Newborn Screening for Severe Combined Immunodeficiency Disorder

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

REPORT

Executive Summary

In January 2010, the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) recommended to the Secretary of the Department of Health and Human Services the addition of Severe Combined Immune Deficiency (SCID) to the Recommended Uniform Screening Panel.[1] The Secretary accepted the recommendation in May 2010 and requested that SACHDNC submit a report in May 2011 on the status of newborn screening for SCID.[2] This report summarizes the current status of screening newborns for SCID in state-based newborn screening programs and proposes next steps for implementation.

Newborn screening to identify and treat infants with SCID and to educate and support families, public health providers, and health care providers has been successfully piloted in the State and Territory newborn screening programs of California, Louisiana, Massachusetts, New York, Puerto Rico, and Wisconsin, and in the Navajo Nation. These pilot studies currently cover approximately 25 percent of births in the United States. To date, 961,925 newborns have been screened and 60 infants, or approximately 1 in 16,032, have been identified with some form of immune deficiency. Fourteen infants with SCID (~1 in 68,000) have been diagnosed and received treatment. No missed cases of SCID have come to the attention of the newborn screening programs conducting the pilots.

The combined State and Federal efforts to address SACHDNC recommendations represent a model of collaboration across HHS agencies, as well as among State public health newborn screening programs.

- Highly accurate molecular methods have been developed and validated.
- Model protocols for screening have been employed, including high-throughput, automated testing in States with a large number of births and screening offsite for States with a small number of births.
- An international database to assess laboratory performance and participation in a national quality assurance program enabled real-time quality improvement.
- Emerging findings from the pilots are advancing understanding of SCID and triggering new research efforts.
- The sharing of expertise and lessons learned facilitated the timely resolution of positive screens and refinement of the screening effort.

The tools and knowledge generated through the pilot studies will be available for ongoing collaborations as other states consider implementing newborn screening for immune deficiency. As screening for SCID continues and expands, collaboration between the Federal agencies and States will increase our understanding of immune deficiencies and improve our ability to identify and treat affected infants.

Introduction

In September 2007, Severe Combined Immune Deficiency (SCID) was nominated to the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) for addition to the Recommended Uniform Screening Panel (RUSP). An evidence review was undertaken and the evidence report was discussed by SACHDNC in February 2009. At that time, SACHDNC voted not to add SCID to the RUSP, noting specific gaps in evidence that should be addressed before SCID could be added to the RUSP: (1) prospective identification of at least one confirmed case of SCID through a population-based newborn screening program, (2) demonstrated willingness and capacity of additional states to implement newborn screening for SCID, (3) reproducibility of the screening test and continuance of a false positive rate of less than 0.1 percent, and (4) creation of a laboratory proficiency testing program through the Centers for Disease Control and Prevention's (CDC) National Quality Assurance Program. In January 2010, the nomination of SCID to the RUSP was again brought to SACHDNC. At that time, SACHDNC reviewed the activities undertaken to address the evidence gaps and voted to recommend to the Secretary of the Department of Health and Human Services (HHS) the addition of SCID to the RUSP and related T cell deficiencies to the list of secondary targets,[1] with the understanding that the following activities would take place in a timely manner:

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

2. The Health Resources and Services Administration (HRSA) 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 deficiencies;

3. CDC shall develop and distribute to performing laboratories suitable dried blood spot specimens for quality control and quality assurance purposes.

In May 2010, the Secretary adopted the recommendation to add SCID as a core condition to the RUSP, and related T cell deficiencies to the list of secondary targets and requested that SACHDNC submit a report in May 2011 on the status of States' implementation of this recommendation, including surveillance activities conducted through the Newborn Screening Translational Research Network (NBSTRN).[2] This report summarizes the current status of screening newborns for Severe Combined Immunodeficiency (SCID) in State-based newborn screening programs, as requested by the Secretary in May 2010.

Background

Immunodeficiency disorders, including SCID, are characterized by the lack of a functioning immune system. Babies born with SCID appear healthy but are extremely vulnerable to infection. Exposure to common infections and live vaccines is life threatening. SCID leads to death in infancy unless treatment, usually stem cell transplantation, is provided.[3-4] Variations or "misspellings" in the DNA sequence of more than 13 different genes can cause SCID or a form of combined immunodeficiency. In most cases, the misspelling occurs in a newborn with no family history of SCID. Since SCID is not apparent at birth and early recognition is essential for lifesaving treatment, SCID has been recognized as a candidate for newborn bloodspot screening for many years.[5] However, no laboratory test for detecting SCID on newborn bloodspots was available until the current testing platform for screening for SCID was developed and validated for population-based screening by NIH in 2005.[6] This screening test detects SCID through the absence of a by-product normally generated during the development of the T cell, an important part of a functioning immune system. Since patients with SCID have few or no T cells, the absence of this by-product, T cell receptor excision circles (TRECs), identifies SCID regardless of the underlying genetic defect or DNA variation. The TREC test uses molecular methods to count the TRECs present in DNA isolated from dried blood spots. In 2005, the TREC test was brought to the attention of SACHDNC at its inaugural meeting, and SACHDNC monitored its development and testing.

