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

Summary of 29th Meeting
January 31 – February 1, 2013
Webinar

The Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) was convened for its 29th meeting at 9:30 a.m. EST on Thursday, January 31, 2013, as a webinar. The meeting was adjourned at 1:02 p.m. EST on Friday, February 1, 2013. In accordance with the provisions of Public Law 92-463, the meeting was open for public comment.

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I. Committee Business: January 31, 2013

A. Welcome and Roll Call

Joseph A. Bocchini, Jr. M.D.
Committee Chair
Professor and Chairman
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Dr. Bocchini welcomed the webinar participants, offered helpful hints for managing the webinar interfaces, and took the roll for the first day of the twenty-ninth meeting of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC). Voting members present were: Dr. Don Bailey, Dr. Jeffrey Botkin, Dr. Carla Cuthbert, Dr. Denise Dougherty, Dr. Alan Guttmacher (late arrival), Dr. Kellie Kelm, Dr. Michael Lu (late arrival), Dr. Stephen McDonough, Dr. Dietrich Matern, Dr. Alexis Thompson, Ms. Catherine Wicklund, and Ms. Andrea Williams. Dr. Sara Copeland served as the Designated Federal Official.

Nonvoting organizational representatives participating in the webinar were:

- American Academy of Family Physicians (AAFP): Dr. Frederick Chen
- American Academy of Pediatrics (AAP): Dr. Beth Tarini (late arrival)
- American College of Medical Genetics (ACMG): Dr. Michael Watson
- Association of Public Health Laboratories (APHL): Dr. Susan Tanksley
- Department of Defense (DoD): Ms. Theresa Hart
- Genetic Alliance: Ms. Natasha Bonhomme
- March of Dimes: Dr. Edward McCabe (late arrival)
- National Society of Genetic Counselors (NSGC): Ms. Cate Walsh Vockley
- Society for Inherited Metabolic Disorders (SIMD): Dr. Carole Greene

Dr. Bocchini welcomed the new organizational representatives to the committee: Ms. Lisa Bujno, Association of Maternal and Child Health Programs; Dr. Tanksley, Association of Public Health Laboratories; and Ms. Vockley, National Society of Genetic Counselors.

B. Approval of September 2012 Minutes

Committee members offered no comments on the minutes of the SACHDNC's September 2012 meeting. All of the committee members present voted to approve the minutes. Dr. Lu arrived after the vote, and was marked as absent for this vote.

C. Anticipated Cancellation of the May 2013 Meeting

Dr. Copeland reported that the authorization for the Newborn Screening Saves Lives Act, which authorizes the SACHDNC, will expire on April 24, 2013. The SACHDNC can continue work under the contracts and grants that are currently in place if the funds appropriated by Congress have not been used. The Committee will not be able to convene or conduct business after the expiration of the Act. As a result, the Health Resources and Services Administration (HRSA) proposed cancelling the May 2013 SACHDNC meeting, unless the Act is reauthorized prior to its expiration and the agency can make the necessary logistical arrangements in time. Alternately, the Committee could hold an abbreviated meeting in early April to discuss the Pompe disease condition nomination.

Committee Discussion

- Dr. Bocchini asked whether the Condition Review Workgroup (CRW) would be prepared to provide the data needed to make a decision about Pompe in early April. Dr. Copeland stated that

the CRW would continue working through March and April in an effort to have the data ready for an early April vote.

- Several Committee members expressed concerns about the quality of the data that will be available if the vote is moved up into April, but agreed that the meeting should take place if possible.
- In response to Dr. Botkin's concerns about approving a condition as part of a webinar instead of an in-person meeting, Dr. Copeland stated that most future Committee meetings will be held as webinars, given the ongoing budgetary uncertainty.
- Dr. Copeland responded to Dr. Chen's question concerning the likelihood of Congress reauthorizing the Act by stating that HRSA did not have a good sense of the intent of Congress. Ms. Bonhomme stated that there are several sponsors for the reauthorization, and there is optimism about it. She cautioned that reauthorization is not certain. Dr. McCabe reported that the March of Dimes' Office of Governmental Affairs is working on the reauthorization, which is a priority for the organization.

Dr. Bocchini asked the Committee members to express their preference for expediting the vote on Pompe prior to the expiration of the Committee's authorization. Voting in favor of expediting the vote if the required data is available were: Dr. Bailey, Dr. Botkin, Dr. Cuthbert, Dr. Dougherty, Dr. Kelm, Dr. McDonough, Dr. Matern, Dr. Melissa Parisi, Dr. Thompson, Ms. Wicklund, and Ms. Williams. None of the members present voted against holding the meeting in April.

II. Condition Review Decision Matrix

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

Dr. Kemper presented highlights of the *Users' Guide to the SACHDNC Decision Matrix*. In September 2012, the Committee approved the use of the updated decision matrix to support the development of recommendations concerning conditions nominated for inclusion in the Recommended Uniform Screening Program (RUSP). However, the Committee wanted additional review and clarification before making the final determination on how the matrix will be used to make a recommendation.

The matrix is based on a two-step process that first considers net benefit and then considers the capability of state newborn screening (NBS) programs to adopt comprehensive screening.

The matrix ranks the certainty of net benefit from "A" (high degree of certainty that adoption of screening will result in net benefit) to "D" (high or moderate certainty of a negative net benefit). Screenings rated as "L" have a low certainty of having a net benefit. Other factors to be taken into consideration when using the matrix include the overall public health burden, birth prevalence, benefits of early detection and treatment, and harms related to screening, diagnosis, and treatment for both affected and unaffected children. Dr. Kemper expressed his opinion that conditions rated as D or L should include guidance on the information or steps needed to resolve uncertainty.

Feasibility is broken into four categories ranging from high feasibility (1 – most programs are ready to screen) to low feasibility (4 – most programs are unlikely to screen). Technical and clinical feasibility are the central issues related to determining screening capability. Careful assessment of readiness can identify issues to be resolved and guide implementation. Established screening tests, a clear approach to diagnostic confirmation, and accepted treatments and follow-up plans are necessary to ensure the technical and practicality of screenings. Feasibility is the driving factor for the implementation of most newborn screening.

Dr. Kemper used several conditions discussed by the Committee over the past few years as examples to illustrate how each would have fit into the matrix and how ratings could change over time based on altered circumstances. In each case, the rating matched the original decision of the Committee.

