# CT Children's CLASP Guideline

*The Role of Primary Care in the Evaluation & Management of Out-of-Range Newborn Screens*

## INTRODUCTION

Newborn screening (NBS) is the well-established practice of testing all babies in their first days of life for certain disorders and conditions that can hinder normal growth and development. This testing is required in every state and is usually done before the baby leaves the hospital. The conditions screened for with NBS can cause serious health problems that start in infancy or childhood. Since these infants can appear healthy at birth, early detection with newborn screening allows doctors, and their care teams, to start treatment and to prevent morbidity and mortality.

When a baby is 24-48 hours old, blood taken by heel stick is sent to the Connecticut Department of Public Health (DPH) at the State Laboratory for screening. Screening tests are currently available for more than 60 disorders in CT. The CT newborn screening panel is based on the recommendations of the US Department of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children. With advances in NBS over the coming years, we expect more conditions to be added to the Recommended Uniform Screening Panel (RUSP).

***See Appendix #1 for a list of current disorders screened for in Connecticut.***

**The Connecticut Newborn Screening Network, or "the Network,"** was formed in 2019. Funded through the CT DPH, and based at Connecticut Children's Medical Center, the Network responds to all reports of infants who have a NBS that flags out of range. The Network supports the CT DPH Newborn Screening Program in the triage, short-term follow-up, education, reporting, and long-term follow-up of out-of-range NBSs. In coordination with the infant's primary care provider (PCP) or hospital-based medical provider (HBMP), the Network will begin the diagnostic work-up, and provide support to the healthcare team and family as needed. If an infant confirms positive for a disorder, the Network will coordinate treatment and long-term follow-up for the condition identified, working with PCPs, hospitals, and specialists statewide.

**Network staff are always happy to speak with you, your office, and families regarding any NBS-related questions or concerns:**
**Monday-Friday 8:30 am - 4:30 pm**
**Phone: 860.837.7870**
**Fax: 860.837.7871**
**Email: cndtn@connecticutchildrens.org**

**Genetic Counseling Services for Families of Infants With an Out-of-Range NBS**

The Network offers no-cost, direct-to-patient, telehealth services with a NBS Genetic Counselor to all families in CT who have an infant who has had an out-of-range NBS. To schedule a telehealth visit with a NBS genetic counselor, families should call (860) 837-5759.

***See Appendix #2 How Can a Genetic Counselor Support Your Practice and Families***

**NBS Registry**

The Network has established an electronic NBS Registry for patients referred or treated through the Network. The network will measure, track, and report on medical, developmental, and behavioral health outcomes from birth to age 21 years.

## INITIAL EVALUATION AND MANAGEMENT

**Roles of PCPs and Network Coordinators:**
Upon receipt of an out-of-range result, a Network Coordinator will contact the newborn's PCP or HBMP to obtain brief information about the baby and to discuss next steps.

Based on the results of the initial screen and/or subsequent diagnostic testing and clinical status, clinical care teams will determine which infants need to be connected with a subspecialist, and how soon. Families will meet with the appropriate specialist in genetics, endocrinology, hematology, neurology, or immunology.

- **LABS and NEXT STEPS:** When a NBS is identified as out-of-range, the Network will contact your office with recommendations and next steps. These recommendations are based on American College of Medical Genetics and Genomics (ACMG) ACT Sheets and Algorithms, agreed-upon workflows formed in an agreement between specialty providers at both Connecticut Children's and Yale, and review with the specialty provider on-call.
- For some conditions, the Network will communicate the recommended labs to your office for you to place the orders (e.g., CH). For other conditions, the confirmatory labs will be obtained directly by the specialty care team (e.g., SMA).
- **As a service to your office, the Network offers to place orders for metabolic, and some genetic, referrals at Quest. However, we are aware that many families and providers have other lab preferences. Please note that you can place diagnostic lab orders wherever you feel most comfortable. Lab choice is ALWAYS parent and provider choice.**
- **If you do choose to order the recommended labs at a non-Quest draw station, your office will be responsible for monitoring lab results and faxing them to the Network at (860) 837-7871.** Once received, the Network will review the results with the geneticist on-call and inform your office of the next steps (closing the NBS case, scheduling a visit with a specialty provider, genetic testing, etc.).
- Please refer families to this webpage for tips on preparing their newborn for a blood draw and collecting a urine sample:

www.connecticutchildrens.org/search-specialties/newborn-diagnosis-treatment-network/pre-diagnosis-resources/

If you are interested in learning more about the condition your patient referred for, we recommend www.medlineplus.gov as a reputable and reliable website.

**Communication and documentation of NBS results with family:**

- PCP practice will have a conversation with parents regarding their child's NBS results. This includes both in *and* out-of-range NBS results. Practices may choose to communicate normal results electronically or in person.
- Most bloodwork takes 2-3 weeks to result, urine labs can take approximately 3 weeks, and genetic testing takes approximately 4 weeks to result.
- PCP practice will document NBS results in the child's chart by the 1-month visit. This includes both in *and* out-of-range NBS results.
- If you, your practice, or the family has any questions or concerns regarding next steps and the status of work up, please call the Network at (860)837-7870.
- Receiving out-of-range NBS results can be traumatic for some families. Consider screening for post-partum depression and refer for treatment as needed.

