Discretionary Advisory Committee on Heritable Disorders in Newborns and Children

Summary of 1st Meeting
May 16-17, 2013
Webinar

The Discretionary Advisory Committee on Heritable Disorders in Newborns and Children (DACHDNC) was convened for its 1st meeting at 1:00 p.m. EDT on Thursday, May 16, 2013, as a webinar. The meeting was adjourned at 2:19 p.m. EDT on Friday, May 17, 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: May 16, 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. Joseph Bocchini welcomed the webinar participants to the first meeting of the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children (DACHDNC), which was chartered to fulfill the same mission as its predecessor committee, the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC). He provided a brief overview of the meeting agenda, offered instructions on how to attend the meeting in webinar format, and conducted roll call for the first day of the meeting. Voting members present were: Dr. Don Bailey, Dr. Bocchini, Dr. Denise Dougherty, Dr. Alan Guttmacher, Dr. Charles Homer, Dr. Kellie Kelm, Dr. Fred Lorey, Dr. Michael Lu, Dr. Stephen McDonough, Dr. Dietrich Matern, Ms. Catherine Wicklund, and Ms. Andrea Williams. Ms. Debi Sarkar served as the Designated Federal Official (DFO).

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
- American College of Medical Genetics (ACMG): Dr. Michael Watson
- Association of Maternal and Child Health (AMCHP): Ms. Lacy Fehrenbach (alternate for Ms. Lisa Bujno)
- Association of Public Health Laboratories (APHL): Dr. Susan Tanksley
- Association of State and Territorial Health Officials (ASTHO): Dr. Christopher Kus
- Department of Defense (DoD): Dr. Adam Kanis
- Genetic Alliance: Ms. Natasha Bonhomme
- March of Dimes: Dr. Edward McCabe
- National Society of Genetic Counselors (NSGC): Ms. Cate Walsh Vockley
- Society for Inherited Metabolic Disorders (SIMD): Dr. Nicola Longo (alternate for Dr. Carole Greene)

Dr. Bocchini welcomed the new DoD representative to the committee, Dr. Kanis.

II. Subcommittee Reports

Representatives from each subcommittee summarized their most recent meetings, which were held earlier in the day.

A. Subcommittee on Laboratory Standards and Procedures

Susan M. Tanksley, Ph.D.
Manager, Laboratory Operations Unit
Texas Department of State Health Services
Austin, TX

Dr. Tanksley reported that the Subcommittee began its meeting by reviewing its priorities:

- To review new enabling and disruptive technologies;
- To provide guidance to state newborn screening (NBS) programs concerning laboratory implementation, integration, follow-up, and quality assurance; and,
- To establish a process for the regular review and revision of the Recommended Uniform Screening Panel (RUSP).

The Subcommittee's discussion focused on an update on the Clinical and Laboratory Standards Institute guidelines for Severe Combined Immunodeficiency (SCID), which falls under the second priority. Dr. Tanksley informed participants about a monthly Newborn Screening Translational Research Network (NBSTRN) conference call that provides guidance on laboratory implementation, follow-up, and quality assurance.

The Subcommittee also discussed the new NBSTRN SCID guideline, *NBSO 6A: Newborn Bloodspot Screening for Severe Combined Immunodeficiency by Measurement of T-Cell Receptor Excision Circles*, which was published in April. The document includes sections on SCID terminology, biology, biological and clinical features, real-time polymerase chain reaction assays, implementation of the assays, follow-up activities, communication, and diagnostic testing. Appendices can serve as aids to NBS programs as they implement SCID screening. Appendix A lists four categories of conditions that might or might not be picked up by the assays and the associated immune deficiency. Dr. Tanksley briefly described each category and a new type of assay that might be added to the guideline in the future.

Possible future Subcommittee agenda items included the implementation of Pompe disease screening, pending the DACHDNC's vote on May 17; the tyrosinemia type 1 survey report; genomic sequencing initiatives in the NBS realm; and the possibility of presenting the Mayo study that compares technologies for lysosomal storage disorders scheduled for completion in the autumn.

B. Subcommittee on Education and Training

Don Bailey, Ph.D., M.Ed.
Distinguished Fellow
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Dr. Bailey reminded the participants that the Subcommittee's charge is to review education and training (E&T) resources, identify gaps in E&T, and make recommendations regarding parents, the public, health professionals, screening program staff, and hospital and birthing facility staff.

The Subcommittee discussed the challenges inherent in meeting by webinar instead of in person. The members agreed that webinars are particularly challenging because they eliminate the opportunities for contact with the various advocacy groups and stakeholders with which the Subcommittee interacts, making it more difficult for the Subcommittee to accomplish its mission. On behalf of the Subcommittee members, Dr. Bailey requested that Dr. Bocchini, in his role as DACHDNC Chair, make a request to the Secretary of Health and Human Services (HHS) to reinstate at least some regular in-person Committee meetings.

Dr. Bailey summarized the Subcommittee's discussions concerning its three priority areas:

- **Priority C, Guidance for Advocacy Groups on the Nomination and Review Process**: An ongoing project of the Subcommittee is the development of public-friendly summaries of successful evidence reviews and unsuccessful condition nominations. These summaries are targeted toward groups considering making a nomination and are designed to help them prepare successful nomination packages. Atlas Research developed a draft document and the Subcommittee working group chairs are reviewing the document, which will be sent out to all Subcommittee members for review and feedback. The earliest the final draft will be ready for full Committee review is September.
- **Priority B, Promote NBS Awareness among the Public and Professionals**: The Subcommittee continues to provide support and input on the NBS 50th anniversary awareness campaign conducted by APHL with support from the Centers for Disease Control and Prevention (CDC). The Subcommittee also discussed awareness goals that it should take on after the completion of the anniversary campaign. The members decided to return to the issue of cross-state harmonization of screening targets, which has been a goal of the Committee since its inception. Because all states have not adopted the RUSP, there are discrepancies among the various state programs. Subcommittee members identified state legislators, state NBS advisory boards, and state public health departments as potential target audiences. The proposed focus of the effort would be educating these groups about the existence of the DACHDNC, its process for making recommendations, and the reasons that all states should be screening for the same conditions. The members anticipated that the Subcommittee would focus on integrating and coordinating the activities of other groups doing this type of work, as the Subcommittee does not have the resources to undertake a campaign of its own.
- **Priority A, Track, Provide Input, and Facilitate National E&T Initiatives**: The Subcommittee has been working on a project to identify a heritable condition that is not on the RUSP and for which screening and treatment would occur at a later point in child development. In January, the Subcommittee identified three exemplar conditions. The Subcommittee discussed fragile X syndrome in light of six questions it anticipates asking about each exemplar condition. Questions address current patterns of identification of affected children, harms associated with later identification, the possibility of ameliorating these harms through earlier identification, the feasibility and desirability of population screening for the condition, the benefits of population screening, and the stakeholder groups that could be engaged in this effort. The Subcommittee plans to review a similar report from CDC and the Genetic Alliance for implications for its own work. The Subcommittee anticipates reviewing the remaining exemplar conditions in September and January 2014 and preparing a draft report for DACHDNC in the spring of 2014.

Committee Discussion

- Dr. Bocchini asked whether the Committee members supported the Subcommittee's request to reinstate in-person meetings. A Committee member advocated for a mix of in-person meetings, which facilitate interaction with advocacy groups, and webinars, which do not require travel. Another Committee member favored in-person meetings because they support the development of relationships between the various groups and within the Committee itself.

- A Committee member asked whether harmonization would refer only to those states that have not fully adopted the RUSP or whether it would also include states that have added conditions that are not on the RUSP. Dr. Bailey indicated that the initial focus should be on full adoption of the RUSP. He anticipated that the issue of inclusion of conditions not currently on the RUSP would be addressed in future discussions. A Committee member recommended that the Committee should look into ways to encourage states to incorporate new screenings into their panels as they are added to the RUSP, with an emphasis on the states that do not have a process for doing so.
- Dr. Tanksley reported that the APHL's Newborn Screening Technical Assistance and Evaluation Program (NewSTEPs) is starting an assessment of the education needs of state administrators, policy makers, and legal departments. The assessment will use key informant interviews to identify an educational role for NewSTEPS. NewSTEPS plans to work with groups such as the E&T Subcommittee to develop more informational and educational tools for these groups. APHL's Newborn Screening and Genetics and Public Health Committee also plans to work on this issue. Dr. Bailey hoped that this type of work would be done primarily by groups such as NewSTEPS and that the Subcommittee could serve as the underlying stimulus and provide needed feedback.
- An organizational representative noted the need for more information concerning population-based screening after the newborn period, including related insurance issues. Dr. Bailey replied that the Subcommittee had only begun to discuss issues concerning the timing of screening, who would do it, and associated payment mechanisms.
- An unidentified participant used the web chat function to ask about the assistance and guidance that would be provided to those groups that have already nominated a condition that was not approved. Dr. Bailey anticipated that the Subcommittee would address this in more depth in the future.

Ms. Williams requested that Dr. Bocchini consider preparing a formal request to the Secretary to reinstate in-person meetings. The Committee discussed and agreed with that Dr. Bocchini prepare a formal request to the Secretary to reinstate in-person meetings.

C. Subcommittee on Follow-Up and Treatment

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

Dr. Kus reported that the Subcommittee recapped the information presented during the previous Committee meeting concerning the applicability of lessons learned from early hearing detection and intervention to Critical Congenital Heart Disease (CCHD) screening. Two of the lessons learned related to electronic reporting between state health departments, hospitals, and providers and to the importance of state-level data for developing the screening system. The Subcommittee anticipates developing a draft paper on this subject and presenting it to the Committee in September.

The Subcommittee also discussed the presentation on the Patient Protection and Affordable Care Act (ACA) given during the previous Committee meeting. The members discussed the need for a follow-up panel that deals with the possible effects of the ACA on children in the NBS program. Issues that could be addressed by the panel include payment for screening and follow-up treatment, the effects of the state-level benchmark plans on coverage for this population, and the effect of Accountable Care Organizations on outcomes for this population. Dr. Kus hoped that a panel discussion on the ACA could be included in the September DACHDNC agenda. The Subcommittee also discussed how it would track the ACA implementation and its effects on

children with heritable conditions, specifically with regard to measures of how well this population is covered under the ACA.

A discussion occurred on the direction of its work of the Subcommittee on developing a framework for assessing outcomes of NBS, using sickle-cell disease as an exemplar condition. The Subcommittee has been working in the correct direction and will continue to develop a framework that could be applied to many conditions.

