2011 Annual Report to Congress

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

Committee Report

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EXECUTIVE SUMMARY

Health and development in newborns and children depends on a complex interaction between genetic and environmental factors. Many important genetic conditions are identified by newborn screening, a longstanding public health program that provides early identification and follow-up for treatment of infants affected by certain genetic, metabolic, hormonal, infectious, and/or functional conditions. Screening detects disorders in newborns that, if left untreated, can cause physical and/or intellectual disabilities, serious illness, and even death. The Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) was chartered in February 2003 to advise the Secretary regarding the most appropriate application of technologies, policies, guidelines, and standards for effectively reducing morbidity and mortality in newborns and children having or at risk for heritable disorders.

The 110th Congress enacted the Newborn Screening Saves Lives Act of 2008 (the Act) to amend the authorizing legislation, the Public Health Service (PHS) Act, 42 U.S.C. 300b-10, which established the Heritable Disorders Program, SACHDNC, and associated grant programs. The Act added several programs and further defined activities for SACHDNC. This report fulfills a requirement of the amending legislation: an annual report to Congress, the Secretary of the Department of Health and Human Services (HHS), the Interagency Coordinating Committee established by the legislation, and State Health Departments, to be submitted 3 years after the date of enactment of the Act.

As instructed in the Act, Part I of the report discusses peer-reviewed newborn screening guidelines formulated by SACHDNC. The report details the process by which conditions come under SACHDNC consideration for addition to the recommended uniform screening panel (RUSP). The extensive, ongoing efforts of SACHDNC to adhere to the most rigorous process possible for the systematic review of scientific evidence regarding the addition of conditions to the RUSP also are described. Part I then explores other SACHDNC guidelines pertaining to components of the newborn screening system, including follow-up; management and treatment; education; and special topics such as newborn screening and health care reform, the retention and use of residual dried blood spots, and sickle cell disease. For each of these issues, background information, SACHDNC recommendations, and actions of SACHDNC and the HHS Secretary (when applicable) are highlighted.

At the request of SACHDNC, Part II of the report was written to include a description of the implementation of programs where the Act specifies that SACHDNC serves as an advisor, a platform for coordination and information sharing, or a consulting body, such as the Clearinghouse of Newborn Screening Information, the Interagency Coordinating Committee on Newborn and Child Screening, the Hunter Kelly Research Program and a laboratory quality program.

The report concludes with an examination of current and future opportunities and challenges in newborn screening and their possible effect on State newborn screening programs, as well as implications for SACHDNC, Federal health officials, and Congress as leaders of the Nation's efforts to prevent the potentially devastating consequences of heritable disorders in newborns and children.

INTRODUCTION

Health and development in newborns and children depends on a complex interaction between genetic and environmental factors. In 2000, Congress recognized the need for Federal input to assist States with improving access to and the quality of services available to newborns and children at risk for heritable disorders. The Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) was chartered in February 2003 to advise the Secretary regarding the most appropriate application of technologies, policies, guidelines, and standards for effectively reducing morbidity and mortality in newborns and children having, or at risk for, heritable disorders. SACHDNC assists the Secretary of the U.S. Department of Health and Human Services (HHS), specifically by providing (1) advice and recommendations concerning the grants and projects authorized under the Heritable Disorders Program; (2) technical information to develop policies and priorities for this program 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; and (3) recommendations, advice, or information that may be necessary to enhance, expand, or improve the ability of the Secretary to reduce the mortality or morbidity in newborns and children from heritable disorders.

What Is Newborn Screening?

Newborn screening is the practice of testing all babies for certain disorders and conditions that can hinder their normal development. Babies with these conditions appear healthy at birth but can develop serious medical problems later in infancy or childhood. Early detection and treatment can help prevent intellectual and physical disabilities and life-threatening illnesses.

Newborn screening usually begins with a hearing screen and/or blood test 24–48 hours after the baby is born.

The blood test is performed by pricking the baby's heel to collect a few drops of blood. The blood is placed on a special piece of paper and sent to a laboratory for analysis. Sometimes a repeat blood test is required, particularly if the first test was done before the baby was 24 hours old. If the results of the test are abnormal, additional testing is required to confirm the result. Parents are notified within a few days of the first test if retesting is necessary.

The hearing test uses a soft earphone or other instrument that is placed in the baby's ear.

Source: National Institutes of Health, National Library of Medicine, *Genetics Home Reference*, http://ghr.nlm.nih.gov/nbs

SACHDNC's activities to date have addressed some broad issues in heritable disorders in newborns and children. SACHDNC has focused much effort on newborn screening, where there was opportunity to make significant impact to remedy disparity, address gaps, and develop models that can be applied more broadly to the issues of heritable disease in newborns and children. Screening detects disorders in newborns that, if left untreated, can cause physical and/or intellectual disabilities, serious illness, and even death. Since the inception of newborn screening in the 1960s, more than 150 million infants have been screened for certain genetic and congenital disorders.

Technological advances in newborn screening have led to significant program expansion and also have spurred the need for SACHDNC to concentrate its work in this area to help State newborn screening programs respond. In response to the changing environment, the 110th Congress enacted the Newborn Screening Saves Lives Act of 2008[I] (the Act). The Act amends the authorizing legislation, the Public Health Service Act, 42 U.S.C. 300b-10, which established the Heritable Disorders Program (HDP), SACHDNC, and two associated grant programs. The HDP was established to facilitate the creation of Federal guidelines on newborn screening; to assist State newborn screening programs in meeting Federal guidelines; to improve education, outreach, and coordinated follow-up care; and to improve laboratory quality and surveillance for newborn screening. The 2008 amending and reauthorizing legislation established several additional programs and instilled SACHDNC with specific responsibilities as follows:

- Making systematic evidence-based and peer-reviewed recommendations regarding screening for heritable disorders;
- Developing a model decision matrix for newborn screening expansion and updating the recommended uniform screening panel (RUSP) based on such a decision matrix;
- Considering ways to ensure that all States attain the capacity to screen for the RUSP with support from grant funding, if necessary, provided for in the Act; and
- Providing recommendations, advice, or information dealing with various components of the newborn screening system.

Suggested Topics of the Newborn Screening Saves Lives Act of 2008 for Recommendations, Advice, or Information From SACHDNC

1. Follow-up activities
2. Implementation, monitoring, and evaluation of newborn screening activities
3. Technologies used in screening
4. Availability and reporting of testing for conditions for which no treatment exists
5. Conditions not in the RUSP that are treatable with Food and Drug Administration-approved products or other safe and effective treatments
6. Use of minimum standards and related policies and procedures by States such as terminology
7. Quality assurance, oversight, and evaluation of State newborn screening programs
8. Public and provider awareness and education
9. Cost and effectiveness of State newborn screening, medical evaluation systems, and intervention programs
10. Identification of causes, public health impacts, and risk factors related to heritable disorders
11. Coordination of surveillance activities to assess and enhance monitoring of newborn disease

This report fulfills a requirement of the reauthorizing legislation (Section 1111(e)): an annual report to Congress, the Secretary, the Interagency Coordinating Committee established in the legislation, and State Health Departments to be first submitted 3 years after the date of enactment. As instructed in the Act, Part I of the report discusses peer-reviewed newborn

[I] The Newborn Screening Saves Lives Act of 2007 was enacted on April 24, 2008. A House Resolution subsequently was enacted on May 27, 2008, making technical corrections, including the renaming of the act as the Newborn Screening Saves Lives Act of 2008.

screening guidelines formulated by SACHDNC. The report details the process by which conditions come under SACHDNC consideration for addition to the RUSP. The extensive, ongoing efforts of SACHDNC to adhere to the most rigorous process possible for the systematic review of scientific evidence regarding the addition of conditions to the RUSP also are described. Part I then explores other SACHDNC guidelines pertaining to components of the newborn screening system, including follow-up; management and treatment; education; and special topics such as newborn screening and health care reform, the retention and use of residual dried blood spots, and sickle cell disease. For each of these issues, background information, SACHDNC recommendations, and actions of SACHDNC and the HHS Secretary (when applicable) are highlighted.

At the request of SACHDNC, Part II of the report was written to include a description of the implementation of programs where the Act specifies that SACHDNC serves as an advisor, a platform for coordination and information sharing, or a consulting body, including the Clearinghouse of Newborn Screening Information, the Interagency Coordinating Committee on Newborn and Child Screening, the Hunter Kelly Research Program and a laboratory quality program. Part II also includes the implementation of the other activities authorized by the Act such as the establishment of the Contingency Plan for Newborn Screening and a grant program to evaluate the effectiveness of newborn screening programs.

The report concludes with an examination of current and future opportunities and challenges in newborn screening and their possible effect on State newborn screening programs, as well as implications for SACHDNC, Federal health officials, and Congress as leaders of the Nation's efforts to prevent the potentially devastating consequences of heritable disorders in newborns and children.

PART I

SACHDNC Structure and Responsibilities

SACHDNC consists of 15 voting members, including the following voting ex officio members: the Administrator of Health Resources and Services Administration (HRSA), the Directors of the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the Agency for Healthcare Research and Quality (AHRQ), and the Commissioner of the Food and Drug Administration (FDA) or their designees. SACHDNC members are selected based on their expertise and qualifications necessary to contribute to the accomplishments of SACHDNC's objectives. Through its recommendations regarding newborn and child screening programs, SACHDNC plays a leading role in the promotion of public health in the United States. Therefore, SACHDNC members appointed by the Secretary include:

- Medical, technical, or scientific professionals with special expertise in heritable disorders or in providing screening, counseling, testing, or specialty services for newborns and children at risk for heritable disorders;
- Individuals with expertise in ethics and infectious diseases who have worked and published material in the area of newborn screening; and
- Members of the public having special expertise about or concern with heritable disorders.

Appointed SACHDNC members serve as individuals, not as representatives of organizations or interest groups. Members are invited to serve for overlapping terms of up to 4 years. A quorum for

the conduct of business by the full SACHDNC is a simple majority (eight) of the voting members. SACHDNC also includes up to 12 nonvoting liaisons or organizational representatives, as determined to be necessary by the Secretary, to fulfill the duties of SACHDNC.

Subcommittees

SACHDNC has three established subcommittees. All subcommittee findings are presented to SACHDNC in an open meeting, and this information is openly deliberated.

1. The Education and Training Subcommittee reviews existing educational and training resources, identifies gaps, and makes recommendations regarding the following five groups: health professionals, parents, screening programs staff, hospital and birthing facility staff, and the public.
2. The Laboratory Standards and Procedures Subcommittee defines and implements mechanisms for the periodic review and assessment of the following:
   - The conditions included in the uniform panel,
   - Infrastructure services needed for effective and efficient screening of the conditions included in the uniform panel, and
   - Laboratory procedures used for effective and efficient testing of the conditions included in the uniform panel.
3. The Follow-Up and Treatment Subcommittee engages in a multistep process that
   - Identifies barriers to short- and long-term follow-up of newborn screening results specific to the challenges in integration of health care systems, financing of services, and information technology;
   - Develops recommendations for overcoming identified barriers in order to improve short- and long-term follow-up of newborn screening results; and
   - Recommends mechanisms for establishing accountability for newborn screening follow up guidelines.

Workgroups

SACHDNC forms subgroups or workgroups of SACHDNC as a resource for gathering, analyzing, and preparing information for SACHDNC such as research data, published literature, and expert opinion on a specific topic. The SACHDNC Chair appoints workgroup members, and these members need not be SACHDNC members. All workgroup findings are presented to SACHDNC in open meeting, and this information is openly deliberated. Workgroups are dissolved upon completion of an assigned task.

Current SACHDNC Workgroups	**Previous SACHDNC Workgroups**
• Carrier Screening • External Review • Internal Nomination and Prioritization Review • Newborn Screening Education • Evidence Evaluation Methods	• Health Information Technology • Medical Foods and Formulas • Research • Residual Blood Spots • Critical Congenital Heart Disease • Sickle Cell Disease Carrier Screening

SACHDNC Responsibilities

SACHDNC duties include (1) making evidence-based recommendations regarding disorders for which newborns and children should be screened; (2) evaluating and updating SACHDNC's RUSP; (3) providing advice to grants and other activities supported under the HDP, a program to improve the ability of States to provide newborn and child screening for heritable disorders; and (4) providing recommendations, advice, or information on a variety of policies that affect the Secretary's ability to reduce mortality or morbidity from heritable disorders in newborns and children.[II]

The SACHDNC process for developing recommendations for the RUSP (discussed further in the following section of the report) is designed to be streamlined, consistent throughout the review process, transparent and evidenced based. With respect to the HDP, SACHDNC may provide advice and recommendations to the Secretary concerning grants and projects, supply technical information to the Secretary for the development of policies and priorities for the administration of HDP grants, or consider ways to ensure that all States attain the capacity to screen for the conditions on the RUSP and include in such consideration the results of grant funding of the HDP.

SACHDNC Newborn Screening Guidelines: The RUSP

In 2002, HRSA's Maternal and Child Health Bureau (MCHB) commissioned the American College of Medical Genetics (ACMG) to convene an expert panel to develop a report outlining a process to standardize guidelines for newborn screenings. At that time, the Nation's newborn screening programs were not screening uniformly for conditions. Some States mandated screening for as few as four conditions and others as many as 50.

The ACMG panel evaluated 81 heritable conditions and assigned 29 conditions to a core newborn screening panel. The panel assigned 25 conditions to a secondary tier because these conditions lacked efficacious treatment or the natural history of the disease was not well-understood. These 25 secondary tier conditions are revealed in the course of screening the core panel or through the diagnostic process for the core panel. The remaining 27 conditions were determined inappropriate for newborn screening at that time because of the lack of a suitable population-based screening tool or efficacious treatment.

In September 2005, SACHDNC strongly and unanimously recommended that the Secretary initiate appropriate action to facilitate adoption of the ACMG expert panel's recommended screening panel by every State newborn screening program. In October 2008, SACHDNC received notice that Secretary Leavitt had deferred making a determination until further information was available. SACHDNC reaffirmed the recommendation in November 2009 that the Secretary facilitate adoption by all State newborn screening programs of the ACMG

[II] SACHDNC recommendations are published on the SACHDNC Web site. Occasionally, SACHDNC recommendations alsoare reprinted in scientific journals. Implementation and evaluation of the impact of the recommendations is the responsibility of the relevant HHS program and not the SACHDNC. However, HHS programs will develop an implementation and evaluation plan for each set of recommendations and periodically report information relevant to the implementation and evaluation activities to the SACHDNC and others who may be involved in implementing the recommendation (e.g., State public health agencies, organizations and institutions, health care payers, private practitioners).

recommended uniform screening panel (now SACHDNC's RUSP) as the panel would provide the Federal guidance necessary to help States voluntarily bring their programs into alignment with the most current standards.

