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

2013 Annual Report

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Mission of the SACHDNC

The U.S. Department of Health and Human Services (HHS) Secretary's Advisory Committee on Heritable Disorders in Newborns and Children[I] (SACHDNC) was chartered in February 2003. The SACHDNC provides the Secretary with recommendations, advice, and technical information regarding the most appropriate application of technologies, policies, guidelines, and standards for: (a) effectively reducing morbidity and mortality in newborns and children having, or at risk for, heritable disorders; and (b) enhancing 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.

This report fulfills the legislative requirement to submit an annual report to Congress, the Secretary, the Interagency Coordinating Committee on Newborn and Child Screening, and State Health Departments.

[I] Authority: Public Health Service Act, Title XI, §1111 as amended (42 U.S.C. 300b-10)

Executive Summary

The Secretary's Advisory Committee on Heritable Disorders in Newborns and Children advises the Secretary of the U.S. Department of Health and Human Services. The Committee's guidance and information serves to enhance the states' ability to apply the most current technologies, policies, guidelines, and standards for effectively reducing morbidity and mortality in newborns and children having, or at risk of, heritable disorders. Heritable disorders can be present at birth and comprise a group of conditions that, undetected, can cause intellectual disabilities, physical disabilities, life-threatening diseases, and/or death. Newborn screening for heritable disorders is a longstanding public health program that provides early identification and follow-up for the treatment of infants affected by certain genetic, metabolic, hormonal, infectious, and/or functional conditions. The intent of newborn screening, along with follow-up, diagnosis, disease management and treatment, evaluation, and education, is to prevent the potentially devastating consequences of disabilities, life-threatening diseases, or death for newborns and children.

Listed below are highlights of the SACHDNC's work during calendar year 2012.

- The Committee approved the condition nominations for Pompe disease and Mucopolysaccharidosis I for review by the Condition Review Workgroup.
- A report, *Implementing Point-of-Care Newborn Screening*, was submitted to the Secretary.
- An enhanced description was developed for the medical home, and for strategies to improve linkage to the medical home, for children with heritable disorders.[II]
- The Committee supported activities related to the harmonization of newborn screening quality indicators and case definitions across the country.
- A condition review matrix was refined as a methodological tool for systematically evaluating the magnitude and certainty of the net benefit of screening and the capacity of state newborn screening programs to implement screening for nominated conditions.
- A report entitled, *Improving Data Quality and Quality Assurance in Newborn Screening by Including the Blood Spot Screening Collection Device Serial Number on Birth Certificates*, was issued by the Committee. Based on this report, four recommendations on improving data quality and quality assurance in newborn screening were forwarded to the Secretary.
- For the 50th Anniversary of Newborn Screening Campaign in 2013, the Committee supported the Centers for Disease Control and Prevention and the Association of Public Health Laboratories in planning and organizing activities for the campaign.

[II] Description contained in the paper *Family-Centered Coordinated Co-Management for Individuals with Heritable Conditions*, developed by the Medical Home Workgroup of the National Coordinating Center for the Regional Genetic and Newborn Screening Service Collaboratives.

- The Committee approved a report, developed by the Follow-Up and Treatment Subcommittee on *Insurance Coverage of Medical Foods for Treatment of Inherited Metabolic Disorders*, to inform federal and state policy makers about the financial burden regarding treatment of children with inborn errors of metabolism and bring awareness to the need for improved insurance coverage of medical foods.

Report

This report discusses activities undertaken by the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) from January to December 2012, including guidelines on peer-reviewed newborn screening (NBS) follow-up and treatment in the U.S. The discussion portion of this report is subdivided into sections that are aligned with the Committee's legislative duties.

1. Advice and Recommendations: Grants and Projects

> The Advisory Committee shall—
>
> (1) provide advice and recommendations to the Secretary concerning grants and projects awarded or funded under section 300b–8 of this title;

During 2012, no updates occurred regarding the provision of advice and recommendations to the Secretary concerning grants and projects.

2. Technical Information

> The Advisory Committee shall—
>
> (2) provide technical information to the Secretary for the development of policies and priorities for the administration of grants under section 300b–8 of this title;

During 2012, the SACHDNC submitted the report *Implementing Point-of-Care Newborn Screening* to the Secretary, to provide insight and information regarding: (a) newborn point-of-care (POC) screening from various viewpoints (e.g., public health, provider, newborn nursery); (b) the POC screening definition; (c) identifying key considerations for inclusion of POC screening; (d) major challenges; (e) screening criteria; and (f) implementation guidelines (Bocchini, March 2012, POC).