Committee Discussion

- Dr. McCabe reported that the March of Dimes' Office of Governmental Affairs is doing a lot of work related to the ACA and that the organization would like to be involved in the panel.
- Dr. Watson reported that the Health Resources and Services Administration has added a focus on the ACA and how genetic diseases are represented in the essential health benefits. ACMG is developing assessments to determine what is and is not represented in the ACA.

With no additional comments on the subcommittee reports. Dr. Bocchini thanked the members for their participation and adjourned the meeting until 10:00 a.m. the next morning.

III. Committee Business: May 17, 2013

Joseph A. Bocchini, Jr. M.D.
Committee Chair
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Louisiana State University
Shreveport, LA

Dr. Bocchini welcomed the Committee members, organizational representatives, and other webinar participants to the second day of the meeting. After reviewing the guidelines for participating in the webinar, he took the roll. Voting members present were: Dr. Bailey, Dr. Bocchini, Dr. Coleen Boyle, Dr. Dougherty, Ms. Melissa Parisi (alternate for Dr. Guttmacher), Dr. Homer, Dr. Kelm, Dr. Lorey, Dr. Lu, Dr. McDonough, Dr. Matern, Ms. Wicklund, and Ms. Williams. Dr. Christopher DeGraw served as the alternate for Dr. Lu during the afternoon session. Ms. Sarkar served as the DFO.

Nonvoting organizational representatives participating in the webinar were:

- AAFP: Dr. Chen
- AAP: Dr. Tarini
- ACMG: Dr. Watson
- AMCHP: Ms. Lacy Fehrenbach (alternate for Ms. Bujno)
- APHL: Dr. Tanksley
- ASTHO: Dr. Kus
- DoD: Dr. Kanis
- Genetic Alliance: Ms. Bonhomme
- March of Dimes: Dr. McCabe
- NSGC: Ms. Vockley
- SIMD: Dr. Georgianne Arnold (alternate for Dr. Greene)

IV. Public Comment

Dr. Bocchini acknowledged the many letters received by the SACHDNC and the DACHDNC supporting the addition of Pompe disease to the RUSP.

Dean Suhr, Advocate, MLD (Metachromatic Leukodystrophy) Foundation: Mr. Suhr hoped to convene a town hall meeting to discuss the requirement that a viable therapy must exist before a condition can be added to the RUSP. The meeting would provide an opportunity for industry representatives, DACHDNC representatives, and advocates to share their perspectives and insights. Screening for conditions without viable therapies would prevent prolonged diagnostic odysseys and result in improved quality of life for patients and affected families.

Tiffany House, President, Acid Maltase Deficiency Association: Ms. House requested that the DACHDNC add Pompe disease to the RUSP. Diagnostic odysseys for patients with the infantile form of the disease can be fatal. For late onset patients, the average time to diagnosis is 10 years, during which they suffer from deterioration of their conditions as well as emotional and psychological stress. Earlier diagnosis has the potential to empower patients and their families through knowledge about the disease and enable them to make informed decisions concerning their lives and medical treatments. Inclusion of the Pompe disease screening on the RUSP will save the lives of patients with the infantile form and prevent the diagnostic odyssey faced by late-onset patients.

Alicia Blackington, United Pompe Foundation: Ms. Blackington shared her experience as a late-onset Pompe patient, her diagnostic odyssey, and her participation in three Genzyme clinical trials. She stressed that she would have made different choices for her life had she known about her disease earlier. Ms. Blackington reported that the time required for diagnosis ranges from six months to 10 years, at which point damage has already been done. Having early knowledge of one's diagnosis is priceless.

Priya Kishnani, Clinician, Duke University Medical Center: Dr. Kishnani described the advances in treatment options for Pompe patients (and the resulting improvement in outcomes) and stressed the importance of early diagnosis (before two months of age). She stressed that many of the questions raised since the condition was nominated have been answered. Genotyping can predict which patients will have classic infantile Pompe disease, methods exist to deal with patients with pseudodeficiency, and there is an extremely low rate of false positives in screening. Dr. Kishnani stressed the importance of NBS for Pompe disease both for lifesaving purposes and for quality of life and informed life choices.

V. Final Evidence Review – Pompe Disease

A. Summary of the Condition Review Workgroup Report

Alex Kemper. M.D., M.P.H., M.S.
Condition Review Workgroup
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Duke University
Durham, NC

Dr. Kemper thanked the members of the Condition Review Workgroup (CRW) for their work on the Pompe disease nomination. He indicated that he would be responsible for describing key findings from the systematic evidence review, Dr. Lisa Prosser would address the projected population-level benefits of adding the Pompe disease screening to the RUSP, and Mr. Jelili

Ojodu would report on the current capacity of state NBS programs to undertake comprehensive screening for Pompe disease.

Pompe disease is caused by a deficiency of acid α-glucosidase (GAA), which leads to the accumulation of lysomal glycogen. It is an autosomal recessive disorder with more than 300 identified mutations. There are two main categories of Pompe disease: infantile form and late-onset form. The infantile form, in which onset occurs within the first year of life, is considered the more severe form. Infantile Pompe disease with cardiomyopathy is considered the "classic" form and is characterized by progressive hypertonia and cardiomyopathy. Death usually occurs during the first year of life if the disease is not treated. Infantile-onset Pompe disease without cardiomyopathy is the "non-classic" form. These patients survive longer without treatment, but usually die in early childhood. Individuals with late-onset Pompe disease generally develop symptoms after one year of life; most seek care in adulthood. These individuals typically receive their diagnoses eight to 10 years after developing symptoms. Death generally occurs 27 years later. The disease is characterized by mild weakness, slowly progressive myopathy, and variable long-term outcomes without treatment including wheelchair dependence, ventilator assistance and respiratory failure.

Pompe disease carriers have below normal GAA enzyme activity levels and can be identified by screening.

Individuals with pseudodeficiency have low measured GAA enzyme activity levels but do not develop the disease. Pseudodeficiency is associated with two specific mutations and can be diagnosed through genotyping.

Individuals who are cross-reacting immunologic material (CRIM) positive (CRIM+) make some endogenous enzyme, which may or may not be functional. CRIM negative (CRIM-) individuals make no enzyme. CRIM- individuals can develop high titres of antibodies that neutralize enzyme replacement therapy (ERT) and lead to poor outcomes. Mutation analysis can be used to determine whether a patient is CRIM+ or CRIM-.

NBS for Pompe disease is based on GAA enzyme activity measured in dried bloodspots. Screening can be done in one of three ways: fluorometric assay, tandem mass spectrometry, and digital microfluidics. There is no available data on the relative performance of these three methods in high-throughput settings; research on this is underway, and results should be available in approximately one year.

Diagnosis is based on low functional GAA enzyme levels. Genotyping can rule out pseudodeficiency, identify carriers, predict which form an individual will have, and predict CRIM status. Diagnosis of Pompe disease is a two-step process consisting of an initial positive screening result followed by a blood sample used to confirm low GAA enzyme activity level and to conduct genotyping.

Dr. Kemper reported that the CRW received input from a panel of technical experts, reviewed 73 reports, and benefited from a series of key informant interviews that helped put the information gathered by the Workgroup into context.

The overall incidence of Pompe disease in the United States is approximately 1 in 28,000. The infantile-onset form affects approximately 28 percent of those with Pompe disease. Approximately 85 percent of the infantile-onset form of Pompe cases are the classic form and the remainder are the non-classic form. Approximately 75 percent of the individuals with classic infantile-onset Pompe disease are CRIM+. Approximately 72 percent of Pompe disease cases are the late-onset form. Pseudodeficiency occurs in less than one percent of births in the United States.

Dr. Kemper summarized the finding of the anonymous dried bloodspot study conducted by the University of Washington. Out of approximately 112,000 samples, four were consistent with late-

onset Pompe disease, four were consistent with carriers, three were consistent with carriers with one pseudodeficiency allele, and six were consistent with heterozygotes for pseudodeficiency. This study identified no cases of infantile Pompe disease. Based on these figures, the data can be extrapolated to an estimated incidence of one in 27,800. Based on the study findings, approximately 0.015 percent of screened babies would require diagnostic recall for blood samples or GAA enzyme activity level tests and genotyping. The overall predictive value based on genotyping was 24 percent across all types of Pompe disease.

Dr. Kemper also reported on the data available from the Missouri NBS screening program, which began screening for Pompe disease on January 15, 2013. Through April 29, the State screened almost 26,000 samples and found one case of likely classic infantile Pompe disease, one case of non-classic infantile-onset disease, one case of late-onset Pompe disease, two carriers, one case of pseudodeficiency, and three false positives. Based on these figures, the overall incidence of Pompe disease, regardless of type, would be one in 8,657. The overall positive rate (those requiring diagnostic follow-up) would be 0.03 percent, and the overall positive predictive value would be 33 percent. Because of the small number screened, Dr. Kemper cautioned that these numbers could change over time.

The Taiwan NBS program has used fluorometric assays to test almost 474,000 samples. From these samples, the program identified nine cases of infantile-onset Pompe disease and 26 cases of later-onset Pompe disease (later onset cases include the non-classic infantile form of the disease). Over time, the algorithm used has changed; early on, the threshold for a positive screening result was much lower than it is now. The false positive rate was higher due to the higher proportion of individuals with pseudodeficiency. The screening program now uses a two-tiered approach. Using modeling to apply the two-tiered system to earlier results, the program determined that it would not have missed any of the infantile-onset patients and would have detected 24 of the 26 later-onset patients. The overall incidence for the Taiwan program is one in 16,919, with an overall positive rate of 0.053 percent. The overall positive predictive value is greater than 90 percent.

Prior to the availability of ERT, Pompe patients had a median age at symptom onset of two months of age with median age of diagnosis of 4.7 months. The median age at which infantile-form patients required mechanical ventilation was 5.9 months (29 percent of babies) and the median age of death was 8.7 months. When patients receive ERT by six months of age, Pompe patients had a 95 percent reduction in their risk of death and an 87 percent reduction in the risk of invasive ventilation at 52 weeks. Overall survival at 36 months was 72 percent and 49 percent remained ventilator free. These results came from an early study of the effectiveness of ERT, which was conducted prior to the availability of immunotherapy techniques now in use. As a result, the four CRIM- individuals in the study had significantly worse outcomes. Dr. Kemper presented data from the Pompe Disease Registry that suggests that there is an improvement in survival rates at two and three years of age for infants that begin ERT prior to three months of age when compared to infants beginning ERT treatment at or after three months of age. Similar differences appear with regard to ventilator free survival. When this analysis is applied to the babies detected by the Taiwan screening program, the rates of survival and ventilator-free survival are better (these individuals are all still alive).

