

## 6.2 Severe Combined Immunodeficiency (SCID) Screening Pilot **DRAFT**

### General Information:

On August 9, 2010, the Genetic Disease Screening Program implemented a pilot program to screen for Severe Combined Immunodeficiency (SCID) and related disorders. SCID is a genetic disorder characterized by the absence of T cells and B cells, causing an inability to fight infections. Without early diagnosis and treatment, affected infants usually die from severe infections in the first year of life. Bone marrow transplantation done by 3.5 months of age restores a functional immune system as long as the diagnosis is made before devastating infections occur.

Screening methodology: Measurement of T-cell receptor excision circles (TRECs) in DNA extracted from dried blood spots using polymerase chain reaction (PCR).

Confirmatory testing: CBC differential and blood lymphocyte evaluation by flow cytometry performed on a whole blood specimen.

### POLICY:

- During this pilot, which will continue until SCID is officially added to the California newborn screening panel, all newborn screening specimens will be sent to GDL from the NAPS Labs for testing. PerkinElmer (PE) staff at GDL will perform testing on the filter paper specimens Monday through Friday. **Filter paper repeat specimens should therefore be collected and sent to GDL via Golden State Overnight courier service Monday-Thursday.**
- Confirmatory testing will be performed at Quest Diagnostics. While they operate 7 days a week, their patient service centers (PSCs) that collect the specimens are closed on Sundays, and most of them are closed on Saturdays as well. For that reason, **specimens should, if possible, be collected Monday-Friday.** Drs. Jennifer Puck (principal investigator of the pilot project) and Joseph Church, immunologists, will interpret results.
- All babies who have positive confirmatory results will be referred to Dr. Puck at UCSF or Dr. Church at Children's Hospital Los Angeles (CHLA) for diagnostic evaluation. Babies in counties to the north of Kern, San Luis Obispo, and San Bernardino counties will be referred to Dr. Puck. Babies in those three counties and counties south of them will be referred to Dr. Church. As with all NBS Program screened-for disorders, a referral will be made to CCS to facilitate authorization for diagnostic services.
- Dr. Church or Dr. Puck must be informed of all babies who are known to have or are suspected of having an immunodeficiency, regardless of the results of

the initial SCID screen. Dr. Church or Dr. Puck will determine appropriate follow-up e.g., whether to collect another filter paper specimen for a repeat SCID screen (if initial screen was a DAF) or to proceed directly to confirmatory testing.

- Follow-up of non-negative SCID screens will be similar to F/U for the other disorders, except that SCID has not been added to SIS yet, and therefore documentation will occur solely in SIS case notes and tracking events. All other pilot data will be maintained in a GDSP SCID Database, which is not accessible to ASCs.
- **Follow-up of DNA Amplification Failures (DAFs) and Positives reported late Friday or any afternoon before a holiday:**

GDL is closed on weekends and holidays and GSO doesn't pick up packages on Sunday, so babies requiring repeat filter paper specimens should be reported to MDs and followed up on the next business day.

#### **NICU babies**

1. DAFs (initial and 2<sup>nd</sup> DAF) can be reported on the next business day.
2. Positive SCID screens are to be reported to the NICU/Neonatologist within 24 hours.
3. Specimen collection/transport to Quest Diagnostics should generally occur Monday to Friday. However, if there is a sense of urgency due to the baby's condition, Quest may be able to have their courier pick up and deliver a specimen to them on weekends/holidays (**call [866] 894-6920**). If it is not possible, collection should occur on next business day. GSO may be utilized to pick up specimens from non-Quest contracted hospitals, Monday-Friday and deliver them to Quest Diagnostics Laboratory .

#### **Babies who have been discharged to home:**

1. DAFs (Initial and 2<sup>nd</sup> DAF) can be reported on the next business day
  2. Babies with 0-5 TRECs: immediately contact PCP (may be on-call MD) and ask PCP to determine condition of baby. If stable, with no signs of infection, PCP should instruct family to avoid exposing baby to crowds and live vaccines, and to take baby to hospital emergency department if baby becomes ill before confirmatory specimen could be obtained. Arrangements should be made to have a confirmatory specimen obtained on following business day. However, if a specimen can be collected at the hospital when the baby is there, Quest may be able to arrange for pick-up (**866-894-6920**). If the hospital does not have a contract with Quest, GSO should be utilized to pick up and deliver the specimen to Quest Diagnostics
  3. Babies with 6-25 TRECs: report on next business day.
- When a baby has expired, enter date and cause of death on the Client Profile screen