The Committee noted in the report that POC screening encompasses physiologic tests that are administered and interpreted outside the laboratory but close to the site of direct delivery of medical care, such as birth hospital or nursery. In turn, POC NBS describes those practices in which results are obtained at the bedside, with oversight from public health agencies for the detection of a state-specified list of conditions (e.g., hearing screening, pulse oximetry for Critical Congenital Heart Disease, or CCHD). The report stated that POC NBS, with appropriate infrastructure, provides opportunities to expand universal NBS for additional treatable disorders, which may lead to timely diagnosis and quality medical care for potentially life threatening heritable conditions (Bocchini, March 2012, POC).

3. Systematic Evidence-Based and Peer-Reviewed Recommendations

> The Advisory Committee shall—
>
> (3) make systematic evidence-based and peer-reviewed recommendations that include the heritable disorders that have the potential to significantly impact public health for which all newborns should be screened, including secondary conditions that may be identified as a result of the laboratory methods used for screening;

The SACHDNC reviews nominated heritable conditions and decides if sufficient evidence is available to assign nominated conditions to an external evidence review by the Condition Review Workgroup (CRW). When nominated heritable conditions are assigned to the CRW, the CRW performs an independent, evidence-based review to determine the suitability and potential net benefit of screening for the nominated condition, based upon the systematic evaluation of results of controlled trials, observational studies, case studies, expert opinion, focus groups, cost-effectiveness analysis, policy analyses, and ethical analysis. Based on the CRW review, the SACHDNC votes to recommend, or not recommend, adding the nominated condition to the recommended uniform screening panel (RUSP). The Secretary of Health and Human Services (HHS) makes the final decision on whether to add, or not add, a recommended condition to the RUSP.

During 2012, the SACHDNC reviewed nominations for 22q11 (Bocchini, May 2012) and X-linked Adrenoleukodystrophy (ALD) (Bocchini, October 2012), but determined that there was not sufficient evidence to assign these conditions forward to the CRW. The committee also requested that the CRW conduct a formal evidence review of Mucopolysaccharidosis I (MPS I) and Pompe disease during 2012.[III] As of December 2012, these reviews were still in progress.

The CRW presented their findings on Hyperbilirubinemia/Kernicterus to the Committee in January 2012. Based on the data provided by the CRW, the Committee voted to not add this condition to the RUSP, basing their decision on the need for greater evidence in clinical validity and effectiveness[IV] (Bocchini, February 2012).

4. Decision Matrix

> The Advisory Committee shall—
>
> (4) develop a model decision-matrix for newborn screening expansion, including an evaluation of the potential public health impact of such expansion, and periodically update the recommended uniform screening panel, as appropriate, based on such decision-matrix;

During September 2012, the SACHDNC approved the updated condition review matrix as a methodological tool for categorizing and assigning value to nominated conditions to support the development of specific recommendation to the SACHDNC about the nominated condition and enhanced transparency in the process of which nominated conditions do and do

[III] Pompe disease was previously submitted in 2006 and reviewed in 2008, but the SACHDNC did not recommend adding the condition to the RUSP at that time due to the need for additional studies.
[IV] Refer to the topic Hyperbilirubinemia/Kernicterus in Appendix B.

not get recommended for addition to the RUSP. The revised decision matrix creates a more formal approach to rating the magnitude and certainty of the net benefit of screening all newborns for nominated conditions, and adds a consideration of the capacity of state newborn screening programs to implement population-wide screening for nominated conditions by evaluating the feasibility and readiness of states to incorporate screening into their newborn screening programs (Kemper, 2012).

5. State Capacity to Screen

The Advisory Committee shall—

(5) consider ways to ensure that all States attain the capacity to screen for the conditions described in paragraph (3), and include in such consideration the results of grant funding under section 300b–8 of this title;

The Committee heard updates on the Federal Plan of Action for implementing CCHD screening from the National Institutes of Health (NIH), the Health Resources and Services Administration (HRSA), and the Centers for Disease Control and Prevention (CDC). In addition, representatives from the states of New Jersey and Indiana presented to the Committee their respective processes of implementing CCHD screening. Presentations included best practices and lessons learned.