Committee Discussion

- Dr. Bocchini stated that one of the best ways to evaluate the revised matrix and application of a rating would be to plug the Committee's previous decisions into the matrix, to determine if it provides an effective means of making decisions based on the available evidence for each of the previous decisions.
- In response to Dr. Botkin's question concerning the use of an evidence-based process for assessing feasibility and capability for state programs, Dr. Kemper replied that one of the principal criteria is the ability to screen. Evidence review includes the evaluation of test characteristics, but does not address many aspects of feasibility and readiness.
- Ms. Wicklund asked how information would be gathered from individuals working in the public health sector, including those responsible for returning and responding to screening results. Dr. Kemper stated that the collection of this information would be the responsibility of the APHL.
- Dr. McDonough was concerned about the application of the matrix. The Committee should not place unreasonable burdens on rare conditions that might not receive A or B net benefit ratings, but could be quickly and easily screened in the future. Many A3 conditions should be approved. He recommended that conditions rated A4 receive a recommendation for capacity building. He also expressed concerns over the definition of moderate certainty, and how various metabolic disorders will fit into A or B ratings. Additionally, the Committee's use of the matrix to rate new conditions should be consistent with previously recommended conditions. He advocated for a delay in the vote on the matrix and for the opportunity to collect written comments from public advocacy groups and researchers.
- Dr. Bocchini pointed out that the goal of the matrix is to provide transparency for the decision making process.
- Dr. Copeland reminded the Committee that the underlying legislation requires recommended conditions to have an assessment of the public health impact. The new matrix is an attempt to quantify the impact.
- Dr. Bailey asked whether the Committee was voting on framework that will provide consistency to its recommendations or on specific points used to rate conditions. Dr. Bocchini indicated that the vote concerned specific decision points.
- Dr. Kemper noted that there is always uncertainty with regard to evidence; the issue is the magnitude of the uncertainty of the net benefit. The central question is whether adding a newborn screening for all newborns nationwide will make a difference.
- Dr. Matern wanted more information about the way in which the matrix would be applied and about APHL's work with the states. He cautioned that a low feasibility rating could give states an excuse to avoid screening. Dr. Botkin agreed that the Committee should not overemphasize feasibility, especially where tests exist but states are not ready to implement them immediately. He also supported reviewing some of the conditions originally included in the RUSP, in light of improvements in the evidence review process.
- Dr. Bailey asked how the Committee would approach conditions that are easy and inexpensive to screen and have no treatment but could benefit from early intervention. Dr. Bocchini replied that this should be taken into consideration in the Committee's future discussions.
- Dr. Greene and Dr. Watson noted the need to define benefit and feasibility. Dr. Green emphasized the importance of incorporating pilot studies as the Committee implements any matrix that it adopts.
- Dr. Tanksley recommended gathering information from states to determine the impediments to implementation. The Committee's recommendation could serve as an impetus to states to adopt screening.
- Dr. Chen stated that AAFP is supportive of the Committee's use of the decision matrix.
- Dr. Botkin pointed out that the different circumstances in each state could result in very different levels of feasibility. The Committee's recommendations need to be flexible enough to acknowledge this variability.

Committee Use of the Matrix
The Committee now focused on clarifying the rating categories used in the matrix.

As proposed, conditions that fall below an A rating for net benefit will not be added to the RUSP. For screenings that receive a B designation, the Committee's recommendation will identify gaps in the evidence and suggestions for improving the rating. These conditions would be eligible for expedited review once the gaps are filled. Conditions receiving a net rating of C, D, or L must be resubmitted for consideration.

With regard to the public health impact designation, conditions receiving a rating of A1 or A2 would require little to no additional discussion as they exhibit significant benefit, readiness, and feasibility. These conditions could be recommended for inclusion in the RUSP. Conditions receiving a rating of A3 or A4 would require additional discussion within the Committee concerning their feasibility or readiness. Of particular interest would be demonstration projects that could move these conditions into a higher category.

Committee Discussion and Vote

- Dr. Matern asked whether a condition rated as A3 or A4 would be recommended to the Secretary of Health and Human Services (HHS). Dr. Bocchini indicated that these conditions would be brought to the Secretary based on the final vote of the Committee. The recommendation would include a discussion of the problems related to feasibility and how they could be addressed. Dr. Matern was concerned that the Secretary would have rejected some of the Committee's earlier recommendations if they came with significant discussions concerning gaps in feasibility. Dr. Kemper noted that the Severe Combined Immunodeficiency (SCID) recommendation included a statement concerning the need for extra support for states to adopt the screening. Dr. McCabe added that tandem mass spectrometry would have fallen into the category when it was first adopted for screening.
- Dr. Matern asked how readiness ratings would be assigned, given that each state has a different level of readiness. Dr. Kemper stated that he hoped to avoid a strict point system and rely on the Committee's knowledge, experience, and deliberations to correctly categorize each condition.
- Dr. Kemper responded to a question about data collection by stating that the Committee would use a stratified sample of states for each evaluation.
- Dr. McDonough was concerned that approval of B1 conditions could be delayed while the Committee collected sufficient data to raise the rating. He recommended that the Committee receive an annual update on current research regarding conditions previously given a B rating.
- Dr. Bailey noted that there is a difference between being moderately certain that there will be a benefit and being moderately certain that new data will prove the benefit. Dr. Kemper stated that the Committee would count any benefit toward net benefit.
- Dr. Bocchini stressed that conditions that affect a small number of patients but result in great benefit for those patients could receive an A rating based on the strong outcome.
- Dr. Bailey was concerned that early intervention would never be shown to have a dramatic impact.
- Dr. Botkin observed that the matrix is embedded in the understanding that data will rarely be ideal. Committee members must exercise judgment and flexibility with regard to ratings. Additionally, the Committee should emphasize the development of the infrastructure needed to ensure that the required studies can be done in a timely fashion.

A participant recommended the elimination of the word "however" in box A2 of the matrix. Dr. Thompson recommended adding the word "most" in reference to the public health departments in box A2 and A3 to indicate that the Committee does not require an absolute statement from all public health departments.

Dr. Bocchini asked for a motion to vote on the adoption of the matrix. Dr. Botkin moved to approve the matrix as amended, and Dr. Dougherty seconded the motion. The Committee approved the motion, with 10 members voting for the motion and three members voting against. There were no abstentions.

III. Public Comment

Kristi Wees, Parent/Advocate, Babyfoodsteps: Ms. Wees is the parent of a child with a suspected mitochondrial disease and an advocate who served on the 2012 Babies First Test Consumer Task Force. She encouraged the Committee to consider children whose diseases are not identified at birth and experience late onset symptoms. According to the European Mitochondrial Disease Network, one-third of children with metabolic disorders resulting in toxic accumulation or energy production experience late onset symptoms, with onset occurring any time after the first year. Late onset of nearly all metabolic conditions suggests that genetics and heritability are not the only factors involved in their onset or progression; environment must play a role in the epigenetic manifestations and heterogeneity of the affected populations. She encouraged the Committee to consider environmental factors—including food additives, preservatives, pesticides, prescription and over the counter pharmaceuticals, vaccinations, and industrial chemicals—in its deliberations.

