



# NEWBORN SCREENING *News*

Spring 2013

THE CALIFORNIA NEWBORN SCREENING PROGRAM

## New Addition to Newborn Screening: Severe Combined Immunodeficiency (SCID)

SCID is a primary immune deficiency, often referred to as the “bubble boy disease”. California began screening newborns for SCID in August, 2010 as a pilot project. Once our regional screening laboratories complete standard newborn screening for other diseases, the dried blood spots are sent overnight to the state’s Genetic Disease Laboratory Branch in Richmond for SCID testing. All positive and incomplete results have been followed up since August

2010, but negative results were not reported. We have been working since 2010 to incorporate SCID screening into our Screening Information System (SIS). Beginning March 1st, 2013, SCID will be fully integrated into California’s Newborn Screening Program. SCID results will be included in the standard Newborn Screening result mailers which will be reformatted to allow for their inclusion. Due to the additional time needed to obtain the SCID

screening result, **result mailers will take an extra ten to fourteen days** (see OST article in this newsletter). As with all disorders, as soon as a positive test result is available, the Area Service Center staff will contact the physician of record with recommended follow up.

Disorder Category	Number
SCID/Leaky SCID/Omenn syndrome	20
Variant SCID	10
Syndromes with T-Cell Lymphopenia	12
Secondary T-Cell Lymphopenia	15
T-Cell Lymphopenia due to Preterm Only	18

Screened for SCID through December, 2012- 1,188,473

## Ideal Time to Screen Babies: 24 - 48 Hours of Age\*

One of the greatest challenges of a newborn screening program is timing specimen collection so that it occurs early enough to assure that affected babies are diagnosed and put on treatment before symptoms or permanent damage occur, but not so early that some disorders can be missed. With the number of disorders screened for now up to 80, it is impossible to screen at the optimal time for each of them. However, the California Newborn Screening (NBS) Program’s vast

experience in screening over 16 million newborns has led us to believe that while babies should be screened sometime between 12 to 96 hours of age, the ideal time to screen is 24 - 48 hours after birth. Here’s why:

- Screening before a newborn is 12 hours of age can cause an amino acid disorder to be missed, i.e., the analyte measured may not yet have had a chance to become elevated. For that reason babies must be at least 12 hours of age when screened. Exception: a baby must be screened prior to a red blood cell transfusion, regardless of age.
- Screening before a baby is at least 24 hours of age increases the odds of the specimen falsely testing positive for primary congenital hypothyroidism due to a normal thyroid stimulating hormone (TSH) surge that occurs after birth. *Positive screens, which necessitate confirmatory testing and evaluation of the baby, are frightening and*

*stressful for families. While the Program’s goal is to identify almost all babies having the screened-for disorders, it also strives to minimize false positives.*

- The time from specimen collection to the time results are reported out can be anywhere from 3-4 days to a few weeks (depending on which test is positive). Some of the disorders, such as galactosemia and congenital adrenal hyperplasia, can be lethal in the first week(s) of life if not treated. Therefore, specimen collection should occur by 96 hours of age, or the 4th day of life.

\*California’s regulations state that babies should be screened as close to discharge as is practical, and those babies remaining in the hospital after 6 days of age are to be screened on the 6th day. However those regulations were written when the program screened for only 4 conditions and are currently in the process of being changed to reflect the times cited in this article.

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## Cystic Fibrosis (CF)

Cystic Fibrosis (CF) is an autosomal recessive inherited disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. It is a multi-systemic condition that can affect the respiratory, gastrointestinal and reproductive tracts. Early diagnosis and intervention have been shown to decrease morbidity and mortality in CF patients. For this reason, CF was added to the panel of disorders detected by the California Newborn Screening Program on July 16, 2007.

In order to meet the needs of California's diverse population and minimize the burden of false positive tests, a comprehensive four-step screening model was created. The steps include: (1) Measurement of immunoreactive trypsinogen (IRT) on all Newborn Screening samples (2) Testing of all IRT positive samples for the California 40 CFTR Mutation Panel (3) Testing of all samples that have one panel mutation by more precise CFTR DNA Sequencing for a second possible mutation and 4) Referral and follow-up of all screen positive children

at a CCS-approved Cystic Fibrosis Center.

In the first four years of CF screening (July 16 2007-June 30, 2011) 2,082,378 newborns were tested. 830 infants were determined to be screen positive for CF by either step 2 or step 3 of the testing procedure. Of those, 302 have been diagnosed with CF (169 by step 2 and 133 by 3). This means that approximately 1 of every 3 babies identified as screen positive was diagnosed with CF.