On February 25, 2010, SACHDNC recommended the addition of Severe Combined Immunodeficiency (SCID)—a deadly disorder that can be treated if identified in the newborn period—to the list of core conditions. Related T-cell lymphocyte deficiencies also were added to the RUSP list of secondary targets. On May 21, 2010, the Secretary adopted SACHDNC's RUSP (screen for the identified 29 core conditions; report on the identified 25 secondary conditions) as a national standard for newborn screening programs. Additionally, the Secretary adopted SACHDNC's recommendation to add SCID as a core condition to the RUSP, and related T-cell lymphocyte deficiencies to the list of secondary targets.

On October 15, 2010, SACHDNC recommended the addition of critical congenital cyanotic heart disease (CCCHD) to its RUSP. On April 20, 2011, the Secretary referred SACHDNC recommendations to the Interagency Coordination Committee on Newborn and Child Screening (ICC) authorized by the Act "for additional review and input regarding implementation." The Secretary requested a proposed plan of action from the ICC to "address identification of effective screening technologies, development of diagnostic processes and protocols, education of providers and the public, and strengthening service infrastructure needs for follow-up and surveillance." The ICC plan is to be reported to the Secretary by July 19, 2011.

Evolution of the Nomination and Evidence Review Process

SACHDNC makes recommendations regarding additional conditions to be included in the RUSP based on scientific evidence regarding the potential net benefit of screening. SACHDNC has established a nomination form and detailed evidence review process to determine the suitability of screening for nominated inherited disorders. The development of the evidence review process began with a meeting in October 2006 of a Decisionmaking Criteria Workgroup and a group of experts in pediatrics, genetics, and public health.[1] Participants reviewed the nomination form and discussed issues in evidence review for genetics, pediatrics and newborn screening, the evidence evaluation process, and the expertise needed for the Evidence Review Workgroup.

SACHDNC published details about its process to nominate and review conditions to the RUSP.[2] The report, *Advancing the Recommended Panel of Conditions for Newborn Screening*, outlined fundamental principles for the nomination and review process: "(1) The deliberative process will be rigorously evidence-based, even for relatively rare conditions; (2) The procedures for the creation of a deliberative system and the system itself will be transparent and accessible to the scientific and lay public; (3) The process will be consistent across the different phases of the review process and applied to all of the proposed conditions."[3] Nomination of conditions began in June 2007. The same year, MCHB entered into an agreement with the Massachusetts General Hospital for Children's Center for Child and Adolescent Health Policy to outline and initially test a process for systematic evidence development that could support and continue to guide the evidence review process. The Duke Clinical Research Institute also participates in this effort.[4] The first full review, in which SACHDNC voted to send the nominated condition to the Evidence Review Workgroup, was completed in October 2008.

Process for Nomination of a Condition to the RUSP

Step 1: Submission of a completed nomination form to the Executive Secretary for an administrative review prior to evaluation by SACHDNC.

Step 2: Administrative review by the designated Federal official or the Executive Secretary to determine the completeness of the form, which is sent to the Internal Review Workgroup of SACHDNC.

Step 3: Internal review by the Nomination and Prioritization Workgroup. If the nominated disorder is found to have sufficient evidence based on the condition (e.g., incidence, significance), the screening test (e.g., analytical and clinical validity), and the treatment (e.g., efficacy), the nominated condition will be assigned to the Evidence Review Workgroup for an evidence-based review.

Step 4: Review by the Evidence Review Workgroup. The Evidence Review Workgroup completes a systematic evidence review (SER) report and submits it to SACHDNC for further evaluation and recommendation.

Step 5: SACHDNC review of the SER report. Using the questions outlined in the analytic framework of the Process for the Evaluation of the External Review of Evidence on Conditions Nominated for Universal Newborn Screening, SACHDNC conducts the review. Additional factors also may be weighed, such as expert opinions and ethical, legal and public heath issues.

Step 6: SACHDNC recommendation. SACHDNC will make a specific recommendation regarding the outcome of the nomination. The Decision Protocol is used to decide on one of the following recommendations: addition to the current core panel of screened conditions, a requirement for more data prior to making a recommendation, or rejection.

Step 7: SACHDNC presents its recommendations to the Secretary of HHS.

SACHDNC since has continued to periodically update its evidence review process as required in the Act. In the March 2010 publication *Committee Report: Method for Evaluating Conditions Nominated for Population-based Screening of Newborns and Children,* SACHDNC describes the process to complete the evaluation of conditions nominated for newborn screening.[5] Specifically, the article explains the analytic framework, related key questions, and criteria for assessing evidence that SACHDNC uses to evaluate systematic evidence reviews. The paper also provides the decision matrix used to adopt SACHDNC recommendations regarding additions to the RUSP.

Decision Matrix for SACHDNC Recommendations[6]			
Category	**Recommendation**	**Level of Certainty**	**Magnitude of Net Benefit**
1	Recommend adding the condition to the uniform panel	Sufficient	Significant
2	Recommend not adding the condition, but instead recommend specific additional studies	Insufficient, but the potential for net benefit is compelling enough to recommend additional studies to evaluate	Potentially significant and supported by contextual considerations
3	Recommend not adding the condition based on current knowledge	Insufficient, and substantial additional evidence is needed to make a conclusion about net benefit	Unknown
4	Recommend not adding the condition based on current knowledge	Sufficient	Zero or net harm

Another SACHDNC publication, *An Evidence Development Process for Newborn Screening*, recounts the evolution of the evidence review process, including expansion of activities with Massachusetts General Hospital for Children's Center for Child and Adolescent Health Policy and Duke Clinical Research Institute to include the promulgation of specific evidence reviews by the group, with the main purpose of providing timely information (but not recommendations) to SACHDNC to help inform their decisionmaking regarding new conditions nominated for addition to the panel.[7] These changes to the process have "helped to strengthen a complex analysis and decision system by providing balanced evidence, taking into account available high-quality data, expert opinion, and other levels of evidence, in a transparent manner. The methods developed and the identification of areas of missing data may also help investigators begin to standardize the clinical and laboratory data they collect pertaining to the newborn screening and diagnosis of rare disorders and their outcomes and focus future research efforts in the most needed areas."[8]

The external Evidence Review Workgroup systematically reviews scientific evidence regarding the potential net benefit of screening for nominated conditions and prepares reports to assist SACHDNC. Thus far, the topics evaluated by the Evidence Review Workgroup include screening for SCID, Pompe disease, Krabbe disease, Hemoglobin H disease, and CCCHD. Currently, the Evidence Review Workgroup is evaluating screening for neonatal hyperbilirubinemia. Of these conditions, SACHDNC has voted to add SCID and CCCHD to the RUSP. If SACHDNC votes to add a condition to the panel, the recommendation to the HHS Secretary is accompanied by the following: "(1) a summary of evidence and strength of recommendation(s); (2) recommendation(s) of other professional groups; (3) discussion of rationale for SACHDNC recommendation(s) that will explicitly state the basis on which the recommendations were made, i.e., a sufficient body of evidence based on results of controlled trials, observational studies, case series, expert opinion, focus groups, cost- effectiveness analysis, policy analyses, ethical analysis, and other inputs; and (4) recommended subsequent surveillance, research, education, and program evaluation activities, if applicable."[9]

SACHDNC Recommendation for Nominated Conditions to the SACHDNC RUSP as of April 2011[III]			
Condition	**Nomination**	**Evidence Review**	**Recommended Uniform Screening Panel (RUSP)**
SCID	September 2007	Approved for evidence review January 2008	Approved for addition to the RUSP January 2010
Pompe disease	October 2007	Approved for evidence review January 2008	Not approved for addition to RUSP October 2008
Niemann-Pick disease	December 2007	Not approved for evidence review October 2008	N/A
Fabry disease	December 2007	Not approved for evidence review August 2008	N/A
Krabbe disease	January 2008	Approved for evidence review August 2008	Not approved for addition to RUSP September 2009
Spinal muscular atrophy	June 2008	Not approved for evidence review November 2008	N/A
Hemoglobin H disease	April 2009	Approved for evidence review September 2009	Not approved for addition to RUSP May 2010
CCCHD	October 2009	Approved for evidence review January 2010	Approved for addition to the RUSP September 2010
Neonatal hyperbilirubinemia	July 2009	Approved for evidence review January 2010	Decision pending

One of the greatest challenges in evaluating conditions for addition to the panel is the paucity of scientifically valid data. To address this, the Evidence Review Workgroup also interviews domain experts and searches for important unpublished data. Appropriately summarizing different levels of data is challenging. However, new meta-analytic techniques and approaches to mathematical modeling have been developed. SACHDNC has convened a panel of experts in these techniques to assist the Evidence Review Workgroup in adopting these new approaches.

Incidence and Prevalence of Conditions on the RUSP

The Evidence Review Workgroup and SACHDNC consider the incidence (number of new cases over a specified time period)[10] and prevalence (proportion of the population that has a health condition at a point in time)[11] of a condition in evaluating whether to add a condition to the RUSP. The reported incidence of conditions on the RUSP reveals instances in which newborn screening has made a critical difference in the lives of children. The table[12] below provides the incidence of 27 of the original 29 conditions on the RUSP as observed in four States from 2001 to 2006. The table also estimates the incidence of these conditions in 2006 in the United States by using the data from actual observed incidence from four States (California, Massachusetts, North Carolina, and Wisconsin) to derive the national estimated number of cases (6,439). Unfortunately, because not all States screened for all conditions on the RUSP at that time, many of these cases were not detected by newborn screening, resulting in serious health consequences.

[III] See http://www.hrsa.gov/heritabledisorderscommittee/correspondence/CorrespConditionNominators.htm for SACHDNC letters that explain votes not to conduct an evidence review or not to add a condition to the RUSP following evidence review.

Data from a CDC survey of 44 States, two Territories, and Washington, DC, revealed 3,261 cases of permanent hearing loss (not included in the table below) identified in 2006.[13]

Estimated Number of U.S. Children Who Would Have Been Identified With Disorders in 2006 Using the ACMG-Recommended Newborn Screening Panel, Based on Incidence of These Disorders in Four State Newborn Screening Programs in 2001–2006, by Disorder

Disorder	Observed Number of Cases CA, MA, NC, and WI (2001–2006)	Number of Births CA, MA, NC, and WI (2001–2006)	Rate per 100,000 CA, MA, NC, and WI (2001–2006)	95% CI CA, MA, NC, and WI (2001–2006)	Estimated Number of Cases US (2006)	95% CI US (2006)
Phenylketonuria (PKU; includes clinically significant hyperphenylalaninemia variants)	254	4,884,217	5.20	(4.76–5.68)	215	(197-235)
Maple syrup urine disease	14	2,214,329	0.63	(0.42–0.94)	26	(17–39)
Homocystinuria	6	2,214,329	0.27	(0.14–0.50)	11	(6–21)
Citrullinemia I	13	2,214,329	0.59	(0.38–0.89)	24	(16–37)
Argininosuccinic acidemia	4	2,214,329	0.18	(0.08–0.39)	7	(3–16)
Isovaleric acidemia	19	2,474,313	0.77	(0.54–1.08)	32	(22–45)
Glutaric acidemia type I	23	2,474,313	0.93	(0.68–1.26)	38	(28–52)
Hydroxymethylglutaric aciduria	2	2,474,313	0.08	(0.02–0.24)	3	(1–10)
Multiple carboxylase deficiency	2	2,474,313	0.08	(0.02–0.24)	3	(1–10)
Methylmalonic acidemia (mutase deficiency)	30	2,474,313	1.21	(0.93–1.58)	50	(38–66)
Methylmalonic acidemia CblA,B	7	2,474,313	0.28	(0.16–0.50)	12	(6–21)
3-Methylcrotonyl-CoA carboxylase deficiency	60	2,474,313	2.43	(2.01–2.92)	100	(83–121)
Propionic acidemia	9	2,474,313	0.36	(0.22–0.60)	15	(9–25)
Beta-ketothiolase deficiency	4	2,474,313	0.16	(0.07–0.35)	7	(3–14)
Medium-chain acyl-CoA dehydrogenase deficiency	143	2,460,473	5.81	(4.90–6.85)	239	(212–269)
Very long-chain acyl-CoA dehydrogenase deficiency	41	2,460,473	1.67	(1.20–2.26)	69	(55–86)
Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency	8	2,460,473	0.33	(0.14–0.64)	13	(8–23)
Trifunctional protein deficiency	1	2,460,473	0.04	(0.00–0.23)	2	(0–7)

Disorder	Observed Number of Cases CA, MA, NC, and WI (2001–2006)	Number of Births CA, MA, NC, and WI (2001–2006)	Rate per 100,000 CA, MA, NC, and WI (2001–2006)	95% CI CA, MA, NC, and WI (2001–2006)	Estimated Number of Cases US (2006)	95% CI US (2006)
Carnitine uptake defect	26	1,256,869	2.07	(1.35–3.03)	85	(63–113)
Hb SS	777	4,403,132	17.65	(16.78–18.56)	1128	(1,063–1,200)
Hb SC	326	4,403,132	7.40	(6.85–8.01)	484	(442–532)
Hb S/β thalassemia	74	3,673,283	2.02	(1.70–2.38)	163	(131–205)
Primary congenital hypothyroidism (excluding secondary, transient, or other)	2544	4,884,217	52.09	(50.67–53.55)	2156	(2,097–2,216)
Biotinidase deficiency (including partial)	19	1,268,943	1.50	(1.06–2.10)	62	(44–87)
Congenital adrenal hyperplasia (excluding non 21-hydroxylase deficiency)	121	2,474,313	4.89	(4.29–5.57)	202	(178–230)
Classical galactosemia plus variant (excluding GALK and GALE)	264	4,884,217	5.41	(4.95–5.90)	224	(205–244)
Cystic fibrosis (including nonclassical)	270	895,410	30.15	(27.66–32.87)	1248	(1,145–1,360)
TOTAL					**6439**	**(6,282–6,596)**