Dean Suhr, Advocate, MLD Foundation: Mr. Suhr recommended that the Committee consider eliminating viable therapy as a consideration for the uniform panel. Quality of life is equally as important as a viable therapy for patients with a condition that does not have a viable therapy. By screening for these conditions, families can prepare for the effects a disease will have on their child. Such a change would have significant implications for the infrastructure needed to support families with a diagnosis but no therapy. He stated that he would contact Committee members individually to discuss this issue in anticipation of a formal recommendation from the MLD Foundation.

Jane Larkindale, Vice President for Research, Muscular Dystrophy Association (MDA): Dr. Larkindale focused her comments on the Duchenne muscular dystrophy (DMD) community. MDA is leading the search for new treatments for DMD and improving the use of existing treatments. Recent studies indicate that early treatment for DMD yields better outcomes for patients. Early intervention is both practical and robust. The Duchenne community has a well-organized national infrastructure and is well positioned to address new initiatives. The community is ready act through research, advocacy, and infrastructure. MDA is prepared to work with the Committee and other partners on shared goals of optimizing health outcomes in children with genetic neuromuscular disorders.

Amber Salzman, President, Stop ALD Foundation: The Foundation was grateful for the review of the adrenoleukodystrophy (ALD) NBS nomination during the September 2012 meeting. Dr. Salzman updated the Committee on the status of the large pilot study being conducted by the Mayo Biochemical Genetics Laboratory. Approximately one-half of the 100,000 samples have been screened. The Foundation and the Kennedy Krieger Institute and the Mayo Clinic have arranged for the confirmation sequencing of the ALD-positive samples. The Foundation planned to present the data and scientific detail during the Committee's May meeting, and hope to be granted an expedited review. Due to the cancellation of the May meeting, Dr. Salzman requested that Committee review the additional ALD data at the same time as it votes on Pompe in April. This would allow ALD to take its place in the queue for review.

Tiffany House, President, Acid Maltase Deficiency Association: Ms. House advocated on behalf of all Pompe patients for the Committee to recommend Pompe disease for inclusion on the NBS panel. Pompe has an approved treatment, enzyme replacement therapy (ERT), that can slow and sometimes reverse the disease. Early intervention generally leads to the best results. Unfortunately, the path to diagnosis is often difficult and long. It takes, on average, 10 years for a late onset patient to be diagnosed. By the time diagnosis is made in late onset Pompe patients, there can be significant, irreversible muscle damage. Newborn screening for Pompe would remove the significant delays in diagnosis. Ms. House shared her experience as a late onset patient who was not diagnosed until age 11, by which time her lung function, walking, and posture had been significantly affected. NBS would enable Pompe patients to be diagnosed at birth and monitored so that treatment can be initiated before irreparable damage occurs. Addition of Pompe to the screening panel would change countless lives for the better.

George Fox, Parent of a Pompe Patient: Mr. Fox shared his experience as the parent of a child with Pompe. He firmly believed that NBS would have resulted in a better quality of life for his son. While each patient responds differently to ERT, the earlier treatment is started, the better the prognosis is in general.

Mr. Fox's son began ERT at eight months of age after six months of increasing weakness. Had the child been diagnosed with Pompe earlier, he would be much stronger today. Now 10 years old, Mr. Fox's son requires round-the-clock ventilation, is 100 percent dependent on others for his movement, and requires a nasogastric feeding tube. Newborn screening for Pompe will save lives and preserve quality of life that would otherwise be lost forever. In the most severe forms of the disease, pre-symptomatic treatment is a must. Mr. Fox requested that the Committee add Pompe disease to the RUSP.

Sarah Wilkerson, Board Member, Save Babies through Screening Foundation: Ms. Wilkerson spoke from the perspective of both a mother and an advocate. Her son died after living for only a few days. One day later, his newborn screening showed that he had medium-chain acyl-CoA dehydrogenase deficiency. Even minor delays in receiving newborn screening results can have life or death consequences. Ms. Wilkerson advocated for the use of couriers to deliver samples to the laboratory in all states. Thirty states still allow the use of the Postal Service to deliver samples. Generally, hospitals in more rural areas rely on the Postal Service, and batch samples together until there are enough to warrant sending them to the state lab, adding delays to the process. She urged the Committee to consider the sensitivity of the timing of the test and to encourage the use of courier services for delivery of samples.

Priya Kishnani, Clinician, Duke University Medical Center: Dr. Kishnani advocated for the quick diagnosis of Pompe patients that NBS provides. Starting babies on ERT before six months of age has been generally accepted as good practice and was supported by the clinical trials that led to the Food and Drug Administration's (FDA) approval of ERT. Diagnosis as late as six months of age is proving to be too late. In cases of classic infantile Pompe, treatment should begin within days, as evidenced by the Taiwan newborn screening data and clinical experience worldwide. Diagnoses of late onset Pompe disease often come too late to prevent significant muscle damage. Early, pre-symptomatic diagnosis is very important. There are existing tools and treatment algorithms in place to manage both infantile and late onset Pompe disease. Dr. Kishnani expressed her hope that the Committee's report would be made available for public and expert comment prior to being put up for a vote.

IV. Update on Pompe Condition Nomination

A. Natural History of Pompe Disease

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Pompe disease is an autosomal disorder caused by a deficiency of acid α-glucosidase, which affects approximately one in 40,000 births. Dr. Kemper provided an overview of Pompe disease, including a description of the classic and nonclassic infantile and late onset forms, age of diagnosis for each type, enzyme function and psuedodeficiency, genotype-phenotype correlation, screening, diagnosis, and treatment. He also reviewed the results of Taiwan's long-term screening effort. The CRW will use the Taiwan data along with the results of screening efforts in Illinois (digital microfluidics and multiplex tandem mass spectronomy for multiple lysomal storage diseases [LSDs]), Missouri (LSDs with digital microfluidics), New Jersey and New Mexico (still planning for screening), and Washington (developing a multiplex enzyme assay pilot study) in its review.

Systematic Evidence Review
The CRW identified 78 articles for data extraction. Additionally, the CRW convened a Technical Expert Panel consisting of seven experts to understand the literature and develop the decision tree model.

Dr. Kemper reviewed the data from the Taiwan screening study, which screened more than 473,000 newborns. The CRW will work to clarify the data used based on nomenclature for later onset. The

workgroup plans to address the difference between later onset and late onset disease in the Taiwan study, and whether the Taiwan study can be generalized to the United States.

Dr. Kemper addressed the benefits and harms associated with the treatment of infantile Pompe disease. Findings of a 52-week ERT trial show improved survival compared to historical controls, with most individuals developing IgG antibodies regardless of their cross-reacting immunologic material (CRIM) status.