- If case is closed before resolution for other reasons (e.g. lost to follow-up, parent refusal, etc.), enter appropriate tracking event in SIS

See SCID Flow Chart (Att.# A) for test steps/actions/cut offs

**Attachments:**

- A** Flow Chart
- B** Mailer #1: Initial Positive
- C** Mailer #2
- D** Mailer #3
- E** Mailer #4
- F** Parent letter #1
- G** Parent letter #2
- H** PMD letter #1A
- I** PMD letter #1B
- J** PMD letter #2
- K** PMD letter #3A
- L** PMD letter #3B
- M** PMD letter #4
- N** PMD letter #5
- O** PMD letter #6A
- P** PMD letter #6B
- Q** *Why Does My Baby Need More Testing for Severe Combined Immunodeficiency*
- R** *Why Does My Baby Need Another Newborn Screening Test*
- S** Severe Combined Immunodeficiency (SCID) Fact Sheet
- T** SCID Letter to Providers
- U** PSC Checklist (specimen collection/handling Instructions for confirmatory testing)
- V** Non-Quest Lab Specimen collection/handling instructions for confirmatory testing
- W** Instructions for Repeat Testing (filter paper)
- X** Golden State Overnight (GSO) Mailing Instructions
- Y** Quest Test Request Form
- Z** PSC list (Northern CA and Southern CA)

**PROTOCOL:**

<b>Respons. Person/Staff</b>	<b>Action</b>
PerkinElmer (PE) staff at GDL	<ul style="list-style-type: none"> <li>• Receives all NBS specimens from NAPS labs.</li> <li>• Runs test (measures TRECs) on specimens</li> <li>• Within 24 °: e-mails to GDSP Program Development and Evaluation Branch (PDEB) file of non-negative screens (i.e., positive or DNA amplification failure) listing accession numbers, with results/interpretation. Notes number of tests in file on e-mail subject line. (“#SCID f/u: 7”)</li> </ul>
GDSP Program Development & Evaluation Branch Research Analyst (PDEB RA)	<ul style="list-style-type: none"> <li>• Receives list of above non-negative results and repeat negatives; enters information into GDSP SCID Database</li> <li>• Verifies that number of screens received matches number noted in e-mail subject line from PE</li> <li>• Reports results to appropriate ASC/designated NBS Coordinator via an e-mail message and fax containing results mailer. Enters confirmation of contact in GDSP SCID DB</li> <li>• Sends e-mail to all ASCs, noting ASCs that are receiving cases for follow-up that day.</li> <li>• If result mailer was sent to ASC before 2 pm, and ASC hasn’t sent acknowledgement by 4 pm, phones ASC to ask if results were received. If mailer was sent to ASC after 2pm, and ASC hasn’t acknowledged it by 10 am the next day, phones ASC.</li> <li>• Enters case note in baby’s SIS record with confirmation-of-contact information (i.e., who was notified and when).</li> <li>• Sends coordinator names, accession numbers of initial and repeat SCID specimens received by GDL.</li> </ul>

