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

Summary of 28th Meeting
September 13-14, 2012
Washington, DC

The Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) was convened for its 28th meeting at 8:40 a.m. on Thursday, September 13, 2012, at the Hubert Humphrey Building in Washington, DC. The meeting was adjourned at 2:12 p.m. on Friday, September 14, 2012. In accordance with the provisions of Public Law 92-463, the meeting was open for public comments.

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CONTENTS

I. Committee Business: September 13, 2012

A. Welcome, Roll Call, Minutes, and Administrative Business

Joseph A. Bocchini, Jr., M.D.
Committee Chair
Professor and Chairman, Department of Pediatrics
Louisiana State University
Shreveport, Louisiana

Dr. Bocchini welcomed everyone and took roll call for the first day of the twenty-eighth meeting for the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC). The following voting members were present: Dr. Colleen Boyle, Dr. Jeffrey Botkin, Dr. Sara Copeland, Dr. Christopher DeGraw (alternate for Dr. Michael Lu), Dr. Charles Homer, Dr. Kellie Kelm, Dr. Fred Lorey , Dr. Dietrich Matern, Dr. Stephen McDonough, Dr. Melissa Parisi, Dr. Alexis Thompson, Dr. Kishena Wadhwani (alternate for Dr. Denise Dougherty), and Ms. Catherine Wicklund.

The following nonvoting, organizational liaison representatives to the Committee were also present:

- American Academy of Family Physicians (AAFP): Dr. Frederick Chen
- American Academy of Pediatrics (AAP): Dr. Beth Tarini
- American College of Medical Genetics (ACMG): Dr. Mike Watson
- American College of Obstetricians and Gynecologists (ACOG): Dr. Nancy Rose
- Association of Public Health Laboratories (APHL): Dr. Jane Getchell
- Child Neurology Society: Dr. Bennett Lavenstein
- Department of Defense (DoD): Dr. Mary J. H. Willis
- Genetic Alliance: Ms. Natasha Bonhomme
- March of Dimes: Dr. Joe Leigh Simpson
- Society for Inherited Metabolic Disorders (SIMD): Dr. Carol Greene

Committee members had no comments or corrections to the minutes of the SACHDNC's 27th meeting held on May 17-18 2012. Dr. Bocchini requested and received a voice to approve the minutes.

- *Motion #1: To approve the minutes of the 27th meeting of the SACHDNC held on May 17-18, 2012. Motion approved by voice vote.*

Dr. Bocchini provided an update on Committee correspondence. The SACHDNC received a letter from Secretary Sebelius in response to the Committee's letter to the Secretary recommending a linkage between newborn screening (NBS) vital numbers and birth certificates. The Secretary has referred the recommendation to the Interagency Coordinating Committee for review and input. Dr. Bocchini expects the Interagency Coordinating Committee to report by March 2013.

II. Update on RUSP Conditions

A. Newborn Screening Case Definitions and Quality Indicators: Update

Jelili Ojodu, MPH
Director, NBS and Genetics
Association of Public Health Laboratories

Newborn Screening Case Definitions Update
Mr. Ojodu gave an update on activities related to Newborn Screening (NBS) case definitions. Mr. Ojodu noted that currently the state of surveillance makes it difficult to compare disorder cases across data systems, screening programs, and patient conditions. Harmonizing NBS case definitions across the country will help establish uniform criteria for disease reporting. The Health Resources and Services

Administration (HRSA) has convened a number of workgroups (metabolic, pulmonology, endocrinology, immunology, and hemoglobinopathy), since January 2011 to assist with the harmonization of NBS diagnoses for surveillance and epidemiological purposes. A meeting with the state newborn screening programs was held in July 2012 to review NBS case definitions submitted by clinicians. The next steps are to validate the definitions that the groups developed. Several states have volunteered to participate in a pilot, facilitated by the Association of Public Health Laboratories (APHL), to beta test the recommended NBS case definition modules for different disorder categories. After the pilot tests, case definitions will be presented to SACHDNC for recommendation and, if recommended, they will be considered the national standard and used nationally in the surveillance of NBS disorders.

Newborn Screening Quality Indicators Update

Mr. Ojodu gave an update on activities related to NBS quality indicators. Twenty-five state NBS programs were brought together in July 2011 to examine the quality indicators currently used in their state and determine which indicators can feasibly be collected, in an effort to harmonize quality indicators across the country. During the meeting, participants also developed and outlined program needs including laboratory and short-term follow-up quality indicators. Participants also summarized the utility of current quality indicators and outlined others that should be collected for the next generation of NBS data repository. Meeting activities for quality indicators included the labeling of categories, the inventory of indicators within a category, and defining key indicators. A final list was narrowed down to ten key quality indicators such as unsatisfactory specimens due to improper collection, parental refusal, eligible infants receiving valid NBS test, and unsatisfactory specimens.

In July 2012, a meeting was held to jointly discuss NBS case definitions and quality indicators. The New Jersey NBS Program presented on beta testing of the ten NBS quality indicators developed at the 2011 meeting to show that it was feasible for states as well as effective. The next steps are to continue to refine the NBS quality indicators.

Mr. Ojodu also noted that the data collected on NBS case definitions and quality indicators would feed into a newly funded 5-year cooperative agreement with HRSA called NewSTEPS. NewSTEPS is a NBS technical assistance and data repository. NewSTEPS will engage actively with states and provide a number of key educational training programs for all components in the NBS system.

Committee Discussion

- Mr. Ojodu stated, in response to a Committee member's question, that background information on NBS case definitions and quality indicators was included in the briefing book. The tables developed for the case definitions for each condition can be provided to Committee members. Quality indicators are currently being refined but they can also be made available to everyone on the Committee for comment.
- Mr. Ojodu replied to a Committee member's question on key barriers to state buy-in, noting that states would be more likely to buy-in if they have a vested interest in improving their program and in harmonizing surveillance efforts across the country. One barrier is that states are faced with executing additional activities with fewer resources.
- Mr. Ojodu stated, in response to a Committee member's question on variability in state NBS programs, that the level of variability is not as large as one would think. State NBS programs have made an effort to close the gap in the conditions they screen for. A Committee member noted that where there is variability, standardization is necessary for accurate measurement.
- Mr. Ojodu commented that data collected in the NBS information system over the past 14 years will be provided to APHL. The data will be populated into the database and matched to the refined and harmonized quality indicators.
- Dr. Watson noted that the screened positive definition affects the follow-up system. Mr. Ojodu noted that states attending the meeting felt it was important to collect that information.