Dr. Kemper used the Taiwan experience to look more deeply at the benefits of screening and early initiation of treatment. NBS leads to significantly earlier diagnosis (diagnosis at 22 days instead of at 3.6 months). Infants with the infantile form who were diagnosed through screening had a 100 percent survival rate at two years of age; those who were diagnosed clinically had a survival rate of 89 percent. The first group was 100 percent ventilator free at two years, and 67 percent of the second group were ventilator free.

The development of antibodies to ERT in CRIM- patients, all of whom have the classic infantile form of the disease and require ERT, can lead to poorer outcomes. When immunotherapy is administered in early infancy, it can protect against the development of neutralizing antibodies. A

small study indicates that initiation of immunotherapy after ERT has been started is not as effective in protecting against the development of antibodies.

There have been no trials of pre-symptomatic use of ERT for patients with late-onset Pompe disease. Treatment decisions are generally based on clinical findings. There are no standards for follow-up. When considering early detection of late-onset Pompe disease, harms such as central line placement, economic costs, and psychosocial harms, should be taken into consideration. ERT for symptomatic individuals has been shown, in a randomized clinical trial, to improve respiratory status and motor function. A key consideration is that pre-symptomatic treatment could benefit late-onset Pompe patients by protecting against muscle damage. Muscle damage cannot be reversed by ERT, so post-symptomatic treatment might have limited benefits.

Dr. Kemper summarized the findings of the CRW:

- Screening identifies newborns with all forms of Pompe disease, not just those with the infantile form.
- Pseudodeficiency is less common in the United States than it is in East Asia; therefore, the United States should not experience the problems with false positives that have occurred in East Asian populations.
- There is good evidence that early identification of infantile Pompe disease, as compared to clinical detection, improves outcomes.
- Most cases of infantile Pompe disease occur in CRIM+ patients.
- Immunotherapy in CRIM- persons appears to improve outcomes. Early immunomodulation seems to be more effective than late immunomodulation.
- Most cases of Pompe disease identified by NBS will be the late-onset form.
- There is no direct evidence that pre-symptomatic treatment of late-onset Pompe disease is related to better outcomes; however, there is biologic plausibility that it would be.

B. Assessing Population-Level Benefits Using Decision Analysis

Lisa Prosser, Ph.D., M.S.
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Associate Professor, Department of Health Management Policy
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Dr. Kemper alerted the DACHDNC members that the results of the decision analysis (DA) presented were not the same results as those in the report that they received prior to the meeting. Since the report was distributed, additional data from the Pompe Disease Registry became available. This data has been incorporated into Dr. Prosser's presentation.

Dr. Prosser described DA as a validated approach for evidence synthesis that can be used as an alternative or complement to traditional meta-analysis. DA is particularly useful in situations where there is little published evidence available. The objective of this part of the condition review process is to use simulation modeling to project population-level health benefits. DA allows for the explicit identification of assumptions and the identification of key areas of uncertainty, which can be used for planning future research.

The Workgroup developed a computer simulation model to evaluate outcomes for universal NBS for Pompe disease versus outcomes for clinical evaluation. The model used data collected during the evidence review and included primary data available through the evidence review, registry data, and published data. The Workgroup conducted three expert panels to review the structure of the model, review the assumptions used to guide transitions within the model, and identify additional sources of data. The number of cases identified, the number of deaths averted, and the number of ventilator-dependent cases averted were the key health endpoints identified for the

model. Key modeling assumptions were: all identified cases of Pompe disease would be eligible for ERT, key outcomes would be assessed for infantile-onset cases only, and the additional number of late-onset cases identified by NBS is unknown.

Dr. Prosser summarized the results of the DA modeling. Assuming that the annual number of U.S. newborns is four million, the CRW projected that an average of 134 cases of Pompe disease would be identified each year. Of these cases, 40 would be infantile-onset cases, and 94 would be late-onset cases. Based on available information, 40 to 70 percent of the late-onset cases would not be detected clinically in the absence of screening. Approximately 10 false negative results could be expected, with all of these cases being late-onset cases. Based on the Taiwan algorithm, the workgroup anticipated that there would be approximately 130 false positives per year.

The modeling suggested that 40 cases of infantile-onset Pompe disease would be identified by NBS (as compared to only 36 through clinical identification). Of these, 34 would have cardiomyopathy and six would not. By comparison, clinical screening would have identified the same number with cardiomyopathy and only two without cardiomyopathy.

With regard to health outcomes, the modeling indicated that the benefits of NBS include earlier identification and treatment of infants with infantile-onset Pompe disease with cardiomyopathy and an increase in the number of identified infantile-onset Pompe patients without cardiomyopathy. Key health outcomes associated with NBS include approximately 13 averted deaths each year and 26 additional cases that would not require invasive ventilation.

Dr. Prosser explained that the model only projected health benefits for infantile-onset cases. The modeling indicated that there would be an increase in survival rates and a reduction in the number requiring invasive ventilation.

Dr. Prosser indicated that additional information, including the input parameters, assumptions, and model schematic, would be shared with the Committee.

C. Evidence Review and Public Health Impact Assessment

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Association of Public Health Laboratories
Silver Spring, MD

Mr. Jelili Ojodu reminded the meeting participants that, in 2011, the HHS Secretary charged the SACHDNC with including a public health impact assessment component in the evidence review for conditions that are being considered for addition to the RUSP. In response to this requirement, APHL conducted a public health impact assessment of states' readiness to add conditions to their screening panels and of the feasibility of doing so. APHL surveyed 13 states. Selection criteria included participation in a regional collaborative, newborn population size, state mandates concerning use of the RUSP, use of state laboratories versus use of outside facilities, second screening requirements, academic affiliations, current status of Pompe screening, laboratory equipment, and experience with NBS screening for similar conditions.

APHL conducted the survey in two phases. The first phase consisted of an electronic survey, which had a 100 percent response rate. The second phase consisted of in-depth telephone interviews with representatives of the NBS programs such as laboratories, state NBS laboratory directors, and, in some cases, follow-up coordinators. These interviews helped APHL understand the thought processes related to the answers provided on the survey.

APHL identified the processes used by states to add conditions to their screening panels. These processes included making changes to state rules or statutes, obtaining funds to conduct the

screenings, and conducting an implementation phase or pilot project (e.g., conducting validation of test methodologies, educating NBS system personnel, etc.). The chief factor determining whether a condition will be added to a state's NBS panel is the authorization to screen for it. Once the authorization to screen is in place, other factors, such as funding, securing equipment and reagents, validating the method, staffing, training, creating protocols, and updating information technology systems, come into play. All of these factors can result in a one-to-two-year implementation timeline. Stakeholders involved in adding new conditions to state screening panels include state NBS advisory committees, state health officials, legislators, state boards of health, state public health departments, and advocacy groups.

The survey also asked about feasibility (i.e., the existence of an NBS screening test, a clear approach to diagnostic confirmation, and a clear approach to follow-up) and readiness (i.e., having all of the resources needed for screening, diagnostic confirmation, and follow-up as well as the authorization to screen).

Concerning feasibility, there was no consensus among the surveyed states concerning the best way to screen for Pompe disease. Fifty-five percent of the program directors surveyed were comfortable with their states' ability to provide diagnostic confirmation of Pompe disease, and 45 percent were uncertain. Seventy-three percent of the program directors were very comfortable with their program's ability to provide or facilitate appropriate treatment. Sixty-four percent of the program directors were comfortable with their programs' ability to provide follow-up services for Pompe disease screening. State NBS programs still need to develop follow-up methods and procedures as they relate to late-onset Pompe cases prior to implementing screening.

With regard to readiness, 83 percent of state programs rely on the assistance of state NBS advisory committees and state health officials to add new conditions to their NBS panels. Seventy-three percent of the program directors reported not having enough funding to immediately implement Pompe disease screening. Fifty-eight percent of states require changes to state rules to add a new condition to their NBS panels; the remaining states require legislative action to add a new condition to their panels.

Another factor that was important to a state's readiness to begin Pompe disease screening was staffing. Seventy-three percent of the surveyed states identified staffing as the most significant barrier to the implementation of screening, indicated that they would not have adequate staff to begin screening immediately, or noted that there was a shortage of metabolic specialists and other individuals trained to handle Pompe cases. Fifty-five percent of program directors have had problems in the past recruiting staff with the needed expertise. Additionally, short-term follow-up programs need to develop protocols and educate hospitals and providers on how to handle out-of-range screening results. Finally, several states noted that they have not been able to secure funding for screening for SCID only three of the surveyed states have added SCID to their panels.

Mr. Ojodu reported that the processes related to validation of the methodologies and platforms related to population screening for Pompe disease are still underway. There is much uncertainty concerning follow-up for treatment of Pompe disease detected through NBS and a great need for more educational materials for hospitals and providers concerning how to handle out-of-range results, especially for the early-onset form of the condition.

Committee Discussion

- Dr. Lorey reported that he reached out to colleagues in other states in his role as the DACHDNC representative for state public health programs and shared some of the comments he received. There was general consensus on the need for a large-scale pilot project before recommending the addition of Pompe disease. He also heard concerns about the actual amount of improvement realized as a result of ERT, the addition of Pompe disease representing a departure from basic NBS criteria regarding treatment and outcomes, and the proportion of late-onset versus early-onset cases. The majority of cases detected by NBS were late-onset, and there is no evidence that outcomes for these cases

are improved by early treatment. The pilot studies identified a very low number of early-onset cases. Additionally, the prevalence rates are somewhat misleading as they appear to include all types of Pompe disease and pseudodeficiency. Finally, many states are still not screening for SCID, which was added to the RUSP in 2010, even though it did not have similar concerns associated with it.