SCID Newborn Screening Pilot Studies

In 2007, scientists in Wisconsin (State Laboratory of Hygiene and Medical College of Wisconsin) and the New England Newborn Screening Program of the University of Massachusetts Medical School both developed high throughput TREC assays to screen births in Wisconsin and Massachusetts on a trial basis.[7-8] In 2008, a partnership among the Wisconsin State Laboratory of Hygiene, Children's Hospital of Wisconsin and the Jeffrey Modell Foundation led to the first pilot study screening all births in a State. Federal funding from CDC was then made available to continue the pilot study in Wisconsin and to initiate a second statewide pilot in Massachusetts. These two CDC-funded pilots are scheduled to conclude in October 2011. A third pilot study at the University of California at San Francisco began in 2009 and is screening up to 2000 births at two Arizona hospitals on the Navajo reservation (the Navajo Nation has a high incidence of SCID).

The pilot studies in Wisconsin and Massachusetts led to screening and follow-up algorithms, created educational materials for families and health care providers, hosted multiple State training programs in use of the assay, and partnered with CDC in the development of proficiency materials that are now available to all State newborn screening programs.[9-10] Investigators from these three pilots presented their findings to SACHDNC in January 2010 and, at the time, reported they had successfully screened more than 200,000 newborns. Although no cases of classic SCID (total failure of the immune system) were found, they did identify infants with immunodeficiency disorders (SCID variant, partial failure of the immune system) that required medical intervention, documented the feasibility of screening for SCID, provided valuable information to SACHDNC, and paved the way for larger efforts.[11-12]

Expansion of SCID Newborn Screening Pilot Studies

To increase the likelihood of detecting classic SCID cases, NIH increased the screening sample size through a larger pilot project initiated in 2010 with Health Research, Inc. (HRI), a not-for-profit corporation affiliated with the New York State Department of Health. The NIH-funded project enabled HRI and collaborators to provide evidence for the feasibility of screening technologies and to expand SCID newborn screening pilot studies to four additional States and Territories: New York, California, Louisiana, and Puerto Rico. The NIH-funded research priorities for this project were to:

- Assess screening technologies for SCID,
- Establish immediate confirmatory tests and procedures for presumed positive results,
- Ensure capacity and resources for tracking positive cases and arrange for appropriate follow-up care and referral in a timely manner, and
- Verify administrative structures necessary for a prospective pilot testing of SCID, including ability to obtain approval for human subject research.

The NIH initiative enabled screening to begin in two States with a large number of births, New York (236,656) and California (510,000). In addition, ongoing screening efforts in Wisconsin expanded to include Louisiana and ongoing efforts in Massachusetts expanded to include Puerto Rico. The efforts in New York and California were also supported with funds from the Jeffrey Modell Foundation (New York and California) and from PerkinElmer, Inc. (California). Piloting SCID screening in States with a large number of births provided evidence that TREC screening is compatible with a high-throughput, automated environment. Sending samples for screening from Louisiana to Wisconsin and from Puerto Rico to Massachusetts established feasibility for a regional approach to SCID screening, while the ongoing screening in Wisconsin and Massachusetts provided information about screening over several years.

Development, Validation, and Quality Assessment of SCID Newborn Screening Technologies

Investigators in New York, California, Wisconsin, and Massachusetts each developed high-capacity assays based on the principles of the NIH-developed research assay.[6] These assays, called laboratory developed tests (LDTs), were developed and validated independently by each laboratory. While the Food and Drug Administration (FDA) currently does not regulate this class of *in vitro* diagnostics, each laboratory is regulated by the Centers for Medicare & Medicaid Services through the Clinical Laboratory Improvement Amendments (CLIA) Act.[13-14] To support the quality assurance measures required by CLIA, CDC provided dried blood spot reference materials for within-laboratory quality control and between-laboratory proficiency testing. As of April 2011, results obtained from 11 newborn screening laboratories, including all pilot labs (California, New York, Massachusetts, and Wisconsin), showed excellent analytic validity (how well the test predicts the presence or absence of TREC). The tests showed 100 percent sensitivity (how often the test results are positive when TRECs are present) and more than 99 percent specificity (how often the test results are negative when TRECs are not present) in discriminating abnormal from normal TREC content in the reference materials.