III. Public Consideration and Condition Nominations

A. Public Comment

Dean Suhr, President and Co-Founder, MLD Foundation. Mr. Suhr expressed support for the Committee and recognized the need for viable Metachromatic Leukodystrophy (MLD) therapies. Mr. Suhr noted that rare disease foundations and families have experienced a change in sentiment around diagnostic screening for conditions when no viable therapy is available. The sentiments are related to quality of life, access to services, accelerating the gathering of data and patient communities necessary to access the science and therapies. Dr. Suhr made himself personally available to start reviewing and changing the policy related to those particular criteria.

William Morris, Grey's Gift Memorial Foundation. Mr. Morris expressed his appreciation for the Committee's hard work. Mr. Morris noted that many states are not currently running secondary NBS panels, and encouraged the Committee to make a statement on state secondary NBS panel compliance by 2015.

Sarah Wilkerson, Save Babies Through Screening. Ms. Wilkerson is a parent and advocate whose son Noah passed away unexpectedly when he was 4 days old of a rare genetic disorder called Medium Chain Acyl-CoA Dehydrogenose Deficiency (MCADD). Noah's condition would have been 90% treatable if diagnosed in time. Ms. Wilkerson described the variable screening processes between the state of Colorado, where she was living during Noah's birth, and her home state of Missouri. Ms. Wilkerson notes that in Missouri there are four state labs that run continuously and have blood sample policies for processing and shipping. Missouri has not lost a child to MCADD since 2004. In Colorado, they do not have these policies. Colorado uses the U.S. postal service to send batches to the lab, often waiting until a large number of batches are ready before mailing and the lab is closed on evenings, weekends, and holidays. Ms. Wilkerson recommended that all states screen within 24 hours of life, no longer condone use of the U.S. postal service for transporting samples, and that the state lab process results within 48 hours of receiving blood samples. Ms. Wilkerson noted that days, minutes, and seconds matter—parents deserve to know whether their child has a condition as soon as possible.

Sarah Wilkerson, Save Babies Through Screening (comments read on behalf of Christine McCormick). September is National NBS Awareness Month. Since 1998, Save Babies Through Screening has been the only organization solely dedicated to advocacy of NBS. The Save Babies Through Screening website is a valuable resource to the public, and resources are also readily accessible by email as well as a toll-free number. Save Babies Through Screening recently created a toolkit that was distributed through social media by several groups as well as an educational video on blood spot prevention. For 14 years, Save Babies Through Screening has been a passionate and dedicated voice for babies. NBS would not be where it is today without dedication of individuals.

Dr. Gerald Raymond, Johns Hopkins Medicine and Kennedy Krieger Institute. This is what we know about Adrenoleukodystrophy (ALD) and why it is important for NBS: (a) ALD affects 1 in 17 thousand people, (b) we understand the natural history of the disorder, and (c) it affects the adrenal glands. Those affected are elevated in Adrenocorticotropin (ACTH), a hallmark of adrenal insufficiency. ALD often goes unannounced with tragic results. Neurological presentation affects 25% of at-risk boys, bone marrow transplants are highly effective, and an opportunity exists to intervene in an asymptomatic population. Presently, a standard blood panel is offered as a clinical diagnostic test, and we hope to move this forward to the Recommended Uniform Screening Panel (RUSP).

Taylor Kane. Ms. Kane, a 13 year old ALD carrier, presented her perspective as a teenager whose father, uncle, and cousin were lost to ALD. Ms. Kane explained how genetic counseling at the Kennedy Krieger Institute helped her understand what being a carrier of the ALD gene means in terms of potential symptoms and having children in the future. While this knowledge can be scary at times, Ms. Kane was happy that she knows her options, unlike her father, uncle, and cousin who were not screened as newborns. Ms. Kane recommended NBS for females to enable them to know whether they are a carrier of the ALD gene and

take the necessary precautions if they choose to have children in the future. Ms. Kane hoped that doctors would find a cure so that boys and men would no longer have to suffer from ALD.

Spencer Barsh, Stop ALD Foundation. Mr. Barsh, 12 years old, offered his perspective as a child with ALD. Mr. Barsh had an older cousin who was diagnosed with ALD after many years of misdiagnosis, and this diagnosis led to Mr. Barsh being tested and discovering that he had ALD. Mr. Barsh believes that if NBS had been available when his cousin was born, his cousin would have known about his condition before it was too late. Since Mr. Barsh's mother discovered that she was a carrier, she has taken precautions to ensure that her second child, a girl, does not have ALD or is an ALD carrier. Mr. Barsh strongly urged NBS for all babies, noting that families should not have to suffer as his family did.

Ann Moser, Johns Hopkins Kennedy Krieger Institute. Ms. Moser gave a history of Hugo Moser's contributions to ALD research at the Kennedy Krieger Institute. Dr. Moser had been interested in plasma research since 1978 and helped to develop the plasma assay in 1981. Dr. Moser went on to develop Lorenzo's oil. When plasma is normalized, boys are 75% less likely to get brain disease. It was Dr. Moser's dream to identify boys with ALD early, and he suggested to the Committee that ALD be added to the screening. In order to develop NBS test for ALD, Kennedy Krieger contacted an expert who was interested in helping to develop a test. Finally, in 2006 they found an indicator. In order to validate the indicator, they obtained newborn bloodspots from various states. The findings of that study were published in 2009, and we then developed a NBS procedure using bloodspots. In December 2008, together with the Maryland State NBS Laboratory, we started a pilot study screening for ALD in 5,000 newborns born in the local Baltimore hospitals. We did not find one false positive. On behalf of researchers, support groups, and families worldwide, Ms. Moser requested that the screening panel be added to screening of all newborns.

B. Final Condition Review Matrix

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

Dr. Kemper presented an update of the Condition Review Workgroup's progress in revising and refining the condition review process. Dr. Kemper displayed three separate matrices containing components of the revised condition review process. These matrices were presented to the Committee at the 27th meeting of the SACHDNC, and Dr. Kemper updated them based on the comments received.