During this time, the program was notified of 24 CF cases which were not picked up by screening. This means that 302 of 326 diagnosed cases of Cystic Fibrosis were found by Newborn Screening for a detection rate of 93%. As it is not possible to detect 100% of CF cases without greatly increasing the number of false positives, providers should remain alert for signs and symptoms of CF regardless of screening results.

These numbers indicate an incidence of 1 in 6395 for classical CF in the California population as a whole. The incidence of CF in the Caucasian population of California

was 1 in 3511 and the incidence in the Hispanic population was 1 in 7641.

Among the 830 screen positive infants, another 399 have been identified as having CFTR Related Metabolic Syndrome (CRMS). In the California program, CRMS describes infants identified by high IRT on NBS who have normal or mildly elevated sweat chloride values and 2 or more CFTR mutations, of which only 1 is clearly a CF-causing mutation. These individuals do not meet CF Foundation guidelines for the diagnosis of CF, but benefit from monitoring at a CF center to be vigilant for possible signs or symptoms associated with CF.

In addition to the screen positive CF cases, 1171 infants were found to have one CFTR mutation after sequencing and determined to be carriers. They did not receive referrals to a CF center or sweat testing. These families and their physicians were notified of the carrier status and provided a toll free number for genetic counseling by phone and advice about further parent testing.

## Red Blood Cell Transfusions and Screening

Hemoglobin and galactosemia screening results will be invalid for 3 months if a newborn has been transfused with whole blood or packed red blood cells prior to specimen collection (based on the life span of red blood cells). For this reason, newborn screening providers are instructed to collect a newborn screening specimen before a transfusion is started, even if the baby is less than 12 hours old. Unlike some of the other disorders, galactosemia and hemoglobin screening are not time-sensitive, and results are valid on a baby screened at less than 12 hours of age. Another specimen collected at least 24 hours

post-transfusion should provide valid results for the other disorders.

In the event that a baby is not screened prior to transfusion, the NBS Program recommends that he/she be tested for hemoglobinopathies and offers the options of either having the baby immediately tested via DNA (which is performed on white blood cells), or testing the baby's blood three months after the last transfusion utilizing electrophoresis. These tests are performed at no additional charge.

Galactosemia testing (for babies who were transfused prior to specimen collection) is recommended if

the baby is symptomatic or if there is a family history of the disorder. As with hemoglobin testing, the baby's DNA is tested along with galactose-1-phosphate uridyl transferase (GALT).

If the provider of a baby who was screened after a transfusion wishes to have the baby tested for either galactosemia or hemoglobinopathies, he/she should contact the Newborn Screening Area Service Center servicing the area. Staff will arrange to have a whole-blood specimen collected and sent to the designated confirmatory laboratory.

## California's Newborn Screening Information Technology Updates

The Program's goal is to screen every baby born in California. Occasionally, for a variety of reasons, a baby is not tested. The earlier the untested baby is identified and tested, the lower the risk of harm (see Ideal Time to Screen in this newsletter). Currently, the NBS Program sends newborn screening test results via mail or email in PDF format to hospitals/midwives and physicians. If a result isn't received by 14 days post discharge, NBS regulations require the hospital to fill out an NBS-Missing Result (MR) form and send it to the State.

The newborn screening program has undergone expansion over the last decade with increased transit and lab processing time as a consequence. To help providers receive NBS status notification and timely results, several projects are in current production or in pilot development. Licensed Perinatal Health Care facilities can sign up to participate in two of the three options at this time.

### Online Specimen Tracking (OST) to Verify Specimen Receipt By The Program

To prevent delays in identifying untested babies, OST enables hospitals to look online to verify that a specimen was actually received at the newborn screening lab within seven days or less. If the hospital doesn't see the specimen listed, the hospital should enter the information on the baby whose specimen was not received. Once entered, the system will try to match it to an existing screening record. If no specimen is found, the case will be turned over to the Area Service Center (ASC) for follow up. The entire process will be much quicker under this new system. The hospital can view the status of the reported missing specimen online. In addition to reporting missing specimens, OST can be used to request another mailer to be sent to the hospital that collected the specimen. Online Specimen Tracking (OST) began the first week of November 2012 and most hospitals have been trained. The remaining perinatal facilities should be trained near the time SCID is fully integrated in March, 2013 (see article about SCID addition on page 1). In order to be in compliance with the state's reporting regulations, please sign up for training by contacting [Melinda.Chan@cdph.ca.gov](mailto:Melinda.Chan@cdph.ca.gov).