- Dr. Kemper responded to Dr. Lorey's comments about the incidence of Pompe by stating that the figures he presented included all forms of Pompe disease but did not include carriers or cases of pseudodeficiency. ; Most of the information on outcome benefits of ERT comes from small case series and case studies. The larger case series do not address ERT therapy.
- Dr. Prosser clarified that the slide presented by Dr. Kemper concerning outcomes among clinically detected cases using ERT treatment, before or after three months of age, was based on data from the Genzyme Pompe Disease Registry and showed the expected benefits derived from ERT treatment of patients diagnosed through clinical detection. The following slide showed the expected benefits of ERT treatment for individuals diagnosed through NBS. The modeling combined the data from the registry for patients in both age groups to identify an average age of initiation of ERT treatment based on clinical detection. The comparison group is based on the data from the Taiwan study, where there were no children in the group of five newborns screened and treated who were dead or ventilator dependent.
- In response to a question concerning the pre-symptomatic treatment of individuals with late-onset Pompe disease and the existence of treatment guidelines for late-onset cases, Dr. Kemper reported that the existing guidelines focus on observing muscle weakness or inflammation, which is diagnosed by increased levels of creatine kinase (CK). MRIs are being used to detect muscle damage earlier than it can be detected using biomarkers. The main question is when therapy should be started, specifically whether it should begin when CK is elevated or weakness develops (the current approach) or whether it should begin earlier. He was unaware of any studies concerning the role of genetic counseling in reducing harm.
- In response to a question concerning the survival curves for early detection of classic infantile Pompe disease, Dr. Kemper indicated that all of the individuals identified through screening are alive and ventilator free. He did not know the current age of these patients. He noted that it is difficult to determine the point at which early intervention, versus clinical intervention, makes a difference.
- Dr. Prosser clarified the data used in the simulation model for the comparator for clinical identification. The model used the combined data from the Pompe Disease Registry for the primary analysis of the 13 deaths. The model did not differentiate between those in the less-than-three-month category and those in the less-than-one-year category. The model evaluated the whole group of infantile-onset cases. The CRW conducted a sensitivity analysis using the combined data, which provided the lower boundary estimate for the number of deaths and the number of ventilator-free cases. The greatest benefit of NBS would be for the cases with delayed identification and treatment.
- A Committee member noted that there is very little difference in survival or ventilator dependence among those identified by NBS and those identified through early identification. Dr. Kemper stated that the small number of cases makes it difficult to explain and encouraged the DACHDNC members to pay close attention to the case studies concerning motor development.
- In response to a request for more information about outcomes for those receiving the earliest possible treatment as a result of NBS, Dr. Kemper indicated that the babies that received treatment very early had better motor development than those who started later. He stressed that there are many factors to consider regarding the age of initiation of therapy.
- A Committee member asked whether biomarkers could be used to test the hypothesis that pre-symptomatic treatment for late-onset cases might prevent muscle damage. Dr.

Kemper, cautioning that he was going beyond the evidence, indicated that MRIs and CK measurement could serve as proxies for biomarkers.

- Returning to the survival curves discussed previously, a Committee member noted that there is no distinction between those detected early and those detected through screening. Dr. Kemper stated that babies that are screened enter treatment significantly earlier than those identified clinically. Without Pompe disease NBS, there are probably some babies who would die from the disease before they could be diagnosed.
- Asked to compare the likelihood of being able to clinically identify individuals earlier, the level of surveillance, and population care in Taiwan with a larger country such as the United States, Dr. Kemper acknowledged that Taiwan has much experience with Pompe disease and may be more familiar with it, but he stressed that the disease is still rare. In areas where screening did not occur, diagnosis took several months and babies did not enter into treatment until four or five months of age.
- Concerning how well Pompe disease fits within the NBS screening criteria, Dr. Matern believed that it fit as well as cystic fibrosis. He pointed out the need for treatment guidelines for late-onset patients diagnosed by NBS and for clarification concerning an acceptable false positive rate. The incidence of Pompe disease in the Missouri data might be a result of the small number screened to date; the study on which he is working had an incidence of 1 in 25,000, with two cases of late-onset disease in 50,000 screens. Dr. Kemper agreed that the Missouri data should be examined carefully given the small number of screenings. He anticipated that the state would adjust its screening threshold as it gains more experience.
- In response to a request to clarify the APHL's findings concerning feasibility, Mr. Ojodu indicated that the phrase about providing/facilitating treatment was not separated in the question. He added that the difference in the positive response rates only reflected a single state. A Committee member recommended distinguishing the provision and facilitation of treatment in the future as they are different things. Dr. Tanksley explained that the Texas Department of State Health Services answered the question in terms of the whole NBS system within the state, not just the NBS program.

General Discussion

- An organizational representative was concerned that a significant number of patients could fall into a grey zone between affected and unaffected if the diagnostic cut offs are not definitive. Dr. Kemper replied that the reports reviewed by the CRW and the expert interviews indicated that genotyping could be used to definitively establish whether an individual is a carrier, has pseudodeficiency, has infantile Pompe disease, or is predicted to have late-onset Pompe.
- An organizational representative pointed out that the genotype/phenotype correlation is much tighter for Pompe disease than for other conditions and anticipated that there would be variation within the correlation based on the experience with other conditions. Dr. Matern reported that his ongoing study encountered variances on a regular basis.
- In response to a question concerning the way in which the feasibility and readiness components would be factored into the recommendation decision, Dr. Bocchini indicated that these issues would be discussed in more detail later in the afternoon.
- An organizational representative stated that there are existing practice guidelines concerning the contents of a diagnostic work-up of an asymptomatic individual as well as guidelines for handling individuals with the infantile form. These guidelines include follow-up intervals.
- In response to a question about the timing and sequence of NBS for Pompe disease, Dr. Kemper replied that Missouri recalls babies with positive screens for a blood sample that is used to confirm low enzyme activity level (one day to process) and for genotyping (two to three days). Generally, laboratories that conduct confirmatory testing run samples once a week because of the low volume; Dr. Matern reported that the Mayo Clinic, which test Missouri's samples, makes an exception for the state and adjusts its schedule to ensure a speedy turn around. Confirmatory laboratories will need to address this issue.

- Dr. Kemper answered a question about Taiwan's two-tier screening approach by explaining that the test is not genetic; instead, Taiwan uses a second punch from the original dried blood spot to conduct a different test.
- A Committee member asked how states would fund treatment for individuals diagnosed through NBS. Dr. Kemper indicated that most children who require ERT would obtain it through the Medicaid program.
- With regard to states' ability to implement Pompe disease screening compared to that for CCHD and SCID, Mr. Ojodu stated that Missouri's experience shows that it can be done. Readiness and feasibility issues relate to programmatic issues (e.g., authority to screen, funding for treatment, availability of follow-up, establishing testing fees, and passing the required statutes). Dr. Bocchini stressed the importance of basing the Committee's decision on the available data rather than comparing it to other conditions that are in the process of being implemented.

VI. Committee Members' Review, Discussion, and Vote on Pompe Disease

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A. Recommendation to DACHDNC for Screening for Pompe Disease

Dr. Homer reviewed the decision matrix that was used to inform the liaison group's evaluation of the evidence presented earlier in the day. In order for the DACHDNC to make a recommendation to move forward with incorporating a new screening into the RUSP, it needs to have a significant benefit and a high level of certainty of the benefit.

The Liaison Group divided its consideration of Pompe disease screening test into two parts. The group looked at the benefits of screening for both the infantile form and the late-onset form. Ultimately, the decision to add the screening to the RUSP must be based on the performance of the single test.

The evidence was clear that screening results in earlier diagnosis of the infantile form than clinical identification. Earlier treatment with ERT results in better outcomes for infants. Dr. Homer expressed a high level of confidence, based on the evidence, that infants identified through screening and treated with ERT have better outcomes than historical controls. The Liaison Group believed that the evidence showed that available screening tests for Pompe disease are extremely sensitive for the infantile form. With appropriate algorithms, such as the two-step Taiwan algorithm, there is a very high level of specificity (few false positives). Dr. Homer indicated that the point estimates generated by the DA modeling indicated that there is a significant benefit associated with screening for Pompe disease with regard to the infantile form. The modeling indicated that screening for Pompe disease would result in 13 lives saved and 26 individuals who would survive without need of ventilation in a cohort of four million births.

The modeling also indicated a high level of certainty, where certainty relates to the possibility that additional science could change the results. The Group agreed that there is a very small likelihood that additional science would change the results and that there is high certainty of significant benefit for the infantile form of the disease.

With regard to the later-onset form of the disease, the Group determined that it needed to know that screening would result in a benefit and with confidence that there is no associated harm in order to make a recommendation to add Pompe disease to the RUSP. The Liaison Group also thought it was important to provide guidance concerning the need for additional studies, as there is no direct data concerning the effect of treatment prior to the onset of symptoms in late-onset Pompe disease. It is clear that treatment after diagnosis results in improved lung function and physical mobility. There is biologic plausibility of the benefit of early treatment. With regard to harms associated with screening and late-onset Pompe disease, studies indicate that there is a similar symptom profile for those receiving placebo and those receiving ERT. There was a higher level of allergic reaction and antibody development among the ERT group, but these seemed to be relatively easy to manage. Additional factors considered by the group regarding late-onset Pompe disease included the credible hypothesis that pre-symptomatic ERT treatment is beneficial, the minimal nature of associated harms, the diagnostic odyssey, and the preference for early knowledge that individuals have Pompe disease. The Liaison Group believed that this provides an optimal context for a trial of alternative strategies for treatment of late-onset Pompe disease.

With regard to the readiness and feasibility of state implementation of Pompe screening, Dr. Homer indicated that states would not be able to implement screening immediately. There is still some uncertainty about which screening test is the optimal one; however, all of the tests are acceptable. Regardless of the approach adopted, there would still be a need for resources for training, staffing, acquiring equipment, and establishing relationships with specialists. The group did not believe that these challenges are different than those faced in implementing other screenings. As a result, the group categorized screening for Pompe disease as not being ready for immediate implementation but not having insurmountable barriers (A2 category on the matrix). Dr. Homer summarized that the Liaison Group recommended adding Pompe disease to the RUSP. The group believed that the condition would fall into the A2 category of readiness on the decision matrix and estimated that the implementation of this screening would require between one and five years. The group also believed that the Committee should recommend that support be provided for a trial or study of alternative strategies for early treatment of late-onset Pompe disease.

Committee Discussion

- Concerning the implication of categorizing a screening as an A2 or A3, Dr. Bocchini explained that the categories referred primarily to the time states would need to implement a screening. A rating of A1 would mean that the evidence indicates that inclusion in the RUSP could be accomplished rapidly in that little needed to be done for implementation; an A2 rating indicates that it is expected that states could prepare and implement the screening within a five-year timeline. These rankings would not affect the Committee's decision concerning the evidence of high benefit or high certainty of benefit.
- A Committee member asked whether the additional study concerning the benefit of early treatment of late-onset patients was factored into the estimated implementation timeframe. Dr. Homer indicated that the A2 rating referred to the ability to effectively implement the testing process and establish referral networks to connect patients to services.
- Dr. Homer replied affirmatively to a Committee member's question about whether the recommendation is to move forward, with the condition that new observational or clinical trial data be collected as implementation rolls out.
- A Committee member asked whether the group considered placing screening for infantile Pompe on the recommended panel and screening for the late-onset form on the secondary panel. Dr. Kemper replied that it is not possible to screen for only the infantile form. The Committee member suggested that identifying the late-onset form as a secondary

condition would highlight the need for more studies that clarify the health benefits of screening for late-onset Pompe.