To collect, aggregate, and analyze de-identified screening data generated during the pilot, NIH provided a subcontract to the HRSA/Maternal and Child Health Bureau (MCHB)-funded

Laboratory Performance Program to develop a SCID data portal as an expansion of a HRSA/MCHB-funded Region 4 Regional Genetic and Newborn Screening Service Collaborative effort.[15] The subcontract was administered through the NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development's NBSTRN, which was established to provide infrastructure resources for research in newborn screening. Access to the SCID data portal is widely available to any State newborn screening program, clinician, or researcher around the world interested in learning about or contributing to the understanding of the performance of SCID newborn screening assays. The aggregation of laboratory performance data in real-time during a pilot represents a useful model of translating a novel genomic technology to a high-throughput public health setting while using the latest in language standardization and electronic information exchange.[16-17]

Interim Pilot Study Results

Through March 2011, SCID newborn screening has been piloted in six States and one Territory (Wisconsin, Massachusetts, New York, California, Louisiana, and Puerto Rico) and the Navajo Nation, covering approximately 25 percent of total births in the United States during this time period and totaling 126 months of continuous screening (Table 1 and Figure 1). In all, 961,925 newborns have been screened, 364 newborns had a positive screen requiring additional testing and resulting in 60 cases of diagnosed immune deficiency (Tables 1 and 2). Fourteen cases of classic SCID, six cases of SCID variant, and 40 cases of Non SCID have been identified, diagnosed, and treated (Table 1, Figure 2). All infants with immunodeficiency disorders identified through the pilot studies have received treatment and are being followed by appropriate health care teams. Almost 80% (11/14) of the SCID patients received bone marrow transplants and are currently between 1 month and 10 months post-transplant (Figure 3). The remaining 20% (3/14) are receiving enzyme replacement, a treatment option for one type of SCID, Adenosine Deaminase Deficiency (ADA). Additional information regarding health outcomes is being collected and will be reported at a later date.

Although the pilots are still in progress, there are emerging findings that are important to note.

- A zero TREC value consistently means that the infant is at significant risk for SCID or a profound T cell lymphopenia. Future investigations of this valuable biomarker will accelerate research in immunology.
- The incidence of SCID and T cell deficiencies appears to be higher than previously reported (Table 3). Past studies reported the incidence of SCID as 1 in 100,000, and the newborn screening pilots are finding a range of incidences from a high of 1 in 34,159 (New York) to a low of 1 in 161,707 (Massachusetts). Past estimates of Non SCID have been difficult since this category comprises a number of distinct disorders that average around 1 in 20,000 (Table 3, Figure 4). The pilots are finding a range of incidences from a high of 1 in 9,705 (Puerto Rico) to a low of 1 in 121,854 (Wisconsin).
- The number of boys versus girls diagnosed with SCID in the pilots is consistent with past studies (Table 5). Past studies found the majority of SCID cases were male (79%)[3] and New York and California found that six of the nine SCID cases (67%) are male.
- The number and type of SCID at a molecular level appears to be different than previously reported (Table 5). Past reporting of the molecular type of SCID found that 48% of cases

are X-linked (IL2RG mutation), making this the most common cause of SCID.[3] The pilots in New York and California completed the molecular studies for eight of the nine SCID cases and found 66% (7/8) are consistent with autosomal recessive inheritance (Table 5). X-linked SCID was found in one case or 11% of the total.

- The subpopulation variability of SCID and T cell deficiency patients appears to be different than previously reported (Tables 4 and 5). Past reporting of the race or ethnicity of SCID patients followed long-term found that the majority (81%) are Caucasian, 9% African American and 6% Hispanic.[3] The pilots in New York and California found that six of the nine (65%) SCID cases are Hispanic, 2 (22%) are African American, and 1 (11%) is Asian (Table 5).

The emerging findings raise important questions. Analysis of future data will help answer these questions. Although the New York, California, Louisiana, and Puerto Rico NIH-funded pilots end in June 2011, and the CDC-funded pilots in Massachusetts and Wisconsin end in October 2011, efforts to analyze the pilot findings will continue.

Efforts in Nonpilot States

State adoption of SACHDNC's recommendation is voluntary, and the rules and regulations governing the addition of a new screening test vary by State. Nonetheless, consideration of SCID newborn screening by States not involved in the pilots has been extensive. All State newborn screening programs were invited to participate in monthly calls in which the principal investigators from the pilot States discussed their experiences, reviewed data portal entries and answered questions. Currently one-third of States participate in these monthly calls. In October 2010, CDC, the Association of Public Health Laboratories, and the HRSA-funded National Newborn Screening and Genetics Resource Center hosted a meeting devoted to SCID newborn screening.[18] The meeting was attended by 192 laboratory technicians, follow-up professionals and immunologists from 48 States and three countries. In addition, laboratory scientists from 28 U.S. newborn screening programs attended a supplementary laboratory workshop.