## 6.2 SCID SREENING PILOT

### Positive screens (initial positives or DNA amplification failure x2)

NBS Coordinator	<ul style="list-style-type: none"><li>• Immediately verifies receipt of case(s) in e-mail to PDEB-RA</li><li>• Contacts PMD/neonatalogist to inform him/her of positive SCID Screen or DNA Amp. Failure x2 and describes SCID Pilot Project<ul style="list-style-type: none"><li>a. Refers questions to Dr. Jennifer Puck (Northern CA) or Dr. Joseph Church (Southern CA)</li><li>b. Informs PMD that attached informational brochure (Att.#Q) is being sent to the baby's family if the baby is at home and not in an NICU</li><li>c. Informs PMD that further testing is required</li><li>d. Assists PMD in making arrangements to have venous blood specimen collected at a Quest Patient Service Center (PSC) (See Att#Z for list of PSCs) when possible and sent to Quest Diagnostics for confirmatory testing</li><li>e. Completes Quest TRF (Att. #Y): In upper left rectangle , enter patient information, placing NBS accession number in field PATIENT I.D. NO. At bottom of form check box for SCID Immunophenotyping Panel, Neonatal, Flow Cytometry</li><li>f. Faxes PSC checklist (Att.#U) and completed Quest TRF (Att. # Y) with Dr. Puck or Dr. Church noted as ordering MD, to designated PSC convenient for family.</li><li>g. Makes arrangements to have specimen collected by another laboratory/collection facility (e.g., lab of hospital of birth) when there is no PSC nearby or when baby is an in-patient at a hospital Provides collector with collection/handling/transport instructions (Att#V) and GSO label, unless facility is contracted with Quest and this specimen can be sent along with other specimens going to Quest</li><li>h. Instructs PMD to withhold rotavirus vaccine (usually administered at 2 mo. of age) and other <i>live</i> vaccines e.g., BCG, until SCID is ruled out.</li><li>i. Instructs PMD to order only irradiated, leukoreduced cytomegalovirus (CMV)-negative blood products if transfusion is needed.</li><li>j. Faxes to PMD/neonatalogist (if baby is still in hospital):<ol style="list-style-type: none"><li>1. Cover letter confirming positive screening results (Att. #H or #I) or 2<sup>nd</sup> DNA Amplification Failure (Att.#K or #L) and required follow-up.</li><li>2. Results mailer of positive screen (Att.#B) or 2<sup>nd</sup> DNA amplification failure screen (Att.#D)</li><li>3. Brochure <i>Why Does My Baby Need More Testing for Severe Combined Immunodeficiency</i> (Att. #Q)</li><li>4. SCID Fact Sheet (Att.#S)</li></ol></li></ul></li></ul>
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	<p>5. Letter to providers about pilot (Att.#T) if provider does not know about pilot</p> <ul style="list-style-type: none"> <li>• E-mails a copy of MD cover letter to Quest Diagnostics, Drs. Puck and Church to alert them to incoming specimen. Includes in message: PCP's/neonatologist's phone number, TREC/Actin results from both DAF samples, gestational age at birth, birth weight, clinical status of baby, whether baby is in North or South region</li> <li>• Uses Tracking Event 142 to place case on ASC Headline Case List</li> <li>• Documents actions, contacts (including times/dates) in SIS case notes</li> <li>• Updates demographic information in SIS (with any changes in names, PMD, mother's phone number, etc) if indicated.</li> <li>• After 3 days, sends cover letter (att.#F) and above brochure to mother if baby is at home (brochure is NOT sent if baby is in the hospital).</li> </ul>
Quest Diagnostics	<p>E-mails Coordinator and Drs. Puck and Church that specimen was received.</p> <ul style="list-style-type: none"> <li>• Assigns specimen a case number</li> <li>• Conducts confirmatory testing (CBC differential and flow cytometry) on venous blood specimen.</li> <li>• Contacts Drs. Puck and Church (within 24 hours) by phone or e-mail to inform them of confirmatory test results.</li> <li>• Faxes all results to Dr. Lorey (who will provide them to PDEB RA) and to Drs. Puck and Church for review, interpretation within 1 to 2 days</li> </ul>
PDEB-RA	<ul style="list-style-type: none"> <li>• Scans confirmatory results, e-mails them to ASC coordinator</li> </ul>
Dr. Puck or Dr. Church	<ul style="list-style-type: none"> <li>• Reviews all confirmatory test results within 24 hours, and e-mails interpretation to PDEB RA, Dr. Lorey, and NBS coordinator, citing case number.</li> <li>• For tests deemed positive: <ul style="list-style-type: none"> <li>a. Contacts PMD to discuss results and follow-up recommendations including referral to CCS-approved Pediatric Immunology Center (PIC)</li> <li>b. Documents activities (e.g., contacts, referrals made, etc.), treatment plan, date of diagnosis, etc., in SIS case notes. (If Drs. Puck and Church are prevented from making entries in SIS, e-mails information to Coordinator).</li> <li>c. Completes Case Resolution form (3.21 A) per request of coordinator.</li> </ul> </li> </ul>