- **Net Benefit Assessment Matrix**: Assesses the magnitude and certainty of net benefits, determining whether the harms outweigh or closely balance the benefits and the level of certainty by which net benefits can be assigned. A significant magnitude and high certainty of net benefit is preferred.
- **Readiness and Feasibility Matrix**: Assesses the readiness and feasibility of implementing comprehensive NBS from a state public health department perspective. Ready and high feasibility is preferred.
- **Combined Matrix**: combines net benefit assessment with readiness and feasibility to illustrate the revised review process. A significant magnitude of benefit with high certainty of net benefit along with high or moderate feasibility is preferred.

Committee Discussion and Vote

- Dr. Kemper, responding to a question on assessing the readiness of public health departments, said that APHL would collect qualitative and quantitative data to give some insight into assessment.
- Dr. Kemper explained to the Committee that readiness and feasibility are considered separate dimensions because it is important to carefully capture the nuances between them.
- A Committee member noted that the U.S. Preventative Services Task Force uses a different review process in that they recommended depression screening even when the healthcare system did not have the resources for implementation. Dr. Kemper noted that former chairs of the U.S. Preventative Services Task Force have reviewed the materials and submitted their input. Dr. Copeland noted that

the Committee has to consider the public health impact in their criteria while the U.S. Preventative Services Task Force does not.

- Several Committee members observed that there would be some struggle with recommending a "B" rating to the screening panel. Dr. Copeland noted that once gaps are identified the condition would come back to the Committee and go through condition review in an expedited manner.
- One Committee member felt that the process should occur in stages. Once a condition passes through the net benefit assessment matrix, it would be able to go on to the readiness and feasibility matrix. Dr. Kemper explained that breaking the process up into two steps would add additional time to the process and that the Committee previously decided to use the combined matrix.
- Dr. Copeland noted that, in terms of readiness and feasibility, ratings are determined by an average of states across the nation. A condition would not be eliminated based on one state's lack of readiness.
- Dr. Bocchini commented that the Nomination Committee will also need to have guidance and procedures that incorporate the feasibility and readiness component.
- A Committee member recommended that conditions falling into the "A2" and "A3" categories be incorporated into a technical assistance program to assist states in implementing the recommendations.

The following motion, made by Dr. McDonough and seconded by Dr. Botkin, was approved (12 votes for, none against, Wadhwani abstaining):

- *Motion #2 (APPROVED): To approve the condition review matrix as an organizational tool for categorization and assigning a letter value in order to nominate a condition. This does not include the second portion on how the matrix will be used to make a recommendation.*

C. Adrenoleukodystrophy: Nomination and Prioritization Report

Fred Lorey, PhD
Committee Member
Genetic Disease Screening Program
California Department of Public Health

Dr. Lorey presented a report and recommendation on X-linked Adrenoleukodystrophy (ALD) from the Committee's Nomination Review and Prioritization Workgroup. Dr. Lorey provided the following summary:

- **The nominated condition is medically serious and the case definition and disease spectrum are well defined.** ALD is an adrenal insufficiency resulting in neurodegeneration. By clinical determination in the U.S., the estimated combined male and female frequency of ALD is 1:17,000.
- **The screening test has analytic validity.** Some literature has been published on the screening test to establish analytic validation. Early onset cases are readily detected in current studies. There are three studies in process for this disorder, prospective and retrospective:
    - Pilot #1: 1,000 newborn samples were run, using tandem mass spectrometry with or without chromatographic separation of Lysophosphatidylcholine species, including 17 known blinded cases. One case was misidentified.
    - Pilot #2: Prospective study of 5,000 newborns using tandem mass spectrometry, with no cases detected.
    - Pilot #3: Currently studying 100,000 prospective cases in addition to known cases.
- **The screening test has clinical validity.** Screening newborns for ALD has clinical utility in preventing or ameliorating adverse health outcomes through effective treatments. Testing and diagnostic processes approved by the FDA exist, including plasma testing and MRI screening.
- **Effective treatment is available.** Defined treatment protocols, FDA approved drugs, and treatment are available for ALD. Hormone replacement therapy is the standard of care for primary adrenal insufficiency. Hematopoietic stem cell transplant (HCT) is the only effective long-term treatment for ALD. However, HCT must occur prior to manifestation of symptoms to achieve optimal survival and clinical outcomes. It is imperative to implement adrenocortical function testing by three months and serial neuroimaging by three years; therefore, timely diagnosis is critical.

Although the Workgroup noted several positive aspects in most of the areas of consideration, the review should not move forward until the largest and latest pilot study on the screening test is complete and data are published.

The Nomination Review and Prioritization Workgroup provided the following recommendation to the full Committee

- *Do not send ALD forward to the Condition Review process for condition review and public health impact.*

Committee Discussion and Vote

- Committee members noted that the test cost is $2 per sample, but when multiple conditions are included the test becomes proportionally less expensive
- Dr. Lorey commented that no newborn spots have been obtained from late onset patients. In response to a question on racial and ethnic considerations, it was noted that the bloodspots obtained are from a heterogeneous group.
- A Committee member stated that many criteria have been met and the literature is evolving. Dr. Copeland noted that the barrier for inclusion is at the Committee's discretion. Dr. Bocchini observed that, since the study is currently underway, the data would not be available for the condition to move forward to condition review.
- Dr. Matern noted that the study will be complete later next year. The test is conducted by reinjecting the extracted and prepared blood spot sample when you find an abnormality. The idea of the study is to provide data on the efficiency and effectiveness of the test. In receiving 1,000 samples each week, they are able to screen in real time.
- A member of the public inquired about the specificity of the screenings and wondered whether the full range of disorders would be picked up. The Committee noted that the most common biochemical abnormality does have a spectrum within it, while other secondary disorders fall into broad groups like Zellweger or single enzyme disorders.
- Dr. Bocchini stated that there are two conditions in the queue currently under reviewed.

The following motion, made by Dr. Botkin and seconded by Dr. Thompson, was approved (10 votes for, 1 vote against, Wadhwani and Matern abstaining):

- *Motion #2 (APPROVED): To accept the advice of the Nomination and Prioritization Workgroup to not bring this condition forward to condition review at this time. The Workgroup will make the Committee aware, on an ongoing basis, of the pilot prospective study progress to enable the Committee to readdress the nomination when data is likely to be available.*

D. Update on Pompe Nomination

Alex Kemper
Condition Review Workgroup
Associate Professor, Department of Pediatrics
Duke University

Mr. Kemper presented an update from the Condition Review Workgroup on condition (i.e. evidence) review for Pompe disease. Two technical expert panel teleconferences were held. The technical expert panel calls represented the broad gamut of expertise from clinicians to genetic epidemiologists and researchers active in the field publicly acknowledge how helpful these experts were in identifying the most salient issues. Teleconferences were used to develop a case definition, identify key questions and sources of information, delineate standard screening and diagnosis process, and to describe the process and timing of immune therapy relative to enzyme replacement treatment (ERT). During the teleconferences it was found that there are variable approaches to screening and treatment initiation. It was also found that there is no standard protocol for the management of those with later-onset Pompe disease.