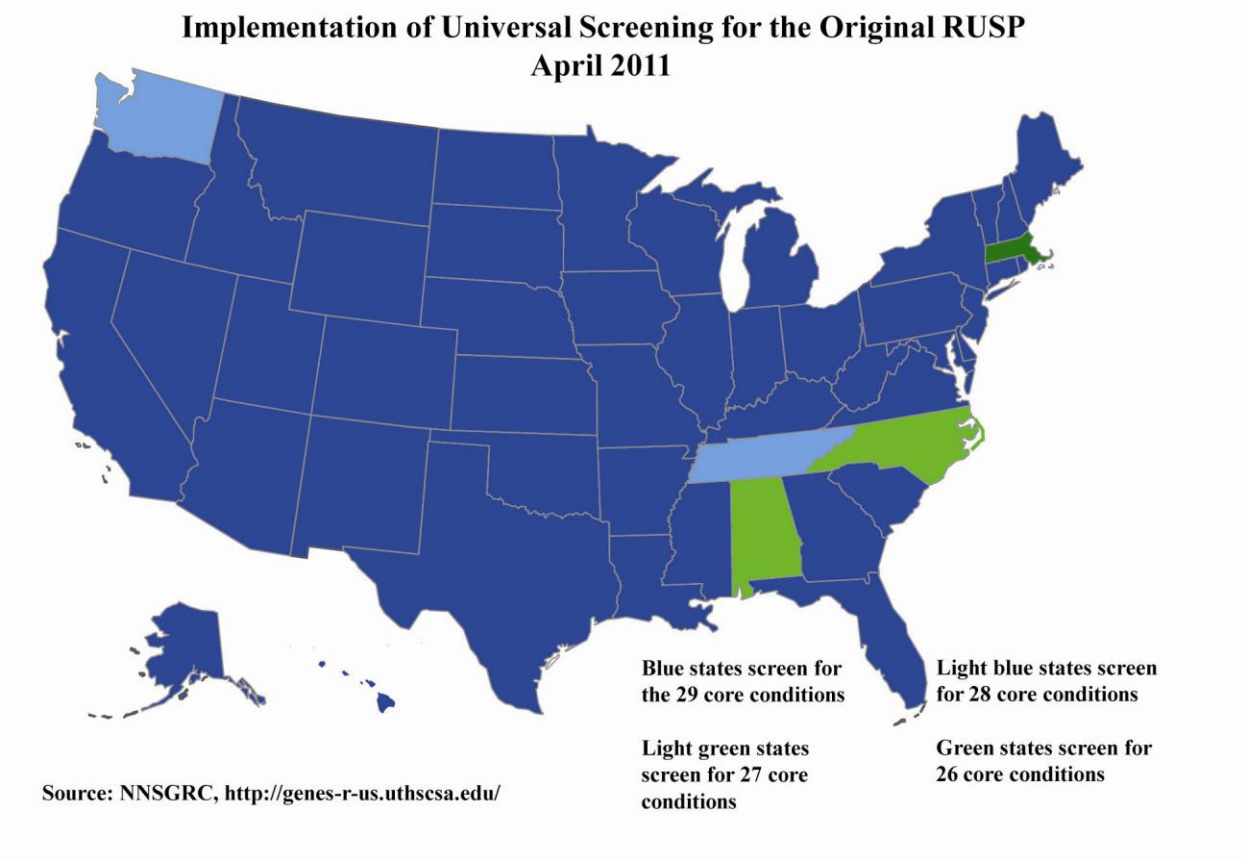
In its review of SCID, the Evidence Review Workgroup noted that one study estimated the annual incidence of SCID as a minimum of 1 in 105,000 births.[14,15] The group found an average prevalence of 8 per 10,000[IV] among neonates eligible for pulse oximetry screening—the screening method used to detect CCCHD—based on a literature review of 11 studies.

State Implementation of the RUSP

States determine the list of conditions screened for as part of the State newborn screening program. Currently, State newborn screening programs are mandated to screen for more than 35 conditions on average, and almost all have adopted the core conditions on the RUSP. The map below depicts the widespread State adoption of the core conditions on the original RUSP as of April 2011. (See Appendix A for tables of conditions screened for in the States.) The States that have not adopted 100 percent of the original RUSP of 29 conditions are lacking legislation or other state policies for a **statewide mandate** for specific conditions. For example, the following 10 states do not have a statewide universal mandate for hearing screening, although it is universally offered even without the mandate (Arizona, Colorado, Georgia, Idaho, Maine,

[IV] This figure includes asymptomatic newborns and excludes prenatally diagnosed CCCHD babies, symptomatic newborns found prior to pulse oximetry screening, and those who have a syndrome commonly associated with CCCHD.

Nebraska, New Hampshire, North Dakota, South Dakota, and Washington). Alabama, North Carolina, and Tennessee exclude tyrosinemia type I from their State newborn screening panels. Alabama and North Carolina also exclude screening for methylmalonic acidemia and carnitine uptake deficiency, respectively. In addition, Massachusetts does not mandate screening for three of the recommended conditions (trifunctional protein deficiency, 3-methylcrotonyl-CoA carboxylase, and multiple carboxylase], and Washington does not mandate screening for 3-methylcrotonyl-CoA carboxylase. Despite the lack of a mandate, both Washington and Massachusetts State newborn screening programs consider these conditions likely to be detected as a result of the screening technology utilized.



In light of SACHDNC's addition of SCID to the panel, many State programs are actively considering implementation of screening for SCID. Five States (New York, California, Massachusetts, Louisiana, and Wisconsin) and Puerto Rico are currently screening all births (almost 25 percent of total U.S. births) as part of initial data gathering efforts, and two States (Pennsylvania and Texas) are screening a portion of their births. In addition, five States (Maryland, Michigan, Minnesota, Illinois, and Iowa) have received approval to begin SCID screening as soon as possible. Once these States are actively screening, approximately 35 percent of babies born in the United States will be screened. Eighteen States are in various stages of fact finding and are focused on investigations of analytical platforms, cost analysis, development of referral and treatment services, and recruitment of necessary personnel. The pilot studies in California, New York, Massachusetts, Wisconsin, Louisiana, and Puerto Rico have resulted in more than 900,000 newborns or 25% of the births in the United States, being screened. Sixty

infants or approximately 1 in 12,000, were identified with some form of immune deficiency. Nineteen infants with SCID (~1 in 46,000) have been diagnosed and received treatment. No missed cases of SCID have come to the attention of the newborn screening programs conducting the pilots.

States may progress more slowly with respect to the implementation of screening for CCCHD. Most States will require additional infrastructure in order to implement screening and establish systems for quality assurance of CCCHD screening. Like hearing screening, screening for CCCHD does not involve testing of dried blood spots. Rather, hospital staff measure pulse oximetry on site with immediately accessible results.

Other SACHDNC Guidelines: Components of the Newborn Screening System and Special Topics

In addition to the screening panel, SACHDNC has issued newborn screening guidelines that address other components of the newborn screening system, including follow-up, management and treatment, and education. SACHDNC also has formulated guidelines on other special topics as needed, including newborn screening and health care reform, the retention and use of residual dried blood spots, and sickle cell disease.

Follow-Up

In April 2007, SACHDNC convened a group of health care policy experts, public health specialists, generalist and specialist care providers, allied health care providers, and the families of affected individuals to request their input regarding long-term follow-up (LTFU) after newborn screening.[16] The product of this meeting, SACHDNC report *Long-Term Follow-Up After Diagnosis Resulting From Newborn Screening: Statement of the U.S. Secretary of Health and Human Services' Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children*, defines the key features of LTFU, the goal of which is to ensure the best possible outcome for individuals with disorders identified through newborn screening.[17] The report expands the concept of LTFU from data management to systematic and comprehensive care of affected individuals.[18] In addition, SACHDNC identifies core components of LTFU, which include care coordination through a medical home, evidence-based treatment, continuous quality improvement, and new knowledge discovery. The Follow-Up and Treatment Subcommittee of the SACHDNC later convened a workshop titled *Overarching Questions in Long-Term Follow-Up and Treatment in Newborn Screening* on September 23, 2009. Invited participants included experts from various sectors of the public health and health care systems that interface with or are critical to LTFU after newborn screening to help define critical questions.[19] A SACHDNC statement resulting from the workshop, which was approved in January 2011, titled *What Questions Should Newborn Screening Long-Term Follow-Up Be Able to Answer?*, outlines questions that "follow the central components of long-term follow-up (LTFU)—care coordination, evidence-based treatment, continuous quality improvement, and new knowledge discovery—and are framed from the perspectives of the state and nation, primary and specialty health care providers, and the impacted families."[20] These questions are intended to lead to a set of quality measures to improve LTFU programs.[21]

Management and Treatment

SACHDNC subsequently targeted one aspect of LTFU identified in the report—management and treatment—through a series of letters and publications. On April 7, 2009, SACHDNC sent a letter to the HHS Secretary that contained recommendations (see Appendix C) to ensure that families receive insurance coverage for essential components of treatment through the following: "1) a more uniform approach toward coverage by health care payers of medical foods and foods for those conditions recommended by SACHDNC and 2) specific amendments to Medicaid legislation to ensure more uniform coverage by State Medicaid programs."[22] The letter was resubmitted to the office of the HHS Secretary in May 2009 following the appointment of Secretary Kathleen Sebelius. In March 2010, the issue was revisited in a SACHDNC white paper, *Heritable Disorders, Newborn Screening and Health Care Reform*,[23] which recommended the closure of gaps in insurance coverage for medical foods and foods modified to be low in protein per the SACHDNC letter sent in April 2009.

Heritable Disorders, Newborn Screening, and Health Care Reform

The *Heritable Disorders, Newborn Screening and Health Care Reform* white paper addresses other barriers to newborn screening system improvement in the context of the health care reform discussion that was taking place among policymakers. The three additional recommendations targeted the billing process for newborn screening services; payment methods for an integrated system of care coordination through the medical home framework; and the adoption and further definition of the Newborn Screening Use Case, which was developed by the subgroup on newborn screening of the American Health Information Community's Personalized Healthcare Workgroup and released in December 31, 2008,[24] within the Department's health information exchange endeavors.

The **Newborn Screening Use Case** is intended to address

- The ability to order and communicate the results from screenings in various clinical domains;
- The ability to communicate initial screening results, confirmatory testing orders, and results and information specific to referral and management of the patient;
- The ability to report newborn screening information to public health; and
- The ability to share de-identified newborn screening information with the clinical research community without requiring additional data collection or data entry.

Source: U.S. Department of Health and Human Services, *Newborn Screening*, http://www.hhs.gov/healthit/usecases/nbs.html

In June 2010, SACHDNC discussed data that indicated families face a substantial out of pocket financial burden in providing treatment for children with heritable disorders detected through newborn screening and made additional recommendations (see Appendix C) to help close gaps in insurance coverage as HHS develops regulations to implement health care reform. While the HHS Secretary adopted three out of four recommendations on health care reform, the recommendation pertaining to the closure in gaps in insurance coverage for medical foods was not adopted (as of September 2010). In a December 2010 letter, the HHS Secretary responded that the Office of the Secretary was awaiting the results of a Department of Labor survey on

employer-sponsored plans and advice from the Institute of Medicine on essential health benefits before making a final decision on this issue.[25]

Education

SACHDNC has taken several steps to provide guidelines for improved parent and provider education about the newborn screening system. The Subcommittee on Education and Training reported on its work to SACHDNC in December 2006. The group emphasized the importance of education that occurs within a prenatal clinical setting and the role of professional organizations and entities most frequently involved in prenatal education such as obstetricians and nurse midwives.[26] Based on the Subcommittee findings, in an April 2007 letter, SACHDNC recommended that the Secretary "develop and fund a mechanism to study the distribution of existing newborn screening educational materials and acquisition of knowledge about newborn screening by expectant parents in the context of the healthcare provider-patient relationship." SACHDNC also endorsed the Subcommittee's emphasis on education during the prenatal period so that parents are informed in advance of the birth of their baby and have the opportunity to better understand and discuss the benefits of newborn screening.[27]

In an effort to improve primary care provider education about medical genetics and genomic medicine, SACHDNC, NIH, and HRSA convened a workshop to identify practical strategies to educate primary care physicians involved in maternal and child health in June 2009. Subsequently, SACHDNC released a paper, *A Blueprint for Maternal and Child Health Primary Care Physician Education in Medical Genetics and Genomic Medicine*, that summarized the workshop and the working group recommendations that arose during the meeting to address the lack of well-trained and available experts in medical genetics and genomic medicine, including (1) developing a targeted curriculum for residency training programs, (2) incorporating assessments of genetics and genomic medicine into the initial board certification process and the process for maintenance of certification, (3) providing continuing medical education opportunities at national meetings, (4) establishing an Internet-based repository of recommendations for primary care providers, and (5) forming a learning collaborative to link primary care providers and specialists to evaluate strategies to improve care and understand barriers to and facilitators of genetics and genomic medicine into primary care and to gather data about health care providers' educational needs.[28]

SACHDNC adopted two of the workgroup's suggestions and recommended (in a September 2009 letter) that the HHS Secretary develop and fund a "Learning Collaborative" in genetics and primary care training to support increased genetic literacy amongst primary care providers and provide additional resources to increase public awareness of the newborn screening system. The Secretary adopted both recommendations. As a result, in 2010, HRSA established a project pairing representatives from primary care practices with genetics and genomic medical expertise through the formation of the Genetics in Primary Care Institute (GPCI). The project is funded as a Special Project of Regional and National Significance by MCHB. Following a development phase, an implementation and project evaluation period planned over a 3-year period, the GPCI will submit a final report to SACHDNC. The Clearinghouse for Newborn Screening Information and Resources (discussed further in Part II of this report) funded under the Act fulfills the second Secretary-adopted recommendation to increase public awareness about newborn screening.

Sickle Cell Disease Carrier Screening

SACHDNC's Sickle Cell Disease Carrier[V] Screening Workgroup was established to consider issues related to athletes and sickle cell disease carrier screening in light of policymaking and recommendations from the National Collegiate Athletic Association (NCAA). NCAA interest in the issue arose from a lawsuit in which the family of a student who was unknowingly a carrier for the genetic mutations for sickle cell disease died following intense exercise. The family asserted that the student's carrier status placed him at increased risk of exercise-related sudden death.[29] In 2009, NCAA recommended that institutions test student athletes to determine their carrier status for sickle cell disease status. In April 2010, NCAA adopted a policy that testing for sickle cell disease carrier status is required for Division I student athletes unless proof of a prior test or a signed waiver refusing testing and releasing an institution from liability is submitted.[30]

Based on the findings of the workgroup and currently available research, SACHDNC cautioned in its October 2010 report, *Screening College Athletes for Sickle Cell Disease Carrier Status*, that the need to single out athletes who are carriers of the mutation for sickle cell disease is unwarranted. Alternatively, the report outlined five recommendations to the HHS Secretary (see Appendix C) concerning clinical guidelines for carrier screening generally and for sickle cell disease specifically, which acknowledge the following: (1) testing for sickle cell disease carrier status is genetic screening, and (2) follow-up counseling and education and mechanisms to protect the privacy of the student athlete and prevent stigmatization and discrimination should accompany screening. SACHDNC also stated that further research is necessary to understand the suggested association of sickle cell disease carrier status and the increased risk of exercise-related sudden death.[31] The Secretary's response to these recommendations is in progress.