To ascertain interest in SCID testing among non-participating States, the Immune Deficiency Foundation (IDF) and NBSTRN conducted a nationwide survey and found that all State programs have actively considered implementing SCID newborn screening (Figure 5).[19] One state (Pennsylvania) is screening a portion of births, and two states are conducting small pilots (Texas and Arizona). Ten States (Colorado, Delaware, Florida, Iowa, Illinois, Michigan, Minnesota, North Carolina, New Jersey and Rhode Island) and the District of Columbia have presented SCID screening to their State advisory boards and received approval to begin screening as soon as logistically possible. Once these States are actively screening, more than 50 percent of babies born in U.S. States and Territories will be screened for SCID.

Twenty-eight State newborn screening programs are in various stages of assessment of analytical platforms, cost analysis, development of infrastructure for referral and treatment services, and recruitment of necessary personnel (Figure 5). Four States work with a regional partner who performs the screening test and are dependent on the regional partner to begin screening. There have been no instances of State advisory boards choosing not to implement SCID screening to date. Sixteen States participate in a monthly conference call to share experiences and expertise.

A small number of States report they prefer or require an FDA cleared or approved kit to begin screening. IDF and NBSTRN will continue to monitor State implementation until all newborns in the United States are screened at birth for SCID.

Education Materials Relevant to Screening and Treatment of SCID and Related T Cell Deficiencies

To support families and to encourage the adoption of SCID newborn screening, IDF launched several efforts, including a Web page for parents, a SCID newborn screening toolkit for use by families to educate policymakers, and a brochure to warn providers about the dangers of administering the live rotavirus vaccine to infants with SCID.[20] The six pilot State newborn screening programs also created and distributed educational materials for the parents of newborns with a positive screen and/or a confirmed diagnosis.[21-24] To support primary care providers and facilitate timely diagnosis and treatment, HRSA/MCHB funded the development of SCID clinical decision support materials, or ACT sheets,[25] through its National Coordinating Center for the Regional Genetic and Newborn Screening Service Collaboratives. As SCID newborn screening adoption increases, a directory of clinical specialists in pediatric immunodeficiencies and related T cell deficiencies will be developed for use by newborn screening programs, families, and health care professionals.

Lessons Learned and Next Steps

Seventeen months after SACHDNC recommended screening all newborns in the United States for SCID and related T cell deficiencies, one-fourth of births are being screened through pilot programs funded by multiple Federal and State agencies and private foundations. Most States have begun active consideration of SCID newborn screening, and several more States are planning to begin screening in the near future. In January 2011, IDF reported to SACHDNC several issues that may be delaying the implementation of SCID screening, including lack of cost benefit information, budgetary concerns (cost estimates for technology infrastructure estimated at $500,000–$1 million), prior commitment to implement other screening tests mandated by State legislation, lack of the widespread availability of experts in immunodeficiency within a State for diagnosis and treatment, and lack of an FDA-approved or -cleared assay.

NIH and CDC will continue to support the adoption of SCID newborn screening through ongoing efforts including technical assistance, publication of pilot project results, screening and follow-up protocols, creation of a long-term follow-up dataset to determine impact of screening on health outcomes, and creation of an expert work group to refine screening, diagnosis and treatment protocols and guidelines. CDC recently announced an opportunity to fund up to two newborn screening programs that had not yet implemented SCID screening before January 2011.[26] The NIH-funded Primary Immune Deficiency Treatment Consortium is working to identify factors, including early identification through newborn screening, that influence health outcomes in patients with immune deficiencies.[27]

In conclusion, the recommendation by SACHDNC to begin screening for SCID has almost certainly saved lives. In addition, the screening program has improved scientific understanding of immune deficiencies, including the molecular etiology and racial and ethnic distributions of molecular subtypes; expanded clinical knowledge of the care and treatment of SCID; and

emphasized the relevance of early diagnosis and intervention. The recommendation has also been a triggering event for the majority of State newborn screening programs to implement or start the process to implement newborn screening for SCID. Screening for SCID represents the largest expansion of newborn screening since the advent of tandem mass spectroscopy a decade ago and the RUSP five years ago. SCID screening is a DNA-based molecular test and State newborn screening programs will develop expertise in DNA-based technologies and/or create networks to share existing regional expertise to implement screening for SCID or DNA-based screening for other disorders. Both approaches to SCID screening establish valuable infrastructure, health information exchange and expertise within the State Newborn Screening Programs, and will be leveraged for future expansions of the RUSP.