6. Recommendations, Advice, or Information

The Advisory Committee shall—

(6) provide such recommendations, advice or information as may be necessary to enhance, expand or improve the ability of the Secretary to reduce the mortality or morbidity from heritable disorders, which may include recommendations, advice, or information dealing with—

A. Follow-Up Activities

(A) follow-up activities, including those necessary to achieve rapid diagnosis in the short-term, and those that ascertain long-term case management outcomes and appropriate access to related services;

In May 2012, the SACHDNC voted to acknowledge the enhanced description of the medical home and strategies for improving linkage to the medical home for children with heritable disorders presented in the paper *Family-Centered Coordinated Co-Management for Individuals with Heritable Conditions*. Report recommendations include identifying innovative programs; incorporating care planning, co-management, and family access functions into electronic health records and related information systems; systematically evaluating preferences, concerns, and needs; promoting outcomes-based research; conducting trainings; and developing methods to incentivize medical home services (Kemper, 2012).

B. Implementation, Monitoring, and Evaluation

(B) implementation, monitoring, and evaluation of newborn screening activities, including diagnosis, screening, follow-up, and treatment activities;

During the SACHDNC's May 2012 meeting, the Follow-Up and Treatment Subcommittee presented a report on *Insurance coverage of Medical Foods for Treatment of Inherited Metabolic Disorders*, developed through a survey of parents that concerned the insurance coverage of medical foods and supplements and modified low-protein foods in the treatment of children with inborn errors of metabolism. The Committee reviewed and acknowledged the report's significance in conveying the challenges parents face in paying for these treatments due to lack of insurance coverage (Berry, 2012).

The SACHDNC appointed an ad-hoc workgroup to engage a multidisciplinary stakeholder group in collecting and documenting perspectives on public health, personal health, and health care system readiness and requirements concerning expanded population-based carrier screening for genetic conditions. During September 2012, the Committee received an update concerning ongoing workgroup efforts to examine population-based carrier screening from five components: (a) social, (b) economic, (c) psychological, (d) education and communication, and (e) testing issues.

Also, in recognition of newborn screening and its value, the SACHDNC requested an update from the CDC's National Center on Birth Defects and Developmental Disabilities and the Association of Public Health Laboratories (APHL) on the multistate analysis of single test versus second screen routine testing in NBS for hypothyroidism and congenital adrenal hyperplasia. The study examined the effects and utility of a routine second screen administered on newborns. Currently, 22.4% of all newborns in the U.S. receive a second screen, regardless of the outcome of their first screen, to reduce the chance of missing early signs of heritable disorders (Shapira, 2012).

Researchers found that in about 12% of cases of primary congenital hypothyroidism and about 38% of cases of congenital adrenal hyperplasia (both classical and nonclassical types), the disorders were detected in infants on the second screen and not on the first screen. Additionally, the data suggest that characteristics such as sex, race/ethnicity, birth weight, and age at collection all contributed to whether the conditions were more likely to be identified in the first or second screen (Shapira, 2012).

C. Diagnostic and Other Technology

(C) diagnostic and other technology used in screening;

During 2012, no updates occurred regarding diagnostics and other technology used in screening.

D. Availability and Reporting of Testing

(D) the availability and reporting of testing for conditions for which there is no existing treatment;

During 2012, no updates occurred regarding the availability and reporting of testing for conditions for which there is no existing treatment.

E. Conditions Not Included in RUSP

(E) conditions not included in the recommended uniform screening panel that are treatable with Food and Drug Administration-approved products or other safe and effective treatments, as determined by scientific evidence and peer review;

During 2012, no updates occurred regarding conditions not included in the RUSP that are treatable with Food and Drug Administration-approved products or other safe and effective treatments.

F. Minimum Standards and Related Policies and Procedures

(F) minimum standards and related policies and procedures used by State newborn screening programs, such as language and terminology used by State newborn screening programs to include standardization of case definitions and names of disorders for which newborn screening tests are performed;

The SACHDNC supported activities related to the standardization of NBS case definitions and quality indicators. Each diagnosis resulting from NBS is confirmed in a manner determined appropriate by state consultants and clinicians. Without uniformity, the true prevalence and incidence of these disorders remain unknown. The goals of the case definitions project were to develop uniform surveillance case definitions for NBS conditions detected through state NBS programs and harmonize definitions across programs for national monitoring of babies' health outcomes. The project is currently in progress, and is undergoing pilot testing in various states.

The purpose of the NBS quality indicators project is to examine quality indicators currently used in states and determine which indicators can feasibly be collected, to harmonize quality indicators across the country. The project also examined the utility of current quality indicators and determined other quality indicators that states should collect. A list of ten key quality indicators was compiled and beta tested in New Jersey. The project is ongoing, and will continue to beta test and refine the quality indicators.