Questions that the CRW still needs to evaluate include:

- What is the current approach to CRIM- status and how important is CRIM- status to outcomes?
- How significant is the development of antibodies to ERT in CRIM+ individuals?
- How do outcomes vary by genotype?
- Have additional harms associated with treatment been identified?
- How does the net benefit of screening change based on CRIM status or classic versus nonclassic type?
- What are the benefits and harms associated with pre-symptomatic detection of late onset Pompe disease, especially the psychosocial implications for parents?
- What are the costs associated with newborn screening for Pompe, including assuring access to ERT?

Next steps for the CRW include completing the evidence tables and quality scores, reviewing unpublished data, and conducting interviews with experts in the field.

B. Decision Analysis and Newborn Screening

Lisa Prosser, Ph.D., M.S.
Associate Professor, Department of Pediatrics and Communicable Diseases
Associate Professor, Department of Health Management Policy
University of Michigan
Ann Arbor, MI

Decision analysis (DA) is a systematic approach to decision making. As part of the condition review process, it can provide a mechanism for evidence synthesis and a method for specifying assumptions. The application of DA to conditions nominated for inclusion in the RUSP includes the development of simple models and the identification of key health outcomes. The objective of DA for Pompe disease is to project health benefits and potential harms for the key health outcomes. Steps in the DA process include design of the DA model (computer simulation); expert panel review of the model structure, assumptions, and outcomes; identification of key outcomes, parameters, and assumptions; and application of the computer simulation model to projected outcomes, with an emphasis on ranges to reflect the uncertainties associated with the input parameters.

The proposed model includes two arms: one simulates a hypothetical cohort undergoing NBS and one simulates a similar hypothetical clinical identification group. The NBS model follows newborns through two years of life, with two years being a key health outcome for the model. The clinical identification portion of the model focuses on newborns that are not at any known increased risk for Pompe disease. Dr. Prosser anticipated presenting the model to the Committee during its next meeting.

Key outcomes of the model include five screening outcomes for newborns (true/false positives, true/false negatives, and repeat screens) for a hypothetical U.S. newborn cohort. For two-year outcomes, the model will project the number of cases of Pompe identified by NBS compared with clinical diagnosis for classic early infantile and late or later onset disease. The model will also project the number of cases expected to die within two years after diagnosis by an NBS program and by clinical identification. For those projected to live past two years, the model will project the number needing ventilator assistance and the number that will not require a ventilator. The model will allow the CRW to project key health outcomes and associated ranges and identify key parameters. The results of the DA model will provide transparency regarding the

assumptions used in the process and highlight knowledge gaps that can inform future data collection and research.

Next steps in the DA process for Pompe include developing the modeling parameters, reviewing the parameter inputs with the expert panel, and conducting a base case and sensitivity analysis to obtain ranges for projected outcomes.

C. Public Health Impact Assessment

Jelili Ojodu, M.P.H.
Director, Newborn Screening and Genetics Program
Association of Public Health Laboratories
Silver Spring, MD

In June 2011, HHS Secretary Kathleen Sebelius charged the SACHDNC with including a public health impact assessment in its evidence-based review for conditions being considered for the RUSP. To support this charge, the Committee tasked APHL with conducting several surveys of state laboratories concerning NBS. The objectives of the surveys were to identify potential health impacts of adding new heritable conditions to the RUSP on the state NBS programs and to assess the feasibility of adding Pompe disease to selected states' screening panels.

APHL selected a 10-state sample for the survey. APHL considered several factors when developing the sample, including participation in a regional collaborative, newborn population size, state mandates to add conditions recommended by SACHDNC, testing facilities, and number of screenings. Condition-specific screening factors considered by APHL included laboratory and analytic requirements, equipment, and experience with screening for similar conditions. States selected for the survey were Delaware, Illinois, Iowa, Massachusetts, Minnesota, Nebraska, Oregon, South Carolina, Texas, and Washington.

Data collection will occur in two phases. APHL has already sent out an electronic survey to assess the states' genetic program and condition-specific characteristics. APHL received nine responses and anticipates receiving the final survey soon. The second phase will consist of in-depth, structured telephone interviews concerning each state's NBS program. This phase will occur over the next several months.

Preliminary survey findings show:

- 56 percent of the responding states require 6 to 12 months to make a decision about adding a condition to their screening panels
- 22 percent test for Pompe using anonymous samples
- 11 percent are considering screening for Pompe but not yet testing samples
- 78 percent conduct no screening for Pompe
- 67 percent are not currently considering routine Pompe screening
- 67 percent do not have authority to implement Pompe screening

Common challenges to implementing screening for Pompe include funding, staffing, laboratory space, and equipment and instrumentation. Fifty-six percent of the responding states indicated that they could begin screening for Pompe disease once these hurdles are overcome.

Committee Discussion

- Dr. McDonough suggested that APHL use the telephone interviews to ask states about the implementation timeline for Pompe, especially if they have not already implemented SCID and Critical Congenital Heart Defects (CCHD) screenings.
- Dr. Kemper, responding to a question about long-term outcomes, indicated that the CRW would include information on cognitive development and motor development in its report.
- Dr. Botkin requested more information on the clinical implications for children with late onset Pompe in the newborn period. Dr. Kemper reported that the CRW did not find any published protocols for managing newborns with late onset Pompe.

- Dr. Matern asked whether the CRW is investigating clinical readiness for follow up after Pompe screening. Dr. Kemper replied affirmatively. Dr. Ojodu stated that questions concerning the management of the condition will be part of the interviews.
- Dr. Matern suggested including Missouri in the survey as it recently began screening for four lysosomal conditions. Dr. Kemper indicated that APHL plans to contact the Missouri program concerning its screening process.
- Dr. Matern suggested that APHL ask the single state considering Pompe screening whether it is also considering other lysosomal screenings as part of a multiplex assay. Dr. Bocchini noted that it would be helpful to know which states are multiplexing screenings for Pompe and which are not. Dr. Kemper agreed to identify the conditions that are included in the multiplex screening along with Pompe disease.

V. Population-Based Carrier Screening

Meredith Weaver, Ph.D., Sc.M, C.G.C.
Associate Project Manager
American College of Medical Genetics and Genomics
Bethesda, MD

Dr. Weaver reviewed the activities of the Population-Based Carrier Screening Workgroup, which gathered and analyzed information on population-based carrier screening. In August 2010, HRSA partnered with the American College of Medical Genetics and Genomics (ACMG) to administer data collection, conduct analysis, and report findings. In January 2011, the workgroup defined the criteria to be used for each issue. Data collection took place in April, May, and June of that year. The workgroup provided a progress report to the Committee in May 2012 and submitted an interim report summarizing the high-level findings of the project in September.

Final Report
Areas of consensus mirrored the well-accepted principles of carrier screening, including those related to informed consent, knowledge of conflict of interest, and insurance coverage. Areas where there was a lack of consensus related to evolving technologies and moving carrier screening into the public health domain.

