possess a gene that predisposes them to certain types of disease.[4] Others may wish not to know, or to keep secret, otherwise unapparent genetic conditions that testing of blood specimens can reveal.[5] Others might consent to the use of their tissue for some research uses but find others profoundly objectionable.[6] Still others may simply believe that their genetic information is nobody's business, and certainly not the government's business. Others are justifiably concerned about the future potential for law enforcement or other forensic uses of the samples.[7]

That some individuals object to the use of newborn samples without notice or consent is not a matter of conjecture. Parents in Texas sued their state's newborn screening program for taking newborn blood samples and storing them indefinitely for undisclosed research purposes.[8] In describing the harm to their children that they perceived, the parents cited many of the above privacy concerns. They told the court that "blood spots contain deeply private medical and genetic information" and they were "concerned about the potential for misuse of that information and fear the possibility of discrimination against their children and perhaps even relatives through the use of such blood samples and research activity thereon."[9]

---

[4] The Genetic Information Nondiscrimination Act represents a step toward addressing this concern, but by no means eliminates it. Pub. L. No. 110-233, 122 Stat. 881 (2008).

[5] Such conditions include the potential for diseases such as Huntington's disease and Alzheimer's disease.

[6] For example, The Havasupai Indians provided researchers with DNA samples for the purpose of studying the tribe's high rate of diabetes. Tribe members were astonished to discover that their DNA had been used for other purposes, including studying the tribe's origins in a way that cast doubt on their ancestral stories. Amy Harmon, *Indian Tribes Win Fight To Limit Research Of Its DNA*, New York Times (Apr. 21, 2010). They sued, and recently won a settlement that included return of their DNA samples. Other individuals might object to having his or her genetic information used for research on the link between race and violence. Henry T. Greely, The Uneasy Ethical and Legal Underpinnings of Large-Scale Genomic Biobanks 8 Annual Review of Genomics and Human Genetics 343 (September 2007).

[7] The ability to access DNA is of interest to law enforcement, as is obvious from the continuing expansion of the Federal Bureau of Investigation's Combined DNA Index System (CODIS). FBI Website, CODIS Combined DNA Index System. http://www.fbi.gov/hq/lab/html/codisbrochure_text.htm. In Sweden, the police have already used newborn screening biobanks in a criminal case. Lori Andrews, *Should Infant DNA Later Be Used In Forensics*, On The Edges Of Science And Law, http://blogs.kentlaw.edu/islat/2009/06/should-infant-dna-later-be-used-in-forensics.html.

[8] Beleno v. Texas Department of States Health and Human Services, Case No. 09-cv-00188, First Amended Complaint (filed 9/29/2009).

[9] Beleno v. Texas Department of States Health and Human Services, Case No. 09-cv-00188, First Amended Complaint at 4 (filed 9/29/2009).

In other words, people care about the ways in which their genetic material is used. When the government collects, stores, and uses blood samples pursuant to a mandatory program, it must take these concerns seriously.

"Anonymization" Does Not Negate Civil Liberties Concerns Surrounding the Use of Newborn Blood Samples.

Some argue that secondary uses of newborn blood samples raise no privacy or consent issues because they can simply be anonymized. Because the samples contain DNA, however, it cannot be assumed that such de-identification is possible. It is unarguable that individual identification is currently possible in cases where a reference sample is available, and it has been estimated that such unique identification is possible with as few as 75 single-nucleotide polymorphisms (SNPs).[10] Moreover, recent developments in genetic testing to predict ethnicity and facial characteristics[11] indicate that it is quite conceivable that genotype alone may one day be sufficient for identification.[12]

To the extent phenotypic information accompanies DNA samples, the risk of individual identification is increased.[13] Logic dictates, and experience has shown, that most meaningful research cannot occur on samples unaccompanied by at least some phenotypic information, and some research requires extensive demographic, medical history, or other information. Finally, even to the extent that DNA and other personal information are delinked, the power to relink information can be abused—either by researchers themselves or by rogue employees or hackers.[14]

In sum, it is simply insufficient to assert that secondary uses are permissible, or that individuals' privacy and autonomy concerns are addressed, because samples are "anonymized." Such a position is out of step with forensic DNA technology as it exists currently and as it will likely develop in the very near future.

Express, Informed Consent Requirements Are Essential to Reconciling Public Health Research with Individuals' Rights of Privacy and Self-Determination.

The way to take civil liberties concerns seriously is by requiring that informed consent be obtained for essentially all collection, storage, use and dissemination of newborn blood spots. The only exception to this requirement should be the narrow set of circumstances previously described, in which the individual child would be harmed by inaction and significantly benefitted by medical intervention. In all other cases, and especially with regard to the expanding array of

---

[10] Lin, Z., A.B. Owen and R.B. Altman, "Genomic Research and Human Subject Privacy," Science, Vol. 305, no. 5681 (9 July 2004), p. 183.
[11] *See* Cho, M.K. and P. Sankar, "Forensic Genetics and Ethical, Legal and Social Implications Beyond the Clinic, *Nature,* Vol. 36, no. 11 (November 2004), pp. S8-S12. *See also* "Retinome," DNA Witness, available at: http://dnaprint.humid.e-symposium.com/dnawitness/retinome.html
[12] McGuire, A.L. and R.A. Gibbs, "No Longer De-Identified," Science, Vol. 312 (21 April 2006).
[13] Greely 8 Annual Review of Genomics and Human Genetics at 351.
[14] *Id.* at 350-51.

secondary uses to which newborn blood is put, express and informed consent must be obtained. To date, these uses have occurred without public knowledge, exploiting the trust and goodwill parents extend to the newborn screening program. This state of affairs cannot continue.