G. Quality Assurance, Oversight and Evaluation

(G) quality assurance, oversight, and evaluation of State newborn screening programs, including ensuring that tests and technologies used by each State meet established standards for detecting and reporting positive screening results;

In January 2012, the SACHDNC issued a report on *Improving Data Quality and Quality Assurance in Newborn Screening by Including the Blood Spot Screening Collection Device Serial Number on Birth Certificates*, and submitted the following recommendations to the Secretary of Health and Human Services:

- The Secretary should encourage state NBDS programs to utilize the unique serial number on each initial newborn screening specimen collection device to aid in electronic tracking and identification. To facilitate national harmonization, the format of this number should be in a standard format that includes a checksum character to assure quality control of the computerized input of the serial number.
- The Secretary should work with the National Association for Public Health Statistics and Information Systems (NAPSIS) toward a goal of including the NDBS serial number on the birth certificate, to facilitate confirming access of all newborns to timely newborn screening and to provide an external mechanism for evaluating specific demographic data recorded on the birth certificate. The use of these data for improving electronic health information and service quality should be emphasized.
- The Secretary should work with the National Center for Health Statistics (NCHS) toward a goal of including a field for the NDBS serial number (consistent with recommendations in Clinical and Laboratory Standards Institute LA4-A5) in the next revision of the U.S. Standard Certificate of Live Birth. Inclusion of this field should be 'required' because NDBS is a required activity in all states and comparison of birth certificates to NDBS specimen records represents the most efficient way to confirm screening universality.
- The Secretary should encourage State birth registrars and state newborn screening program directors to consider ways in which electronic data validation of the demographic information, collected by the NDBS and EBRS activities, can be used for cross validation and data quality improvement (Bocchini, March 2012, Improving Data Quality).

The Secretary responded to the Committee stating that further analysis is needed before a decision is made (Sebelius, September 2012). Currently, the Committee's report is under review by the Interagency Coordinating Committee on Newborn and Children Screening (ICC). For more information, refer to the topic *Improving Data Quality in Newborn Screening* in Appendix B.

H. Public and Provider Awareness

(H) public and provider awareness and education;

During April 2012, the SACHDNC's Education and Training Subcommittee, in conjunction with HRSA's Maternal and Child Health Bureau's Genetic Services Branch, convened a meeting to discuss strategies to inform and educate expectant parents, health care professionals, policymakers, and the general public about NBS. The CDC and APHL intend to incorporate these suggested strategies into organizing

efforts for campaign planning (with the SACHDNC's involvement) to recognize the 50th Anniversary of Newborn Screening. Two planned activities for the campaign include a Newborn Screening Symposium, scheduled for May 5–10, 2013 in Atlanta, Georgia, and a National Newborn Screening Commemorative Event, scheduled for next year in Washington, D.C.

I. Cost and Effectiveness

> (I) the cost and effectiveness of newborn screening and medical evaluation systems and intervention programs conducted by State-based programs;

The SACHDNC considers the insight into rapidly evolving genetic technology, with its associated costs and effectiveness, to be critically important in supporting the Secretary in reducing the morbidity and mortality in newborns and children having, or at risk for, heritable disorders. In September 2012 the SACHDNC heard a synopsis on *Translating Genomic-Based Research for Health*, a discussion held during an Institute of Medicine workshop on Assessing the Economics of Genomic Medicine. The workshop was designed to discuss the clinical implementation of genetic and genomic technologies by examining the costs associated with the development and use of genetic and genomic information in the care of individual patients (Wicklund, 2012).

J. Causes, Public Health Impacts, and Risk Factors

> (J) identification of the causes of, public health impacts of, and risk factors for heritable disorders; and

Identifying the cause, public health impact, and risk factors for heritable disorders continues to be a focus of the SACHDNC. In September 2012, the SACHDNC heard a report on the progress of the Pregnancy and Health Profile Screening and Risk Assessment Tool, developed in a partnership between the National Coalition for Health Professionals in Genetics, Genetic Alliance, March of Dimes, Partners Healthcare, and HRSA. The risk assessment tool integrates genetics and NBS information into a health history to assist genetic clinical decision making, educate patients and providers, and address the life course of the female patient. The ability to integrate genetic and NBS information assists providers in detecting risk factors and mitigating harm, thus lessening the impact of heritable disorders on the public health system (Scott, 2012).

K. Coordination of Surveillance Activities

> (K) coordination of surveillance activities, including standardized data collection and reporting, harmonization of laboratory definitions for heritable disorders and testing results, and confirmatory testing and verification of positive results, in order to assess and enhance monitoring of newborn diseases.