- Regarding reporting for screenings on a secondary panel, Dr. Lorey believed that reporting would not be required if the screening itself was not required. A Committee member expressed concern that adding late-onset Pompe to the RUSP as a secondary target would eliminate the benefits of being able to follow identified individuals longitudinally.
- A Committee member believed that there could be primary and secondary targets if molecular testing was included in the screening process. Regarding the categorization of the screening, he believed that the DACHDNC should either recommend the screening or not recommend it. If the recommendation is not clear, states will be slow to implement the screening.
- A Committee member did not believe that the NBS program would be responsible for discriminating between the infantile and the late-onset forms.
- With regard to secondary targets, a Committee member noted that it is not clear that states would differentiate between primary and secondary targets for Pompe in a way that they have not for other conditions.
- A Committee member indicated that the secondary targets identified by the Committee became mandated targets in many states. Once individuals are identified as potential late-onset patients, they will be followed through the health care system, which will result in an accumulation of data at the local provider level. The challenge will be collecting the information in a centralized manner, given the long time between identification and the beginning of therapy. It might be possible to do a retrospective study using dried bloodspots, but it would be difficult to link clinical information with a dried bloodspot in a state program due to consent issues and the length of time that the bloodspots are kept. An organizational representative pointed out that secondary targets are identified through differential diagnosis in the process of screening for the core condition.
- Responding to a question concerning the impact of including a timeline for implementation in its recommendation, Dr. Bocchini did not think that any recommendations approved by the Secretary included a timeline for implementation. Including a timeline in the recommendation would only acknowledge that there would be a period of time before all states would be able to include the screening in their panels.
- A Committee member indicated that the matrix was an internal tool designed to help the Committee explore state readiness. The final recommendation would only address whether a condition should be included in the RUSP. Dr. Bocchini stated that the Secretary asked the Committee to include a public health impact statement; therefore, it is essential that the impact assessment is included in the recommendation.
- Dr. Tanksley, in her role as an NBS program representative, expressed her appreciation of the estimated implementation timeline and her confidence that the state NBS programs could implement screening for Pompe disease.
- A Committee member strongly disagreed with the slide that indicated that there were no major barriers to implementation and argued that the barriers for Pompe disease are significant. The estimate of lives saved does not include a time factor (e.g., death averted for a year or permanently) and was based on the Taiwan study and modeling. There is very little data available for the United States, especially for late-onset cases. He objected to the hypothesis that early intervention helps late-onset patients because there was no data to support it. NBS programs have not tracked late-onset disorders before, which makes implementation more difficult.
- A Committee member believed that length of life should not have an impact on the Committee's decision.
- A Committee member noted that if studies are needed before screening can begin, it will not be possible to identify sufficient cases pre-symptomatically and obtain the required evidence without a screening program. He did not believe that adoption of the screening should be delayed.

- In response to a question about laboratory readiness, Mr. Ojodu stated that only Missouri is in the validation stage of NBS population screening for Pompe disease. The other methods discussed have not been fully validated for population NBS. Dr. Matern believed that the reagents for the tandem mass spectrometry method are available. There have been issues in the past with the availability of hardware or reagents for the fluorometric assay method; this has been working smoothly over the last several months. The necessary reagents are not available for the immunocapture method of screening.
- Mr. Ojodu added that any mass spectrometry machines used for population NBS screening for Pome disease would have to be dedicated machines, which represents a significant cost to NBS programs and to the NBS system. Dr. Matern pointed out that any condition that has come before the Committee in recent years would require additional equipment in the laboratory. Some laboratories would have the capacity to conduct mass spectrometry work on their existing equipment due to limited populations.
- A Committee member recommended that the Committee continue to discuss the issues of conducting formal pilot programs to better understand the clinical phenotype-genotype relationship and how it relates to Pompe disease NBS.
- A Committee member shared her belief that separating the infantile form of Pompe disease from the later-onset form is an artificial separation and encouraged the Committee to avoid dividing the condition into primary and secondary targets. Another member pointed out discriminating between the two forms would require molecular testing.
- An organization representative expressed concerns about the level of certainty of evidence if the Committee combines early-onset and late-onset forms. He believed that combining the two forms would move the certainty into the moderate category and call into question the significance of the overall benefit. Dr. Homer reiterated his belief that the evidence concerning the infantile form was strong. Because one could not assert, with any level of certainty, that there is benefit for early identification for the late-onset form, he believed the thresholds for certainty should be different.
- A Committee member indicated that he was confused about the primary and secondary screening categories and the implications of separating the two forms. Once children are identified, they will need to be connected to appropriate services, regardless of genotype. Ideally, those with the late-onset form would be entered into a tracking study or an active study.
- Dr. Bocchini believed, based on the discussion, that it would be difficult to have primary and secondary targets. If Pompe disease is a single target, the evidence concerning outcomes for early identification or treatment of asymptomatic individuals will evolve in a scientific, prospective way.
- A Committee member advocated for adding Pompe disease to the RUSP based on the benefit associated with infantile screening. Any research that comes after the addition can be addressed later.

B. Committee Vote on Pompe Disease Nomination

Dr. Bocchini opened the floor for a recommendation concerning the addition of Pompe disease to the RUSP as a category A2 on the decision matrix.

Dr. McDonough made a motion to recommend the addition of Pompe disease to the RUSP as a category A2 on the decision matrix. He acknowledged that there are concerns about identifying a category instead of simply making a recommendation for addition. Dr. Bailey seconded the motion.

Dr. Boyle asked whether the DACHDNC could make a recommendation for a formal, multi-state pilot program to help guide implementation. Dr. Matern indicated that this is already happening in

Missouri; Illinois, New Jersey, and New Mexico will follow soon. Dr. Boyle indicated that a formal study would allow for the collection of standardized, systematic data over time.

Dr. Boyle made a motion that the recommendation be made to use the data from the states that are currently implementing Pompe disease screening as a pilot study, to clarify issues such as determining the best screening test and best protocol. Dr. McDonough indicated that he was willing to incorporate this into his motion, if the Committee members were supportive of it.

An unidentified participant asked that the motion be reframed for greater clarity. Dr. Boyle explained that states that are or will soon be implementing Pompe screening would coordinate activities to develop systematic information to develop a framework. Dr. Matern stated that Mayo received funding from the National Institute of Child Health and Human Development and NBSTRN to set up such a process. He believed that states should be invited to enter data and help others move implementation forward. Any additions to the recommendation might have unintended consequences when it comes to implementation. Dr. Parisi agreed that making a recommendation with multiple qualifiers could complicate the interpretation of the recommendation. She believed that the coordination would occur whether or not it is included in the recommendation.

Dr. Bocchini indicated that the DACHDNC had been instructed that the recommendation should only address whether Pompe disease should be included in the RUSP. Any other recommendations should be included in the letter to the Secretary. The Committee could continue to track the implementation of Pompe disease screening and make states aware of outcomes, as it is currently doing for other conditions. Dr. Bocchini called for a vote on Dr. McDonough's original motion, which did not include any recommendations concerning pilot studies or tracking of identified cases.

> *The DACHDNC members voted to approve the motion to recommend the inclusion of Pompe disease on the RUSP, with 11 members voting for the motion and two members voting against it. Two members were absent and did not cast votes.*

Dr. Bocchini noted that there was general consensus that the Committee adopts the guidance provided by the members concerning the evidence review and the public health impact as well as the additional recommendations concerning the late-onset form of Pompe disease.

VII. Adjournment

Dr. Bocchini thanked all of the individuals who worked to ensure that the DACHDNC was chartered in time for this meeting. He also thanked the CRW for providing a thorough summary of the available data, the public health impact, and the DA data.

With no additional business to address, Dr. Bocchini adjourned the meeting at 2:19 p.m.

Appendix A – Written Public Comments

From: Karen Kacures
To: Vasquez, Lisa (HRSA)
Subject: Fwd: New Born Screening for Pompe Disease
Date: Sunday, May 12, 2013 4:32:36 PM

---------- Forwarded message ----------
From: **Karen Kacures** <kkacures@gmail.com> Date:
Wed, Jan 16, 2013 at 12:00 PM
Subject: New Born Screening for Pompe Disease
To: lvasquez@hrsa.gov

To whom it may concern,

I am an adult with Pompe disease. I was diagnosed after having symptoms for over 12 years. Newborn screening would prevent future patients from suffering for years like I did. Now that there is a enzyme replacement treatment available that is working well for so many people, including me, newborn screening would help people access this treatment before ever showing symptoms and having the muscle damage like I have suffered.

Since both of my children are carriers of the Pompe gene, I worry about future generations of my family and how newborn screening would help them so they may never go through the time and expense of going from one specialist to another being mis-diagnosed with many disorders with similar symptoms.

I know so many others in the Pompe community who have similar stories and it took years for their diagnoses also. Please consider putting Pompe disease onto the new born screening panel.

Thank you for your consideration.

Karen Kacures
213 So. Buffalo Pass
Georgetown, Texas 78633

kkacures@gmail.com

From: Krystal
To: Vasquez, Lisa (HRSA)
Subject: Letter of support for Pompe Screening at birth (w/ info)
Date: Monday, May 13, 2013 7:47:54 AM

Sorry, I forgot to include my information:

Krystal Hayes
315 Baird ln
Bracey, VA
4346365107

Mother of child with Pompe Disease and also Registered Nurse

>
> Hello, my name is Krystal and I'm the mother of Haley Hayes, a child with infantile onset Pompe disease. Haley was diagnosed at the age of 6.5 months and her heart was extremely enlarged and barely functioning at that point. Haley has done well on the enzyme over the years but because of the delayed diagnosis, her skeletal muscles remain very weak. We are thankful the enzyme replacement returned her heart to normal, however the delay in diagnosis has left my wonderful 7 year old 'firecracker' unable to stand, walk, or be independent. She has a tube in her stomach for supplementary nutrition and people have a difficult time understanding her. All of these the things we know would be improved if Haley had been diagnosed earlier, or even at birth. Screening at birth is a simple procedure that could drastically improve the lives of many that would be diagnosed earlier and would even save some from passing away before a diagnosis was reached.
>
> Krystal Hayes
>
>
> Sent from my iPad

Written Comments Richard Cotton

Scientific Director -Human Variome Project International Limited

I am writing to support the reauthorization of the Newborn Screening Saves Lives Act urgently. This is not only to save lives but in anticipation that data will be shared globally and that the activity will save lives globally. This is the purview of the Human Project: www.humanvariomeproject.org

From: Brad Crittenden
To: Vasquez, Lisa (HRSA)
Subject: Newborn screening for Pompe Disease
Date: Monday, May 13, 2013 6:36:32 PM

Hello Lisa,

I am a patient in Canada with Adult Onset Pompe Disease. I am also the President of the national Pompe patient group in Canada.