The activities recommended by SACHDNC fostered collaboration among HHS agencies and enabled each agency to focus on their areas of expertise while sharing tools and infrastructure resources with stakeholders in public health and clinical health care teams. Highlights from this teamwork are

- Quality control and improvement materials to ensure accurate tests distributed by CDC to the pilot states;
- Clinical decision support tools supported by HRSA (ACT sheets) to guide infants' health care providers; and
- Expanded pilots and databases enabling the diagnosis, treatment, and long-term follow-up of SCID cases contracted by NIH.

This report on State implementation efforts affirms SACHDNC's system of evidence-based review of conditions nominated for addition to the RUSP and subsequent recommendations to begin newborn screening for nominated disorders and lays an effective foundation for future efforts to improve the health of newborns.[28-29]

Table 1. Summary of Pilots

State	Start of Screening	Number of Months Screening	Annual Births or Number Studied	Number of Infants Screened as of April 30, 2011	SCID[a]	SCID Variant[b]	Non SCID[c]
WI	1/1/2008	40	69,232	243,707	4	0	7
MA	2/1/2009	27	77,022	161,707	1	0	14
Navajo Nation	2/1/2009	27	2,000	1,297	0	0	0
NY	9/30/2010	7	236,656	136,635	4	0	12
CA	8/1/2010	9	510,000	358,000	5	6	3
PR	8/1/2010	9	45,620	29,115	0*	0	3
LA	10/1/2010	7	65,268	31,464	0	0	1
	Total	126	1,005,798	961,925	14	6	40

*One infant with suspected SCID expired before diagnosis confirmed.

a. SCID: Deleterious mutation in the DNA of one of the following genes, resulting in total failure of normal function of the protein encoded by that gene, whether IL2RG, JAK3, IL-7Ra, RAG-1, RAG-2, ADA, CD45, Artemis/DCLRE1C, CD3δ, CD3ε, CD3ζ, DNA PKc, or DNA Ligase IV. These proteins are crucial to the normal development of lymphocytes; therefore, any defect in one of these genes will result in a significant problem with immune function and associated susceptibility to infection. AKT2 defects, which cause severe lymphopenia and granulocytopenia, may have low TRECs but also poor amplification of peripheral blood DNA due to low numbers of nucleated blood cells. Patients with SCID have fewer than 300 autologous T cells per mL of blood, and their proliferative responses to the mitogen PHA are less than 10 percent of normal control responses. Some SCID patients do not have defects in any of the above genes, suggesting that additional disease genes for SCID remain to be discovered.

b. SCID variant: Variation in the DNA of one of the following genes resulting in impairment of functioning of the protein encoded by that gene. Also known as “leaky SCID”; Combined Immunodeficiency (CID); or Omenn syndrome, a particular clinical entity with skin rash, eosinophilia, and T cells that represent expansion of a restricted thymic output. CID and Omenn syndrome may be due to hypomorphic variations in the above SCID genes or may be caused by defects in genes such as PNP, AK2, Cernunnos, Coronin-1A, RMRP, or WHN/FOXN1. In addition, there are SCID variant patients s for whom defects in known genes are not found.

c. Non-SCID: Other defects either related directly to a component of the immune system with an associated malfunction or related to the loss of a section of DNA (e.g., DiGeorge syndrome, Jacobsen syndrome) or, in some cases, abnormal gain of DNA (e.g., Down syndrome/trisomy 21). Multisystem syndromes may be associated with variable severity of defects in immune function along with other serious health problems, including heart defects and developmental delay. The non-SCID category is a mixed group and includes individuals with a variety of genetic defects as well as infants who have poorly developed immune systems due to premature birth. Lymphopenia of prematurity, idiopathic T cell lymphopenia, DiGeorge syndrome/del(22)(q11.2), CHARGE syndrome, Jacobsen syndrome/del(11)(q24.1-11qter), Down syndrome/trisomy21, thymectomy, and RAC2 deficiency may be associated with low or undetectable TRECs in some cases. There are additional defects of cellular immunity, including CD25 and ataxia telangiectasia, in which TRECs may or may not be abnormal. There are insufficient data at this time to predict whether these conditions may be detected by TREC newborn screening. In addition, there are many non-SCID immunodeficient patients for whom a genetic cause is not found.

Note: In many T cell immunodeficiencies, the best treatment may be either hematopoietic stem cell transplantation or thymus transplantation because these infants are susceptible to life-threatening infections, as are the classic SCID and SCID variant babies. The confirmatory tests used to follow up babies with abnormal newborn screen results, along with additional specialized immune testing, can help the pediatric immunologist to make decisions regarding the severity of immune dysfunction and the need for transplantation for these infants. These infants would not be picked up without newborn screening, and they are often in just as much need of significant treatment as the more well recognized SCID babies. In addition, some babies require supportive care with intravenous immunoglobulin (IV IgG) and antibiotics, even when a transplant is not needed.