Infantile Pompe disease can present itself in the classical form, as a rapidly progressive disease characterized by prominent cardiomegaly, hepatomegaly, weakness and hyptonia, and death due to

cardiorespiratory failure usually in the first years of life. It can also present as a nonclassical form, with a slower progression and significantly less severe cardiomyopathy than the classic form. Later onset forms cover a wide spectrum including childhood, juvenile, muscular variant, and adult-onset.

An initial literature search through PubMed and EMBASE on glycogen storage disease type II and Pompe disease resulted in 2,000 abstracts. Grey literature was also collected from the American College of Medical Genetics, the American Academy of Pediatrics, the National NBS Resource Center, the March of Dimes, the Acid Maltese Deficiency Association, the International Pompe Association, the United Pompe Foundation, the Food and Drug Administration, Genzyme Corporation, and Online Mendelian Inheritance in Man. Many recent articles relate to immunomodulation. Many case studies were found to focus on later-onset Pompe disease.

To ensure transparency, the Condition Review Workgroup will post the protocol for the review process. The Workgroup is currently completing abstraction of data from the literature review and an analysis of grey literature. Key informant interviews will also be conducted in areas of uncertainty. Dr. Prosser at the University of Michigan is currently preparing a decision analytic framework for net benefit modeling, and the Workgroup is now beginning to work with APHL to examine public health readiness and feasibility.

Committee Discussion

- Mr. Kemper noted that Pompe disease is the first condition in condition review, and it will be presented to the full Committee in January.
- Mr. Kemper, in response to a question on early detection of later-onset Pompe disease, noted that individuals with later-onset disease would be identified through NBS but may not show any symptoms for years. The case study aims to tease out whether early intervention makes a difference in these cases. Mr. Kemper hopes to find a standard algorithm for how individuals with later onset disease progress through the follow-up system.
- Dr. Copeland stated that the high cost of treatment complicates early detection, for even detecting the condition one year early increases health costs by $200,000 per year.
- Committee members noted that additional information and a discussion on late-onset forms would be helpful in January.

E. Ethical Issues: ELSI and the Advisory Committee

Jean McEwen, JD, PhD
Program Director
Ethical, Legal, and Social Implications Program, NHGRI/NIH

Dr. McEwen presented on the Ethical, Legal, and Social Implications (ELSI) Program and the National Institutes of Health (NIH) National Human Genome Research Institute (NHGRI).

Dr. McEwen discussed the NHGRI strategic plan for the future of genomics research published in 2011 in Nature Magazine. The strategic plan evolved from understanding the structure of genomes (1990-2003) and the biology of genomes (2004-2010) to understanding the biology of disease and advancing the science of medicine (2011-2020) as well as improving the effectiveness of healthcare (beyond 2020). Dr. McEwen commented that, as we move forward, interactions with patients, research participants, and the general public becomes increasingly important. In recognition of this, this broad rubric of genomics in society and ethical issues cuts across all areas and will become increasingly important in the future.

The strategic plan considers four sets of ethical issues: psychosocial and ethical issues in genomics research, psychosocial and ethical issues in genomic medicine, legal and public policy issues, and broader societal issues.

- **Psychosocial and ethical issues in genomics research** include protection of research participants; perceptions of risks and benefits; diversity of research cohorts; role of race and ethnicity; and community engagement.

- **Psychosocial and ethical issues in genomic medicine** include genomic uncertainty; direct to consumer testing; effectiveness of diagnostics, therapeutics, and behavioral change; pre-implementation, prenatal and postnatal genetic diagnosis; and constructs of race and ethnicity.
- **Legal and public policy issues** include intellectual property; insurance reimbursement; regulation of genetic testing, pharmacogenomics and therapeutics; genetic discrimination/stigmatization; and applications of genetic information in a non-medical setting.
- **Broader societal issues** include concepts of health and disease; individual and group identity; insights on human origins genetic determinism, free will, and individual responsibility.

ELSI was established in 1990 in the anticipation of addressing the ethical, legal, and social implications of genetic and genomic research. NHGRI research is mainly multidisciplinary, and almost half of the studies involve multiple methods such as standard empirical surveys, focus groups, interviews, archival materials, and ethnographic information. The ELSI website features a searchable database. Funding mechanisms include regular research grants, small research grants, conference grants, exploratory research grants, post-doctoral training grants, career development grants, and administrative supplements, including minority supplements.

In 2004, the ELSI Research program launched the Centers of Excellence to foster trans-disciplinary research; facilitate translation of research into health, research, and public policies; and train the next generation of ELSI researchers. The program currently supports six full centers plus two exploratory centers. Each center as a specific focus, ranging from intellectual property to behavioral genetics, with the goal of reviewing the area of focus comprehensively and translating the findings into policy and practice.

Dr. McEwen noted current tensions in the program. ELSI wants to encourage basic fundamental research versus research translation. Dr. McEwen stated that experts are called in to provide consultation, but such experts are at risk of losing their objectivity or independence. Looking into the future, ELSI hopes to turn these tensions into opportunities by setting priorities within the current and future funding climate. A working group will advise on some of these priorities.

Committee Discussion

- Dr. McEwen noted that there is collaboration between other NIH institutes and ELSI research opportunities. Dr. McEwen also cited general interest in implementing a trans-NIH bioethics initiative, but commented that funding is not available.
- Dr. Homer asked whether findings or recommendations from the research could potentially be incorporated into the condition review matrix. Looking at previous research may inform the Committee's ability to consider ethical issues in the condition review process. To shed light on this question, Dr. McEwen recommended that the Committee review published literature on the NHGRI website.