The recommendations focus on five main areas from a high-level perspective:
- It is desirable to consider the social issues addressed by the workgroup and the feasibility of examining them further.
- It is desirable to consider economic issues and the feasibility of examining them further.
- Psychological issues (e.g., available psychological support, implications of using information gained by screening, etc.) must be considered prior to administering population-based carrier screening.
- Education and communication issues to must be considered prior to administering any type of screening.
- It is desirable and important to consider many testing issues and the feasibility of examining them further.

The report focuses on the points that should be considered when conducting a population-based carrier screening program, both in a general sense and with respect to specific conditions.

At this time, the Committee needs to determine the level of support that it wishes to give the report. Dr. Weaver indicated that the proposed level of support is to affirm the value of population-based carrier screening and forward the report to the HHS Secretary for informational purposes only.

Dr. Copeland added that the Committee requested the report in response to the early stages of direct-to-consumer testing. There was never an intention to develop a panel similar to the RUSP because of the great variability in the impacted populations. The report provides a framework for considerations that a group or population interested in carrier screening might want to address.

Committee Discussion

- Responding to a question about the availability of the report, Dr. Copeland indicated that it would be posted on the Committee's website.
- Dr. Thompson inquired whether the workgroup tested the recommendations in the report by using an existing screening as an example. Dr. Copeland stated that the workgroup did not test the recommendations. The purpose of the report is not to set standards; instead it provides a framework and questions to guide consideration of adoption of population-based carrier screening.
- Dr. Thompson recommended developing a process similar to that used for the RUSP to identify conditions that should be screened for carrier status. Dr. Copeland indicated that it is not the intention of the current report to address the process for recommending conditions. The workgroup might consider doing so at a later point in time.
- From a strategic point of view, Dr. Guttmacher did not see any additional benefit in presenting the report to the Secretary. The report summarizes the conventional wisdom of a diverse group of stakeholders but does not ask the Secretary to take any significant action. Dr. Copeland noted that more of these types of issues will come before the Secretary as genome sequencing moves forward. The report will inform the Secretary about existing resources and work already done by the Committee.
- Dr. Cuthbert reported that similar questions about sending the report to the Secretary had been asked at the Centers for Disease Control and Prevention (CDC). The document should include an explanation of how it could be used to support decision making as new issues come forward.
- Dr. Copeland indicated that the executive summary and introduction could be reformatted to include the framework, reasoning, and etiology, which would be useful for the both the Secretary and for a more general audience. Dr. Guttmacher supported this approach.
- Ms. Cate Walsh Vockley asked whether the workgroup considered the potential to identify individuals who are affected by the conditions for which carrier screening is being done and whether the document should include a discussion of this. Dr. Weaver stated that the workgroup did not consider this issue, but it could be added to the introduction.
- Dr. Carol Greene recommended that the background information make the distinction between identifying pre-symptomatic individuals and carrier testing. The report should also address cases where carriers could be at risk of developing symptoms.
- Dr. McCabe, who serves as the editor-in-chief of *Molecular Genetics and Metabolism*, offered to work with the workgroup to develop an article that could be published in parallel to the report.

Based on the feedback received, Dr. Copeland indicated that the workgroup would revise the executive summary and introduction, and have an additional discussion about the report during the next Committee meeting.

The Committee divided into subcommittees, and held individual subcommittee webinars for the balance of the afternoon.

VI. Committee Business: February 1, 2013

A. Welcome and Roll Call

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

Dr. Bocchini welcomed the webinar participants to the second day of the meeting. Dr. Copeland took the roll for the second day. Voting members present were: Dr. Bailey, Dr. Botkin, Dr. Cuthbert, Dr. Denise Dougherty, Dr. Kelm, Dr. Lorey, Dr. Lu (late arrival), Dr. McDonough, Dr. Matern, Dr. Parisi (for Dr. Guttmacher), Dr. Thompson, Ms. Wicklund, and Ms. Williams.

Nonvoting organizational representatives participating in the webinar were:

- AAFP: Dr. Frederick Chen
- AAP: Dr. Beth Tarini
- ACMG: Dr. Michael Watson
- Association of Maternal and Child Health Programs (AMCHP): Dr. Lisa Bujno
- APHL: Dr. Susan Tanksley
- Association of State and Territorial Health Officials (ASTHO): Dr. Christopher Kus
- DoD: Ms. Theresa Hart
- Genetic Alliance: Ms. Natasha Bonhomme
- March of Dimes: Dr. Edward McCabe
- NSGC: Ms. Cate Walsh Vockley
- SIMD: Dr. Carole Greene

VII. Update on State Implementation of Screening and Data Collection for CCHD and SCID

A. CCHD Implementation and Data Collection Update

Marci Sontag, PhD
Assistant Professor, Concentration Director
Director of Epidemiology, NewSTEPs (Newborn Screening Technical assistance and Evaluation Program)
Colorado School of Public Health Department of Epidemiology
Aurora, CO

Dr. Sontag provided an update on the implementation of NBS for CCHD and data reporting across the country based on data collected by the Newborn Coalition, by the NewSTEPs survey of states, and by HRSA's Regional Genetics Collaborative. CCHD was added to the RUSP in September 2011. Subsequently, HRSA funded six demonstration projects in five states and the Northeast region to implement CCHD screening. Several other states are either conducting CCHD NBS or working toward implementation.

The legislative process for adding new conditions to the screening panel vary by state. Twenty-nine states have introduced legislation to implement the screening. Legislation is actively pending in 10 states. Four states that do not require legislation have implemented CCHD screening. The rest are considering screening or waiting for more information to become available.

The primary barrier to the implementation of CCHD screening is time and resources, specifically with regard to setting up data systems and developing surveillance systems. The second major challenge is convincing public health decision makers that the proposed algorithm and implementation approach will function as planned. Additional barriers identified by the NewSTEPs survey were buy-in from hospitals and clinicians and challenges related to the algorithm. The majority of states anticipated being able to begin screening more than six months but not more than three years after making the decision to screen.

NewSTEPs sought to determine the minimal data set for state collection needed for local use and national reporting. In general, the role of public health data in CCHD screening relates to quality assurance, surveillance, and quality improvement. Public health data collection could include aggregate data on whether or not a test was done, data on babies who failed the screening, or all available data on all screenings. Many national stakeholders are working together to think through the data collection issues. Some states are modifying existing systems. Others are considering adopting commercial systems or developing their own new systems. NewSTEPS is developing a national NBS repository and quality indicators to track metrics in state screening programs.

Next steps include developing technical assistance to help states implement CCHD screening. NewSTEPS is also working to identify partners and resources to assist states.

B. SCID Implementation Update

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

The implementation of screening for SCID represented the largest expansion of NBS since the advent of tandem mass spectrometry and the development of the RUSP. Because screening for SCID uses a DNA-based molecular test, state NBS programs have had to develop new areas of expertise or identify regional partners with the necessary expertise.