NBS Coordinator	<ul style="list-style-type: none"> <li>•</li> <li>• For positive confirmatory tests:             <ol style="list-style-type: none"> <li>a. Initiates CCS Referral Protocol to designated CCS-approved Pediatric Immunology Center (PIC).</li> <li>b. Offers assistance to PIC in patient tracking to assure that family receives needed services (e.g., arranging for PHN to locate a family).</li> <li>c. Documents activities in SIS case notes. Cuts and pastes Dr. Puck's or Church's interpretation into SIS case notes.</li> <li>d. Follows case through diagnosis, initiation of treatment plan (e.g., "Bone Marrow Transplant scheduled")</li> <li>e. Faxes PMD test results along with cover letter (Att.#O or #P) that includes immunology consultant's interpretation and recommendations for follow-up.</li> <li>f. Resolves case per Case Resolution Protocol (3.20).</li> </ol> </li> <li>• For negative confirmatory tests:             <ol style="list-style-type: none"> <li>a. Contacts PMD by phone to inform him/her of negative test results, and sends cover letter (Att.#N) /test results and interpretation, verifying conversation</li> </ol> </li> </ul>
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### Initial NBS Tests Deemed DNA Amplification Failure

NBS Coordinator	<ul style="list-style-type: none"> <li>• Looks in SIS for possible match of specimen, which may eliminate need to collect another specimen from the baby. If not already matched, links the two, and alerts PDEB-RA who will request SCID result of other screen from PE staff. before reporting results out. If a baby with an initial DAF is suspected of having or has been diagnosed with an immune deficiency, consults with Drs. Church and Puck as to whether to repeat the filter paper SCID screen or proceed to flow cytometry.</li> <li>• Contacts PMD/neonatalogist by phone to inform him/her of DNA Amplification Failure (i.e., inconclusive results) and describes SCID Pilot Project             <ol style="list-style-type: none"> <li>a. Refers questions to Dr. Jennifer Puck or Dr. Joseph Church.</li> <li>b. Informs PMD that another filter paper heel stick blood specimen is required</li> <li>c. Assists in arranging for collection of new heel stick specimen <b>to be sent to GDL via GSO courier (Att#W, #X). Repeat</b> specimen</li> </ol> </li> </ul>
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	<p>will be Type 21, Lab 62.</p> <p>d. Faxes specimen collection/handling instructions (Att.#W and #X) to collector: Use NBS TRF; check “other” on “Reason for Test,” and write in “SCID Repeat”</p> <p>e. Instructs PMD to withhold rotavirus vaccine (usually administered at 2 mo. of age) and/or other <i>live</i> vaccines until SCID is ruled out.</p> <p>f. Instructs PMD to order only irradiated, leukoreduced cytomegalovirus (CMV)-negative blood products if transfusion is needed.</p> <p>g. Documents actions in SIS case notes and tracking events</p> <p>h. Faxes PMD/Neonatologist:</p> <ol style="list-style-type: none"> <li>1. Mailer #2 (Att.#C), reporting failure to amplify DNA and need for another heel stick specimen)</li> <li>2. Cover letter (Att.#J)</li> <li>3. SCID Fact Sheet (Att#.S)</li> <li>4. Brochure <i>Why Does My Baby Need another Newborn Screening Test?</i> (Att.# R)</li> <li>5. Letter to Providers about Pilot (Att.#T ) if PMD request information about pilot</li> </ol>
PE staff at GDL	<ul style="list-style-type: none"> <li>• Tests 2<sup>nd</sup> filter paper specimen</li> <li>• Provides PDEB-RA with hard copies of TRFs of received repeat specimens</li> <li>• E-mails results to PDEB RA</li> </ul>
PDEB RA	<ul style="list-style-type: none"> <li>• Uploads results and enters TRF into GDSP SCID Database</li> <li>• Informs Coordinator by e-mail of results</li> <li>• Enters actions in SIS case notes</li> </ul>
NBS Coordinator	<ul style="list-style-type: none"> <li>• Sends above brochure (Att.# R) to mom 3 days after contacting PMD, with cover letter (Att#G), if baby is at home (does not send brochure to mom if baby is in hospital).</li> <li>• If repeat test is negative, sends results (Att.#E) and cover letter to PMD (Att#M)</li> <li>• If test is positive, informs MD by phone, sends results mailer (AttI) to MD with cover letter, and follows protocol above (Positive tests)</li> <li>• If test is again a DNA amplification failure, contacts MD, faxes results mailer (Att.#D ) and cover letter, and follows protocol above (Positive Tests).</li> <li>• Documents activities in SIS using case notes.</li> </ul>