IV. Committee Business: September 14, 2012

A. Welcome and Roll Call

Joseph A. Bocchini, Jr., M.D.
Committee Chair
Professor and Chairman, Department of Pediatrics
Louisiana State University
Shreveport, Louisiana

Dr. Bocchini welcomed everyone and took roll call for the second day of the twenty-eighth meeting for the Secretary's Committee on Heritable Disorders in Newborns and Children (SACHDNC). The following voting members were present: Dr. Colleen Boyle, Dr. Jeffrey Botkin, Dr. Sara Copeland, Dr. Christopher DeGraw (alternate for Dr. Michael Lu), Dr. Charles Homer, Dr. Kellie Kelm, Dr. Fred Lorey, Dr. Dietrich Matern, Dr. Stephen McDonough, Dr. Melissa Parisi, Dr. Alexis Thompson, Dr. Denise Dougherty, and Ms. Catherine Wicklund.

The following nonvoting, organizational liaison representatives to the Committee were also present:

- American Academy of Family Physicians (AAFP): Dr. Frederick Chen
- American Academy of Pediatrics (AAP): Dr. Beth Tarini
- American College of Medical Genetics (ACMG): Dr. Mike Watson
- American College of Obstetricians and Gynecologists (ACOG): Dr. Nancy Rose
- Association of Public Health Laboratories (APHL): Dr. Jane Getchell
- Child Neurology Society: Dr. Bennett Lavenstein
- Department of Defense (DoD): Mary J. H. Willis
- Genetic Alliance: Ms. Natasha Bonhomme
- March of Dimes: Dr. Joe Leigh Simpson
- Society for Inherited Metabolic Disorders (SIMD): Dr. Carol Greene

V. Advisory Committee, Subcommittees, Workgroups Reports

A. Subcommittee Report on Education and Training

Beth Tarini, MD, MS, FAAP
Organizational Representative

Ms. Tarini, in the absence of Subcommittee chair Dr. Bailey, presented a progress update on the Education and Training Subcommittee's priorities and projects and identified goals for the January 2013 SACHDNC meeting. The Subcommittee's charge was to review existing educational and training resources, identify gaps, and make recommendations regarding two categories: 1) parents and the public, and 2) health professionals.

Ms. Tarini gave an update on member organizations. The American Academy of Pediatrics has released an EQIPP NBS quality improvement course titled *NBS: Evaluate and Improve Your Practice*. The course is to help providers document and record positive screening results and provide tips on how to discuss those results with families. A genetic literacy in primary care colloquium will be held at the AAP Annual Meeting in October 2012, and the Genetics in Primary Care Institute will continue their quality improvement initiative in the late spring of 2013. The AAP is also in the process of developing a pediatric family history tool, in collaboration with National Coalition for Health Professional Education in Genetics and HRSA.

Priority A: To track, provide input, and facilitate integration of national initiatives on Committee-initiated activities. Conduct a scan to determine major education and training needs that extend into areas other than NBS, using a prototype condition through which training and education gaps could be identified.

- To determine possible prototype conditions, input was solicited from all subcommittee members (i.e., Education and Training, Long-Term Follow-up and Treatment, and Laboratory Standards and Procedures) as well as SACHDNC members and the regional collaboratives.
- The condition must not be currently on or previously considered for the RUSP, is a specific heritable condition, has a specific known genetic ideology, and has screening featuring available procedures and preventing costly diagnostics.
- A list of ten possible prototype conditions to present to the full Committee include: Duchenne Muscular Dystrophy, Ehlers-danlos Type IV, Familial Adenomatous Polyposis, Franconi's Anemia, Fragile X, Friedreich's Ataxia, Long QT Syndrome, Marfan Syndrome, Turner Syndrome, and Wilson's Disease.

Priority B: To promote NBS awareness among the public and professionals. Support and provide input to the 2013 NBS Awareness Campaign and develop recommendations for the SACHDNC in promoting ongoing awareness and support for NBS beyond the 2013 campaign.

- Centers for Disease Control and Prevention (CDC) and APHL gave a briefing on 50th anniversary plans, which include an APHL NBS symposium meeting in May 2013, a book documenting

achievements in NBS, a celebration event in Washington, D.C. to coincide with September 2013 SACHDNC meeting, and a day on the hill, a traveling exhibit of NBS artifacts, and social media messaging.
- Next steps include involving advocacy groups to spread awareness and creating standardized messages for use by member organizations to increase awareness of NBS. After 2013, the subcommittee will create a toolkit for individual states to use as they celebrate their 50th anniversaries for NBS.

Priority C: Provide better guidance for advocacy groups and others regarding the nomination and review process. Increase public transparency for what we do, the rationale behind the decisions, and to provide feedback regarding next steps as well as support future nominators in preparing successful application packages.

- In collaboration with the Condition Review workgroup, developing public-friendly website information, beginning with a public-friendly condition review summary.
- Next steps include seeking clarity on technical constraints to revisions to the SACHDNC website, working on harnessing the potential of SACHDNC and NBS clearinghouse websites for material dissemination, and creating a subcommittee to assist with the creation of public-friendly documents, starting with a past condition review.

Committee Discussion

- A Committee member suggested that the subcommittee narrow the prototype conditions list further before bringing it to the full Committee for a vote.
- Committee members recommended looking at conditions that have been brought forward by the public, or those with high incidence rates, as areas of concern.
- Ms. Tarini noted that the subcommittee attempted to get away from the newborn age period while remaining within the pediatric age range, selecting conditions that represented a broader age spectrum.
- A Committee member suggested that, as a matrix is created to analyze these conditions, it would be helpful to determine the number of existing advocacy groups for each condition.

B. Subcommittee Report on Follow-up and Treatment

Carol Greene, MD
Organizational Representative

Dr. Greene gave a progress update on the Follow-up and Treatment Subcommittee priorities and projects. Dr. Greene began with an update on changes in Committee membership. Dr. Greene gave an update on member organization projects, including a publication on connecting NBS blood spots and birth certificates, a revised manuscript for publication on the coverage of medical foods and supplements, and a publication on key considerations for point-of-care NBS.

Priority A: Facilitate screening program implementation and follow-up. Assess the challenges of point-of-care tests, beginning with hearing screening follow-up as a case study. Connecting point-of-care testing with dried blood spot screening.