The SACHDNC continued their focus on the coordination of surveillance activities by hearing a report during September 2012 on the Ethical, Legal, and Social

Implications Program from the Health National Human Genome Research Institute (NHGRI) of NIH. The report outlined the NHGRI's strategic plan for the future of genomics research, which currently encompasses understanding the biology of disease and advancing the science of medicine as well as improving the effectiveness of health care. The plan considers: (a) psychosocial and ethical issues in genomics research and medicine, (b) legal and public policy issues, and (c) broader societal issues.

In September 2012, the National Center for Preparedness, Detection, and Control of Infectious Diseases at the CDC provided an update to the SACHDNC regarding *Recommendations for Good Laboratory Practices in Biochemical Genetic Testing and NBS for Inherited Metabolic Disorders*. The expected outcomes of implementing these recommendations include improving the quality of laboratory genetic services, enhancing the oversight for genetic testing through the use of the current regulatory framework, and improving the health care outcomes from genetic testing (Chen & Greene, 2012).

Future Forecast

Future plans by the SACHDNC have been grouped into three main categories: education and training, laboratory standards, and follow-up and treatment.

Education and Training

The SACHDNC is examining a list of heritable disorders for which education and training could provide benefit, beyond the newborn period, to providers and patients. Once a final list is determined, the SACHDNC will work with stakeholders to identify infrastructure requirements associated with childhood screening, challenges and opportunities presented by these requirements, and education and training needs related to these conditions. In addition, the SACHDNC will support the APHL's NBS Awareness Campaign by providing input regarding appropriate audiences and messages, as well as support the efforts of the CDC and APHL to commemorate the 50th Anniversary of NBS. Finally, the SACHDNC is working on providing information that will support future nominators in preparing application packages.

Laboratory Standards and Procedures

The SACHDNC is exploring new diagnostic technologies, beginning with a survey of the use of succinylacetone to screen for Tyrosinemia Type I. The Committee will examine the collection and analysis of data from this survey to determine the advantages, limitations and challenges of using succinylacetone as a specific marker for Tyrosinemia Type I. In addition, the Committee is interested in providing guidance to state laboratories concerning conditions that have been newly added to the RUSP, starting with Severe Combined Immunodeficiency (SCID), as well as support the development of NBS quality indicators and case definitions. Furthermore, the Committee is establishing a process to review the RUSP and recommend specific changes as laboratory technology evolves.

Follow-Up and Treatment

The SACHDNC will consider challenges in POC-NBS by examining lessons learned from early hearing detection and intervention (EHDI) that may be applicable to CCHD screening and other POC screening. Issues considered will include integration of POC screening with the bloodspot screening program, and the roles of public health in clinical POC testing, reporting and follow up. The Committee will also develop a framework that can be used to assess the outcomes of NBS. To be certain that any framework will be practical and useful, experts in Sickle Cell Disease (SCD) will be involved to apply the framework to SCD as an example. The framework will be applicable to other conditions with respect to the types of data elements and data sources needed to know if the goals of screening are being achieved. Furthermore, the Committee will also begin to explore the impact of the Affordable Care Act on individuals and families with heritable conditions.

Conclusion

During 2012, the SACHDNC continued to provide recommendations, advice, and technical information to assist the Secretary in efforts to reduce the morbidity and mortality in newborns and children having, or at risk of, heritable disorders.

The SACHDNC continued to make systematic, evidence-based and peer-reviewed recommendations for which all newborns should be screened. The Committee reviewed nominations for 22q11 and ALD, and approved condition nominations for Pompe disease and MPS I to be reviewed by the Condition Review Workgroup. SACHDNC also developed an updated condition review matrix as a methodological tool for systematically evaluating the magnitude and certainty of the net benefit of screening and added an analysis of the capacity of state NBS programs to implement screening for nominated conditions to its decision matrix.

SACHDNC continues to serve in a leadership role in the field of NBS and heritable disorders. The Committee issued and supported reports on implementing POC NBS, improving data quality and quality assurance in NBS, supported strategies for improving linkage to the medical home for children with heritable disorders, and insurance coverage of medical foods for the treatment of inherited metabolic disorders. The Committee also received updates from partners and experts in the field on the Federal Plan of Action, the effects and utility of a routine second screen administered on newborns, the clinical implementation of genetic and genomic technologies, the development of a Pregnancy and Health Profile Screening and Risk Assessment Tool, and recommendations for good laboratory practices in biochemical genetic testing and NBS.