The Retention and Use of Residual Dried Blood Spot Specimens After Newborn Screening

In February 2009, SACHDNC established the Use and Storage of Residual Blood Spots Workgroup. SACHDNC tasked the workgroup with the development of guidelines for States regarding the retention and use of residual dried blood spots after newborn screening. The workgroup solicited input from a variety of stakeholders, including community members, via three Webinars with more than 350 participants. Ultimately, SACHDNC published a report *Considerations and Recommendations for National Guidance Regarding the Retention and Use of Residual Dried Blood Spot Specimens after Newborn Screening* that reviewed the issues facing State newborn screening programs related to the retention and use of residual dried blood spot specimens and laid the foundation for developing national guidance to States. Specifically, SACHDNC encouraged "an approach to guidance that maintains the standard uses of the residual blood specimens by newborn screening programs and upholds the core principles of benefiting infants, families and society, protecting privacy and confidentiality, and ensuring the public's trust while recognizing the research value of residual newborn screening specimens and their potential for advancing science and clinical care." SACHDNC recommendations (see Appendix C) pertaining to State policies on access, use, and disposition

[V] As defined in the National Library of Medicine's Genetic Home Reference, a carrier is "an individual who has a recessive, disease-causing allele at a particular locus on one chromosome of a pair and a normal allele at that locus on the other chromosome" (http://ghr.nlm.nih.gov/).

of residual dried blood spots; education of parents and health care professionals about newborn screening and the potential use of residual dried blood spots; the need for a national dialogue; and the possibility of developing a voluntary national repository of residual dried blood spots were transmitted to the Secretary on October 13, 2010. On April 13, 2011, the Secretary referred the report to the ICC for their review and input regarding possible future implementation of the recommendations. The ICC will submit a report with recommendations for appropriate HHS action by June 1, 2012.

PART II

Programs authorized by the Act for which SACHDNC serves as an advisor, a platform for coordination and information sharing, or a consulting body are outlined below. Descriptions of the project, related achievements, future plans, and challenges are highlighted below.

Section 1109: Improved Newborn and Child Screening for Heritable Disorders

Section 1109 of the HDP authorizes grant programs to (1) improve the ability of State and local public health agencies to provide screening, counseling, or health care services to newborns who have or are at risk for heritable disorders; (2) assist in providing health care professionals and laboratory personnel education and training in newborn screening and new technologies; (3) provide educational programs to parents, families, and patient advocacy groups; and (4) establish and operate a system to assess and coordinate treatment related to congenital, genetic, and metabolic diseases. Thus far, HRSA has established two programs to implement this section of the Act:

- The Regional Genetic and Newborn Screening Service Collaboratives and a National Coordinating Center for the Collaboratives, and
- Newborn Screening Effective Follow-Up projects.

Regional Genetic and Newborn Screening Service Collaboratives

The fundamental goal of the National Coordinating Center (NCC) and the seven Regional Genetic and Newborn Screening Service Collaboratives (RCs) is to improve access to quality genetic health care services within local communities, particularly for newborns and children having or at risk for heritable condition, across the Nation. Section 1109 of the Act allows the NCC and RCs to work toward this goal by providing incentives to States for the enhancement, expansion or improvement of newborn screening programs. These funds help to ensure that, at a minimum, nearly all infants born in the United States receive screening for the conditions in the RUSP, with few exceptions.[VI]

The seven RCs and the NCC were initially funded in 2004 for a period of 3 years as part of the HDP under the Children's Health Act of 2000 (P.L. 106-310). The second stage of HRSA's Regional Genetics and Newborn Screening Services initiative began in 2007 for a period of 5 years. The main goal of this initiative is to improve access to newborn screening and genetic services, especially for medically underserved populations. The goal of each RC is to (1) enhance newborn and child screening and related follow-up services for heritable disorders, including an expansion of LTFU activities; (2) augment workforce capacity through activities such as training and education; (3) enhance subspecialty access by strengthening communications between medical homes and tertiary care centers; (4) enhance genetic counseling services; and (5) strengthen State programs' communication and education to families and health practitioners. Each RC also was responsible for providing the States in its region with access to genetic medicine expertise for

[VI] Most States that have not adopted 100 percent of the original RUSP of 29 conditions do not have a statewide universal mandate for hearing screening. See Part I discussion on State Implementation of the RUSP for further details.

subspecialty care and for the ongoing treatment and management of children identified with genetic disorders through newborn and other screening programs.

Toward this end, the RCs use Federal support to strengthen communication and collaboration among public health agencies, individuals with genetic disorders, families, primary care providers, and genetic medicine and other subspecialty providers. The RCs have utilized distance communication strategies to increase access to genetic services by 47 percent (2009–2010: 1,094 visits; 2008–2009: 517 visits). Ninety-eight percent of States and Territories have evaluated and made recommendations on implementing the SACHDNC-recommended newborn screening panel, with 45 of 50 States screening for all core conditions except SCID (29 of 30 conditions). All States and Territories have systems in place to track entry into clinical management for newborns who are diagnosed with conditions mandated by their State-sponsored newborn screening programs or identified for hearing loss. Finally, 17 percent of States and Territories have systems in place that track receipt of clinical services and/or health outcomes for children with inborn errors of metabolism covered in newborn screening.

While many gains have been realized, the RCs play an important role in overcoming the challenges that remain for state newborn screening programs. Although all programs are increasingly similar with respect the number of conditions for which they screen, substantial variation persists among newborn screening programs in terms of tracking and follow-up mechanisms. LTFU has been the source of priority funding to three RCs: New England Genetics Collaborative (NEGC), Southeast Newborn Screening and Genetics Collaborative (SERC), and Region 4 Genetics Collaborative. These priority projects focus on the following aspects of LTFU:

- The expansion of a State model for follow-up to other States in the region (NEGC);
- Building the business case for LTFU, which is now completed and details the elements of a LTFU information system, and developing the system with evidence and consensus-based guidelines (SERC); and
- Developing a multiregional information system for inborn errors of metabolism. There are 17 participating clinics with 274 cases entered (Region 4).

To harmonize communication practices, the national LTFU workgroup, housed at the NCC, is working with newborn screening laboratories and State programs to determine the most useful types of data to include in LTFU and the form in which it should be provided to state programs for long-term health outcomes evaluation and utility analyses of programs. Activities of the LTFU workgroup include the identification and definition of core administrative, clinical, and laboratory data needed to communicate periodic outcomes of LTFU in a standardized way (expected to be completed by Summer 2011), creation of a LTFU data dictionary and data dashboard (summary) based on core data (in progress), and the identification of optimal time periods for communicating outcomes of LTFU (in progress).

Together these efforts seek to address the inconsistency between state programs of LTFU for individuals with heritable disorders. With the Secretary's official adoption of the RUSP, including SCID, in May 2010, many State newborn screening programs are in the early stages of developing robust LTFU systems that can effectively track health outcomes and evaluate public health programs and systems for these conditions. In the future, as States implement LTFU

systems, the framework of the RCs and the National Coordinating Center will help to ensure equal access to services and quality care following newborn screening over the long term.

Newborn Screening Effective Follow-Up Projects

The activities of the HRSA Effective Follow-Up in Newborn Screening Initiative focus on the use of health information exchange (HIE) to improve the newborn screening system, with attention to both short- and long-term follow-up. Effective follow-up projects are funded by HRSA in Colorado, Indiana, New York, and Utah. Achieving the goal of follow-up requires effective and timely communication and information sharing among patients, families, clinicians, laboratorians, public health agencies, researchers, and relevant community support services. The cooperative agreement is intended to implement models that facilitate meaningful electronic HIE for attaining effective short- and long-term follow-up of children and youths with conditions identified by newborn screening. The models include a method to capture and analyze clinical and related variables to determine health outcomes and will provide an assessment of the impact of LTFU efforts initiated by the newborn screening system.

All four States are taking steps to address vocabulary, coding, messaging, and transport standards to facilitate HIE. These projects also have measures in place to ensure the privacy and security of information. In addition to those activities approved in the initial application, for the remaining year of this initiative, awardees are strongly encouraged to implement ONC's Newborn Screening Use Case and the use of standard electronic messages, documents, and codes as specified in the HRSA and NIH/National Library of Medicine (NLM) *Newborn Screening Coding and Terminology Guide*.

Section 1110: Grant Program to Evaluate the Effectiveness of Screening, Counseling, or Health Care Services

Section 1110 of the Act authorizes programs to evaluate the effectiveness of screening, counseling or health care services in reducing the morbidity and mortality caused by heritable disorders in newborns and children. HRSA funded several projects to address this section of the Act. In March 2011, HRSA and CDC were delegated the authority from the HHS Secretary to implement this Section of the Heritable Disorders Program.

1. ***Newborn Screening from a Family Perspective.*** Four projects were established to evaluate family perspectives on screening for heritable disorders in newborns and children, as well as other newborn screening issues, such as the use and storage of residual blood spots. The Genetic Alliance along with the State Departments of Health in Iowa, Hawaii, and the University of Maryland focused on (1) measurement of parental behavior after receiving false positive screening results; (2) assessment of potential "harm" on children and their families with notification of false positive screening results; (3) determination of the information that would be necessary for parental decision making about screening for conditions that may not have a medically proven treatment; (4) assessment of the impact of carrier identification, particularly on diverse populations and what information may be desired by families; and (5) determination of changes in parental attitudes and responses with increased education and knowledge about newborn screening.

2. ***Laboratory Quality Assurance Activity.*** States were asked to undertake specific newborn screening public health laboratory quality improvement projects such as enhancing newborn screening analytical laboratory test performance across the region. Expected outcomes of the projects were harmonization of case definitions of disorders screened in newborn screening programs, newborn screening panels, and testing methodologies and decreasing the number of false positives. The outcome of the project was a worldwide collaborative effort to achieve clinical validation of cutoff values for newborn screening by tandem mass spectrometry. An unprecedented level of cooperation (47 U.S. State newborn screening programs and 45 countries) has allowed the objective definition of cutoff target ranges for 114 markers to be applied to newborn screening of rare metabolic disorders. The collaborative project paved the way to a collegial and transparent process for clinical validation of newborn screening by tandem mass spectrometry. The collaborative model can be applied to other rare disorders and potentially to any other laboratory tests for rare disorders if a comparable level of cooperation is achieved. The critical factors behind the unanticipated expansion of the collaborative project to become a worldwide initiative have been the gain of mutual trust among participants, the belief of equal standing of all sites regardless of the magnitude of their contributions, and the vision to create tools that motivate users to be actively involved.

Section 1112: Clearinghouse of Newborn Screening Information

To implement this section of the Act, in September 2009, MCHB awarded a cooperative agreement to Genetic Alliance and partners, including the Regional Genetic and Newborn Screening Service Collaboratives, the March of Dimes, and the Association of Public Health Laboratories (APHL), to establish the Newborn Screening Clearinghouse (NBSC). The NBSC was created to increase awareness of newborn screening; improve the understanding and informed decisionmaking capacity of expectant and new parents, health professionals, industry representatives, and the public; and maintain current data on quality indicators to measure performance of newborn screening, such as false-positive rates and other quality indicators as determined by SACHDNC under Section 1111. Current information available in the NBSC includes condition-specific information, contact information for the condition-specific advocacy organizations, information about what conditions each State screens for, data supplied by public health laboratories, and general information about the process of newborn screening. The NBSC does not collect patient-specific or personal information but rather aggregate, anonymized population-based data. The NBSC has made significant progress toward realizing Congress' vision for the NBSC. In Fall 2011, BabysFirstTest.org, a streamlined, customizable newborn screening Web site will be launched.

The NBSC, APHL and HRSA are working together to assess the capabilities of the current National Newborn Screening Information System and plan for the integration of newborn screening quality indicators into the NBSC as required by the Act, including approaches for handling technical solutions to challenges. At present, the NBSC and APHL, in partnership with State newborn screening laboratories, are drafting documents on quality indicators for newborn screening that will include appropriate measures to track the success of newborn screening across the country. APHL will coordinate these activities with input from the NBSC, HRSA, and CDC. The current and proposed information system does not collect patient-specific or personal information but rather aggregate, anonymized population-based data.

With the launch of the Web site, the NBSC will renew its outreach efforts to ensure that the clearinghouse provides a robust tool for public education about newborn screening. The NBSC also will continue to fund innovation in the field through challenge awards

Section 1113: Laboratory Quality

Section 1113 requires the establishment of a laboratory quality program acting through the Director of CDC and in consultation with SACHDNC. CDC's Newborn Screening Quality Assurance Program (NSQAP) must continually broaden its services and produce materials to meet the public health demand for quality newborn screening tests. Annual HHS appropriations provide essential support to CDC's quality assurance programs and efforts to sustain vital newborn screening laboratory competence and capacity in states. The NSQAP is the only comprehensive source of quality assurance materials for dried blood spot testing in the United States. Accurate screening of newborns using dried blood spots helps prevent severe disability and death in thousands of children each year. State public health laboratories test more than 98 percent of all babies born in the United States each year for congenital disorders that can have improved outcomes if diagnosed early. NSQAP develops quality control and proficiency testing materials to maintain and enhance the quality of their newborn screening test results, conducts research, and provides technical support and training for emerging newborn screening technologies.

In conjunction with HHS funds appropriated each year, the Act has allowed NSQAP to expand its activities in support of newborn screening laboratories across the country and worldwide. NSQAP purchased new instrumentation to increase capacity, hired permanent staff, and increased quality assurance material production. Proficiency testing materials are now available for 48 of the 53 primary and secondary disorders recommended by the SACHDNC, including 41 of the 42 disorders detectable by tandem mass spectrometry. In 2010, NSQAP produced, certified, and distributed more than 700,000 dried blood spot quality assurance materials to newborn screening laboratories in the United States and internationally and provided data reports for newborn screening program evaluation. One hundred percent of U.S. States and 67 countries participated in NSQAP's proficiency testing and quality control programs (for a total of more than 500 laboratories). In further support of the accuracy of newborn screening tests, NSQAP continuously evaluates the analytical performance characteristics of the commercial filter paper that State newborn screening programs use as a collection device for dried blood spots.

NSQAP also is involved in newborn screening contingency operations. In collaboration with the APHL, NSQAP maintains a national repository of emergency blood collection cards for newborn screening programs. In 2009, APHL purchased the cards, which are stored at CDC. NSQAP regularly tests these cards to ensure their operational quality and sustainability for use by newborn screening programs. This stockpile of materials is a critical resource for state programs during emergencies, such as natural disasters, or in the event of unexpected, limited commercial availability of collection cards. In 2010, 75,000 of the emergency collection cards were distributed to a State in response to their request for help. Several States have made inquiries regarding the availability of the emergency cards, and the repository is recognized as an important national resource. Reserve blood collection cards must be continually replenished to meet demand and to ensure suitability for use.