*At this time, OST is only available to hospitals but it may be expanded to clinicians in the future.*

### NBS Electronic Results Transmitted Via Secure E-Mail

NBS Results can now be transmitted daily (6 of 7 days) to a hospital's dedicated e-mail address. Perinatal Licensed Health Facilities that participate must be able to receive CDPH secure password protected encrypted e-mail. Facilities print or save the PDF NBS mailers to their hospital systems or patient charts. The project started in 2010 as a pilot and has continued to add new participants monthly. There are currently 50 hospitals participating and several more in the process. Contact Robin Thomas to enroll at [Robin.Thomas@cdph.ca.gov](mailto:Robin.Thomas@cdph.ca.gov)

*For more information about Newborn Screening or any of the topics covered in this newsletter, visit our website at: [www.cdph.ca.gov/nbs](http://www.cdph.ca.gov/nbs)*

### Health Information Exchange (HIE) Pilot

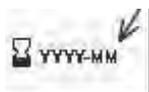
California's NBS Program has started development of a pilot program that will transmit Health Level Seven (HL7) electronic messages of NBS Results. HL7 International is the global authority on standards for interoperability of health information technology with members in over 55 countries. The HL7 files will be transferred by the NBS program to FTP sites which is a secure way to send and receive NBS data. This technology will enable hospitals and clinicians to download the result file from the secure FTP site. From there, hospitals and clinicians can process the file to load the results directly into the patients' electronic medical record. More facilities and offices are implementing electronic patient records as required by Federal HITEC Act.

The pilot partners are Deloitte Consulting as our project lead; Athena Health, Stanford Hospital and Family Health Centers of San Diego as our project participants. The pilot project testing and go live period will be completed in late Fall 2013. Future announcements will be made when state-wide enrollment starts.



## Expiration Date of Test Request Form

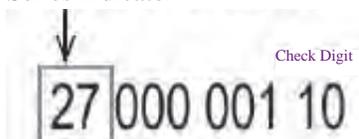
As of August 1, 2007, the Clinical and Laboratory Standards Institute (CLSI), formerly the National Committee for Clinical Laboratory Standards (NCCLS), has imposed an expiration date on filter paper. Currently, the shelf life for printed collection devices is 3 years. As a result, the Newborn Screening Program laboratories will not accept any specimen that is collected on forms after the expiration date. The expiration date is located in the lower right corner of the NBS copy of the Test Request Form. It is located next to the hourglass icon.



Check the expiration date listed next to the hourglass icon.

Every series of California Newborn Screening Specimen Collection Forms, also called the NBS Test Request Forms (or TRFs) has a different expiration date. Any specimen collected after the expiration date, will be deemed inadequate and another specimen will need to be collected for that baby. The form number is located at the top right of the TRF. The series number is the first 2 numbers of the 8 digit form number. The last 2 numbers are check digits, which are used to validate data entry of the form number.

Series Indicator



The forms that are currently in circulation and their expiration dates are:

Form Number (Series)	Expiration Date
27 XXX XXX (27 million series)	July 31, 2014
28 XXX XXX (28 million series)	February 28, 2015

Whenever you receive new shipments of NBS TRFs, please be sure to use all of your older forms before using the new TRFs. Forms are shipped a year or two before their expiration date. If your facility is unable to use the forms during this time, please call us to adjust the number of forms you receive. Please note that you will not receive credit if forms expire. If you have expired forms please dispose of them by placing in your recycle bin, shredder or trash. Please do not leave any expired forms around as they might be used in error, causing an unnecessary inadequate specimen, which may result in a delay in diagnosis.

For more information regarding the expiration date on the Test Request Form please go to our website: [www.cdph.ca.gov/nbs](http://www.cdph.ca.gov/nbs)

If you have any questions, or would like to make changes to future shipments, please email [NBSOrders@cdph.ca.gov](mailto:NBSOrders@cdph.ca.gov).

## Ordering Newborn Screening Supplies

To order Newborn Screening Specimen Collection Forms (TRFs), Special Forms or *Important Information for Parents* (IIP) booklets:

- Call: (510) 412-1542
- Email: [NBSOrders@cdph.ca.gov](mailto:NBSOrders@cdph.ca.gov)
- Order online at: [www.cdph.ca.gov/nbs](http://www.cdph.ca.gov/nbs)



### Newborn Screening Area Service Centers (NBS-ASCs)

Stanford University  
(650) 724-8120

Children's Hospital Central CA  
(559) 353-6416

UCLA Medical Center  
(310) 826-4458

Harbor/UCLA Medical Center  
(310) 222-3751

Rady Children's Hospital San Diego  
(858) 966-8708

Kaiser Permanente, Northern CA  
(510) 752-6192

Kaiser Permanente, Southern CA  
(626) 564-3322

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