

# Implementation of Newborn Screening for Severe Combined Immune Deficiency

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**NBSTRN-CC**  
**February 1, 2013**



American College of Medical Genetics **ACT SHEET**

Using ACT Sheet  
for Combined Immunodeficiency (SCID) and Conditions  
with T Cell Lymphopenia

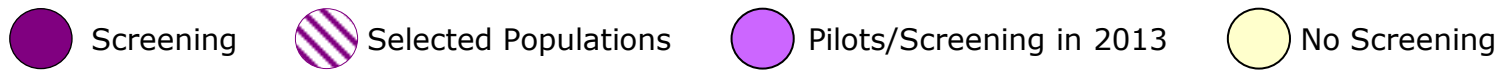
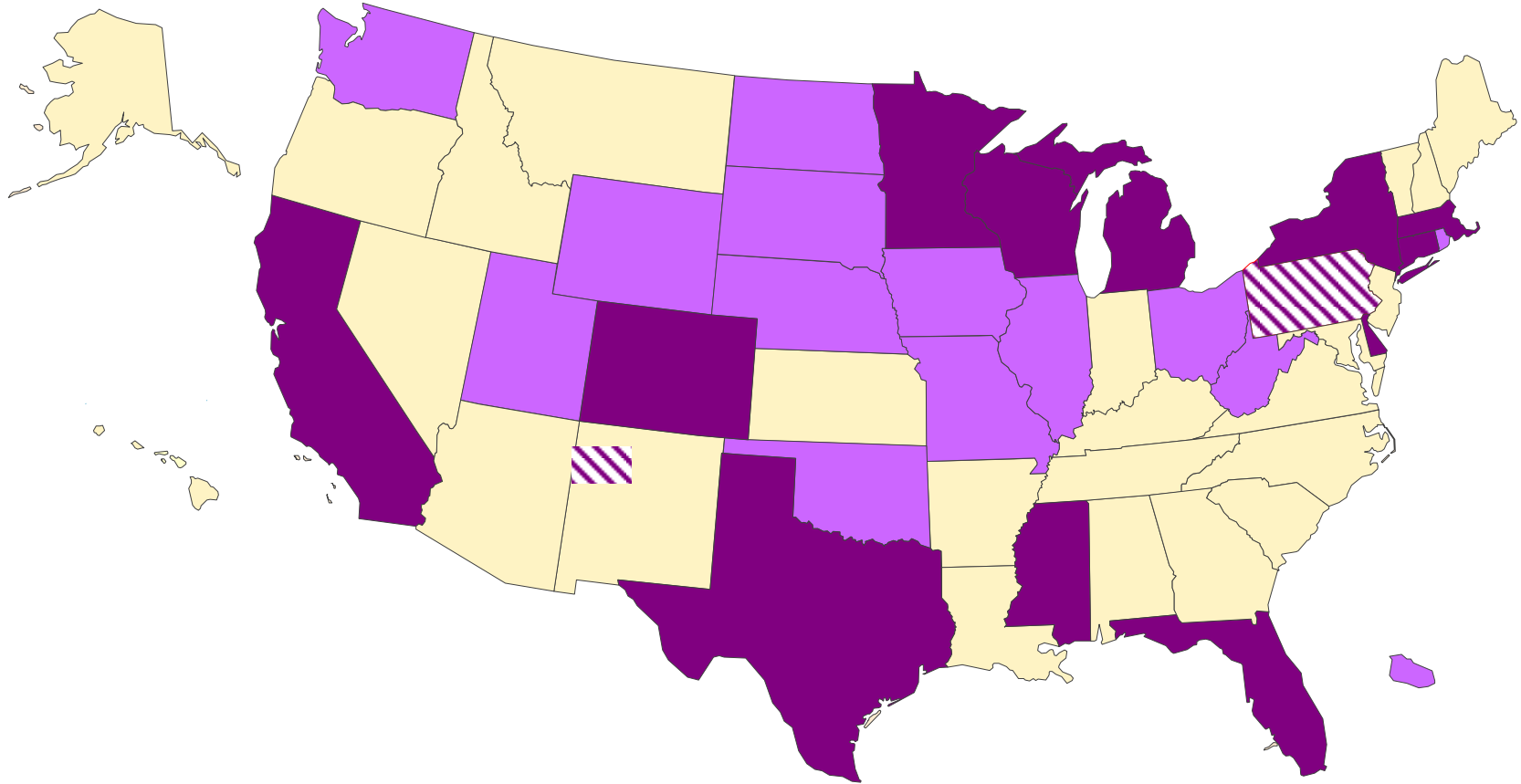
Combined Immunodeficiency (SCID) includes a group of rare but serious, and potentially fatal, conditions in which T lymphocytes fail to develop and B lymphocytes are either absent or compromised. This leads to the term "combined." Untreated patients develop life-threatening infections due to the lack of a screening test for T cell receptor excision circles (TRECc), a byproduct of normal T cell development as well as certain related conditions with low T cells. For example DiGeorge Syndrome with low T cells and low TRECc.