As is the case for most progressive diseases, early diagnosis is critical. Not only does it give the best chance for treatment but, in severe cases, it also gives the family the best use of the time that they have. Quality of life comes in many shapes and sizes. It broke my heart a few years ago when I learned that many Pompe babies were dying before they were even diagnosed. How can we let that happen when it's not necessary? Even more babies suffer irreparable life-changing muscle damage that, in many of those cases, doesn't have to happen. Newborn screening is a very simple thing that empowers parents with knowledge that will help them make informed decisions.

If newborn screening had been in place when I was a child, I would have known that I had Pompe Disease. I would have known why I could never do a sit-up and why I walked funny. I could have been monitored and not misdiagnosed and treated for things I didn't have.

Please carefully consider this and make the right decision for patients and families. I

would be very happy to discuss this further and can be reached at:
112-3201 Wilson St
Penticton, BC Canada V2A 8J3
250-488-2571

Best Regards,
Brad Crittenden

Brad Crittenden, President
Canadian Association of Pompe
brad@pompecanada.com
twitter.com/pompecanada

From: Steve and Allyson Lock
To: Vasquez, Lisa (HRSA)
Subject: Newborn Screening for Pompe Disease
Date: Monday, May 13, 2013 5:29:58 PM

Dear Lisa Vasquez

I am writing to express my support for **newborn screening for Pompe disease**.

If Pompe disease is diagnosed early, treatment with Enzyme Replacement Therapy has much better success. This has been proven to be the case.

It generally takes many years to get a diagnoses for late-onset Pompe disease and all the while our physical health is in decline. With an earlier diagnoses and treatment, much of this physical decline can be avoided. Therefore it is imperative to screen for infant-onset **and** late-onset Pompe disease.

I personally had to experience chronic respiratory failure before a diagnoses was finally found. I'm lucky that I survived that episode, and so many others have had to go through the same thing.
It is clear how important NBS is for infant-onset Pompe disease, and it is also important for late-onset Pompe disease. It would not be ethical to leave out late-onset testing and only test for infant-onset. Both must be done.

Please help us fight this terrible disease by approving **newborn screening for Pompe for both infant-onset and adult-onset**. This **will** save lives and help many many others to live healthier, longer and more normal lives.

Thank you very much for your time.

Yours sincerely

Allyson Lock
President
New Zealand Pompe Network 181c
Willow Park Drive
RD11
Masterton
New Zealand 5871
Phone: +64-6-3704244

Franc

e January 12th

2013

Dear Lisa Vasquez,

Further to information that Tiffany House has passed on regarding Pome & Newborn Screening, I would like you to read my personal view:

If, I as a mother was aware of Pompe at the birth, of course my attitude would have been completely different toward my son who was diagnosed with Late Onset at 15 years old.

He suffered enormously from about the age of nine when challenged with " normal" physical activities, like sports at school, and there was a great deal of searching, wasted anxiety and energy on both our behalves.

I think any parent would agree that one would wish to offer the best for one's offspring, and therefore being forewarned is obviously better prepared to deal with the challenges.

When he received the diagnosis – he was relieved … imagine that – all those years of not understanding why he wasn't like other "normal" children, that he was actually happy to be told that he has Pompe and all that it entails, closely followed by a deep depression. As an adolescent, he was told that his life would not be as he imagined… It is a lot to come to terms with as well as going through puberty.

It is a fine line to tread between being an over – protective parent , which knowledge might accentuate and allowing the child to make mistakes and therefore learn, but in the case of a rare illness, in particular Pompe , I think knowledge would enhance the parental approach, and therefore provide the parent with the ability to prepare the ground which will be undoubtedly be trod, with care, sensitivity and above all with the unconditional love that every parent has toward their child, particularly in the 21st century when there are possible solutions to alleviate some of the effects of the illness.

Your sincerely,

Lucy Golder

Raymond Saich
Australian Pompe's Association 3 Malonga Ave
Kellyville NSW 2155
Australia
Email Rsaich@bigpond.net.au

13th May 2013

Dear Ms. Vasquez,

Subject New Born Screening

On behalf of the Australian Pompe's Association may I offer our support for adding Pompe to the diseases tested with the new born screening program. Here in Australia we have seen a number of tragedies in the last few years of babies born with Pompe disease and it taking too long to be diagnosed.

This delay appears to be worse, when the child is born in a remote area when the few precious weeks when treatment is so vital, are lost in transferring and referring the child from local to regional to metropolitan hospitals and from specialist to another specialist. Pompe is so rare that doctors have never seen it and most specialists, have only read about it. By the time the child is seen at the metropolitan hospital by an experienced specialist the vital time has been lost and the child may have advanced too far for the wonders of ERT to take effect.

If Pompe is diagnosed at birth, under the new born screening program, the child will immediately be referred to the appropriate specialist for confirmation and treatment.

We have talked to and share too many tragedies with parents struggling to cope with the deterioration of their precious child, know that things would have been different if ERT could have been started, weeks or months before, if the child had been diagnosed at birth.

We strongly support the addition of Pompe to the New born screening program.

Yours sincerely,

Raymond Saich President
Australian Pompe's Association

Upon my long 1.5 year journey to a diagnosis, I immediately became proactive, enrolling in all 3 clinical trials for Lumizyme. Now with treatment, it is imperative for early diagnosis BEFORE damage is done. The NBS would give the children the chance to live a normal life and the option of when to start ERT.

Alicia Blackington

Adult on set Pompe Patient
United Pompe Foundation

Aliciablackington@gmail.com

To whom it may concern,

Support for the adoption of newborn screening for Pompe disease

As the parent of a child with Pompe disease I am acutely aware of the need to diagnose the condition early in order to protect the child from the cruel progressive nature of the condition. Even without treatment, progression may be diminished by appropriate diet and exercise, but the initiation of Enzyme Replacement Therapy (ERT) at the earliest opportunity will give the child the greatest chance of survival and improved quality of life.

As the Development Director of a UK charity supporting the Pompe community and in my role as President of the International Pompe Community, I see far too many cases of infantile Pompe disease where treatment is commenced far too late and the child either dies unnecessarily or is committed to a life of extreme disability and the parents to a life of caring for their extremely complex needs.

Screening trials for Pompe disease in Taiwan, Austria and the USA have shown that the technology is effective and specific and there is no reason to leave diagnosis to chance. Children must be diagnosed within the first few weeks of life and even at the most advanced medical centres we find children being diagnosed after four months.

Please make sure that every effort is made to initiate newborn screening for Pompe disease as soon as possible.

With kindest Regards

Allan Muir

Development Director, AGSD---UK

Chairman, International Pompe Association

May 13, 2013

Via: E-Mail

Joseph Bocchini, MD
Committee Chair
Discretionary Advisory Committee on Heritable Disorders in Newborns and Children
U.S. Department of Health and Human Services

Re: Public Comment for Pompe Disease

Dear Dr. Bocchini:

I write to encourage the Committee to add late-onset Pompe disease to the Recommended Uniform Screening Panel.

About six months ago, I was diagnosed with late-onset Pompe disease. I was a newly-married, seemingly-healthy, twenty-nine-year-old vegetarian lawyer. The diagnosis came as a shock to me, my family, and my physicians. The condition was found almost by accident, when doctors conducted a muscle biopsy to consider if I might be a carrier for Duchenne's muscular dystrophy.

Once the shock of the diagnosis wore off, I quickly realized how fortunate I was to have been diagnosed so early. Though I have battled fatigue for years, I have limited muscle involvement. Thanks to the impressive research conducted by doctors at Duke, Columbia, and elsewhere, I can take proactive steps to try to stay healthy and minimize further muscle damage. These steps include changing my exercise routine, adding significantly more protein to my diet, and starting enzyme replacement therapy. If I had not been diagnosed, I would not have made these lifestyle changes, and the damage to my muscles would likely have progressed more aggressively.

With Pompe disease, exercise is supposed to be "submaximal"—a term that was not previously in my vocabulary. I played competitive volleyball for much of my life, including a year of Division III college sports. Looking back, I recognize that my body did not always perform the way I thought it should. I was often sick and consistently had breathing problems. I was even (perhaps wrongly) diagnosed with exercise-induced asthma. But I always pressed on and pushed myself as hard as I could. Now I wonder if I unnecessarily caused muscle damage simply because I did not know the extent of my own limitations.

For years, I have been interested in bioethics and health policy. Before law school, I worked for the Jonsson Comprehensive Cancer Center at UCLA, and in school, I served as the Executive Editor of the *Yale Journal of Health Policy, Law, and Ethics*. Today, about half of my legal practice is healthcare-related. I understand that deciding whether to add a stereotypically "adult" disease, such as late-onset Pompe, to the infant screening panel is a difficult decision. Genetic

discrimination is certainly one concern. Even taking the risks into consideration, I am incredibly grateful I know my diagnosis. And yet, I am equally as grateful that my parents were not told of my condition thirty years ago when I was born. At that time, there would have been nothing my parents could have done to help me, and an early diagnosis would have only led to fear.

However, the reason I am writing you in support of adding Pompe to the screening panel is because of the tremendous medical advancements that have occurred since I was born. Today, there is real value in monitoring patients with late-onset versions of the disease and initiating treatment as early as practicable. Many in our society struggle to live with diseases that have no known treatments, but Pompe patients are lucky. By proactively managing our condition and treating early, we can lead healthier lives. However, one can only be proactive if one knows of his or her condition. It is truly a blessing that I was diagnosed as early as I was, and I hope that all Pompe patients may receive the benefits of early diagnosis and treatment.

For the above reasons, I encourage the Committee to include all forms of Pompe on the Recommended Uniform Screening Panel.