For more than 31 years, CDC has conducted research on materials development and assisted laboratories with quality assurance for dried blood spot screening tests. As States adopt new tests for additional diseases, NSQAP must extend its services to ensure the quality of these test results while maintaining support for its current programs. CDC continues to improve the quality of newborn screening by responding to needs identified by state programs and developing high-quality and rugged laboratory methods that better detect newborn diseases.

In the future, CDC plans to strengthen its repository of quality assurance materials for existing quality assurance programs, such as the hemoglobinopathy and cystic fibrosis programs, based on population-specific needs within the United States. This will allow for expansion and diversity in the inventory to facilitate additional newborn screening laboratory participation and also will address the SACHDNC's RUSP. The agency also intends to provide support and technical assistance as molecular biology technology is incorporated into the routine workflow of newborn screening laboratories. The Newborn Screening Molecular Quality Improvement Program will work alongside the State laboratories to enhance good laboratory practice, determine the educational needs of public health laboratory personnel, and facilitate technology transfer. Finally, CDC will implement quality assurance programs and will apply appropriated yearly funds to support newborn screening implementation for recent additions to the RUSP, such as SCID, in additional States. To complement this effort, CDC will enhance the Newborn Screening Training Program to support emerging and existing technology education for public health laboratorians and leaders.

Section 1114: Interagency Coordinating Committee on Newborn and Child Screening

Section 1114 of the Act requires the Secretary to establish an ICC. The ICC was established to assess existing activities and infrastructure, including activities on birth defects and developmental disabilities authorized under section 317C of the PHS Act, in order to make recommendations for programs to collect, analyze, and make available data on the heritable disorders recommended by SACHDNC, including data on the incidence and prevalence of, as well as poor health outcomes resulting from, such disorders; and make recommendations for the establishment of regional centers for the conduct of applied epidemiological research on effective interventions to promote the prevention of poor health outcomes resulting from such disorders as well as providing information and education to the public on such effective interventions. The legislation indicates that the ICC reports to the Secretary and the appropriate committees of Congress on its recommendations related to the purpose described previously, and carry out other activities determined appropriate by the Secretary.

As per the legislation, ICC membership includes the Director of the CDC, the Administrator of HRSA, the Director of the Agency for Healthcare Research and Quality, and the Director of the National Institutes of Health, or their designee(s). In the future, the ICC must report to the Secretary and the appropriate committees of Congress on its recommendations.

Section 1115: National Contingency Plan for Newborn Screening

Section 1115 of the Act directed CDC to consult with the Administrator of HRSA and State departments of health (or related agencies) to develop a national contingency plan for newborn screening by October 21, 2008, for use by a State, region, or consortium of States in the event of

a public health emergency. The framework and draft of the plan were developed in consultation with national, State, and local partners who convened in September of 2008. The framework then was shared with Congress.

Most sectors of government have developed plans to ensure continuity in the event of disaster or emergency. These plans are generally referred to as Continuity of Operations Plans (COOP). A COOP for a newborn screening program and its public health laboratory should have two basic features: (1) a comprehensive, pre-identified list of all core testing, support activities, and supplies that must be maintained if the laboratory experiences a partial or complete operational disruption; and (2) a prearranged plan of action to ensure that all these core activities are continued without delay.

Contingency planning for an emergency helps to ensure the availability of critical resources and the continuity of operations. Contingency planning also sets standards for entities participating in the activation of the plan. Federal, State, and local entities play critical roles in the screening, diagnosis, referral, and treatment of disorders identified in newborn screening, especially during a public health emergency. Adhering to the established standards and maintaining continuity of testing and follow-up promote optimum execution of the COOP.

In July 2010, CDC and HRSA released the Newborn Screening Contingency Plan (CONPLAN). The CONPLAN's mission guides CDC and HRSA to work with public health newborn screening partners to ensure a comprehensive and uniform system of screening and continuity of care for newborns testing positive. The screening covers infants born in the United States for all SACHDNC-recommended disorders in the event of a public health emergency, as specified in the Act. The CONPLAN was developed for use as a framework by State and local health agencies, laboratories, clinicians, and other organizations that are part of the newborn screening system in the United States. It outlines major supporting actions that each public health official should consider when planning and preparing for newborn screening contingency operations and notes the responsible entities for each action.

The CONPLAN also details key roles and responsibilities for public and private health sectors. It provides a framework for states to develop pre-alert or activation responsibilities with the other key newborn screening entities within their jurisdictions, as well as a list of threats that may disrupt normal public health functions. The plan is based on the assumptions that national and/or regional backup systems and redundancies are required to ensure continuity of newborn screening operations and that preparations for newborn screening contingencies must occur before a public health emergency triggers the need for their implementation. Recommendations related to oversight, coordination, and communications also are included.

The field of emergency preparedness is an evolving one, and the science and systems involved in newborn screening are always improving. The CONPLAN is subject to amendment based on such developments, changes to standard operating procedures in stable situations, or information gathered in disasters. CONPLANs are only as good as the preparation to employ them. They should be reviewed periodically and, where possible, practiced. Areas for improvement can be identified through such exercises. CDC and HRSA will continue to work to upgrade the newborn screening CONPLAN as new technologies develop and lessons are learned through implementation.

Critical considerations in the CONPLAN include the following:

- Many States lack sufficient resources to ensure self-sufficiency through internal backup systems and redundancy through regionalization.
- Few States have the capacity to absorb a significant increase in screening volume for the laboratory and follow-up functions in the case of an emergency.
- Because of a lack of standardized screening requirements across States, a State providing contingency screening for another State may not have the capacity to screen for all conditions for which the State requiring support usually screens.
- Contingency newborn screening programs may not have the medical expertise needed to follow up with infants that test positive.
- States need to adopt the CONPLAN as an annex to their existing plans and update it as needed.

It should be noted that, in its current form, the CONPLAN does not provide detailed recommendations for the facilitation of access to medical foods, pharmaceuticals, and devices. This is an important aspect of preparedness, and further efforts to address this component of strategic objective six should be undertaken. On May 13, 2010, the SACHDNC reviewed and approved the CONPLAN. The Secretary's response to this recommendation is in progress.

Section 1116: Hunter Kelly Research Program

Section 1116 of the Act established the Hunter Kelly Research program and delegated the authority for this program to NIH. The Act authorized research in newborn screening that included identifying, developing, and testing the most promising new screening technologies; experimental treatments and disease management strategies for conditions that can be detected through newborn screening for which treatment is not yet available; and other activities that would improve newborn screening as identified by the NIH Director. Research activities are to take into consideration recommendations from SACHDNC.

Research beginning in the 1960s led to the development of universal screening tests for PKU and congenital hypothyroidism. Immediate initiation of treatment for affected infants to protect their developing brains has significantly reduced intellectual and developmental disabilities associated with these conditions. The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) has long led research efforts at NIH to increase the number of genetic tests and treatments for a wide range of rare and common conditions, now doing so through the Hunter Kelly Newborn Screening Research Program. This program aims to identify, develop, and test new screening technologies and promote innovative research on the management and treatment of conditions that benefit from early identification. The NICHD strongly encourages investigator-initiated research projects that focus on the aims of the Hunter Kelly Newborn Screening Research Program.

Multiple challenges face researchers in the field of newborn screening: the small number of individuals with rare diseases and the geographic distance between patients, multiple competing technologies being used for screening, variability of regulations for screening across states and regions, and the lack of an infrastructure to connect existing resources. To address these and other critical needs, the NICHD, through the Hunter Kelly Newborn Screening Research Program, funds the Newborn Screening Translational Research Network (NBSTRN). The

NBSTRN has developed an infrastructure designed to support researchers who are developing new screening methods, studying candidate disorders being considered for screening, initiating clinical trials that test new therapeutic interventions, and pursuing longitudinal research on the long-term health of children identified through newborn screening programs. Through an organized network of state newborn screening programs and clinical centers, the NBSTRN is implementing a research informatics system for use by investigators; administering a virtual repository of residual dried blood spots available for studies, which allows investigators to search for and request residual dried blood spots nationwide and subsequently acquire the dried blood specimen if approved by the State holding the specimen[32]; and facilitating the timely dissemination of new findings gathered by researchers.

The Hunter Kelly Research Program also supports numerous grants and contracts to develop and improve technologies related to newborn screening. One current project awarded to the Mayo Clinic is comparing different experimental tests that have been developed to screen for Lysosomal Storage Diseases, a group of progressive metabolic disorders not widely screened for at this time, and evaluating their effectiveness in a side-by-side comparison. Another project involves a multistate collaborative effort, with infrastructure support from the NBSTRN, to evaluate screening tools that test for SCID. This multistate project screened approximately 500,000, a sample of newborns that was large enough to identify children with this rare disease and to evaluate the efficacy of the test on a large scale in several State newborn screening laboratories.

The NICHD, the National Institute of Neurological Disorders and Stroke, the National Institute of Deafness and other Communication Disorders, and National Institute of Diabetes Digestive and Kidney Diseases have an ongoing collaborative initiative to stimulate translational research on potential therapeutic interventions for conditions currently screened by States, as well as other high-priority genetic conditions for which screening might be possible in the near future. The initiative has placed special emphasis on research related to some of the high-priority conditions, defined as those for which the development of an efficacious therapy would make the condition amenable to newborn screening. A sample of currently funded projects include research related to new or improved treatments of gamma-hydroxybutyric aciduria, hyperammonemia, Gaucher's disease, spinal muscular atrophy, galactosemia, Krabbe disease, and PKU.

In 2011, the NICHD will award two grants to study the natural history of disorders that are currently identified by newborn screening or could benefit from early identification by newborn screening. A comprehensive understanding of the natural history of a disorder has been identified as a necessary element to facilitate appropriate interventions for infants identified by newborn screening. By defining the sequence and timing of the onset of symptoms and complications of a disorder, a valuable resource will be developed for the newborn screening community.

On December 13–14, 2010, the NICHD, the National Human Genome Research Institute, and the Office of Rare Diseases Research sponsored a workshop, Newborn Screening in the Genomic Era: Setting a Research Agenda. The purpose of the meeting was to identify elements of a trans-NIH research agenda that would lead to the application of new genomics concepts and technologies to newborn screening and child health. The meeting was attended by experts from academia, industry, and Federal agencies in the fields of newborn screening and genomics.

CONCLUSION: The Future of Screening for Heritable Disorders

Vast improvements in the Nation's ability to screen for and prevent adverse outcomes from heritable disorders in newborns and children have occurred since SACHDNC's creation. State newborn screening programs are the beneficiaries of ongoing rapid advances in science, technology and disease prevention. As a result, they are presented with new opportunities that simultaneously pose difficult public policy challenges. As leaders of the Nation's efforts to prevent the potentially devastating consequences of heritable disorders in newborns and children, SACHDNC, Federal health officials, and Congress remain important partners for States as they grapple with ethical, social, technological, financial, and other concerns. These issues must be addressed in order to ensure that all children in the United States have equal access to screening and follow-up services that take advantage of scientific progress and operate in a system capable of incorporating new tools such as HIT that can positively impact the quality of services.

The success of State newborn screening programs hinges to a large degree on public awareness and understanding of the program's goals and the individual's rights. Public mistrust as a result of perceived infringement on privacy and confidentiality could negatively affect this important public health program. Therefore, sensitive issues such as State policies on the retention and use of residual dried blood spots need to be resolved quickly to maintain high public acceptance of screening programs. Ongoing public education about, and awareness of, newborn screening and related policies is integral to securing public trust.

Increased communication among other stakeholders, including clinicians, consumers, public health departments, and laboratories, will improve services for the Nation's babies and their families. HIT is an important tool to facilitate better newborn screening and support communication and coordination efforts. Currently, State newborn screening programs conduct different tests and collect different data. HIT provides a mechanism to link and standardize this information. SACHDNC has recommended that the requirements of newborn screening information [laboratory orders; conditions screened] are included in Federal standards and regulations for HIT. Specifically, ONC developed a Newborn Screening Use Case in 2008 (see Part I, Heritable Disorders, Newborn Screening, and Health Care Reform section for further information), and SACHDNC has endorsed the *Newborn Screening Coding and Terminology Guide*, which is HRSA and NLM guidance on standards for interoperability for electronic reporting of the results of newborn screening tests.[33]

As State newborn screening programs are integrating the use of information technology into their programs, advances in medical technology are poised to transform the newborn screening landscape once again. For example, researchers have applied digital microfluidics, a technique that "manipulates liquids as discrete microdroplets under software control," to a miniature testing platform that allows all laboratory steps involved in newborn screening, including "sampling, sample preparation, sample-processing, mixing, incubation, and detection to waste handling" on a chip.[34] This technology may allow more cost-effective population-based screening and more efficient use of the available specimen collected from newborns, thereby enabling continued expansion of newborn screening tests, if recommended, without requiring additional specimen collection.[35]

Technologic developments have implications for the future of disease management of children affected by heritable disorders identified by newborn screening. Lab-on-a-chip technology allows screening within the clinic setting.[36] Future developments in the medical device industry may permit at home monitoring of newborns and children with heritable disorders. For example, a child with pulmonary or cardiac compromise could remain at home, while the parents participate in the monitoring of the child's health status. This could facilitate the collection of data on treatment response and health outcomes. Such portable monitoring devices could empower parents by providing access to their child's health information in an easily understood format, such as graphs that demonstrate changes in a measurable health data point of interest. Continued coordinated efforts to assist in the implementation of new technologies as they are applied to the screening, diagnosis and management of heritable disorders will help to ensure equal access to improvements in health care across the nation.

Improvements in technology may bring screening for heritable disorders beyond the newborn period to children and adolescents. For example, screening for conditions such as Duchenne muscular dystrophy or fragile X syndrome beyond the newborn period may be deemed beneficial based on the weight of scientific evidence. This will bring up questions about the systems that are appropriate for ensuring that screening outside of the newborn period occurs.

Screening for heritable disorders may affect older children in other ways. The identification of infants or children who may be carriers for conditions that may be passed on to offspring is a current challenge for State newborn screening programs that is expected to grow as an issue of concern in the future. At present, stakeholders in newborn screening contemplate how to handle the identification of carriers for conditions such as cystic fibrosis or sickle cell disease. As technology progresses, information with long-term value will become increasingly available. For example, currently there is screening for rare alleles that result in early-onset disease in the case of homozygotes. Scientific advances may reveal that these rare alleles have implications for heterozygotes by placing them at increased risk for certain adult chronic conditions such as Parkinson syndrome. Together, State newborn screening programs, the public and policymakers will need to consider how to handle information that genetic screening generates at any age that might have few short-term implications but is of importance in the long-term health of individuals. At present, a SACHDNC Workgroup on Carrier Screening is examining criteria for which disorders might be introduced to a panel.