**FOLLOWING ACTIONS:**

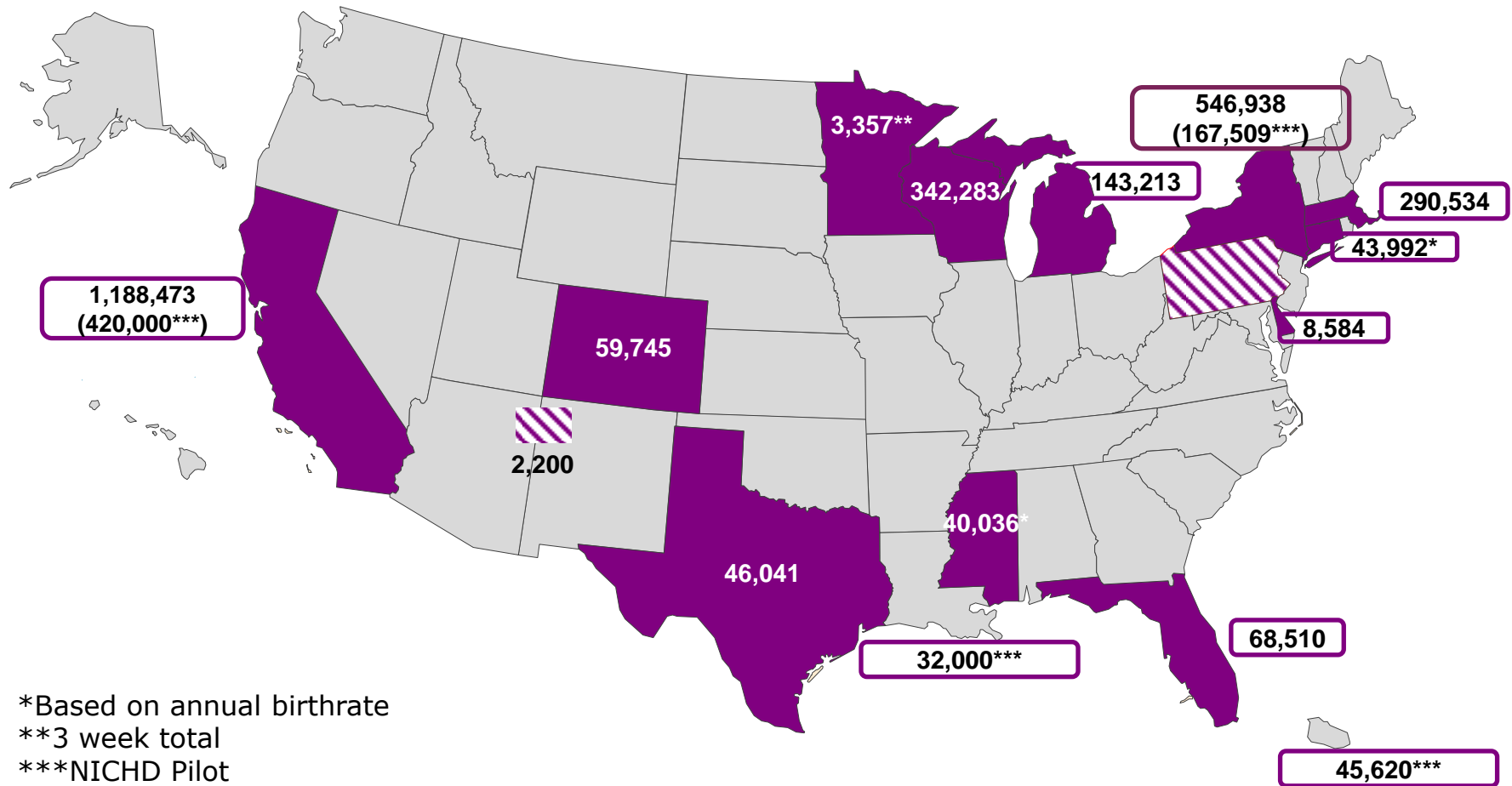
Inform them of the newborn screening result. Point out that additional tests are required to...