Table 2. Number of Negative and Positive Screens by State

Screening Result	State							Total Screened
	WI	MA	Navajo Nation	New York	California	Puerto Rico	Louisiana	
Negative[a]	243,657	161,679	1,296	136,412	357,954	29,107	31,456	961,561
Positive[b]	50	28	1	223	46	8	8	364
Total Screened	243,707	161,707	1,297	136,635	358,000	29,115	31,464	961,925

a Negative: TREC copy number above cut-off point. No further analysis needed.
b Positive: TREC copy number below cut-off point. Case referred for confirmatory diagnostic studies.

Table 3. Incidence of SCID, SCID Variant and Non SCID by State

Diagnosis	Incidence	State					
		WI	MA	NY	CA	Puerto Rico	Louisiana
SCID		1 in 60,927	1 in 161,707	1 in 34,159	1 in 76,500	NA	NA
SCID Variant		NA	NA	NA	1 in 76,500	NA	NA
Non SCID		1 in 121,854	1 in 11,551	1 in 11,386	1 in 76,500	1 in 9,705	1 in 31,464

Table 4. California Incidence in the First Six Months of Screening

Diagnostic Category	Race or Ethnicity	Incidence Rate	95% Confidence Intervals	
			Lower	Upper
SCID	All	1 in 33,000	1 in 20,000	1 in 65,000
SCID	Hispanic Only	1 in 22,000	1 in 9,000	1 in 40,000
All Related T-cell Lymphocyte Deficiencies	All	1 in 22,000	1 in 13, 300	1 in 35,000

Table 5. Clinical Characteristics of Nine SCID Cases in New York and California Pilots

Characteristic		Number of SCID Cases (%)
Sex	Male	6 (67%)
	Female	3 (33%)
Molecular Type of SCID*	Autosomal Recessive (IL-7Ra)	2 (22%)
	Autosomal Recessive (RAG-1)	2 (22%)
	Autosomal Recessive (ADA)	2 (22%)
	X-Linked (IL2RG)	1 (11%)
Race or ethnicity	Hispanic	6 (67%)
	African American	2 (22%)
	Asian	1 (11%)

*Molecular typing on one case is pending.