Wisconsin, Massachusetts, and the Navajo Nation were the first to begin screening. Pilot projects in California, New York, Louisiana, and Puerto Rico rapidly expanded SCID screening. Eight states began screening after the pilot projects. Currently 12 states screen for SCID, which translates into approximately 40 percent of newborns receiving an initial screening. Some states conduct selective screenings. To date, approximately 2.85 million babies representing 45 percent of newborns have been screened. Fourteen states plan to begin pilot projects or statewide screening in 2013. By the end of 2014, ACMG estimates that 60 percent of newborns will receive an initial screening. The remaining states are actively working on legislation or other approaches to expand their screening programs to include SCID.

Resources available to newborn screening laboratories through the CDC and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) include technical assistance, publication of pilot results, screening and follow up protocols, long-term follow up data sets, and expert working groups that work to refine diagnosis and treatment protocols. CDC's Clinical Laboratory and Standards Institute guidance document, "Guideline ILA-36 Newborn Blood Spot Screening for SCID by Measurement of T-cell Receptor Excision Circles," addresses the gamut of information required to begin newborn SCID screening. The Newborn Screening Translational Research Network's (NBSTRN) R4S SCID database module facilitates analytical validation of screening assays. States can use the model to aggregate and share information as they develop and implement new molecular tools.

Additional Resources
HRSA and ACMG produced online clinical decision support materials for health care providers. The Immune Deficiency Foundation created NBS tool kits for SCID advocates, pamphlets, and para-education materials. CDC, APHL, and the Jeffrey Modell Foundation funded two-year fellowships for post-doctoral candidates as well as NBS research concerning immunodeficiencies. The Immune Deficiency Foundation provides educational resources to families and states.

The NICHD-funded NBSTRN provides online resources for researchers such as a website of SCID resources, a virtual dried blood spot (DBS) repository containing several thousand characterized samples for SCID, and the Longitudinal Pediatric Data Resource (LPDR), which is available to clinicians, researchers, and public health partners for the collection of information of screened positive and diagnosed cases. The LPDR is a collaboration between the NBSTRN and the National Institute of Health's (NIH) Primary Immune Deficiency Treatment Consortium to create a longitudinal record for newborns from screening through diagnosis and full life course to support research into the trajectory of identified cases. States can use the LPDR to understand the improvement in health outcomes related to newborn screening for SCID.

Committee Discussion

- Dr. Botkin recommended that the Committee address the need to distinguish between pilot studies that are done for quality assurance purposes and those conducted for research purposes.
- Dr. Sontag stated that the survey did not include specific questions concerning barriers to follow up for CCHD, but indicated that they could be included in future surveys.

- Dr. McDonough asked how the implementation of SCID and CCHD screening would affect states' ability to add screenings for new conditions to their panels. Dr. Brower noted that SCID implementation offered states both an opportunity and a challenge, as it was the first time they used a molecular test as a first tier test. States, facilitated by the HRSA-funded regional collaboratives, shared information and worked with partners to implement their programs.
- Dr. Kus noted that importance of defining the roles of state and federal public health authorities, especially with regard to implementing Secretarial recommendations.

VIII. Update on NIH Genomic Sequencing and Newborn Screening Disorders Initiative

Tiina K. Urv, Ph.D.
Program Director
Intellectual and Developmental Disabilities Branch
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
Bethesda, MD

Dr. Urv updated the Committee on the Genomic Sequencing and Newborn Screening Disorders Initiative, which is a collaboration of NICHD and the National Human Genome Research Institute (NHGRI). In 2010, NICHD, NHGRI, and the NIH Office of Rare Diseases Research sponsored a workshop to identify elements of the trans-NIH research agenda that could lead to the application of new genomics concepts and technologies to NBS and child health. The main takeaways from the workshop formed the basis for the initiative.

Under the initiative, projects must address at least one of the following:

- For disorders currently screened for in newborns, how can genomic sequencing replicate or augment known newborn screening results?
- What knowledge about conditions not currently screened for in newborns could genomic sequencing of newborns provide?
- What additional clinical information could be learned from genomic sequencing relevant to the clinical care of newborns?

Each submitted project must include three components:

- **Genomic datasets** – Datasets must expand the scale of data available for analysis in the newborn period, specifically high-quality nucleic acid data from all or a large portion of the genome of each study participant.
- **Clinical research** – Research must focus on disorders that are currently identified by NBS or that could potentially benefit from early identification by NBS.
- **Ethical, legal, and social implications research** – This component addresses ethical, psychosocial, legal, and economic issues that might result from the implementation of genomic sequencing of newborns.

NICHD and NHGRI anticipate committing $25 million to the effort. The maximum award period is five years, with a maximum annual budget of $1.25 million per year per project. The application due date was November 19, 2012. The review process should be completed in June with the earliest anticipated project start date in July.

Committee Discussion

- Asked about the availability of the sequence data and algorithms generated by the initiative, Dr. Urv stated that availability would depend on the regulations in the states where the research is conducted.

IX. Update on MDS Muscle Disease Symposium on Newborn Screening for Duchenne Muscular Dystrophy

Jerry R. Mendell, M.D.
Professor of Pediatrics and Neurology
Director, Center for Gene Therapy
Nationwide Children's Hospital and The Ohio State University
Director of the Paul D Wellstone Muscular Dystrophy Cooperative Research Center
Columbus, OH

Dr. Mendell reported on the proceedings of a September 2012 symposium on NBS for DMD sponsored by the Muscular Dystrophy Coordinating Committee. The objectives of the meeting included the examination of all available data related to the natural history of DMD, the disease pathogenesis, the NBS method introduced in Ohio, and current therapy.

Natural History of DMD
In DMD, the absence of the dystrophin protein allows muscle fibers to tear. The tears grow larger and more numerous over time leading to scar formation and fiber loss. The natural history of DMD is defined by the pre-steroid era and is characterized by manifestation of the disease as early as 15 months, mean age of diagnosis around age five, wheelchair dependency by 10 years of age, and the appearance of scoliosis by age 12. Death usually occurs after the late teen years.

Newborn Screening for DMD
DMD NBS screening began in 1979, is done in multiple countries, and produces a consistent incidence of approximately 1 in 5,000 newborn males. Generally, the screening protocol is a single tiered system, with rescreening for individuals with elevated creatine kinase (CK) at six weeks of age followed by DNA analysis for DMD mutation. In 2004, the CDC funded a study by Nationwide Children's Hospital in Ohio to develop a two-tiered testing system. Under this new system, the initial DBS sample receives both Creatine Kinase (CK) and DNA testing.

Major outcomes of the study were:

- The proposed two-tier system fits well with standard obstetric practice in the United States.
- The cost to screen is low ($1 per CK screen and $150 for DNA sampling).
- Raising the CK threshold to 1,000 U/L would reduce the need for screening to 40 per 1,000.
- The cost is significantly less that diagnosing a toddler or young child.
- The ability to test for other muscular dystrophy genes is an added value.