Advances in medical and especially DNA technology do not, as some would assert, obviate the need for informed consent. On the contrary, true informed consent is now more important than ever, in light of the abundance of information that can be extracted from a single blood sample, and the ease with which the information can be disseminated.

Specifically, "informed" consent in this context means that each parent consenting to secondary uses of his or her infant's blood knows:

(1) what tissue being collected and what information can be extracted from that tissue;
(2) the period of time over which the sample and any derivative information will be stored;
(3) any and all purposes for which the sample and derivative information will be used; and
(4) to whom and under what circumstances the sample or any data drawn from it may be released to third parties.

In addition, an individual can only be said to have given his or her informed consent if he or she is provided with appropriate privacy notifications sufficiently in advance of the collection of the information so that needed deliberation and consultation can occur prior to the point when a decision must be made. Moreover, each individual must be informed of their right to learn at a later point in time whether and to whom the sample and associated information has been disclosed, and by what means they may later withdraw their consent.

Fortunately, this is not a situation in which there is inherent tension between advancing public health and respecting parents' decisions. A consent process will enable the small percentage of parents who wish to opt out of certain uses of their children's blood spots to do so, while allowing the others to donate their children's blood spots to public health research. When, as in the newborn screening context, tissue and the information it contains is collected from an individual for one purpose but subsequently used for another purpose, it is especially important that the secondary uses be disclosed to the individual. For the state to fail to do so is, simply put, a violation of the public trust.

The Risks of Foregoing Express, Informed Consent Outweigh Any Perceived Benefits.

The more newborn screening programs deviate from express, informed consent, the more they run the risk of losing the public support on which their success depends. Although the public's awareness of the secondary uses of newborn screening samples is currently minimal, it will not remain this way for long. The newborn screening program has come unmoored from its roots in clinical interventions benefitting individual children, and the government has failed to respond to this development with heightened protections for the fundamental rights of individual children and their families. As a consequence, media attention and the concern of organizations like the ACLU are increasingly drawn to this issue.

As individuals increasingly feel that their babies' blood is being taken for one purpose and then used against their will and beyond their control for other unspecified purposes, there is a real risk that the public will lose trust in the newborn screening program. The program saves lives. It would truly be tragic if the expanding use of newborn blood for unconsented-to research were to result in parents declining to have their infants screened in the first instance. Public sentiment that samples are being misused, or that individuals are being misled or not given a say in their use could lead to a political backlash undermining the support upon which those very research projects ultimately depend.

Sincerely,

Catherine Crump
Staff Attorney
American Civil Liberties Union
Speech, Privacy and Technology Project

Mie Lewis
Staff Attorney
American Civil Liberties Union
Women's Rights Project

Christopher Calabrese
Legislative Counsel
American Civil Liberties Union
Washington Legislative Office

5. Andrea Williams
Children's Sickle Cell Foundation, Inc.
Statement to the HHS Advisory Committee
on Heritable Disorders in Newborns and Children
May 14, 2010

To the Chair and Members of the Committee:

I am grateful for another opportunity to address you with my comments today. We heard a lot about sickle cell trait carriers and athletics. As we continue to discuss the recommendations within the scope of the committee, I offer that we keep a bigger picture in mind with regards to sickle cell trait carriers.

This committee has made great strides with regard to the Newborn Screening Program. Your commitment to maintaining balance and focus is observed as you work with the subcommittees to bring about the best possible recommendations. It is that same tenacity and strength that is needed to address the overarching issues with sickle cell trait. There are a growing number of teens and young adults who have been identified as sickle cell trait carriers via the Newborn Screening Program that may not know their sickle cell trait carrier status in spite of quality short-term follow-up efforts that occur within a year of birth sporadically around the nation. Of the STF programs, most started around 2005 and most of them lack the resources to revisit these families as their children reach their teen years.

It seems a logical next step for the Committee to consider adding sickle cell trait as a secondary condition under sickle cell disease and establish a comprehensive Long-term Follow Up initiative (supported with resources from the various organizations e.g. CDC, NIH, HRSA.) that would address the overall needs of the child with sickle cell trait identified by the Newborn Screening Program. The SCT LTFU program would include the health, athletic and genetic information and be offered to the Parent and to the teen/young adult as they transition to adulthood.

It is my hope as a mother of two children with sickle cell trait and one with sickle cell disease that you will take the necessary steps to ensure that this information get to those persons that need it, when they need it the most. This will be another example of how the Newborn Screening Program saves lives!

Thank you.

Respectfully submitted,

Andrea M. Williams