Figure 1.Timeline of SCID Newborn Screening Pilots

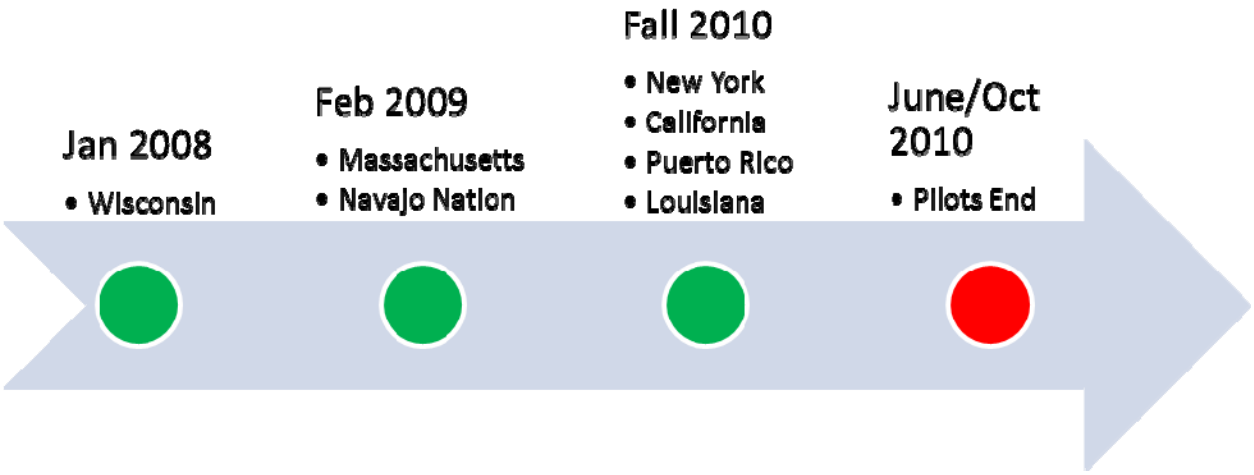


Figure 2: Cumulative Number of Newborns Screened and SCID Cases Diagnosed

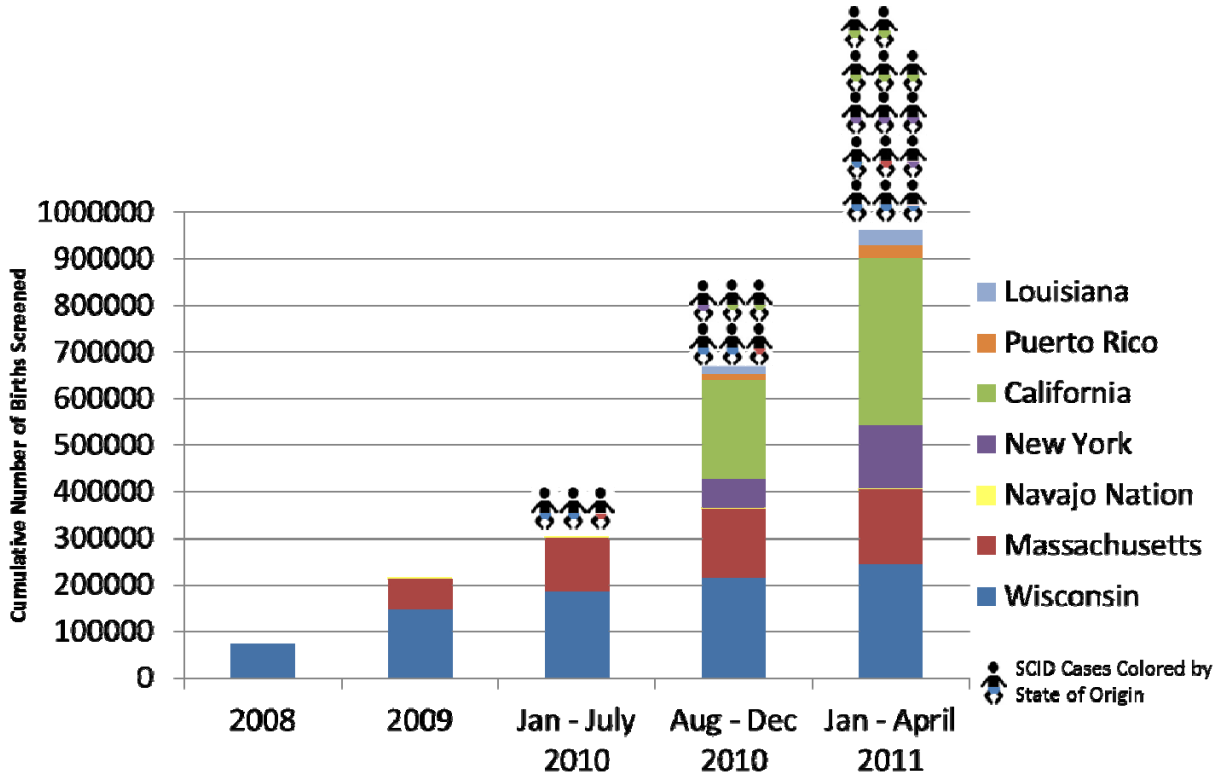


Figure 3: Type of Treatment for SCID Cases (N=14) in All Pilots

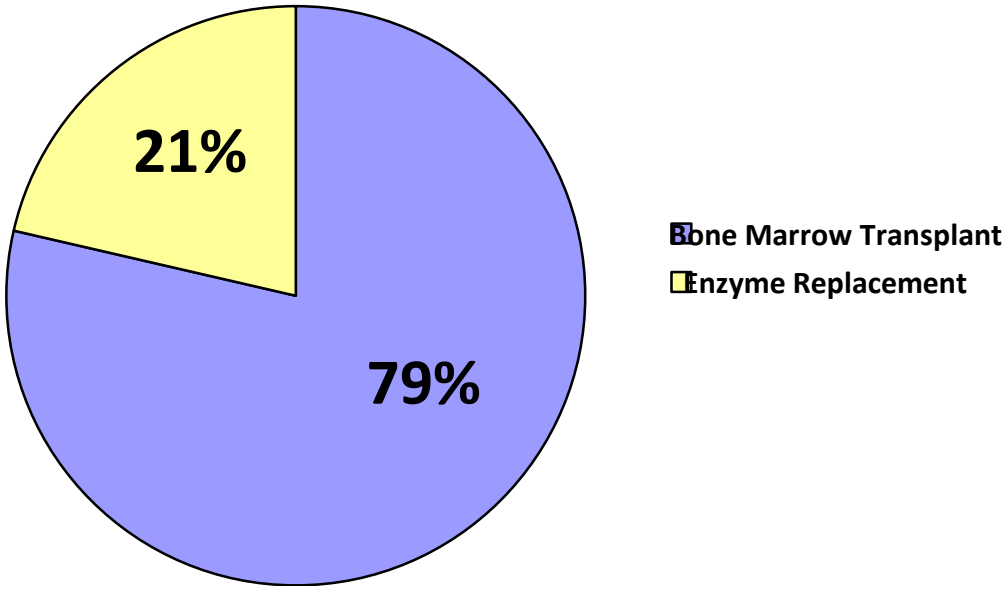


Figure 4: Diagnosis for Non SCID Cases for All Pilots (N=40)