Year	Event
2001	CDC Conference
2005	Assay Discovery
2006	QA Material Development
2008	State Pilots
2010	RUSP Addition
2011	<b>Implementation</b>
2013	Lab Guide

# Implementation Status



# Estimated Newborns Screened Through December 31<sup>st</sup> 2012



Total  
Number of  
Newborns  
Screened  
by  
12/31/12

2.85 M

Percentage  
of Births  
Screened

45%

States  
Planning  
Pilots or  
Screening  
in 2013

12

Estimated  
Percentage  
of Births  
Screened  
by 2014

62%

Clinically  
Diagnosed  
Cases  
Since RUSP  
Addition in  
Non-  
screening  
States

15

## ◆ CDC

- **Conduct Individualized Laboratory Training**
- **Support Laboratory Test Development**
- **Supply Quality Control Reference Materials**
- **Provide Proficiency Testing through NSQAP**

## ◆ NICHD

- **National Pilot Protocols and Algorithms**
- **R4S SCID Data Portal through NBSTRN**
- **Monthly Stakeholder Calls through NBSTRN**
- **Information Resource through NBSTRN**

- ◆ **Clinical Laboratory and Standards Institute (CLSI) Guideline ILA-36**
  - "Newborn Blood Spot Screening for SCID by Measurement of T-cell Receptor Excision Circles"
  - Approved Dec 2012; Publication scheduled for May 2013
  - Addresses laboratory operations, instrumentation, TREC assay protocols, automated methodologies, diagnostic tests, short-term and long-term follow-up.
- ◆ **CDC Cooperative Agreements**
  - Oct 2011-Sep 2013
  - Michigan: More than 150,000 screened; 4 SCID found
  - Minnesota: Completed method development; began screening Jan 2013

- **NBSTRN funded the SCID module for R4S**
- **Facilitates analytical validation of screening assay**
- **Collects clinical information**
- **Tutorials can be arranged at any time**
- **Co-curators**
  - **Roshini Abraham, PhD**
  - **Fred Lorey, PhD**

## Condition Types

SCID

Leaky SCID/Omenn Syndrome

Variant SCID

Syndromes with T cell impairment

Secondary T cell lymphopenia other than preterm alone

Preterm alone

## Conditions by Flow Phenotyping

T-B+NK-

T-B-NK-

T-B-NK+

T-B+NK+

Other



## ◆ **HRSA, ACMG**

- **Clinical Decision Support Materials**
- **ACT Sheets**
- **Available online**

## ◆ **Immune Deficiency Foundation**

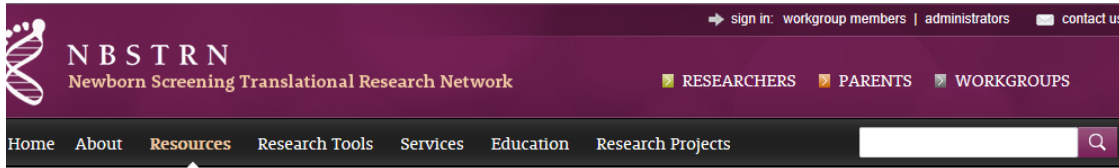
- **SCID Newborn Screening Toolkit for Advocates**
- **Rotavirus Vaccine Pamphlet**
- **Parent Education Materials**

## ◆ **CDC, APHL, and Jeffrey Modell Foundation**

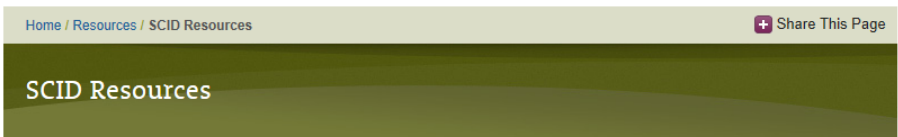
- **Two-year fellowship for post-doctoral candidates**
- **Newborn screening research including immune deficiencies**