Respectfully,

Courtney A. Carrell, JD

Acid Maltase Deficiency Association, Inc
P.O. Box 700248
San Antonio, Tx. 78270
Phone: 210---494---6144
Email: TiffanyLHouse@aol.com

To:Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) Care of: Lisa Vasquez, MPA
Public Health Analyst, Genetic Services Branch
Division of Services for Children with Special Health Needs Maternal and Child Health Bureau
Health Resources and Services Administration 5600 Fishers Lane. Rm 18---A---19
Rockville, MD 20857 301---443---4948---(phone) lvasquez@hrsa.gov

From: Tiffany House
AMDA President Date:May 12, 2013
Re: Newborn Screening for Pompe Disease

To the Members of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC):

My name is Tiffany House and I am the President of the Acid Maltase Deficiency Association (AMDA). The AMDA is a Pompe patient organization that supports over 300 patients in the United States. Our mission is to raise awareness of, and promote research into, Pompe disease. We are also dedicated to educating patients and work with experts from around the world to provide patients with the latest news regarding advances in Pompe Disease treatment and research.

I am writing to you today to express the AMDA's support for adding Pompe Disease to the Federal Newborn Screening Panel. The AMDA supports the Newborn Screening pilot studies that are currently ongoing in the United States, and we believe that Newborn Screening for Pompe should be available to everyone in the United States.

Pompe Disease is a progressive neuro---muscular disease that affects patients at all stages of life and is caused by a partial or complete deficiency of the enzyme acid alpha---glucosidase. The infantile---onset form of the disease, which typically presents in the first 6 months of life, is the most severe form of the disease. These patients do not generally survive beyond one year of age without treatment. Late---onset patients, while generally demonstrating a slower progression, also have reduced life spans as a result of Pompe Disease.

Pompe patients are fortunate that we have an approved treatment in the form of an enzyme replacement therapy (ERT) that has been proven to slow (and sometimes reverse) the effects of this devastating disease. In a pivotal infantile---onset trial, the treatment (Myozyme) was shown to alter the natural course of the disease–patients

were no longer dying before their first birthday. Many of these patients are now eight years old or older (the oldest patients are now over 12 years old).

From the twelve plus years of experience with treating patients with enzyme replacement therapy, the consensus amongst Pompe Disease experts is that early intervention generally leads to the best results. Unfortunately, the path to diagnosis is often long and difficult (in late---onset patients this is primarily because the early symptoms can often be missed because they are so subtle) and by the time a diagnosis is made there is often significant muscle damage.

I know of families that have lost children to Pompe Disease because the disease had progressed too far by the time that they were diagnosed and a treatment was available. Some of these families have gone on to have other children with Pompe Disease who were diagnosed at birth or before as a result of the family history and were able to start treatment before any significant damage has occurred. These children are living and thriving. The lesson is simple–early diagnosis and intervention saved their lives. Even a few months difference in the initiation of treatment can have a profound impact on the path that these children's lives will take. It can mean the difference between life and death.

This is true for late---onset patients as well. In addition to being the AMDA President, I am also a Pompe patient. My first symptoms can be traced back to when I was an infant; however I was not diagnosed until I was almost twelve. While it may seem hard to believe that it took over eleven years to be diagnosed, this is actually the case for the vast majority of late---onset patients and this diagnostic odyssey often takes a significant toll on patients and their families (mentally and physically). By the time I was diagnosed my pulmonary function had decreased to 40% of normal and I was demonstrating noticeable muscle weakness. Within the next four years my pulmonary function continued to decrease, I developed severe scoliosis, and I lost the ability to walk. At sixteen I began enzyme replacement therapy and my condition has improved significantly since then. However, I am confined to a wheelchair and rely on non---invasive ventilatory support via a Bi---Pap machine to survive.

In contrast to my situation is another patient I know, Caitlin. Caitlin was diagnosed at the age of 6–before she had significant developmental impairment and when she had minimal respiratory involvement. She is now almost nine years old and is doing extremely well. She is able to run and play and keep up with her friends. You would not know that she has Pompe to look at her. However, even though she is doing really well, she also has to use a Bi---Pap at night to help her breathe. Even with diagnosis and treatment as early as she had it, there has already been damage to her muscles that may never be reversed.

I understand that there may be a concern in identifying a late---onset condition at birth, but it is my understanding that this concern has been overcome with other conditions that are currently on the newborn screening panel. I would argue that the benefits that can come from this early diagnosis would far outweigh any potential disadvantages. Having the diagnosis before there is any damage would allow patients to be properly monitored so that treatment can be initiated before there is any potential for irreversible damage and it would save patients and their families years of searching for answers.

As the President of the AMDA and as a Pompe patient I ask you to please add Pompe Disease to the Federal Newborn Screening Panel. This simple test can and will save lives. It will allow infantile---onset patients to be identified so that treatment can be initiated before it is too late, and it will allow late---onset patients to be identified and avoid the diagnostic odyssey that results in years of searching and unanswered questions only to find the answers after there has been significant (and sometimes irreversible) damage to our muscles.

Newborn screening for Pompe will change the lives of countless people for the better.

Thank you.

Tiffany House AMDA President

From: pompe.hillary
To: Vasquez, Lisa (HRSA)
Subject: Pompe Disease NBS Support
Date: Monday, May 13, 2013 9:54:55 AM

I am writing to express support for the inclusion of Pompe disease on the federally mandated Newborn Screening Panel. I was diagnosed with late-onset Pompe in 2002, at age
24. I had symptoms for six years and actively pursued a diagnosis. Including Pompe on NBS panels would help many patients avoid this diagnostic odyssey. During the six years that I spent trying to find a diagnosis my health deteriorated considerably. If I had known from birth that Pompe was in my future then I would very likely be much healthier than I am today. There should be no ethical concerns with identifying a disease that may not manifest itself for decades, as knowledge is power. Prevention with Pompe disease progression is compulsory and guidelines for handling late-onset patients identified via NBS can be established by physicians.

Accurate screening tests are available, and treatment for both infant and late-onset Pompe disease has proven effective in recent years. We have a duty to provide future generations with the best chance of living with Pompe disease through early diagnosis. For these reasons, please include Pompe disease on the federally mandated Newborn Screening Panel.

Hillary Gibson
Adult-Onset Pompe Disease Patient pompe.hillary@comcast.net Portland, Oregon USA

From: Gina Fox
To: Vasquez, Lisa (HRSA)
Subject: Pompe Newborn screening.
Date: Monday, May 13, 2013 1:51:23 PM

Hello Lisa, below is my letter to the SAC for my support of newborn screening for pompe disease.

Thank you members of the SACHDNC for taking the time to re-examine Pompe Disease for possible nomination to the recommended uniform screening panel. For my family, there is no question that early diagnosis would have resulted in a better quality of life for our son. While I understand that every patient responds differently to enzyme replacement therapy, it has been my observation that the earlier treatment is started, for the most part, the better the prognosis. I have been a close observer of pompe disease for the last 10 years, not just with my son, but with large portions of the pompe population as a whole. Our son started ERT in March of 2003 when he was 8 months old. It is important to note, that when he was born, the neonatologist labeled him as "strong" in his initial exam. However, in retrospect, he had already begun a slow regression and would soon be failing to thrive.At first his regression was difficult to see. At 3 months of age, during a routine exam, a heart murmur was observed. Hypertrophic Cardio myopathy was the diagnosis.

From 3 months to 6 months we sought the cause of the cardiomopathy. It was during this 3 month period that a dramatic weakening revealed itself. After 3 long months and a battery of tests its was determined that our son had Pompe disease. From 6 months to 8 months, as we tried to get therapy started, our son's strength diminished exponentially to the point where we were barley able to save his life. Had we started treatment, before he was 6 months old, when he was vigorous and strong, it is very safe to say, we would have a much stronger son today. I have seen countless videos and testimony from pompe families around the world to help support this claim. As it stands today, our son is 10 years old and 100% dependent on us for all his movements. He is on a ventilator 24 hours a day. He is also 100% g-tube dependent. He can not sit up on his own or roll over in bed.

He must always have one of us or a nurse by his side. I understand that there are issues that need to be resolved when it comes to newborn screening with pompe disease. To me, these issues pale in comparison to the positives that will come from newborn diagnosis of these desperate children. Not only will newborn screening possibly save some of these kids' lives, but, it most certainly will preserve a quality of life that will be lost forever otherwise. In the most server forms of the disease, pre-symptomatic treatment is a must! I would say, if the SACHDNC's goal is to "reduce morbidity and mortality in newborns and children with heritable disorders" then Pompe is a perfect candidate to achieve this goal. So I would ask you, please add Pompe disease to the recommended newborn screening panel. Thank you.

George Fox
gfox1@bellsouth.net 9241 nw 23rd place
Gainesville , FL 32606
352-328-6571

From: Maria Otero
To: Vasquez, Lisa (HRSA)
Subject: Pseudohypoaldosteronism
Date: Monday, May 13, 2013 2:36:11 PM

We would like to participate in the Meeting on Heritable Disorders in Newborns and Children under the public comments.

Pseudohypoaldosteronism is rare yet an important diagnosis to keep on the differential with the patients that have failure to thrive and/or laboratory abnormalities that are associated with it. How do we increase the awareness of this diagnosis among our already busy and time deprived pediatricians?
The pediatrician is the first physician who gets to see a PHA patient showing the following symptoms: weight loss, vomits which will lead to dehydration and death if not treated. After ordering the an electrolytes test, when the abnormal results are obtained, then the pediatrician will send the newborn to the hospital where will be seen by either endocrinologists or nephrologist
Are there a where patients and families diagnosed with this condition can turn to for help, support, latest information and trials/treatments?
With lack of any support group, two years ago we have created a group on Facebook that have raised awareness and have collaborated with parents who were able to provide information to their own doctors. This condition needs to be added as one of the possible reasons for a newborn to be diagnosed with failure to thrive. We are eager to help you all help the future generation of patients.
Sincerely,

Maria Isabel Otero

From: David Brown
To: Vasquez, Lisa (HRSA)
Subject: Why the US Government Should Support Pompe Screening -- A Personal Story
Date: Monday, May 13, 2013 10:42:14 AM

May 13, 2013

Ms. Lisa Vasquez
Health Resources and Services Administration Department of Health and Human Services
Rockville, Maryland

Dear Ms. Vasquez

Our family has learned that further consideration is being given by the Secretary's Discretionary Advisory Committee on Heritable Disorders in Newborns and Children to recommending federal encouragement of routine screening of newborns for Pompe disease.

For the parents of infants who may be born with the Pompe genetic defect in the future, that is very welcome news.