- The hearing screening follow-up case study is in the early stages, will be the focus of the subcommittee's next teleconference, and will be reported on at the next Committee meeting. Subcommittee members reported on a review of current newborn hearing screening regulations and policies across the country. The use of Electronic Health Records (EHR's) and point-of-care screening was also discussed. The Subcommittee will look at lessons learned around point-of-care screening from the Early Hearing Detection & Intervention (EHDI).
- For the ongoing evaluation of Critical Congenital Heart Defects (CCHD) implementation, the subcommittee will work with a HRSA-funded regional collaborative.

[Note: Priority B is not a separate project, but a reminder to learn the current as well as variable roles and responsibilities in all case studies].

Priority C: Explore the extent to which we can document improved clinical outcomes and determine the full potential of NBS, using Sickle Cell Disease (SCD) as a case study. Focus on developing key questions, understanding data sources, and identifying gaps without duplicating efforts currently underway at HHS.

- Looked at a number of factors, including clinical care in the notification and action regarding carrier status, use of HER's, and gaps in services for patients. Select current key tracking process and outcome indicators that are evidence-based, practical to perform in clinical care, and traceable within EHR.
- Matrices were developed to help organize and review populations that are interested in the questions that are important. A second matrix of data sources can be populated to understand the entire landscape of organizations working on SCD. A reminder to include privacy concerns in conversations about using an EHR to track medical outcomes.
- Next steps include a discussion of possible final products that will be useful for future decisions about implementing NBS, designing future data collection in long-term follow-up, and developing a simple project to provide a focused look at the effectiveness of NBS for SCD in improving health.

Committee Discussion

- Dr. Copeland encouraged the subcommittee to enlist the CCHD grantees in thinking about what questions to ask EHDI.
- A Committee member noted that the SCD case study is not only determining the extent that NBS for SCD fulfilled its promise, it's also informing the model for other conditions.
- A Committee member suggested that, in the matrices, it is also important to consider what the treatments are and how treatment information will be captured and monitored.
- Dr. Copeland stressed the potential for duplication of efforts and reminded the subcommittee that the focus is on how the long-term follow-up system works rather than SCD epidemiology.
- A Committee member recommended that the SACHDNC contribute a voice to encourage unity among multiple federal efforts around establishing measures for systems of care, research, and modeling. Another Committee member recommended interfacing with a transadvisory group. Dr. Copeland noted that a transadvisory group is not meeting at this time, but may in the future.

C. Subcommittee Report on Laboratory Standards and Procedures

Fred Lorey, PhD
Committee Member
Genetic Disease Screening Program
California Department of Public Health

Dr. Lorey presented a progress update on the Laboratory Standards and Procedures Subcommittee priorities and projects.

Dr. Lorey began with updates from member organizations. First, the subcommittee reviewed the article on "Recommendations for Good Laboratory Practices in Biochemical Genetic Testing and NBS for Inherited Metabolic Disorders" in CDC's *Morbidity and Mortality Weekly Report*. The article covered good laboratory practices (GLP's) for genetic testing performed in the screening, diagnosis, monitoring, and treatment of heritable metabolic disorders. The subcommittee felt that the report is not ready for a full Committee vote of support, and will request additional information on how these recommendations could impact state programs. Second, the subcommittee reviewed a draft document from the Clinical Laboratory Standards Institute that addresses detection of Severe Combined Immunodeficiency (SCID) through population-based dried blood spot screening. Volunteers have been requested to provide additional comments to the draft, and the completed document will be particularly valuable to states that have yet to begin screening, because it will cover everything related to the SCID disease and testing.

Priority A: Review of enabling and disruptive technologies

- Begin with the succinylacetone assay, for it has replaced tyrosine as the marker for Tyrosinemia Type I but not all States have begun using it. Propose a presentation on this at the May 2013 meeting.

Priority B: Provide guidance for state NBS programs and make decisions about implementation, integration, follow-up, and quality assurance.

- NBS quality indicators are in development. Subcommittee members discussed the importance of confirming data quality and providing feedback to states based on data received. States could use the new data repository within NewSTEPS for case management, and it is important to discuss the value of data collection with states to increase buy-in for participation.
- NBS case definitions have been developed. Several states have volunteered to beta test the definitions.
- Create a slide deck for state labs after a new condition is added to RUSP. Determine the types of information helpful to state decision makers such as laboratories, hospitals, and legislatures. This is in progress, beginning with the SCID template.

Priority C: Establish a process for regular review and revisions of the RUSP and recommend specific changes to technology when indicated.

- Work with the condition review group to develop lab requirements for their reviews (this is a joint project with all three subcommittees). To this date, SCID and CCHD have been reviewed.

Dr. Lorey subsequently requested self-nominations for the Laboratory Standards and Procedures Subcommittee. Needed categories of expertise include state laboratory staff with molecular expertise, commercial laboratories, clinicians, and pathologists.

Dr. Lorey concluded with an update on Health Information Technology (HIT). A new version of Logical Observation Identifiers Names and Codes (LOINC) for the NBS panel is now available. The National Library of Medicine would like feedback.

Committee Discussion

- A Committee member noted that the consensus on priority C was to let the subcommittees lead the way, with full Committee participation once Priority C is finalized.
- Dr. Bocchini commented that recruitment for the Subcommittee on Laboratory Standards and Procedures is underway for the defined categories.

D. Multistate Analysis of Single Tests or Routine Second Testing in NBS for Hypothyroidism and Congenital Adrenal Hyperplasia: Update

Stuart Shapira, MD, PhD
Medical Officer, Pediatric Genetics Team
NCBDDD, CDC

Dr. Shapira provided an update on a Multistate Analysis of Single Tests or Routine Second Testing in NBS for Hypothyroidism and Congenital Adrenal Hyperplasia, conducted by the National Center on Birth Defects and Developmental Disabilities at the CDC. Dr. Shapira presented a brief history of NBS, which began in the 1960s. At that time, specimens were obtained at 48-96 hours after birth. Pressures to decrease healthcare costs led to early hospital discharge of mothers and newborns before 48 hours of life, affecting NBS. To reduce the chance of missing cases of clinically significant disorders, nine states have mandated a second screen collection on all newborns at 8-14 days of age, regardless of the first NBS result. Currently, the total percent of the U.S. population with a routine second screen is approximately 22.4%.

In February 2006, a project was proposed to the Lab Standards and Procedures Subcommittee of the SACHDNC to investigate the effect of the routine second screen. A protocol development meeting was held in December 2006, with representation from a majority of the states who require second screening, three states who highly recommend second screening, and endocrinologists and federal representatives.