- ◆ **IDF offers educational resources to families and state**
  - **IDF SCID Newborn Screening Campaign website and blog**
  - **Educational guides to be of use to the states in their follow up protocols for SCID screening**
  - **Two educational guides for parents have been developed by IDF and experts in SCID with the help of the New York-Mid-Atlantic Consortium for Genetic and Newborn Screening Services (NYMAC).**
  - **Targeted advocacy actions**
  - **IDF will be holding the IDF 2013 National Conference in Baltimore, MD June 27-29, 2013**

# Resources for NBS Researchers



- Resources
- State Profiles
- Newborn Screening Publications
- Disease Registries
- Gaps in Research
- Links
- SCID Resources >



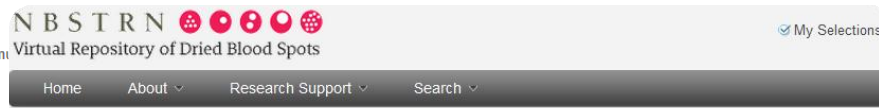
## Statement of Work for National SCID Pilot Study

A collection of educational resources for Severe Combined Immunity Deficiency (SCID) Associated with T Cell Lymphopenia.

- Immune Deficiency Foundation Parent Brochure on SCID Cus screen.
- SCID Parents Guide for Positive Diagnosis

## California State Newborn Screening Program Brochure

- Why Does My Baby Need More Testing for Severe Combined
- Why Does My Baby Need More Testing for Severe Combined

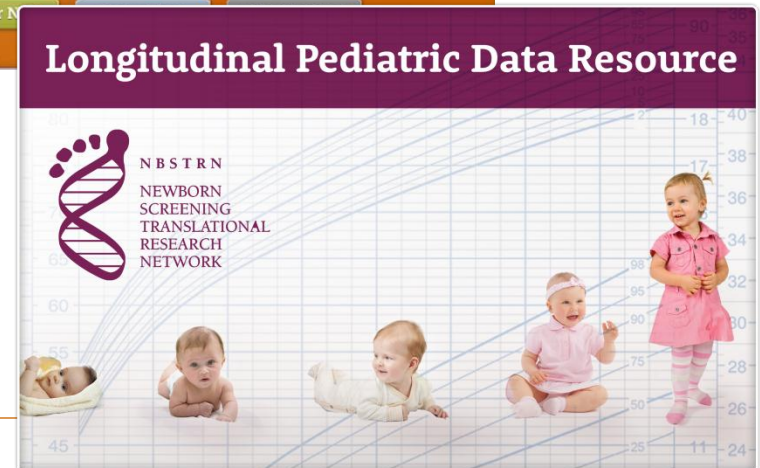



**REQUEST DRIED BLOOD SPOTS FOR RESEARCH**

Search and request de-identified residual dried blood spots (DBS) to use in newborn screening related research projects.

[Register Now](#)

<https://www.nbstrn.org/resources/scid-resources>



**Longitudinal Pediatric Data Resource**

NBSTRN  
NEWBORN  
SCREENING  
TRANSLATIONAL  
RESEARCH  
NETWORK

# Expansion of SCID Newborn Screening Pilots

- ◆ **NIH initiated project to enable additional states to pilot screening – Dr. Michele Caggana, PI**
- ◆ **Key Features**
  - **Initiates pilots in high number birth states (New York, California)**
  - **High capacity assay development (New York, California)**
  - **Regionalization model**
    - **Puerto Rico → Massachusetts**
    - **Louisiana → Wisconsin**
  - **CDC quality assurance program**
  - **Utilize NBSTRN**
  - **SCID data portal**
  - **Monthly conference calls to share expertise**