Our only grandchild, Julian Minh, is a victim of Pompe disease. At birth a ten-pound baby, Julian was seemingly healthy except for unexplained difficulties breathing. After that, he failed to thrive. Weakening muscles prevented him from taking milk by bottle and he took very little by breast. The breathing difficulties worsened and his weight fell to the 20th percentile for six month-olds. By six and one-half months, Julian was showing all the classic symptoms of Pompe. Only then, and after false starts based on the assumption that Julian's problem was simply refusal to take the bottle while his mother was at work, was his affliction was finally diagnosed.

Now, after 14 months of enzyme replacement therapy, Julian is responding well. Nonetheless, it is apparent that the physical damage done in those first months may never be undone. Absent new and more effective therapies, ahead of Julian very likely lies a lifetime in a wheelchair and on a ventilator.

Julian is receiving the best of care from his devoted parents and a talented team of specialists at Seattle's Childrens' hospital. For that we are most thankful. And yet -- if only infants were routinely screened for Pompe in Washington state when Julian was born, our grandchild could likely look forward to a fully normal childhood, adolescence and maturity.

As we understand the economics of care and prevention, inclusion of screening for Pompe in the newborn screening panel will be cost-effective. The benefits of early diagnosis are so apparent that a very good argument can also be made for accelerated genetic screening of adults or children who present any symptoms associated with the onset of Pompe.

From our experience, we also think it very important that there be heightened emphasis on training, including in-service training, for pediatric medical personnel in the recognition of glycogen storage diseases.

For further details, if needed, do not hesitate to contact us by e-mail (nworbd@g- mail.com and btblicsw@gmail.com).
Very sincerely yours,
David and Tuyet Brown 9074 N. Brookview Avenue Fresno, California 93720

From: Jean Public
To: Vasquez, Lisa (HRSA); americanvoices@mail.house.gov; speakerboehner@mail.house.gov; info@taxpayer.net; media@cagw.org; info@theteaparty.org
Cc: letters@newsweek.com; today@nbc.com; dsarjar@hrsa.gov
Subject: Fw: public COMMENT on federal - just another unresponsive govt agency full of insiders
Date: Friday, May 03, 2013 11:35:41 AM

This policy development will end up harming our children. American children used to be healthy, now they suffer from allergies, colitis, autism in huge numbers. American taxpayers have spent trillions of dollars with this do nothing agency and this is just more of the same crap. this is really about money and drug dealers controlling everything. the bribing and lobbying in Washington dc is in fact contaminating everything that emanates from that town. the lobbyists either offer money or new jobs through the revolving door to get what they want. the people are forgotten. absolutely forgotten. YOU SHOULD NOT HAVE TO HAVE EVERY SEAT FILLED WITH INSIDERS. THE ORDINARY AMERICANS SHOUDL HAVE 1/3 OF THE SEATS IN T HSI WASHGTKN INSIDER CROWD. I NOTE YOU HAVE ACED OUT EVERY ORDINARY AMERICAN TO HAVE INPUT INTO THESE POLICIES. TAXPAYERS ARE BEING GOUGED FOR HUGE SUMS WHEN THEY DONT EVEN HAVE A SEAT AT THIS TABLE. SOMETHING IS GOING VERY VERY WRONG IN WASHINGTON DC WITH THIS KIND OF INSIDER SET UP. THIS AGENCY USES AMERICANS AS GUINEA PIG FOR FINDINGS THAT ARE WHAT YOU WANT TO FIND, NOT WHAT IS TRUTH.

THIS AGENCY, WITH THIS SET UP, IS ENTIRELY UNRESPONSIVE TO THE US PUBLIC. WE NEED CHANGE IMMEDIATELY WITH THIS INSIDER SET UP. WE NEED ORDINARYAMERICANS SITTING ON THIS COUNCIL AND THIS COUNCIL SHOUDL BE RESPONSIVE. WE HAVE HAD TOO MUCH UNRESPONSIVENESS IN CONTAMINATED CORRUPT WASHINGTON DC TO THIS POINT. WE ARE TIRED OF DICTATORIAL PRONOUNCEMENTS FROM THIS AGENCY WITH NO TRUTH OR SHRED OF HONESTY AS PART OF IT. THIS COMMENT IS FOR THE PUBLIC RECORD. JEAN PUBLIC 2 GLENWAY FLEMINGTON NJ 08822

[Federal Register Volume 78, Number 84 (Wednesday, May 1, 2013)]
[Notices]
[Pages 25447-25448]
From the Federal Register Online via the Government Printing Office [http://www.gpo.gov/]
[FR Doc No: 2013-10241]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Establishment of the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children and Notice of Meeting
AGENCY: Health Resources and Services Administration, HHS.
ACTION: Notice of establishment of the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children and Notice of Meeting.

Authority: The Committee is governed by Public Health Service Act (PHS), 42 U.S.C. 217a: Advisory councils or committees as well as provisions of Public Law 92-463, as amended, (5 U.S.C. App. 2), which sets forth standards for the formation and use of advisory committees.
SUMMARY: The U.S. Department of Health and Human Services announces the establishment of the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children. This notice also announces the Committee's first meeting.
FOR FURTHER INFORMATION CONTACT: Debi Sarkar, Health Resources and Services Administration, Maternal and Child Health Bureau; Telephone: 301-443-1080; Email: dsarkar@hrsa.gov.
SUPPLEMENTARY INFORMATION:
I. Background and Authority
Under the Public Health Service Act (PHS), 42 U.S.C. 217a, the Secretary of Health and Human Services directed that the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children (DACHDNC) shall be established within the Department of Health and Human Services (HHS). To comply with the authorizing directive and guidelines under the Federal Advisory Committee Act (FACA), a charter

was filed with the Committee Management Secretariat in the General Services Administration (GSA), the appropriate committees in the Senate and U.S. House of Representatives, and the Library of Congress to establish the Committee as a discretionary federal advisory committee. The purpose of the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children (DACHDNC) is to advise the Secretary of Health and Human Services about aspects of newborn and childhood screening and technical information for the development of policies and priorities that will enhance the ability of the State and local health agencies to provide for newborn and child screening, counseling and health care services for newborns and children having, or at risk for, heritable disorders. The DACHDNC will review and report regularly on newborn and childhood screening practices, recommend improvements for newborn and childhood screening programs, as well as fulfill the list of requirements stated in the original authorizing legislation.

II. Structure

The Committee consists of fifteen (15) voting members, including the Chair. The members of the Committee were appointed by the Secretary. Membership is composed of the Chair, Special Government Employees (SGEs) and federal ex-officio members. Federal ex-officio members include the Administrator of the Health Resources and Services Administration; the Directors of the Centers for Disease Control and Prevention; the National Institutes of Health; the Agency for Healthcare Research and Quality; and the Commissioner of the Food and Drug Administration--or their designees. The Chair and other members are (a) medical, technical, public health or scientific professionals with special expertise in the field of heritable disorders or in providing screening, counseling, testing, or specialty services for newborns and children at risk for heritable disorders; (b) experts in ethics and heritable disorders who have worked and published material in the area of public health and genetic conditions; and (c) members from the public sector who have expertise, either professional or personal, about or concerning heritable disorders in order to achieve a fairly balanced membership.

The DACHDNC also includes nonvoting liaisons or representatives from Federal Agencies, public health constituencies, advocacy organizations and medical professional societies, as determined to be necessary by the Chair and/or the Designated Federal Official, to fulfill the duties of the DACHDNC. In addition, the DACHDNC is encouraged to work closely with other relevant HHS entities that focus on reviewing scientific evidence and making recommendations on clinical preventive services.

III. First Meeting of the DACHDNC

Dates and Times: May 16, 2013, 10:00 a.m. to 2:00 p.m.
May 17, 2013, 10:00 a.m. to 2:00 p.m.

Place: Virtual via Webinar.

Status: The meeting is open to the public. For more information on registration and webinar details, please visit the Committee's Web site: http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders.

Purpose: The Discretionary Advisory Committee on Heritable Disorders in Newborns and Children (Committee), as authorized by Public Health Service Act (PHS), 42 U.S.C. 217a: Advisory councils or committees, was established to advise the Secretary of the Department of Health and Human Services regarding the development of newborn screening activities, technologies, policies, guidelines, and programs for effectively reducing morbidity and mortality in newborns and children having, or at risk for, heritable disorders. The Committee's recommendations regarding additional conditions/inherited disorders for screening that have been adopted by the Secretary are included in the Recommended Uniform Screening Panel (RUSP) that constitutes part of the comprehensive guidelines supported by the Health Resources and Services Administration. Pursuant to section 2713 of the Public Health Service Act, codified at 42 U.S.C. 300gg-13, non-grandfathered health plans are required to cover screenings included in the HRSA-supported comprehensive guidelines without charging a co-payment, co-insurance, or deductible for plan years (i.e., policy years) beginning on or after the date that is one year from the Secretary's adoption of the condition for screening.

Agenda: The meeting will include: (1) A final report on the Pompe Condition Nomination for inclusion in the RUSP, and (2) updates on priority projects from the Committee's subcommittees on Laboratory Standards and Procedures, Follow-up and Treatment, and Education and Training.

The Committee is expected to vote on whether or not to recommend to the

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Secretary the addition of Pompe Disease to the Recommended Uniform Screening Panel (RUSP).

Certain proposed agenda items may be subject to change as necessary

or appropriate. The agenda, webinar information, Committee Roster, Charter, presentations, and meeting materials are located on the Committee's Web site at http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders.

Public Comments: Members of the public can submit written comments and/or register to present oral comments during the public comment period of the meeting. All comments, whether oral or written, are part of the official Committee record and will be available for public inspection and copying. Advance registration is required to present oral comments or submit written comments. Individuals who wish to make public comments are required to email Lisa Vasquez (lvasquez@hrsa.gov) by Tuesday, May 7, 2013. The public comment period is scheduled for the morning of May 17, 2013.

Written comments should identify the individual's name, address, email, telephone number, professional or business affiliation, type of expertise (i.e., parent, researcher, clinician, public health, etc.), and the topic/subject matter of comment. To ensure that all individuals who have registered to make oral comments can be accommodated, the allocated time may be limited. Individuals who are associated with groups or have similar interests may be requested to combine their comments and present them through a single representative. No audiovisual presentations are permitted.

Contact Person: Anyone interested in obtaining other relevant information should contact Debi Sarkar, Maternal and Child Health Bureau, Health Resources and Services Administration, Room 18A-19, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857; telephone: (301) 443-1080; email: dsarkar@hrsa.gov. The logistical challenges of coordinating this meeting hindered an earlier publication of this meeting notice.

More information on the Committee is available at http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders.

Dated: April 25, 2013.

Mary K. Wakefield,

Administrator.

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