The coordinated efforts of the SACHDNC and stakeholders—including policymakers, state public health agencies, providers, and the public—will continue to ensure that newborns and children have universal access to high-quality screening, follow-up, diagnosis, disease management and treatment, evaluation, and education, which may prevent the potentially devastating consequences of disabilities, life-threatening diseases, or death.

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Appendix A: Recommended Uniform Screening Panel[1]

Core [2] Conditions [3]
(as of December 2012)

ACMG Code	Core Condition	Metabolic Disorder			Endocrine Disorder	Hemoglobin Disorder	Other Disorder
		Organic acid condition	Fatty acid oxidation disorders	Amino acid disorders			
PROP	Propionic acidemia	X					
MUT	Methylmalonic acidemia (methylmalonyl-CoA mutase)	X					
Cbl A,B	Methylmalonic acidemia (cobalamin disorders)	X					
IVA	Isovaleric acidemia	X					
3-MCC	3-Methylcrotonyl-CoA carboxylase deficiency	X					
HMG	3-Hydroxy-3-methyglutaric aciduria	X					
MCD	Holocarboxylase synthase deficiency	X					
ßKT	ß-Ketothiolase deficiency	X					
GA1	Glutaric acidemia type I	X					
CUD	Carnitine uptake defect/carnitine transport defect		X				
MCAD	Medium-chain acyl-CoA dehydrogenase deficiency		X				
VLCAD	Very long-chain acyl-CoA dehydrogenase deficiency		X				
LCHAD	Long-chain L-3 hydroxyacyl-CoA dehydrogenase deficiency		X				
TFP	Trifunctional protein deficiency		X				
ASA	Argininosuccinic aciduria			X			
CIT	Citrullinemia, type I			X			
MSUD	Maple syrup urine disease			X			
HCY	Homocystinuria			X			
PKU	Classic phenylketonuria			X			
TYR I	Tyrosinemia, type I			X			
CH	Primary congenital hypothyroidism				X		
CAH	Congenital adrenal hyperplasia				X		
Hb SS	S,S disease (Sickle cell anemia)					X	
Hb S/ßTh	S, βeta-thalassemia					X	
Hb S/C	S,C disease					X	
BIOT	Biotinidase deficiency						X
CCHD	Critical congenital heart disease						X
CF	Cystic fibrosis						X
GALT	Classic galactosemia						X
HEAR	Hearing loss						X
SCID	Severe combined immunodeficiences						X

1. Selection of conditions based upon “Newborn Screening: Towards a Uniform Screening Panel and System.” *Genetic Med*. 2006; 8(5) Suppl: S12-S252” as authored by the American College of Medical Genetics (ACMG) and commissioned by the Health Resources and Services Administration (HRSA).
2. Disorders that should be included in every Newborn Screening Program.
3. Nomenclature for Conditions based upon “Naming and Counting Disorders (Conditions) Included in Newborn Screening Panels.” *Pediatrics*. 2006; 117 (5) Suppl: S308-S314.

SACHDNC Recommended Uniform Screening Panel[1]
SECONDARY[2] CONDITIONS [3]
(as of December 2012)

ACMG Code	Secondary Condition	Metabolic Disorder			Hemoglobin Disorder	Other Disorder
		Organic acid condition	Fatty acid oxidation disorders	Amino acid disorders		
Cbl C,D	Methylmalonic acidemia with homocystinuria	X				
MAL	Malonic acidemia	X				
IBG	Isobutyrylglycinuria	X				
2MBG	2-Methylbutyrylglycinuria	X				
3MGA	3-Methylglutaconic aciduria	X				
2M3HBA	2-Methyl-3-hydroxybutyric aciduria	X				
SCAD	Short-chain acyl-CoA dehydrogenase deficiency		X			
M/SCHAD	Medium/short-chain L-3-hydroxyacl-CoA dehydrogenase deficiency		X			
GA2	Glutaric acidemia type II		X			
MCAT	Medium-chain ketoacyl-CoA thiolase deficiency		X			
DE RED	2,4 Dienoyl-CoA reductase deficiency		X			
CPT IA	Carnitine palmitoyltransferase type I deficiency		X			
CPT II	Carnitine palmitoyltransferase type II deficiency		X			
CACT	Carnitine acylcarnitine translocase deficiency		X			
ARG	Argininemia			X		
CIT II	Citrullinemia, type II			X		
MET	Hypermethioninemia			X		
H-PHE	Benign hyperphenylalaninemia			X		
BIOPT (BS)	Biopterin defect in cofactor biosynthesis			X		
BIOPT (REG)	Biopterin defect in cofactor regeneration			X		
TYR II	Tyrosinemia, type II			X		
TYR III	Tyrosinemia, type III			X		
Var Hb	Various other hemoglobinopathies				X	
GALE	Galactoepimerase deficiency					X
GALK	Galactokinase deficiency					X
	T-cell related lymphocyte deficiencies					X