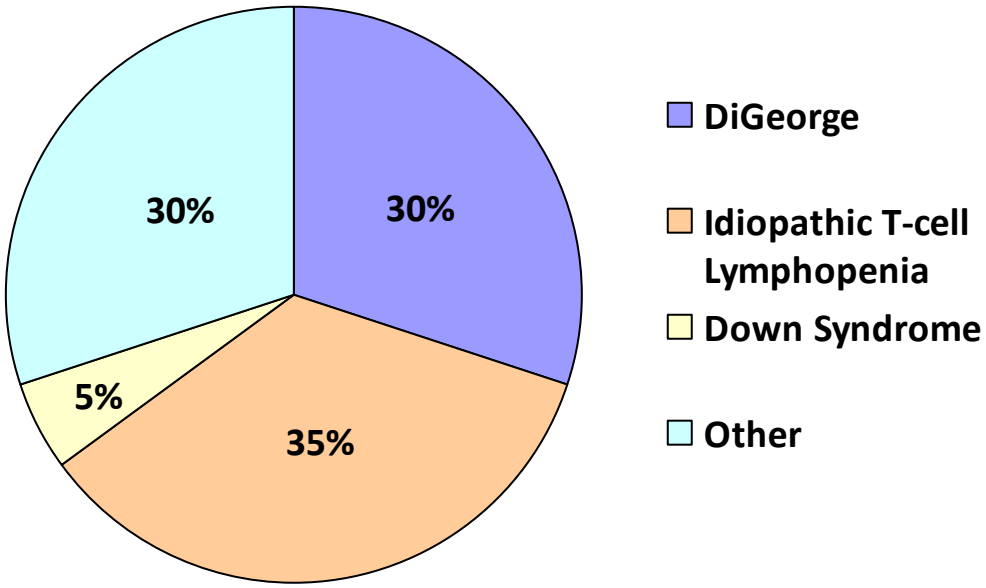
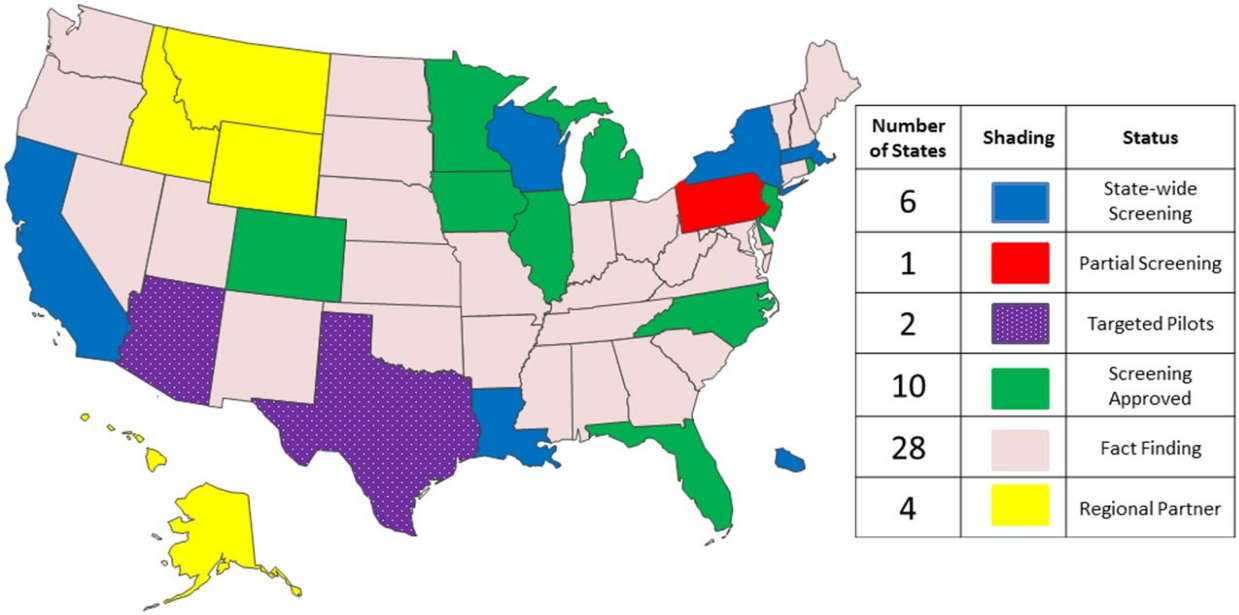


Figure 5. Map of Newborn Screening for SCID Implementation Status



Number of States	Shading	Status
6		State-wide Screening
1		Partial Screening
2		Targeted Pilots
10		Screening Approved
28		Fact Finding
4		Regional Partner

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