Homozygote: an individual who has inherited identical alleles at a particular locus

Heterozygote: an individual who has inherited different forms of a particular gene from each parent, usually one normal and one abnormal

Source: National Library of Medicine, *Genetics Home Reference*, http://ghr.nlm.nih.gov/

Not all needs and challenges are driven by technology. While most birth defects, developmental disorders, and common complex disorders have environmental causes or contributing factors, they are fundamentally heritable disorders. Understanding the genetic contribution to health or developmental problems is critical to the delivery of appropriate health care for each child. In the future, SACHDNC will need to consider how best to encourage development and application of programs and policies that will improve health and developmental outcomes of newborns and children born with any heritable disorder, whether or not the condition is appropriate to be

included in newborn screening or screening of older children. Understanding genetic contribution to disease can lead to identification of more appropriate management and improved accuracy in prediction of outcomes and future needs for families and for communities. The application of genetic technology to pharmacogenetics is already in progress, with pharmacogenetic experts proposing incorporation of genomic information in the prescribing of medications ranging from antidepressants and asthma therapies to management of pain and obesity. The controversies around, and the increasing uptake of, direct to consumer genetic testing are receiving attention, and families are interested in exploring broad genetic testing for their children. Newborns and children will need to be assured of safe and appropriate use of existing and future genetic information and technology that has promise in the treatment of conditions as diverse as PKU, Down syndrome, and asthma. As these technological and system changes unfold, SACHDNC, Federal health officials, and Congress must be prepared to assist and advise States and the public. The coordinated efforts of stakeholders, including policymakers, public health agencies, providers, and the public, will help to ensure that newborns and children have equal access to new genetic technologies as they are incorporated into health and public health services.

Appendix A: Conditions Screened for by State Newborn Screening Programs

Revised from NNSGRC as of April 2011 (http://genes-r-us.uthscsa.edu/nbsdisorders.htm) based on legislation or policies

Table of Core[1] Conditions

STATE	Hearing HEAR	Endocrine CH	Endocrine CAH	Hemoglobin Hb S/S	Hemoglobin Hb S/A	Hemoglobin Hb S/C	Other BIO	Other GALT	Other CF	Other SCID	Additional Conditions Included in Screening Panel (universally required unless otherwise indicated)
Alabama	●	●	●	●	●	●	●	●	●		
Alaska	●	●	●	●	●	●	●	●	●		
Arizona	A	●	●	●	●	●	●	●	●		
Arkansas	●	●	●	●	●	●	●	●	●		
California	B	●	●	●	●	●	●	●	●	A	HHH; PRO; EMA ; OTC, MTHFR (D)
Colorado	A	●	●	●	●	●	●	●	●		
Connecticut	●	●	●	●	●	●	●	●	●		HHH; HIV [2] ; NKH
D.C.	●	●	●	●	●	●	●	●	●		G6PD
Delaware	●	●	●	●	●	●	●	●	●		
Florida	●	●	●	●	●	●	●	●	●		
Georgia	A	●	●	●	●	●	●	●	●		
Hawaii	●	●	●	●	●	●	●	●	●		
Idaho	A	●	●	●	●	●	●	●	●		
Illinois	●	●	●	●	●	●	●	●	●		Pompe, Gaucher, Fabry (B) CPS (D), NKH, 5-OXO, HIV [2]
Indiana	●	●	●	●	●	●	●	●	●		
Iowa	●	●	●	●	●	●	●	●	●		
Kansas	●	●	●	●	●	●	●	●	●		
Kentucky	B	●	●	●	●	●	●	●	●		
Louisiana	●	●	●	●	●	●	●	●	●	A	
Maine	A	●	●	●	●	●	●	●	●		HHH; CPS (D)
Maryland	●	●	●	●	●	●	●	●	●		EMA
Massachusetts	●	●	●	●	●	●	●	●	●	A	TOXO; HHH, CPS (D)
Michigan	●	●	●	●	●	●	●	●	●	C	
Minnesota	●	●	●	●	●	●	●	●	●		
Mississippi	●	●	●	●	●	●	●	●	●		5-OXO; CPS; HHH
Missouri	●	●	●	●	●	●	●	●	●		
Montana	●	●	●	●	●	●	●	●	●		
Nebraska	A	●	●	●	●	●	●	●	●		5-OXO; HHH; NKH (A)
Nevada	B	●	●	●	●	●	●	●	●		
New Hampshire	A	●	●	●	●	●	●	●	●		TOXO
New Jersey	●	●	●	●	●	●	●	●	●		

STATE	Hearing HEAR	Endocrine CH	Endocrine CAH	Hemoglobin Hb S/S	Hemoglobin Hb S/A	Hemoglobin Hb S/C	Other BIO	Other GALT	Other CF	Other SCID	Additional Conditions Included in Screening Panel (universally required unless otherwise indicated)
New Mexico	●	●	●	●	●	●	●	●	●		
New York	●	●	●	●	●	●	●	●	●	●	HIV; HHH; Krabbe Disease
North Carolina	●	●	●	●	●	●	●	●	●		
North Dakota	A	●	●	●	●	●	●	●	●		HHH; NKH
Ohio	●	●	●	●	●	●	●	●	●		
Oklahoma	●	●	●	●	●	●	C	●	●		
Oregon	B	●	●	●	●	●	●	●	●		
Pennsylvania	●	●	●	●	●	●	●	●	●		5-OXO; CPS; G6PD; HHH; NKH (B)
Rhode Island	●	●	●	●	●	●	●	●	●		
South Carolina	●	●	●	●	●	●	●	●	●		
South Dakota	A	●	●	●	●	●	●	●	●		5-OXO; EMA; HHH; NKH
Tennessee	●	●	●	●	●	●	●	●	●		HHH; NKH
Texas	B	●	●	●	●	●	●	●	●	B	
Utah	●	●	●	●	●	●	●	●	●		
Vermont	●	●	●	●	●	●	●	●	●		
Virginia	●	●	●	●	●	●	●	●	●		
Washington	A	●	●	●	●	●	●	●	●		
West Virginia	●	●	●	●	●	●	●	●	●		
Wisconsin	●	●	●	●	●	●	●	●	●	●	
Wyoming	●	●	●	●	●	●	●	●	●		

[1]Terminology consistent with the following report: American College of Medical Genetics. (2006). Newborn screening: Towards a uniform screening panel and system. *Genetics in Medicine, 8* (5 Suppl), S12–S252.

[2]Newborn screened for HIV only if mother was not screened during pregnancy.

Dot "●"indicates that screening for the condition is universally required by Law or Rule and fully implemented

A = universally offered but not yet required

B = Required through hospitals with specific per annum births or by parental request

C = testing required but not yet implemented

D = likely to be detected (and reported) as a byproduct of MRM screening (MS/MS) targeted by Law or Rule

List of abbreviations for the table is available on page 35.

Table of Core[1] Conditions-Metabolic

STATE	Fatty Acid Disorders CUD	Fatty Acid Disorders LCHAD	Fatty Acid Disorders MCAD	Fatty Acid Disorders TFP	Fatty Acid Disorders VLCAD	Organic Acid Disorders GA-I	Organic Acid Disorders HMG	Organic Acid Disorders IVA	Organic Acid Disorders 3-MCC	Organic Acid Disorders Cbl-A,B	Organic Acid Disorders BKT	Organic Acid Disorders MUT	Organic Acid Disorders PROP	Organic Acid Disorders MCD	Amino Acid Disorders ASA	Amino Acid Disorders CIT	Amino Acid Disorders HCY	Amino Acid Disorders MSUD	Amino Acid Disorders PKU	Amino Acid Disorders TYR- I
Alabama	●	●	●	●	●	●	●	●	●	D	●	●	●	●	●	●	●	●	●	
Alaska	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Arizona	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Arkansas	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
California	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Colorado	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Connecticut	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
D. of Columbia	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Delaware	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Florida	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Georgia	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Hawaii	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Idaho	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Illinois	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Indiana	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Iowa	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Kansas	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Kentucky	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Louisiana	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Maine	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Maryland	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Massachusetts	●	●	●	D	●	●	●	●	D	●	●	●	●	D	●	●	●	●	●	●
Michigan	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Minnesota	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Mississippi	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Missouri	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Montana	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Nebraska	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Nevada	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
New Hampshire	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
New Jersey	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
New Mexico	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
New York	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
North Carolina		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
North Dakota	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Ohio	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

STATE	Fatty Acid Disorders CUD	Fatty Acid Disorders LCHAD	Fatty Acid Disorders MCAD	Fatty Acid Disorders TFP	Fatty Acid Disorders VLCAD	Organic Acid Disorders GA-I	Organic Acid Disorders HMG	Organic Acid Disorders IVA	Organic Acid Disorders 3-MCC	Organic Acid Disorders Cbl-A,B	Organic Acid Disorders BKT	Organic Acid Disorders MUT	Organic Acid Disorders PROP	Organic Acid Disorders MCD	Amino Acid Disorders ASA	Amino Acid Disorders CIT	Amino Acid Disorders HCY	Amino Acid Disorders MSUD	Amino Acid Disorders PKU	Amino Acid Disorders TYR- I
Oklahoma	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Oregon	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Pennsylvania	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Rhode Island	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
South Carolina	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
South Dakota	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Tennessee	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
Texas	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Utah	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Vermont	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Virginia	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Washington	●	●	●	●	●	●	●	●	D	●	●	●	●	●	●	●	●	●	●	●
West Virginia	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Wisconsin	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Wyoming	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

[1]Terminology consistent with the following report: American College of Medical Genetics. (2006). Newborn screening: Towards a uniform screening panel and system. *Genetics in Medicine, 8* (5 Suppl), S12–S252.

[2]Newborn screened for HIV only if mother was not screened during pregnancy.

Dot "●" indicates that screening for the condition is universally required by Law or Rule and fully implemented

A = universally offered but not yet required

B = Required through hospitals with specific per annum births or by parental request

C = testing required but not yet implemented

D = likely to be detected (and reported) as a byproduct of MRM screening (MS/MS) targeted by Law or Rule

List of abbreviations for the table is available on page 35.

Table of Secondary Target[1] Conditions

STATE	Fatty Acid Disorders CACT	Fatty Acid Disorders CPT-Ia	Fatty Acid Disorders CPT- II	Fatty Acid Disorders DE-RED.	Fatty Acid Disorders GA-II	Fatty Acid Disorders MCKAT	Fatty Acid Disorders M/SCHAD	Fatty Acid Disorders SC AD	Organic Acid Disorders 2M3HBA	Organic Acid Disorders 2MBG	Organic Acid Disorders 3MGA	Organic Acid Disorders Cbl-C,D	Organic Acid Disorders IBG	Organic Acid Disorders MAL	Amino Acid Disorders ARG	Amino Acid Disorders BIOPT-BS	Amino Acid Disorders BIOPT-RG	Amino Acid Disorders CIT-II	Amino Acid Disorders H-PHE	Amino Acid Disorders MET	Amino Acid Disorders TYR- II	Amino Acid Disorders TYR- III	Other Metabolic GALE	Other Metabolic GALK	Hbg Variant Hbg's
Alabama	●		●		●				●	●	●	●				●	●	●	●	●	●	●			●
Alaska	●	●	●		●			●	●	●	●	●	●	●	●	B	B	●	●	●	●	D	B	B	●
Arizona	D	D	D		D				D		D	D						D	D		D	D			D
Arkansas																									●
California	●	●	●		●		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●				●
Colorado	●	●	●		●		●	●			●	●		●	●			●	●	●	●	●			●
Connecticut	●	●	●	●	●			●				●		●	●			●	●	●	●	●	●	●	●
D. of Columbia	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	A	A	●	●	●	●	●	●	●	●
Delaware	●		●		●	D		●	D	●	D	●	●		●	D	D	●	●	●	●	●	●	●	●
Florida	●	●	●		●			●											●		●				
Georgia	D	D	D		D	D	D	D	D	D	D	D	D	D	A			D	D	D	D	D	B	B	●
Hawaii	●	●	●		●			●	●	●	●	●	●	●	●	B	B	●	●	●	●		B	B	●
Idaho	●	●	●		●			●	●	●	●	●	●	●	●	B	B	●	●	●	●		B	B	●
Illinois	●	D	●	D	●	D	●	●	D	●	●	●	●	●	●	D	D	D	●	●	●	●			●
Indiana	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			●
Iowa	●	●	●		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			●
Kansas																			●						●
Kentucky	A	A	A		A			●	A	A	A	A	A	A	A	D	D	A	●	A	A	A			●
Louisiana																			●						●
Maine	D	D	●		●			●		D	D	●	D		●			●	●	D	●	D	●	●	●
Maryland	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	B	B	●	●	●	●	●	●	●	●
Massachusetts	D	D	A	A	D	D	A	D	D	D	D	●	D	A	●	D	D	A	D	D	D	D	D	D	●
Michigan	●	●	●	●	●	●	●	●	●	●	●	●	●	D	●	●	●	●	●	●	A	A			●
Minnesota	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Mississippi	●	●	●	A	●	A	●	●	A	●	●	●	●	●	●	A	A	●	●	●	●	A	●	●	●
Missouri	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			●
Montana	D		D	D	D	D	D	D	D	D	D	D	D			D	D	D	●	D	D	D			●
Nebraska	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	●	D	D	D	●	●	●
Nevada	●	●	●		●			●	●	●	●	●	●	●	●	B	B	●	●	●	●		B	B	A
New Hampshire	D	D	●		●					D	D	D			●	D	D	D	●	D			●	●	●
New Jersey	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
New Mexico	A	D	A		A			A	D	D	A	A	D	D	D	B	B	A	A	A	A	D	B	B	●
New York	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			●	●	●	●	●			●
North Carolina	●		●		●			●		●		●	●			●	●	●	●	●	●	●			●
North Dakota	●	●	●		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			●
Ohio	●	●	●		●			●		●		●	●		●			●	●	●	●	●			●
Oklahoma	●	●	●		●	D		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			●
Oregon	●	D	●		●			●	D	D	●	●	D	D	D	B	B	●	●	●	●	D	B	B	●
Pennsylvania	B	B	B	B	B		B	B		B	B	B	B	B	B	B	B	B	●	B	B	B	●	●	●
Rhode Island		D																	●				●	●	●
South Carolina	●	●	●	●	●	●	●	●	●	●	●	●	●	●		●	●	●	●	●	●	●	●	●	●

STATE	Fatty Acid Disorders CACT	Fatty Acid Disorders CPT-Ia	Fatty Acid Disorders CPT- II	Fatty Acid Disorders DE-RED.	Fatty Acid Disorders GA-II	Fatty Acid Disorders MCKAT	Fatty Acid Disorders M/SCHAD	Fatty Acid Disorders SC AD	Organic Acid Disorders 2M3HBA	Organic Acid Disorders 2MBG	Organic Acid Disorders 3MGA	Organic Acid Disorders CbI-C,D	Organic Acid Disorders IBG	Organic Acid Disorders MAL	Amino Acid Disorders ARG	Amino Acid Disorders BIOPT-BS	Amino Acid Disorders BIOPT-RG	Amino Acid Disorders CIT-II	Amino Acid Disorders H-PHE	Amino Acid Disorders MET	Amino Acid Disorders TYR- II	Amino Acid Disorders TYR- III	Other Metabolic GALE	Other Metabolic GALK	Hbg Variant Hbg's
South Dakota	●	●	●		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			●
Tennessee	●	●	●	●	●	D		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Texas	D	D	D	C	D	C	C	C	D	D	D	D	C	C	C	D	D	D	●	D	D	D			●
Utah	●	●	●		●	D		●	●	●	D	●	●	D	●	●	●	●	●	●	●	●			●
Vermont	D	D	D		D					D	D	●			D			●	●	D	D	D	●	●	●
Virginia	D	D	D		D	D			D	D	D	D				D	D	D	D	D	D	D	D	D	●
Washington	D		D		D	D			D	D	D	D				D	D	●	D	D					●
West Virginia	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	●	D	D	D	●	●	●
Wisconsin	●		●	●	●	●	●	●	●	●	●	●	●			●	●	●	●	●	●	●			●
Wyoming	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A			A	●	A	A	B			●

[1]Terminology consistent with the following report: American College of Medical Genetics. (2006). Newborn screening: Towards a uniform screening panel and system. *Genetics in Medicine, 8* (5 Suppl), S12–S252.