1. Selection of conditions based upon “Newborn Screening: Towards a Uniform Screening Panel and System.” *Genetic Med*. 2006; 8(5) Suppl: S12-S252” as authored by the American College of Medical Genetics (ACMG) and commissioned by the Health Resources and Services Administration (HRSA).
2. Disorders that can be detected in the differential diagnosis of a core disorder.
3. Nomenclature for Conditions based upon “Naming and Counting Disorders (Conditions) Included in Newborn Screening Panels.” *Pediatrics*. 2006; 117 (5) Suppl: S308-S314.

Appendix B: SACHDNC Recommendations and Secretary Response, 2012

TOPIC	SACHDNC RECOMMENDATION	SECRETARY'S RESPONSE/OUTCOME
Hyperbilirubinemia/ Kernicterus	In a February 21, 2012 letter to the nominators, the SACHDNC responded to the nomination of Hyperbilirubinemia/Kernicterus for inclusion in the RUSP for state newborn screening programs. The Committee stated that they requested a formal review of the scientific evidence by the Condition Review Workgroup. However, the Committee decided not to add Hyperbilirubinemia/Kernicterus to the RUSP. This decision was based on the determination that "screening clinical validity should be improved," " there are significant gaps in the evidence," and "more data are required about the cost effectiveness for Recommended Uniform Newborn Screening Panel (RUSP) addition, as opposed to current practices and standards of care." (Bocchini, February 2012).	N/A
Point-of-Care	In a March 9, 2012 letter to the Secretary, the SACHDNC noted that they voted to support and affirmed the value of the *Implementing Point-of-Care Newborn Screening* report. The report "addresses the importance of establishing POC-NBS implementation standards, ensuring quality assurance, and developing systems of diagnostic confirmation, follow-up, data collection, and program evaluation. The report also provides state public health agencies, clinicians and hospitals with suggested guidance and strategies to implement POC-NBS. This information can help assure high quality, universal access to newborn screening; establish standards of care; and provide mechanisms for effective diagnosis, intervention, and follow-up care." (Bocchini, March 2012, POC).	In a letter dated April 3, 2012, Secretary Sebelius responded to the letter, stating that "the report provides valuable insight and information for the community and providers involved in newborn screening." (Sebelius, April 2012).
Improving Data Quality in Newborn Screening	In a March 9, 2012 letter to the Secretary, the SACHDNC summarized their response to the report, *Improving Data Quality and Quality Assurance in Newborn Screening by Including the Bloodspot Screening Collection Device Serial Number on Birth Certificates*. The Committee issued the following formal recommendations for consideration: "1) The Secretary should encourage state NDBS programs to utilize the unique serial number on each initial newborn screening specimen collection device to aid in electronic tracking and identification. To facilitate national harmonization, the format of this number should be in a standard format that includes a checksum character to assure quality control of the computerized input of the serial number. 2) The Secretary should work with the National Association for Public Health Statistics and Information Systems (NAPHSIS) toward a goal of including the NDBS serial number on the birth certificate, to facilitate confirming access of all	In a letter dated September 7, 2012, Secretary Sebelius responded to the letter by stating that "further analysis of the issues and advice on the Committee's recommendations by relevant Department of Health and Human Services agencies is needed before I can make a decision. Therefore, I am referring the Committee's report to the Interagency Coordinating Committee on Newborn and Children Screening (ICC) for its review and input regarding the Committee's recommendations for the development of quality assurance mechanisms to improve data quality in newborn screening. I will encourage the ICC to submit a report with their analysis, advice, and recommendations by March 31, 2013." (Sebelius, September 2012).

