

CP 3.4 Follow-up of Newborns with Positive Biotinidase Deficiency (BD) Screen

GENERAL INFORMATION/POLICY:

- The Newborn Screening Program screens for profound biotinidase deficiency (equal to or less than 10% normal enzyme activity in the serum) but will detect some newborns with partial biotinidase deficiency (10% -30% normal enzyme activity).
- The NBS Program recommends that all newborns detected with both profound and partial biotinidase deficiency be followed by a CCS-approved metabolic special care center (SCC).
- Confirmatory testing is conducted by Stanford Biochemical Genetics Laboratory.

Cut-offs:

- The cut-off for BD is ≤ 10.00 ERU (Enzyme Response Units). A value equal to or less than 10.00 is considered to be positive.
- Newborns with initial screening values of 6.01 – 10.00 ERU will have a second filter paper NBS test.
- Newborns with initial values of 6.00 ERU and lower will be immediately referred to a Metabolic Center for a diagnostic evaluation including confirmatory testing through Stanford.

Transfusions:

Transfusions of red blood cells (accounting for about 99% of newborn transfusions) are not thought to affect biotinidase levels in babies (as they do galactosemia and hemoglobinopathy screens). Therefore, the BD screen should be considered valid if it is collected at least 24 hours after a red blood cell transfusion. There is a slight possibility that an affected newborn transfused with other blood products can be missed.

Associated Forms/Documents:

- 3.4.1 BD Fact Sheet
- 3.4.2 Stanford BD TRF

3.4 Follow-up of Newborns with Positive Biotinidase Deficiency (BD) Screen

PROTOCOL FOR INITIAL POSITIVE RESULTS (Values of 6.01-10.00 ERU):

Resp. Person	Action
NAPS Lab	<ul style="list-style-type: none"> • As soon as possible but no later than the end of the same day, calls appropriate ASC when initial result is positive. • Enters C of C into SIS.
ASC NBS Coord/Program Specialist	<ul style="list-style-type: none"> • As soon as possible but in no later than 48 hours after notification of a positive, calls the newborn's physician and/or the hospital, if infant has not been discharged, to discuss the biotinidase results; asks for information on the infant's health status. Discusses need for and gives instructions for collection and handling of a second filter paper newborn screening test (to be sent to respective NAPS lab for processing). • Faxes or sends letter to PCP confirming results and specifics of conversation, and sends informational brochure, <i>Why Retest for Biotinidase Deficiency</i>. • Contacts the family directly as requested by the physician to arrange for collection of a second NBS specimen. • Sends parent letter with appropriate informational brochure, <i>Why Retest for Biotinidase Deficiency</i>. • Documents all attempts at notification, interactions with physicians and parents, using tracking events and case notes in SIS.
NAPS Lab	<ul style="list-style-type: none"> • Runs full NBS panel of tests, treating the specimen as if it were an initial NBS. • Enters results into SIS (SIS will match it with the initial specimen and convert the second specimen from type 21 to type 31). • If test/result is positive (value of 10.00 ERU or lower), as soon as possible but no later than the end of the same day, calls appropriate ASC. • Enters C of C into SIS.
ASC NBS Coord.	<ul style="list-style-type: none"> • If the result of the second screen is positive for BD (value of 10.00 ERU or lower), follows protocol for values of ≤ 6.0 ERU, including calling the newborn's physician and/or hospital, alerting to signs and symptoms of BD, discussing and assisting with referral to appropriate metabolic center per CCS protocol.
Metabolic Center	<ul style="list-style-type: none"> • Follows protocol for values of ≤ 6.00 ERU.
ASC NBS Coord.	<ul style="list-style-type: none"> • Closes case as either positive or negative per Case Resolution Protocol (3.20).

3.4 Follow-up of Newborns with Positive Biotinidase Deficiency (BD) Screen

PROTOCOL FOR INITIAL POSITIVE RESULTS (Values of 6.0 ERU or lower):