[2]Newborn screened for HIV only if mother was not screened during pregnancy.

Dot "●" indicates that screening for the condition is universally required by Law or Rule and fully implemented

A = universally offered but not yet required

B = Required through hospitals with specific per annum births or by parental request

C = testing required but not yet implemented

D = likely to be detected (and reported) as a byproduct of MRM screening (MS/MS) targeted by Law or Rule

List of abbreviations for the table is available on page 35.

List of abbreviations for the preceding tables

Table of Core Conditions Conditions/Abbreviations and Names

BIO	Biotinidase	**CF**	Cystic fibrosis	**GALT**	Transferase deficient galactosemia (Classical)	**HB S/C**	Sickle – C disease	**HEAR**	Hearing screening
CAH	Congenital adrenal hyperplasia	**CH**	Congenital hypothyroidism	**HB S/S**	Sickle cell anemia	**HB S/A**	S-βeta thalassemia	**SCID**	Severe Combined Immunodeficiency

Table of Core Conditions-Metabolic Deficiency/Disorder Abbreviations and Names (optional nomenclature)

3-MCC	3-Methylcrotonyl-CoA carboxylase	**CUD**	Carnitine uptake defect (Carnitine transport defect)	**LCHAD**	Long-chain L-3- hydroxyacyl-CoA dehydrogenase	**PKU**	Phenylketonuria/ hyperphenylalaninemia
ASA	Argininosuccinate aciduria	**GA-1**	Glutaric acidemia type 1	**MCAD**	Medium-chain acyl-CoA dehydrogenase	**PROP**	Propionic acidemia (Propionyl-CoA carboxylase)
BKT	Beta ketothiolase (mitochondrial acetoacetyl-CoA thiolase ; short-chain ketoacyl thiolase; T2)	**HCY**	Homocystinuria (cystathionine beta synthase)	**MCD**	Multiple carboxylase (Holocarboxylase synthetase)	**TFP**	Trifunctional protein deficiency
CBL A,B	Methylmalonic acidemia (Vitamin B12 Disorders)	**HMG**	3-Hydroxy 3 - methylglutaric aciduria (3-Hydroxy 3-methylglutaryl-CoA lyase)	**MSUD**	Maple syrup urine disease (branched-chain ketoacid dehydrogenase)	**TYR-1**	Tyrosinemia Type 1
CIT I	Citrullinemia type I (Argininosuccinate synthetase)	**IVA**	Isovaleric acidemia (Isovaleryl-CoA dehydrogenase)	**MUT**	Methylmalonic Acidemia (methylmalonyl-CoA mutase)	**VLCAD**	Very long-chain acyl-CoA dehydrogenase

Table of Secondary Conditions Deficiency/Disorder Abbreviations and Names (optional nomenclature)

2M3HBA	2-Methyl-3-hydroxy butyric aciduria	**CACT**	Carnitine acylcarnitine translocase	**GA-II**	Glutaric acidemia Type II	**MAL**	Malonic acidemia (Malonyl-CoA decarboxylase)
2MBG	2-Methylbutyryl-CoA dehydrogenase	**CBL-C,D**	Methylmalonic acidemia (Cbl C,D)	**GALE**	Galactose epimerase	**MCKAT**	Medium-chain ketoacyl-CoA thiolase
3MGA	3-Methylglutaconic aciduria	**CIT-II**	Citrullinemia type II	**GALK**	Galactokinase	**MET**	Hypermethioninemia
ARG	Argininemia (Arginase deficiency)	**CPT-Ia**	Carnitine palmitoyltransferase I	**H-PHE**	Benign hyperphenylalaninemia	**SCAD**	Short-chain acyl-CoA dehydrogenase
BIOPT-BS	Defects of biopterin cofactor biosynthesis	**CPT-II**	Carnitine palmitoyltransferase II	**IBG**	Isobutyryl-CoA dehydrogenase	**TYR-II**	Tyrosinemia type II
BIOPT-REG	Defects of biopterin cofactor regeneration	**De-Red**	Dienoyl-CoA reductase	**M/SCHAD**	Medium/Short chain L-3-hydroxy acyl-CoA dehydrogenase	**TYR-III**	Tyrosinemia type III

Table of Core Conditions-Additional Conditions Included in the Screening Panel Other Disorders

5-OXO	5-oxoprolinuria (pyroglutamic aciduria)	**G6PD**	Glucose 6 phosphate dehydrogenase	**NKH**	Nonketotic hyperglycinemia
CPS	Carbamoylphosphate synthetase	**HHH**	Hyperammonemia/ornithinemia/ citrullinemia (Ornithine transporter defect)	**PRO**	Prolinemia
EMA	Ethylmalonic encephalopathy	**HIV**	Human immunodeficiency virus	**TOXO**	Toxoplasmosis

Appendix B: SACHDNC Publications

The list of SACHDNC publications below includes journal articles, reports, white papers, and meeting summaries. These documents are available on the SACHDNC Web site at http://www.hrsa.gov/heritabledisorderscommittee/default.htm.

Statement—What Questions Should Newborn Screening Long-Term Follow-Up Be Able to Answer?: A Statement of the United States Secretary for Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children (publication in journal forthcoming)

Briefing Paper—Screening U.S. College Athletes for Their Sickle Cell Disease Carrier Status (October, 2010)

Briefing Paper—Considerations and Recommendations for a National Policy Regarding the Retention and Use of Dried Blood Spot Specimens After Newborn Screening (September, 2010)

Journal Review—An Evidence Development Process for Newborn Screening (March, 2010)

Journal Commentary—A Blueprint for Maternal and Child Health Primary Care Physician Education in Medical Genetics and Genomic Medicine (March, 2010)

Journal Commentary—Method for Evaluating Conditions Nominated for Population-Based Screening of Newborns and Children (March, 2010)

Report—Long-Term Follow-Up After Diagnosis Resulting From Newborn Screening (April, 2008)

Report—Advancing the Current Recommended Panel of Conditions for Newborn Screening (November, 2007)

Meeting Summary—The Road Map to Implement Long-Term Follow-Up and Treatment in Newborn Screening (April 18, 2007)

Meeting Summary—Evidence-Based Evaluation and Decision Process Workgroup Meeting Summary and Recommendations (October 23, 2006)

Appendix C: List of the SACHDNC Recommendations to the HHS Secretary and Outcomes

TOPIC: Critical Congenital Heart Disease	
SACHDNC RECOMMENDATION: On October 15, 2010, SACHDNC recommended to the HHS Secretary the addition of "critical congenital cyanotic heart disease (CCCHD) to the recommended uniform screening panel with the understanding that the following activities will also take place in a timely manner: (1) The National Institutes of Health (NIH) shall fund research activities to determine the care provided and the health outcomes of affected newborns with critical congenital cyanotic heart disease as a result of prospective newborn screening; (2) the Centers for Disease Control and Prevention (CDC) shall fund surveillance activities to monitor the critical congenital cyanotic heart disease link to infant mortality and other health outcomes; (3) the Health Resources and Services Administration (HRSA) shall guide the development of screening standards and infrastructure needed for the implementation of a public health approach to point of service screening for critical congenital cyanotic heart disease; and (4) HRSA shall fund the development of, in collaboration with public health and health care professional organizations and families, appropriate education and training materials for families and public health and health care professionals relevant to the screening and treatment of CCCHD."	**SECRETARY'S RESPONSE:** On April 21, 2010, the Secretary rejected SACHDNC recommendations, stating, "As you noted in your letter, there are 'recognizable evidence gaps' regarding screening for Critical Congenital Cyanotic Heart Disease. After consultation with HHS agency leadership, I have determined that the Advisory Committee's recommendations are not ready for adoption. However, because this is such an important issue, I am referring these recommendations to the newly established Interagency Coordinating Committee on Newborn and Child Screening (ICC) for additional review and input regarding implementation. The ICC includes the National Institutes of Health, Centers for Disease Control and Prevention, Health Resources and Services Administration, Agency for Healthcare Research and Quality, and the Food and Drug Administration. ICC leadership will examine the evidence gaps described by the Advisory Committee, and propose a plan of action to address identification of effective screening technologies, development of diagnostic processes and protocols, education of providers and the public, and strengthening service infrastructure needs for follow-up and surveillance. The ICC will report this plan to me within 90 days, and I will keep you and the Advisory Committee informed."

TOPIC: The use and retention of residual newborn screening blood specimens

SACHDNC RECOMMENDATION: On October 13, 2010, in order to address the potential to advance science and clinical care for newborns, children, their families and society through the use of residual newborn screening blood specimens and to protect those valuable resource for the public good SACHDNC made the following recommendations to the Secretary:

"(1) All State newborn screening programs should have a policy in place that has been reviewed by the State Attorney General or other appropriate legal authority that specifies who may access and use dried blood specimens once they arrive at the State-designated newborn screening laboratory, including further access after newborn screening tests are completed.

(2) All State newborn screening programs should have a policy in place that has been reviewed by the State Attorney General or other appropriate legal authority addressing the disposition of dried blood specimens remaining after newborn screening. Policymakers should consider the value of the specimens as a promising resource for research, the protection of the privacy and confidentiality of families and the necessity of ensuring the public's trust.

(3) All State newborn screening programs should develop a well-defined strategy to educate health care professionals who provide patients with prenatal and postnatal care about newborn screening and the potential uses of residual dried blood specimens.

(4) All State newborn screening programs should create policies that are in compliance with Federal research regulations, ensure that parents are aware of these activities, and consider whether documentation of parents' wishes and willingness to participate are required.

(5) All State newborn screening programs should work proactively to ensure that all families of newborns are educated about newborn screening as a part of prenatal and postnatal care.

(6) The Secretary of Health and Human Services should help improve efforts to educate the public and health care providers about newborn screening and the retention and use of specimens.

(7) The Secretary of Health and Human Services should facilitate a national dialogue among Federal and State stakeholders about policies for the retention and use of residual newborn screening specimens, including model consent and dissent processes.

(8) The Secretary of Health and Human Services should explore the feasibility of establishing a voluntary national repository of residual dried blood specimens, in which families may choose to participate.

SECRETARY'S RESPONSE: On April 13, 2011, the Secretary rejected SACHDNC recommendations, stating, "At this time, the Committee recommendations are not ready for adoption. Therefore, I am referring the Committee's report, Considerations and Recommendations for a National Policy Regarding the Retention and Use of Dried Blood Spot Specimens After Newborn Screening to the Interagency Coordinating Committee on Newborn and Child Screening (ICC) for their review and input regarding possible future implementation of the recommendations. The use of the ICC allows a more formal engagement of the Office of Human Research Protections and Office of Civil Rights, along with the Federal agencies assigned to the ICC by its authorizing legislation. I will encourage the ICC to submit a report with recommendations for appropriate HHS action by June 1, 2012."

TOPIC: Revisions to June 2010 recommendations regarding screening U.S. college athletes for their sickle cell disease carrier status

SACHDNC RECOMMENDATION: On October 11, 2010, SACHDNC recommended to the Secretary the following revisions to recommendations made on June 14, 2010. The revisions were considered refinements to add clarity to the original SACHDNC recommendations, rather than changes in the content of the recommendations (changes below are italicized for emphasis):

"Original: Recommendation 1: All individuals should know their medical risk for various disorders, including their carrier status for various inherited genetic conditions such as sickle cell disease.

Revised: Recommendation 1: All individuals should have the opportunity to find out their risk for various medical disorders, including their carrier status for genetic conditions such as sickle cell disease.

Original: Recommendations 2: Genetic testing or screening should not be a pre-requisite for participation in athletic endeavors.

Original: Recommendations 3: Evaluation and screening for sickle cell disease and other genetic conditions should take place within the individual's medical home. That evaluation should include counseling regarding the implications of the information for the individual and assurance of the privacy of genetic information.

Revised: Recommendation 2 (combining Recommendations 2 and 3): Evaluation and testing for sickle cell disease and other genetic conditions should take place within the individual's medical home. That evaluation should include counseling regarding the implications of the information for the individual and assurance of the privacy of genetic information. Genetic testing should not be a prerequisite for participation in sports, unless deemed medically necessary.

Original: Recommendations 4, 5, and 6: No Changes

Recommendation 3: As part of the individual's annual medical evaluation for participation in sports, all potential athletes should receive education on safe practices for prevention of exercise and heat related illnesses.

Recommendation 4: The Secretary, HHS, instruct SACHDNC to work with the SCDAA, relevant Federal HHS agencies, athletic associations, community based and health care professional organizations to develop guidelines and educational resources about screening for sickle cell trait in all persons, including athletes.