This meeting resulted in proposals for two studies on congenital hypothyroidism (CH) and congenital adrenal hyperplasia (CAH): a five-year retrospective study and a one-year prospective study. However, several states were unable to gain approval for participation in the one-year prospective study.

One-screen states (California and Wisconsin) and two-screen states (Alabama, Delaware, Maryland, Oregon, and Texas) were able to move forward with the retrospective study. Individual-level anonymous data were submitted to the APHL for multivariate analysis, including data elements on demographics, laboratory data, and clinical data. One-screen states used Thyroid-stimulating Hormone (TSH) testing while two-screen states used Thyroxine (T4) testing for the first screen. In two-screen states, if a T4 result is abnormal, their second screen will use TSH. In some cases, one-screen states did a targeted second screening.

- **Congenital Hypothyroidism (CH) results**: In two-screen states, almost 12% of CH were identified on the 2nd screen. Female CH cases were more likely to be identified on the first screen than the second screen. CH cases identified on the first screen were less likely to be extremely low birth weight, less likely to have been transfused prior to screening, and more likely to have the sample collected at greater than 24 hours after birth. When assessed in a multivariate model, the most predictive characteristic for detection on first screen was race. Compared to Caucasians, African-American and Asian/Pacific Islanders were less likely to be identified, whereas Hispanic and other groups were equally likely to be identified. Dr. Shapira noted that the denominator, or total number of cases screened in each state, was unavailable. A proxy from vital records was used to look at the incidence of cases overall as well as according to race/ethnicity. The rate of CH related to total birth was higher in one-screen states than in two-screen states. Among Hispanics, the rate was higher in one-screen states. For Asian/Pacific Islanders, the rate was higher in two-screen states.
- **Congenital Adrenal Hyperplasia (CAH) results**: In two-screen states, 38% of CAH cases were picked up on the second screen. However, the analysis was limited because only Alabama and Texas identified cases on second screen. Race and ethnicity were found to be significant, for cases were less likely to be Hispanic. In a multivariate mode, the only statistically significant variable was the occurrence of sample collection at greater than 48 hours. Cases were more likely to be classical simple virilizing on the second screen.

In two-screen states, 12% of CH and 38% of CAH (including 9% of all classical salt-wasting) cases were detected on the second screen. If the two-screen states only performed the first screen, these cases would not be detected. All of the CH and more than half of the CAH were treated, indicating that they were clinically significant.

Committee Discussion

- Dr. Lorey noted that the large Hispanic population in California could skew the results for one-test states. Dr. Shapira noted that the number of Hispanics was similar in Texas, a two-screen state, and he suspects that the make-up of Hispanics is similar between one-screen and two-screen states.
- Dr. Lorey commented that due to the demographics of the Asian/Pacific Islander population in California, it is important to consider the subpopulations within that category.
- Dr. Tarini observed that an access issue around screening, specifically for African-Americans, could lead to less African-Americans being identified. Getting the denominator might be helpful in determining the number screened. Dr. Shapira added that while the data was not originally requested from states, he is hopeful that states will understand the importance and provide the data in the future for further analysis.
- A member of the public asked whether the Jewish population was looked at separately for CAH, and Dr. Shapira replied that data on religious background was not collected by any of the states.
- A Committee member asked whether the states have the opportunity to look at false positive results. Dr. Shapira responded that data on false positives was not collected from states as it was not within the scope of this study,.

E. CDC Recommendations for Good Laboratory Practices in Biochemical Genetic Testing and NBS for Inherited Metabolic Disorders

Bin Chen, PhD
Division of Laboratory Systems, National Center for Preparedness, Detection, and Control of Infectious Diseases, Coordinating Center for Infectious Diseases, CDC

Dr. Chen reviewed the Center for Disease Control's *Morbidity and Mortality Weekly Report* "Recommendations for Good Laboratory Practices in Biochemical Genetic Testing and NBS for Inherited Metabolic Disorders." Dr. Chen also briefly discussed the results of a participant survey completed by 69 people who had participated in continuing education/training on the recommendations.

Dr. Chen began with a brief background on the process for developing recommendations. In 2009 the Clinical Laboratory Improvement Advisory Committee (CLIAC) convened a Biochemical Genetic Testing (BGT) Workgroup, comprised of 13 experts representing BGT and NBS perspectives to evaluate laboratory standards and guidelines. In 2010, CLIAC reviewed the BGT workgroup report and formulated recommendations. SACHDNC, APHL, and the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) provided additional input to compliment CLIAC recommendations.

The intent of the recommendations is to:

- provide quality management guidance for genetic testing performed for screening, diagnosis, monitoring, and treatment of heritable metabolic disorders;
- consider BGT and NBS separately when practices differ;
- clarify Clinical Laboratory Improvement Amendments (CLIA) requirements and provide additional good laboratory practice recommendations; and
- complement the 2009 CDC guideline for molecular genetic testing.

Highlights of recommended practices include:

- ensuring adequate establishment and verification of analytic test performance and documenting available information on clinical validity;
- providing guidance for patient preparation when appropriate;
- following written criteria for specimen acceptance or rejection;
- referring tests only to CLIA-certified laboratories;
- using control materials to monitor the entire analytic process;
- performing control procedure each day or with each batch;
- providing necessary information for accurate understanding and interpretation of test results; and
- retaining test reports indicating genotypes for at least 21 years.

Recommendations also covered personnel qualifications, competency assessment, quality management system approach, and confidentiality. The intended audience for recommendations include laboratory professions, surveyors, and inspectors; users of laboratory services; standard-setting organizations; professional societies; and IVD manufacturers. The expected outcomes of implementing recommendations include improved quality of laboratory genetic services, enhanced oversight for genetic testing using the current regulatory framework, and improved healthcare outcomes from genetic testing.

F. Prenatal Family History Project: Data and Report

Joan Scott, MS, CGC
Executive Director of NCHPEG

Ms. Scott presented on the Pregnancy and Health Profile Screening and Risk Assessment Tool developed in collaborative effort by the National Coalition for Health Professionals in Genetics (NCHPEG), Genetic Alliance, March of Dimes, Partners Healthcare, and HRSA. The tool was developed to integrate genetics and NBS information into a health history, assist genetic clinical decision-making, educate patients and providers, and address the life-course of the female patient.