Potential Treatments
Dr. Mendell reviewed several studies of the effects of glucocorticoids. Dr. Mendell also described exon skipping, a molecular treatment for DMD.

Committee Discussion

- Dr. Botkin asked whether CK testing, followed by DNA analysis, would identify carrier females. Dr. Mendell indicated that there is no reason to suspect that carriers could not be identified by elevated CK levels. He anticipated adapting models currently used for identifying carriers of other conditions.
- Dr. Mendell, in response to a question about confirmation of DMD by muscle biopsy in the Ohio study, stated that DNA analysis is the gold standard for diagnosis of this disease. It is now possible to identify more than 95 percent of boys with DMD.
- Asked about the parental permission model used for the clinical screening portion of the study, Dr. Mendell stated that the project used a consent model, which was mandated by the CDC.
- Asked about the availability of exon skipping treatment, Dr. Mendell stated that it is under study protocol. There is strong support for presenting it to the FDA. FDA will determine whether it will be fast-tracked.

- Dr. Matern asked whether Dr. Mendell plans to ask the Committee to consider DMD for NBS. Dr. Mendell planned to make a formal nomination to the Committee.
- Ms. Vockley asked if there has been any clinical evidence from follow up concerning false negatives and whether any patients had been identified as having mutations consistent with Becker muscular dystrophy. Dr. Mendell explained that the distinction between DMD and Becker dystrophy in infancy relates mostly to a gene being in or out of frame. He anticipated that it would be difficult to distinguish the disease in infants with in-frame mutations. With regard to false negatives, the researchers asked that all patients receive a CK screen at six months. In general, initial CKs under 2,000 U/L returned to normal. The study protocol called for follow up in MDA clinics for patients with elevated CK levels. He anticipated that a similar approach would be used for an actual screening protocol.

X. Subcommittee Reports

A. Subcommittee on Laboratory Standards and Procedures

Carla Cuthbert, Ph.D.
CDC Ex-Officio (alternate)
Centers for Disease Control and Prevention
Atlanta, GA

Dr. Cuthbert summarized the presentations made during the Subcommittee's meeting.

APHL
Dr. Ojodu reported on the activities of the Newborn Screening and Genetic and Public Health Program at the APHL. This year marks the fiftieth anniversary of NBS, and there will be multiple activities marking the milestone. APHL will send an exhibit on NBS to state houses, NBS laboratories, and health departments in 13 states; participate as an exhibitor at several professional meetings; developing a coffee table book and associated e-book on NBS; and use social media to conduct NBS outreach. APHL will host a reception and awards ceremony in Washington, D.C., in September with the goal of informing elected officials about the benefits of NBS. In May, the Newborn Screening and Genetic Testing Symposium, which is cosponsored by the APHL and the CDC, will take place at the same time as the International Society for Neonatal Screening meeting.

APHL is working with the CDC on the Molecular Assessment Program, which helps states address specific concerns as they implement molecular testing into their routine workflows. The goal is to provide feedback to NBS laboratories on their molecular screening capabilities and suggest improvements through a peer review process. Program staff have conducted site visits in five states.

Dr. Ojodu also provided an update on the NewSTEPs programs. The update included a review of the program's mission, vision, and goals; a summary of the program's accomplishments to date; and the incorporation of quality indicators and case definitions to provide continuous quality improvement.

National Library of Medicine
Ms. Swapna Abhyankar with the National Library of Medicine (NLM) discussed NBS information technology initiatives, with an emphasis on the creation of Logical Observation Identifiers Names and Codes (LOINC) terms for CCHD. NLM worked with Children's National Medical Center, HRSA, the CCHD Technical Assistance Committee, and Oz Systems to create the terms, which align with the HL7 Implementation Guide. The terms have been submitted to the Regenstrief Institute for assignment of codes. NLM is also working on mutation nomenclature and has created a LOINC answer list for cystic fibrosis genetic mutation results. The library is working with the Regenstrief Institute to incorporate the mutation synonyms into the LOINC answer list. To continue this work, NLM needs to collect information from states on the mutations for which they screen and the ways in which they are reported.

Tyrosinemia Type 1 Screening
Dr. Matern addressed the evaluation of markers currently used for NBS for tyrosinemia Type 1. His remarks focused on the shift away from using tyrosine as the testing marker toward the use of succinylacetone (SUAC), which is specific to tyrosinemia Type 1 but not detectable by routine NBS, and the status of states' transition to the use of SUAC. Screening options to be considered include removing tyrosinemia Type 1 from the NBS panel, lowering the cutoff for tyrosine, or implementing an alternative marker.

To date, CDC has interviewed representatives of 14 NBS laboratories, half of which measure SUAC and half of which do not, to identify the challenges related to tyrosinemia Type 1 screening. The Office of Management and Budget recently approved the CDC's request to expand the survey to all U.S. NBS laboratories. Dr. Cuthbert reviewed several of the survey questions and indicated that the Subcommittee would provide a detailed presentation of this topic to the Committee once data collection is complete.

Committee Discussion

- Dr. Bocchini suggested that the tyrosinemia Type 1 report be placed in the *Morbidity and Mortality Weekly Report (MMWR)*. Dr. Cuthbert indicated that the Subcommittee would obtain feedback from the SACHDNC as part of the effort to prepare a MMWR submission.
- In response to Dr. McCabe's question concerning states that do not screen for tyrosinemia Type 1, Dr. Cuthbert indicated that the responses to the full survey should provide a better understanding of the reasons for not screening.
- Dr. Greene pointed out that the Committee would break new ground by recommending screening for a specific metabolite or a specific method of testing. Dr. Cuthbert indicated that the survey includes a question on the impact of a recommendation by the SACHDNC concerning the use of SUAC. Dr. Kus pointed out that the Committee's recommendations of conditions are based, in part, on the analysis of the data provided by a specific test. Dr. Bocchini indicated that an article in MMWR could inform states about the relative value of one procedure over the other, instead of having the Committee make a recommendation on a test.
- Dr. McCabe reminded the Committee that the joint HRSA/AAP committee recommended the standardization of testing and technologies nationwide.
- Dr. Tanksley recommended that the CDC survey include a question concerning the number of diagnosed cases of tyrosinemia Type 1 and the number of infants screened using both methods.
- Dr. Greene cautioned against concluding that the number of infants identified through NBS is equal to the incidence of the disease. There is an expectation that some infants will be missed because tyrosine is not elevated.
- Dr. Matern identified the addition of testing for SUAC to the screening programs as the primary issue, not the test used to conduct the screen.