Recommendation 5: The National institutes of Health and the Centers for Disease Control and Prevention conduct research to ascertain if some athletes with sickle cell trait are at increased risk of exercise-related sudden death."

SECRETARY'S RESPONSE: Pending

TOPIC: National Contingency Plan for NBS

SACHDNC RECOMMENDATION: On June 14, 2010, SACHDNC recommended to the Secretary, "In order to establish a comprehensive national all hazards approach to newborn screening incident response, the SACHDNC recommends that the Secretary of HHS coordinate newborn screening emergency preparedness activities, as defined in the CONPLAN, within HHS's National Response Framework."

SECRETARY'S RESPONSE: Pending

TOPIC: Screening U.S. college athletes for their sickle cell disease carrier status

SACHDNC RECOMMENDATION: On June 14, 2010, SACHDNC recommended the following to the Secretary:

"(1) All individuals should know their medical risk for various disorders, including their carrier status for various inherited genetic conditions such as sickle cell disease.

(2) Genetic testing or screening should not be a pre-requisite for participation in athletic endeavors.

(3) Evaluation and screening for sickle cell disease and other genetic conditions should take place within the individual's medical home. That evaluation should include counseling regarding the implications of the information for the individual and assurance of the privacy of genetic information.

(4) As part of the individual's annual medical evaluation for participation in sports, all potential athletes should receive education on safe practices for prevention of exercise and heat related illnesses.

(5) The Secretary, HHS, instruct SACHDNC to work with the SCDAA, relevant Federal HHS agencies, athletic associations, community based and health care professional organizations to develop guidelines and educational resources about screening for sickle cell trait in all persons, including athletes.

(6) The National Institutes of Health and the Centers for Disease Control and Prevention conduct research to ascertain if some athletes with sickle cell trait are at increased risk of exercise-related sudden death."

SECRETARY'S RESPONSE: Recommendations were revised in the October 11, 2010, letter.

TOPIC: Insurance coverage for medical foods

SACHDNC RECOMMENDATION: On June 14, 2010, SACHDNC recommended to the Secretary that as the Department developed specific regulations for implementation of health reform, the Department would ensure that families with individuals diagnosed with inborn errors of metabolism have access to health coverage that includes the following essential components of treatment:

"(1) Medical foods (as defined by the Food and Drug Administration and, in addition, for those conditions recommended by the Committee) delivered either orally or by tube (both are enteral) and foods modified to be low in protein that are prescribed by a physician should be considered medical benefits (and be included as essential health care services, and should not be restricted to pharmacy benefits);

(2) Individuals of all ages who are diagnosed with one or more of the conditions recommended by the Committee should be considered high risk and HHS regulations should ensure that they can access comprehensive coverage. This can best be accomplished through private health plans or publically supported programs such as Medicaid and high risk pools that cover medically necessary treatments – including medical foods and modified low protein foods; and

(3) Families should have access to these essential benefits irrespective of the source of their health coverage, including private plans, federally supported programs such as Medicaid, the Children's Health Insurance Program, TRICARE, and the Indian Health Service, as well as plans participating in, the Federal Employees Health Benefits program, and should not be subject to state exclusions."

SECRETARY'S RESPONSE: On December 14, 2010, the Secretary rejected SACHDNC's recommendations, stating, "As you are aware, the Department must follow the relevant language of the Affordable Care Act in determining essential health benefits. The statute states that essential health benefits shall include at least ten general categories specified in the law and the items and services covered within these categories. Additionally, the scope of benefits must be equal to that provided under a typical employer-sponsored plan and the determination of the scope of benefits should be informed by a survey conducted by the Department of Labor. The statute also states that benefit packages must be balanced appropriately across service categories and must be constructed in ways that do not discriminate against individuals because of their age or condition.

The Administration and this Department have moved quickly to develop a process for determining essential health benefits. A survey is being conducted by the Department of Labor to inform our determination of a typical employer-sponsored plan. The results are expected in March of next year. We are also seeking advice from the Institute of Medicine on considerations to be taken into account with regard to essential health benefits both initially and over time. The Institute of Medicine will be holding a public workshop on essential health benefits early in 2011 and its report is due at the end of September.

The information you have provided will help inform our ultimate decision about essential health benefits. However, until I have the results of the Department of Labor survey and the Institute of Medicine recommendations, I am not in a position to make determinations about particular benefits."

TOPIC: Health Care Reform White Paper

SACHDNC RECOMMENDATION 1: On March 23, 2010, SACHDNC recommended that the Secretary "encourage the Centers for Medicare and Medicaid Services to convene an expert panel to examine coding changes to streamline the billing process for newborn screening services and to put forth recommendations that enhance the standardization of health care transactions."

SECRETARY'S RESPONSE: On September 23, 2010, the Secretary adopted SACHDNC's recommendation, stating, "The lack of a uniform system of codes for billing and payment for newborn screening services results in an administrative burden on payers, providers, and suppliers. CMS will explore options for using an existing expert panel or convening a new panel to recommend a more uniform system of coding and billing of newborn screening services."

SACHDNC RECOMMENDATION 2: On March 23, 2010, SACHDNC recommended that the Secretary "encourage the Centers for Medicare and Medicaid Services to develop and pilot a payment method for an integrated system of care coordination through the medical home framework for children diagnosed with heritable and congenital disorders as a result of screening."

SECRETARY'S RESPONSE: On September 23, 2010, the Secretary adopted SACHDNC's recommendation, stating, "CMS is convening a new Maternal, Infant, Child Workgroup this year to provide input into State and Federal efforts to address clinical, policy, and payment issues related to neonatal care and outcomes improvement. This recommendation will be forwarded to that workgroup for consideration. I am also asking the new Center for Medicare and Medicaid Innovation, which is charged with testing new payment methods and health care delivery systems for CMS beneficiaries, to consider medical home models for children with heritable and congenital disorders."

SACHDNC RECOMMENDATION 3: On March 23, 2010, SACHDNC recommended that the Secretary "encourage the adoption and further definition of the Newborn Screening Use Case within the Department's health information exchange endeavors, specifically encouraging the Centers for Medicare and Medicaid Services to make use of the Newborn Screening Use Case when defining "meaningful use" of Electronic Health Records and the Office of the National Coordinator for Health Information Technology to further facilitate the adoption of the Newborn Screening Use Case."

SECRETARY'S RESPONSE: On September 23, 2010, the Secretary adopted SACHDNC's recommendation, stating, "This recommendation facilitates a standard approach to newborn screening that would permit the electronic exchange of newborn information with the goal of improving the coordination of care. I will direct CMS to address opportunities to adopt and further define the Newborn Screening Use Case through additional rule making as ONC's plans for implementation of meaningful use of health information technology evolves. I also will ask CMS to assess opportunities to use information from the Newborn Screening Use Case in developing the pediatric electronic health record format, as required under the Children's Health Insurance Program Reauthorization Act of 2009."

SACHDNC RECOMMENDATION 4: On March 23, 2010, SACHDNC recommended that the Secretary "support, as allowable, the closure of gaps in insurance coverage for medical foods and foods modified to be low in protein, as recommended by the Committee in April 2009."

SECRETARY'S RESPONSE: On September 23, 2010, the Secretary respectfully rejected the recommendation, stating, "HHS recognizes that there is a need for policy to address gaps in coverage for medical foods and foods modified to be low in protein that are essential treatments for certain heritable disorders identified in newborn screening but are not typically considered "medical services." We are currently reviewing SACHDNC's June 14, 20lO letter in which many of these same

concerns are raised in the context of enactment of the Affordable Care Act. My forthcoming response to the June 14 letter will address this issue further. I will also ask CMS to review State Medicaid programs to determine if there is opportunity to improve Federal guidance to the states regarding existing coverage for medical foods and foods modified to be low in protein."

TOPIC: Addition of SCID to RUSP

SACHDNC RECOMMENDATION: On February 25, 2010, SACHDNC recommended "the addition of SCID to the uniform panel, and related T-cell lymphocyte deficiencies to the list of secondary targets as a comprehensive entity, with the understanding that the following activities will also take place in a timely manner.

The National Institutes of Health shall fund surveillance activities to determine health outcomes of affected newborns with any T-cell lymphocyte deficiency receiving treatment as a result of prospective newborn screening.

The Health Resources and Services Administration shall fund the development of appropriate education and training materials for families and public health and health care professionals relevant to the screening and treatment of SCID and related T-cell lymphocyte deficiencies.

The Centers for Disease Control and Prevention shall develop and distribute to performing laboratories suitable dried blood spot specimens for quality control and quality assurance purposes."

SECRETARY'S RESPONSE: On May 21, 2010, the Secretary responded as follows: "The Secretary also adopts the Committee's recommendation to adopt the SACHDNC's addition of SCID as a core condition to the Recommended Uniform Screening Panel, and related T-cell lymphocyte deficiencies to the list of secondary targets as a comprehensive entity as a national standard and affirms the SACHDNC's updated Recommended Uniform Screening Panel to screen for 30 core conditions and report 26 secondary conditions.

In addition, I request that the SACHDNC submit a report in May 2011 on the status of States' implementation of this recommendation, including the surveillance activities to be conducted through the Newborn Screening Translational Research Network."

TOPIC: Adoption of RUSP

SACHDNC RECOMMENDATION: On November 22, 2009, SACHDNC reaffirmed its recommendation that the Secretary "facilitate adoption by all state newborn screening programs of the ACMG recommended uniform screening panel (now the SACHDNC's recommended uniform screening panel) which will provide the Federal guidance necessary to help states voluntarily bring their programs into alignment with the most current standards."

SECRETARY'S RESPONSE: On May 21, 2010, the Secretary responded as follows: "The Secretary adopts SACHDNC's recommendations to adopt the SACHDNC's Recommended Uniform Screening Panel (screen for the identified 29 core conditions; report on the identified 25 secondary conditions) as a national standard for newborn screening programs and facilitate the adoption of the SACHDNC's Recommended Uniform Screening Panel by all State newborn screening programs."

TOPIC: Krabbe disease

SACHDNC RECOMMENDATION: On September 1, 2009, SACHDNC recommended "not adding the condition (Krabbe disease) to the core panel now."

SECRETARY'S RESPONSE: On March 21, 2010, the Secretary adopted SACHDNC's recommendation not to add Krabbe disease to the RUSP.

TOPIC: Improve genomic education of primary care physicians

SACHDNC RECOMMENDATION: On September 1, 2009, SACHDNC recommended that the Secretary "develop and fund a 'Learning Collaborative' in genetics and primary care training to support increased genetic literacy amongst primary care providers."

SECRETARY'S RESPONSE: On March 21, 2010, the Secretary adopted SACHDNC's recommendation, stating that HRSA was "establishing a project that pairs representatives from primary care practices with genetics and genomic medical expertise through the formation of a Genetics in Primary Care Training Institute."

TOPIC: Increase public awareness of newborn screening

SACHDNC RECOMMENDATION: On September 1, 2009, SACHDNC recommended that the Secretary "provide additional resources to increase public awareness of the newborn screening system."

SECRETARY'S RESPONSE: On March 21, 2010, the Secretary adopted SACHDNC's recommendation, stating, "The newly funded Clearinghouse for Newborn Screening Information and Resources will bring needed resources to newborn screening education by establishing and maintaining a central clearinghouse of current educational and family support services information, which will include materials, research, and data on newborn screening."

TOPIC: Insurance coverage of medical foods and foods modified to be low protein

SACHDNC RECOMMENDATION: On April 7, 2009, SACHDNC recommended the following

"(1) Federal legislation be enacted to establish a uniform requirement that health plans offer coverage of medical foods and foods modified to be low protein for those conditions recommended by the Committee. Health plans would include Federal insurance programs coverage plans (Children's Health Insurance Program, Tricare, and Medicaid) and those plans governed by the Employment Retirement Income Security Act (ERISA) and would not be subject to state exclusions.

(2) Medicaid's enabling legislation (Title XIX of the Social Security Act) be amended to ensure more uniform coverage by state Medicaid programs of medical foods and foods modified to be low protein for those conditions recommended by the Committee. (Medical foods are not mentioned in the Federal Medicaid statute allowing significant variation across states with respect to the coverage of medical foods. Amending §1905(a) of the Federal statute would encourage best practices and ensure greater uniformity.)

(3) The following specific requirements be included in the legislation:

(a) Medical foods (as defined by the FDA and for those conditions recommended by the Committee) delivered either orally or by tube (both are enteral) and foods modified to be low protein used under the direction of a physician for the treatment of an inborn error of metabolism should be included as medical benefits and not restricted to pharmacy benefits.

(b) Pharmacological doses of vitamins and amino acids used specifically for the treatment of inborn errors of metabolism for those conditions recommended by the Committee under the direction of a physician will be covered.

(c) A minimum yearly coverage should be set for all health insurance plans, including those covered by the Children's Health Insurance Program, TRICARE, and Medicaid and those governed under the ERISA. The Secretary will have authority to set age-specific minimum levels of coverage and periodically update these levels based on a standard cost of living index."

SECRETARY'S RESPONSE: On October 2, 2009, the Secretary responded as follows: "I recognize that medical foods and other foods modified to be low in protein are important treatments for inborn errors of metabolism, and the Department will be further exploring these proposals. SACHDNC's recommendations to enact legislation are beyond the Department's authority. Therefore, I am neither adopting nor rejecting SACHDNC's recommendations."

TOPIC: Prenatal parental education

SACHDNC RECOMMENDATION: On April 4, 2007, SACHDNC recommended that the Secretary "develop and fund a mechanism to study the distribution of existing newborn screening educational materials and acquisition of knowledge about newborn screening by expectant parents in the context of the healthcare provider-patient relationship."

SECRETARY'S RESPONSE: On October 21, 2008, the Administrator of HRSA responded as follows: "We will ask the newly authorized Secretary's Newborn and Child Screening Interagency Coordinating Committee to assess the feasibility of and possible approaches to conducting these studies so that we can develop a cost estimate for conducting the studies if and when funding becomes available."

TOPIC: Adoption of the ACMG recommended uniform screening panel

SACHDNC RECOMMENDATION: On September 9, 2005, SACHDNC "strongly and unanimously recommends that the Secretary initiate appropriate action to facilitate adoption of the ACMG recommended screening panel by every State newborn screening program."

SECRETARY'S RESPONSE: On October 21, 2008, the Administrator of HRSA responded as follows: "Based on the information available now, the Secretary is considering adopting the conditions recommended in the ACMG report as a national standard for newborn screening programs. Before making this determination, the Secretary would like to consider further information including the findings and recommendations of the President Bush's Council on Bioethics related to ethical issues in the current expansion of newborn screening. Therefore, the Secretary will defer making a determination pending further information

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