The Pregnancy and Health Profile tool assists busy primary care providers in translating family history data into clinical care. The tool also engages the patient as an active participant and provides a personalized clinical encounter with clinical decision support and provider and patient materials. Condition support is available for over 20 conditions, including Mendelian congenital conditions, Mendelian pregnancy and lifespan conditions, complex congenital conditions, and complex pregnancy and lifespan conditions.

The tool was implemented in four different clinical settings, and patient and provider feedback data was collected at each site. Data collected during implementation concluded that customization, clinical champions, and IT support are critical to successful implementation. Process recommendations for clinical implementation were identified. Patient satisfaction with using the tool was high; however, providers submitted mixed feedback about decision support.

Next steps include disseminating the prenatal tool for free download, continuing study on the impact of the tool with a prenatal population, developing adaptations for additional clinical settings, and developing web-based and non-English language versions.

Committee Discussion

- A Committee member commented that provider age may have an effect on the comfort of using the tool. However, Ms. Scott noted that the tool was universally accepted among all age groups and any differences in comfort level arose from concerns about workflow.
- Ms. Scott noted that data was collected for 3-4 months; however, additional data may be collected in the future to track long-term pregnancy outcomes.
- Ms. Scott added that the tool is able to pick up major conditions, but clinicians may need to clarify some family history data with patients to ensure quality control.
- Ms. Scott also noted that information collected in the tool would then need to be scanned or entered into the electronic medical record.

G. Carrier Screening Draft Review

Meredith Weaver, PhD, ScM, CGC
American College of Medical Genetics and Genomics
SACHDNC Carrier Screening Taskforce

Dr. Weaver updated the Committee on work completed by the Population-based Carrier Screening Workgroup. In May 2012, SACHDNC charged the Workgroup with engaging a multidisciplinary stakeholder group, using the modified Delphi process, to collect and document perspective on public health, personal health, and health care system readiness and needs for expanded population-based carrier screening for genetic conditions. This work would result in an outline of recommendations and a roadmap of considerations needed prior to implementation of population-based carrier screening. As of September 2012, the points to consider when screening for a condition have been identified. These considerations are both general to the screening process and condition-specific. However, they are not currently intended to be used as a list of which conditions to screen for and when to screen.

The workgroup looked at five components of population-based carrier screening: social issues, economic issues, psychological issues, education and communication issues, and test issues. For each issue, workgroup members considered four parameters: desirability, feasibility, importance, and confidence in judgment. To achieve major consensus, less than 20% of the workgroup could disagree. Dr. Weaver noted that the results from the modified policy Delphi are consistent with popular discourse on population-based carrier screening. General agreement existed for the desirability of issue, and some agreement regarding the importance of issues. There was little agreement regarding the feasibility of assessing, determining, or considering an issue.

Looking forward, a report with recommendations about general carrier screening parameters and criteria for specific conditions will be circulated prior to the January 2013 SACHDNC meeting. Committee

members will be able to review and comment on the report. During the January 2013 meeting, there will be a vote to support the report as a product of the SACHDNC.

Committee Discussion

- Dr. Weaver commented that while carrier screening has been discussed, a distinction has not been made regarding population screening versus universal screening. She added that they did not look at public health data versus clinical data.

VI. Pertinent Meeting Updates

A. IOM Meeting Summary: Assessing the Economics of Genomic Medicine

Catherine Wicklund, M.S., C.G.C.
Committee Member
Northwestern University
Feinberg School of Medicine Center for Genetic Medicine

Ms. Wicklund provided the Committee with a synopsis of the Roundtable on Translating Genomic-Based Research for Health, held at the July 2012 Institute of Medicine (IOM) workshop on Assessing the Economics of Genomic Medicine. The goal of the workshop was to advance discussions around the clinical implementation of genetic and genomic technologies by examining costs associated with the development and use of genetic and genomic information in the care of individual patients.

To assess the economic implications of individual care, workshop participants were presented with a hypothetical exercise in following a 35-year old female smoker over a 15-year period, specifically looking at three points over her lifespan: 1) preconception counseling, 2) a deep vein thrombosis event, and 3) lung cancer care. Three genomic models were considered for each situation: 1) targeted mutation analysis, 2) whole genome sequencing with relevant clinical data but some actionable variants; and 3) whole genome sequencing with all relevant data, actionable variants, and significant secondary findings. The various factors that influence costs were identified along with alternative models of implementation.

A genomic scorecard was presented during the roundtable on the economic utility of genomic screening. Genomic medicine has the potential to shed light on genetic underpinnings of every disease, assess the risk of common diseases, and locate individuals who are at a high risk of preventative disease. The genomic scorecard is a powerful diagnostic tool that could potentially improve the treatment of cancer, prevent rare diseases, and inform reproductive choice. There is less utility in NBS, and no utility in the prevention of common diseases through genomic risk assessment and broad preventative application.

Ms. Wicklund noted that cost effectiveness does not equal cost savings, i.e., expensive interventions are not cost effective. Assessing genomic medicine requires a spectrum of expertise and perspectives, including economic research, technology development, epidemiology research, behavioral research, ELSI/education, and health services. The roundtable came up with 20 additional questions in terms of comparative effectiveness research, health economic methods, health economics applications, and patient-centered outcomes.

Committee Discussion

- Ms. Wicklund noted that the discussion needs to shift away from the cost of early adoption of technology and toward the type of economic burden genomic medicine may place on the healthcare system. When collecting information, it is important to consider the storage and interpretation of data as well as what information is most useful for leveraging behavior change.
- Ms. Wicklund, responding to a Committee member's question on costs, stated that an adult woman was used as an example in this presentation; however, the cost of genetic sequencing may be less for a child if compared to a number of other routinely administered tests.

- A Committee member stated that the IOM meeting was one of the first opportunities to clarify microeconomics versus macroeconomics. The macroeconomic level is critical to our discussions because the world of genomics is no longer in a vacuum.
- Ms. Wicklund noted that planning for another workshop is underway, and that the IOM website contains summaries of each workshop. The February 27th workshop will be on co-development in diagnostics in targeted therapeutics. Drug repurposing will be discussed on June 24th.

B. Adjournment

Dr. Bocchini noted that the next SACHDNC will be held via teleconference in January 31–February 1, 2013.

Dr. Bocchini thanked Committee and audience members for their contributions, and adjourned the meeting at 2:12 pm on September 14, 2012.