B. Subcommittee on Education and Training

Don Bailey, Ph.D., M. Ed.
Subcommittee Chair
Distinguished Fellow
Early Childhood Development
RTI International
Research Triangle Park, NC

The three goals of the Subcommittee meeting were:

- Priority A: Finalize the process by which the Committee reviews conditions for possible screening outside the newborn period and review the status of recommendations for an exemplar condition
- Priority B: Receive an update on the CDC/APHL NBS fiftieth anniversary awareness activities and identify ongoing strategies for NBS awareness after 2013
- Priority C: Review materials on plain language summaries of conditions that have been nominated and reviewed, but not recommended for inclusion in the RUSP

Priority A
The Subcommittee will use an exemplar condition/case study approach to explore the issues that would arise if the Committee were to consider policies and priorities related to screening after the newborn period. During the Subcommittee meeting, the members selected three conditions – fragile X syndrome, long QT syndrome, and Wilson's disease – as exemplar conditions. The Subcommittee plans to work with stakeholders to identify challenges and opportunities, education and training needs, and infrastructure requirements associated with childhood screening related to these conditions and develop a report of lessons learned and next steps for presentation to the Committee during the winter 2014 meeting. The Subcommittee also considered whether each condition, based on initial symptoms, would benefit from population screening or targeted screening.

Priority B
For this priority, the Subcommittee focused its efforts on promoting NBS among the public and professionals by providing input on APHL's 2013 NBS awareness campaign. Since Dr. Cuthbert provided a summary of Dr. Ojodu's remarks about the campaign activities, Dr. Bailey highlighted aspects of the campaign related to the Subcommittee's work:

- The campaign target audiences include expectant parents, clinicians, scientists, policy makers, and state and national media.
- Core messages focus on the benefits of screening and the need to quickly follow up on results.
- The Subcommittee will provide feedback on one of the educational brochures within the next few days.

Priority C
The goals of the Subcommittee's work with the CRW are to increase transparency concerning the Committee's reviews and to support future nominators' preparation of application packets. Plain language summaries of evidence reviews will provide a blueprint for future nominators, as will improved information on the Committee's website. The Subcommittee envisions creating a case study book concerning lessons learned to help future nominators.

HRSA awarded a contract to Atlas Research to help the Subcommittee develop the summary report on evidence reviews. The document will provide an overview of the SACHDNC, describe the RUSP and the process by which conditions are added to it, and present detailed examples of nominations that were not ready for evidence review or inclusion on the RUSP. It will illustrate the challenges and stumbling blocks conditions face as they move through the condition review process. The Subcommittee has already reviewed and provided feedback on draft summaries for two conditions and anticipates having a draft document available for initial review within a few weeks. The final document will be ready for review during the next Committee meeting.

Committee Discussion

- Dr. Bailey responded to a question from Dr. Kus concerning NBS for fragile X syndrome by stating that the Subcommittee recognized that NBS would be possible, but that it is not as ready for implementation as other conditions. None of the selected conditions should be excluded from consideration for NBS.

C. Subcommittee on Follow-up Treatment

Carole Greene, M.D.
Organizational Representative
University of Maryland Medical System Pediatric Genetics
Baltimore, MD

Christopher Kus, M.D. M.P.H.
Organizational Representative
Associate Medical Director
Division of Family Health
New York State Department of Health
Albany, NY

Dr. Greene reported that the Subcommittee meeting began with two reports on ongoing projects:

- **Inborn Errors of Metabolism (IBEM)** – Dr. Susan Berry reported on a HRSA project to develop consensus concerning the collection of outcomes data for children with IBEM detected by NBS. The project achieved consensus on core data elements and outcome measures for 40 IBEMs for a multi-center research project. The project is beginning to develop database reports, accepting more centers into the project, and identifying funding strategies for data collection.
- **NBSTRN** – Dr. Brower provided an update on the LPDR.

Active Subcommittee Projects
The Subcommittee has two active projects supporting its priorities:

- **Early Hearing Detection and Intervention** – This project identifies lessons learned from NBS hearing screening that could be applied to CCHD screening and point of care screenings. The Subcommittee discussed the Newborn Hearing Screening Survey and focused on the use of the NBS card or the electronic birth registration process to obtain hearing screening results, and the importance of linking multiple screening efforts electronically. The Subcommittee anticipates sharing a draft lessons learned document with the full Committee at its next meeting
- **A Framework for Assessing Outcomes from NBS** (formerly known as the Outcomes after NBS project) – The goal of this project is to develop a framework that can be used to determine the data needed to assess whether NBS for a particular condition results in the anticipated benefits. The framework asks basic questions related to detection and direct interventions, access to care, and key outcomes for condition-specific responses, potential measures, data resources, and key components. Next steps include comparing the framework with other standard data element sets, revising the framework based on feedback from stakeholders, identifying gaps in data sources, and presenting the framework and report to the SACHDNC at its next meeting.

Update on Medical Foods
Ms. Christine Brown, Executive Director, National PKU Alliance, provided an update on medical foods from the advocacy perspective. There is no federal authority to require state coverage of medical foods. Additionally, there is no right to appeal if a state's benchmark health insurance plan for the state health insurance exchange does not cover medical foods. Advocates continue to work with Congress in an effort to reintroduce the Medical Foods Advocacy Act.

Ms. Kathy Camp, NIH Office of Dietary Supplements, provided an overview of NIH projects to improve the design and quantity of evidence-based research on medical foods and nutritional supplements. NIH also provides technical support to professional organizations working on evidence-based guidelines as well as technical support concerning systems issues, such as definitions and coding, that could affect access.

Although the Subcommittee is following issues related to medical foods, it has no active projects in this area.

The Subcommittee requested that the Committee include a discussion of the impact of essential health benefits decisions on children with heritable conditions on its next meeting agenda.

Committee Discussion

- In response to a question about the use of the term "justification" in the assessment framework, Dr. Greene noted that the term referred to the reason for screening. The Subcommittee welcomes comments on the framework.
- Dr. Chen noted that the federal government is not generally involved in the development of state essential health benefits packages, which would result in a patchwork of coverage. Dr. Kus highlighted the need to track the limitations of the essential health benefits packages for special needs populations. Dr. Greene thought it would be helpful to compare the percentage of denials, for medically necessary therapies or evaluation, before and after the institution of essential health benefits packages.
- Ms. Brown reported that all of the states have submitted their essential health benefits plans to the Centers for Medicare & Medicaid Services (CMS). They can be found on the CMS website.

XI. Adjournment

Dr. Bocchini thanked the Committee members, liaisons, and organizational representatives for their attention and patience during the webinar. He acknowledged the challenges of meeting virtually, and welcomed comments on the preferred format for future meetings.

Dr. Copeland has resigned her position to accept a new job. Dr. Bocchini thanked Dr. Copeland for her contributions to the work of the Committee and in her help in facilitating the work of the Committee and its Subcommittees, and wished her the best of luck in the next phase of her career.

Dr. Bocchini adjourned the meeting at 1:02 p.m.