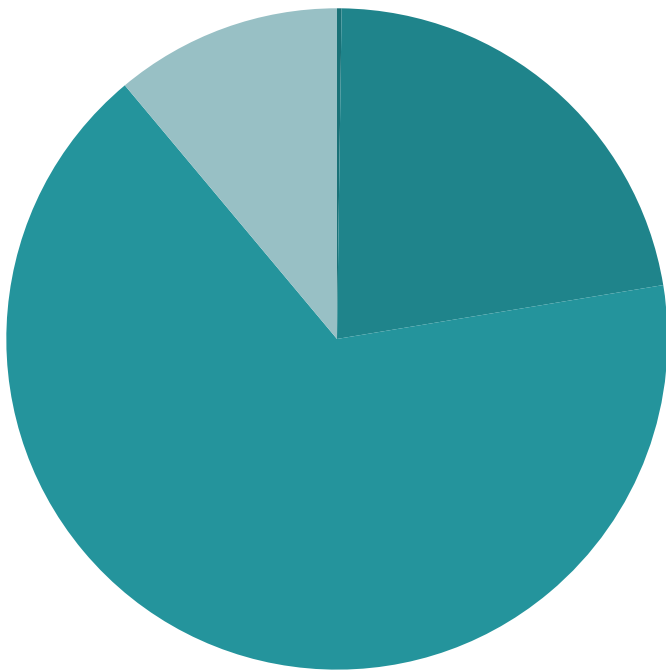


# Characteristics of SCID Cases

## Race or Ethnicity

### New York and California Pilots

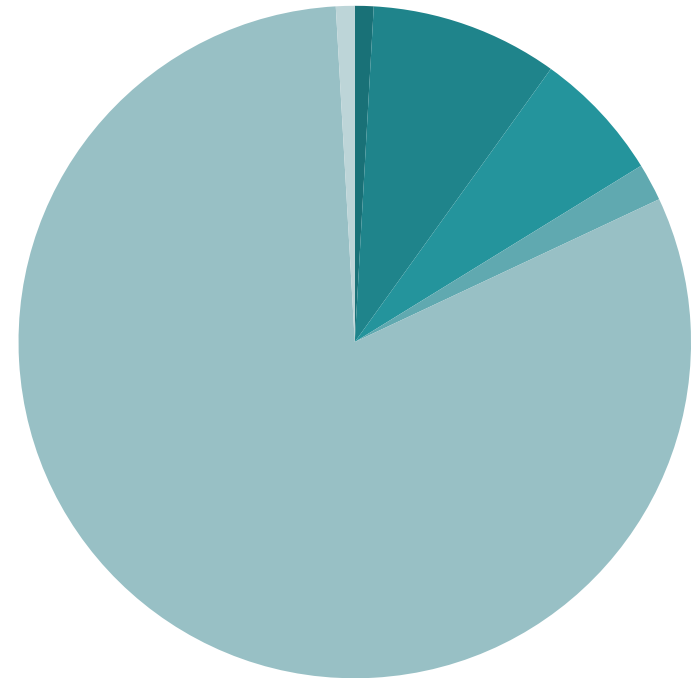
**N = 9**



### Duke Retrospective Study

**N = 111**

- Asian
- African American
- Hispanic
- American Indian
- Caucasian
- Arab



Log In

## Longitudinal Pediatric Data Resource

NBSTRN  
NEWBORN  
SCREENING  
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### Primary Immune Deficiency Treatment Consortium

**You Can Help.**

Rare disease research cannot move forward without the meaningful participation of our patients.

The Primary Immune Deficiency (PID) Treatment Consortium (PIDTC) consists of 13 major centers in North America whose shared goal is to improve the outcome of patients with rare, life threatening, inherited disorders of the immune system. The PIDTC Can Help You:

- Learn more about inherited disorders of the immune system including newborn screening
- Quickly connect with experts in a PIDTC center in your area who diagnose and treat inherited immune disorders
- Learn about treatment options and new research studies for patients with these diseases
- Help answer questions your physician may have about immune disorders
- Connect with patient support groups

**Information for Professionals**  
Physicians, Clinicians, & Researchers

**Coming Soon:**  
Diseases In Depth  
Finding Answers: How can I join the PIDTC

**Information for Patients and Families**  
Take Action: [Learn More](#)

## SCID

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ID

Source of information

State

Birth weight

Neonatal complications

Type of neonatal complications

- Unknown  Yes  No
- Infection/sepsis
  - Antibiotics
  - Hypoglycemia
  - IV fluids
  - Jaundice
  - Premature (< 37 weeks gestation)
  - Transfused
  - Respiratory distress
  - APGAR < 5
  - Seizures
  - Other