Resp. Person	Action
NAPS Lab	<ul style="list-style-type: none"> • As soon as possible but no later than the end of the same day, calls appropriate ASC when initial result is positive. • Enters C of C into SIS.
ASC NBS Coord.	<ul style="list-style-type: none"> • As soon as possible but in no later than 48 hours after notification of a positive, calls the newborn’s physician and/or the hospital, if infant has not been discharged, to discuss the biotinidase results; asks for information on the infant’s health status. Discusses immediate referral to a SCC. • Assists physician with referral to appropriate metabolic center per CCS protocol. Requests information from the physician regarding which SCC is a preferred provider for the family’s insurance. If the preferred center is too distant, a referral can be made to the closest center. • Alerts physician to watch for any signs and symptoms of BD, i.e., skin rash/alopecia, poor muscle tone, seizures, developmental delay, hearing loss, conjunctivitis, ketolactic acidosis, organic acidemia, visual problems (e.g., optic atrophy). Recommends if any symptoms occur while awaiting evaluation by the metabolic specialist, physician should immediately contact the CCS metabolic specialist to discuss the symptoms and treatment. • Unless primary care physician (PCP) objects, contacts the SCC to notify staff of referral and requests that a metabolic specialist contact the PCP regarding follow-up. • Faxes/sends follow-up letter to physician confirming the BD test results on the baby and referral information, along with Biotinidase Deficiency Fact Sheet (3.4.1). • If the baby has been discharged from the hospital, also sends a letter to the parents notifying them of the need for referral to a CCS-approved metabolic special care center and includes the brochure <i>“Why Retest for Biotinidase Deficiency?”</i> • Makes referral to CCS regional office per protocol 7.2 <i>Referral to a CCS Special Care Center or CCS-paneled Specialist</i>, and enters appropriate Tracking Events and case notes into SIS. • If the physician and the ASC coordinator are unable to contact the family within 3 – 4 days from the initial notification makes a referral to public health nursing and arranges for a home visit. • If the metabolic center has difficulty in making contact with the family, offers assistance in making a referral to public health nursing.

3.4 Follow-up of Newborns with Positive Biotinidase Deficiency (BD) Screen

<p>Metabolic Center</p>	<ul style="list-style-type: none"> • Contacts PCP to discuss health status of newborn and follow-up for newborn referred to SCC. Determines if immediate visit at SCC is necessary. Schedules appointment as appropriate • At initial visit assists parent/guardian with completion of CCS application. • Faxes completed CCS application to local CCS office and requests authority for services. See Protocol 7.2 <i>Referral to CCS Special Care Center or CCS-Paneled Specialist.</i> • Orders confirmatory/diagnostic laboratory testing through BD reference lab (Stanford). • Provides information to family on where and when to go for specimen collection. • Bills CCS for diagnostic services per CCS guidelines. • Enters initial appointment status and Metabolic Service Report(s) (MSR) into SIS per vendor agreement requirements. After completing the MSR, enters case notes when additional information is needed to augment or clarify the MSR.
<p>State BD Reference Lab (Stanford)</p>	<ul style="list-style-type: none"> • Reports confirmatory results (positive and negative) to ordering physician within timeframes delineated in contract. • Enters results in SIS.
<p>Metabolic Center</p>	<ul style="list-style-type: none"> • As soon as possible but no later than 48 hours after notification, calls the newborn's primary care physician with confirmatory results. For newly diagnosed newborns, or those newborns requiring additional testing, discusses necessary follow-up. • Develops treatment plan. • Sends follow-up letter to the PMD confirming notification and recommendations, and includes appropriate informational materials on the confirmed disorder. • Enters follow-up information (including case resolution) as appropriate in SIS via the Metabolic Services Report (MSR) per vendor agreement requirements. • Bills private insurance/Medi-Cal/CCS for non-laboratory services related to diagnostic evaluation.
<p>ASC NBS Coord.</p>	<ul style="list-style-type: none"> • Contacts metabolic center within 5 days of referral to determine follow-up plan and verifies that the center has contacted the PCP • Upon request, sends the appropriate informational brochure on the confirmed disorder to the PCP. • If the physician or metabolic center is unable to contact the family with the confirmatory results within one week from the initial notification, assist with initiating a referral to public health nursing and arranges for a home visit. • Reports any unusual occurrences such as missed cases, lost to follow-up cases, delays in contacting family, delays in analysis or reporting of confirmatory results, etc., of potential significance to the NBS Branch nurse consultant/ASC contract liaison.

3.4 Follow-up of Newborns with Positive Biotinidase Deficiency (BD) Screen

	<ul style="list-style-type: none">• Refers case to Child Protective Services (see 7.1) as appropriate and with approval of NBS Nurse Consultant/Contract Liaison.• Contacts metabolic center/primary care physician(s) regularly (at least monthly unless informed via SIS or MD that baby will not be seen for over a month) to follow progress of resolution and documents findings in SIS. Attempts to resolve case by obtaining decision when possible.• Enters appropriate tracking events and case notes into SIS.• Once case is resolved by specialist (as noted on MSR), resolves case in SIS by: confirmed diagnosis and treatment, infant death, noncompliance, no response or lost to follow-up.
--	---