TOPIC	SACHDNC RECOMMENDATION	SECRETARY'S RESPONSE/OUTCOME
	newborns to timely newborn screening and to provide an external mechanism for evaluating specific demographic data recorded on the birth certificate. The use of these data for improving electronic health information and service quality should be emphasized. 3) The Secretary should work with the National Center for Health Statistics (NCHS) toward a goal of including a field for the NDBS serial number (consistent with recommendations in CLSI LA4-A5) in the next revision of the U.S. Standard Certificate of Live Birth. Inclusion of this field should be 'required' because NDBS is a required activity in all states and comparison of birth certificates to NDBS specimen records represents the most efficient way to confirm screening universality. 4) The Secretary should encourage State birth registrars and state newborn screening program directors to consider ways in which electronic data validation of the demographic information, collected by the NDBS and EBRS activities, can be used for cross validation and data quality improvement." (Bocchini, March 2012, Improving Data Quality).	
Adrenoleukodystrophy	In an October 1, 2012 letter to the nominators, the SACHDNC responded to the nomination of X-linked Adrenoleukodystrophy for inclusion in the RUSP for state newborn screening programs by stating "at this time, the Committee has decided to not send the nomination forward to the external condition review group." The Committee further added that the "decision is based primarily on the determination that sufficient prospective data is not yet available from the large pilot study presently underway at the Mayo Biochemical Genetics Laboratory (MBGL)." (Bocchini, October 2012).	N/A

Appendix C: SACHDNC Members

SACHDNC members are appointed by the Secretary or designee, and shall not exceed 15 voting members, including the Chair and Federal Ex-Officio members. The Committee may also include up to 12 non-voting organizational representatives, as the Secretary determines necessary.

The Designated Federal Official from HRSA's Maternal and Child Health Bureau serves as the government's agent for matters related to the management of the SACHDNC's activities, and ensures all procedures are within applicable statutory, regulatory, and HHS General Administration Manual directives.

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Appendix D: Glossary

Term	Definition
22q11	Condition (also referred to as DiGeorge syndrome) caused by a defect in chromosome 22, associated with deficiencies in heart and immune system function, a cleft palate and complications resulting from inadequate calcium in the blood (Mayo, 2013, DiGeorge).
Adrenoleukodystrophy (ALD)	Hereditary condition causing an inability to break down very long-chain fatty acids, resulting in damage to the myelin sheath, nervous system and adrenal glands (Mayo, 2013, Adrenoleukodystrophy).
Critical Congenital Heart Disease (CCHD)	Group of defects present in the heart structure at birth, causing severe and life-threatening symptoms and requiring intervention within the first year of life.
Heritable Disorders	Group of genetically inherited conditions present at birth that, undetected, can cause intellectual/physical disabilities and life-threatening illnesses.
Neonatal Hyperbilirubinemia	Condition distinguished by a build-up of bilirubin in an infant that, untreated, results in severe jaundice and serious health complications (Mayo, 2013, Infant Jaundice).
Newborn Screening (NBS)	Practice of testing babies for heritable disorders and conditions that can hinder their normal development, enabling early detection/treatment and preventing intellectual/physical disabilities and life-threatening illnesses.
Pompe disease	Condition resulting from mutations in the GAA gene that affects the heart and skeletal muscles (NINDS, 2013).
Recommended Uniform Screening Panel (RUSP)	Standard guideline for the newborn screening of heritable conditions, consisting of a list of conditions referred to as a screening panel. This panel provides guidance to the states regarding the latest evidence-based medical recommendations for newborn screening.
Severe Combined Immunodeficiency (SCID)	Primary immune deficiency disease distinguished by the lack of T-cells and B-cell function that, untreated, results in vulnerability to opportunistic infections and early death (SCID, 2013).

Term	Definition
Sickle Cell Disease Carrier	Individual who “carries” sickle cell mutation (i.e., sickle cell trait), is clinically benign under ordinary circumstances, and often asymptomatic. This is due to the carrier possessing a recessive, disease-causing allele on one chromosome and a normal allele on the other chromosome.

Appendix E: Acronyms

ALD	Adrenoleukodystrophy
APHL	Association of Public Health Laboratories
CCHD	Critical Congenital Heart Disease
CDC	Centers for Disease Control and Prevention
CLSI	Clinical and Laboratory Standards Institute
CRW	Condition Review Workgroup
EBRS	Electronic Birth Registration Systems
IBEM	Inborn Errors of Metabolism
ICC	Interagency Coordinating Committee
HHS	U.S. Department of Health and Human Services
HRSA	Health Resources and Services Administration
MBGL	Mayo Biochemical Genetics Laboratory
MPS I	Mucopolysaccharidosis I
NBS	Newborn Screening
NBSTRN	Newborn Screening Translational Research Network
NCHS	National Center for Health Statistics
NDBS	Newborn Dried Bloodspot Screening
NHGRI	National Human Genome Research Institute
NIH	National Institutes of Health
POC	Point-of-Care
RUSP	Recommended Uniform Screening Panel
SACHDNC	Secretary's Advisory Committee on Heritable Disorders in Newborns and Children
SCID	Severe Combined Immunodeficiency