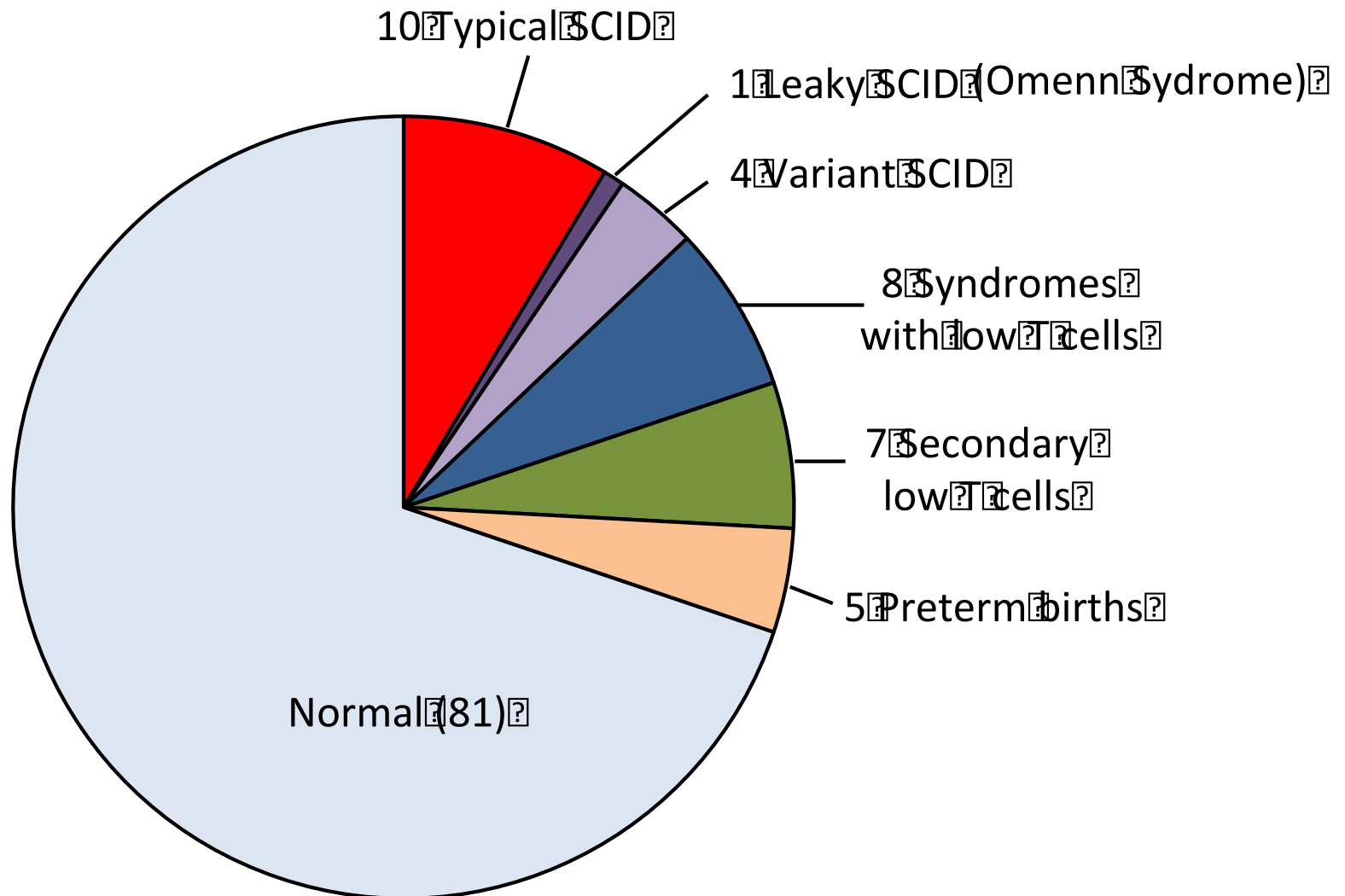
Type of neonatal complications-other, spec

Sex

Race

- Male  Female
- Not reported
  - American Indian/Alaskan Native
  - Asian

# California Cases to Flow Cytometry in First 18 Months



- ◆ **99.91% specificity; missed cases partial ADA, MHC-II.**
- **Of infants called for confirmatory flow cytometry, 30% had clinically significant T cell lymphopenia.**
- **Centralized flow cytometry as a 2<sup>nd</sup> tier test within the screening program permits timely and consistent diagnosis.**
- **All 11 infants with SCID received definitive treatments, with >90% survival at 6-21 months, superior to outcomes reported for SCID without newborn screening.**
- **Newborn screening offers the opportunity to study and treat pre-symptomatic immunodeficient infants with a wide spectrum of T lymphopenic disorders.**



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◆ **Thank you!**