***See Appendices:***
***#3 Initial Intake Questions***
***#4 Signs and Symptoms to Watch For***
***#5 Response to Sickle Cell Trait Results***
***#6 Network Workflow***
***#7 PCP Workflow***
***#8 Guidance on Heel-stick Specimen Collection for PCP Offices***
***#9 Communication of NBS Results to Families***
***#10 Participation in MOC QI Project***

## WHAT TO EXPECT FROM THE FIRST SPECIALTY CARE TEAM VISIT

- History and physical exam
- Review of NBS result and diagnostic testing, if completed
- Initiation of treatment, if appropriate
- Ascertain the need for diagnostic/genetic testing

## LONG-TERM MANAGEMENT (Birth - Age 21)

**BIRTH TO THREE REFERRALS**

Some medical conditions have a high probability of resulting in a developmental delay**. Infants diagnosed with one of these conditions will be automatically eligible for early intervention.** Upon diagnosis, a Network coordinator will alert you that a Birth to Three referral is recommended.
Please see Diagnosed Conditions List: https://www.birth23.org/referral/eligibility/dxcond/

**LONG-TERM FOLLOW-UP**

NBS nationwide is expanding to include long-term health outcomes through reporting of de-identified aggregate data through age 21 years.

Long-term management of the specific condition will be under the direction of the specialty clinical care team. PCPs will remain an invaluable member of the care team as they continue to provide primary and preventive care. The Network will remain involved to assist the care teams and families in identifying care coordination needs, facilitate best-practice care, and minimize those lost to follow-up.

Many of the conditions have the potential to impact long-term health and development. The Network model includes the reporting of developmental and behavioral health issues. **To obtain this information, Network coordinators will leverage existing health information exchanges and patient and family-centered surveys to learn about developmental and behavioral health concerns. Occasionally, the Network may need to contact your office for this information.**

## HOW TO CONTACT THE NETWORK

Monday-Friday 8:30 am - 4:30 pm
Phone: 860.837.7870
Fax: 860.837.7871
Email: cndtn@connecticutchildrens.org

**NBS NETWORK INFOLINE**
Network nurses are always happy to speak with your office and families. Parents and/or providers can contact 860-837-7870 to speak to Network staff from 8:00 am to 4:30 pm Monday to Friday.

***See Appendix #11 Should I Call the Network or the Program?***

**WEEKENDS**
For non-urgent lab results and questions that arise over the weekend, please contact the Network on Monday Morning.

For potentially urgent lab results and/or clinical changes over the weekend, please call the Network at 860-837-7870 and ask to speak to the NBS provider on call or, if you know the care team involved, request to speak the specialist on call for that care team.

*If there is a concern that something is not safe/ok for newborn, refer to ED

## APPENDIX 1: WHAT DISORDERS ARE SCREENED FOR IN CT?

**Amino Acid Disorders**

- Argininemia (ARG)
- Argininosuccinic Aciduria (ASA)
- Benign Hyperphenylalaninemia (H-PHE)
- Biopterin Defect in Cofactor Biosynthesis (BIOPT-BS)
- Biopterin Defect in Cofactor Regeneration (BIOPT-REG)
- Carbamoyl Phosphate Synthetase I Deficiency (CPS)
- Citrullinemia, Type I (CIT)
- Citrullinemia, Type II (CIT II)
- Classic Phenylketonuria (PKU)
- Homocystinuria (HCY)
- Hypermethioninemia (MET)
- Guanidinoacetate Methyltransferase (GAMT) Deficiency
- Maple Syrup Urine Disease (MSUD)
- Ornithine Transcarbamylase Deficiency (OTC)
- Tyrosinemia, Type I (TYR I)
- Tyrosinemia, Type II (TYR II)
- Tyrosinemia, Type III (TYR III)

**Endocrine Disorders**

- Congenital Adrenal Hyperplasia (CAH) (Spanish version)
- Primary Congenital Hypothyroidism (CH) (Spanish version)

**Fatty Acid Oxidation Disorders**

- 2,4 Dienoyl-CoA Reductase Deficiency (DE RED)
- Carnitine Acylcarnitine Translocase Deficiency (CACT)
- Carnitine Palmitoyltransferase I Deficiency (CPT-IA)
- Carnitine Palmitoyltransferase Type II Deficiency (CPT-II)
- Carnitine Uptake Defect (CUD)
- Glutaric Acidemia, Type II (GA-2)
- Long-Chain L-3 Hydroxyacyl-CoA Dehydrogenase (LCHAD) Deficiency
- Medium-Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency
- Medium/Short-Chain L-3 Hydroxyacyl-CoA Dehydrogenase Deficiency (M/SCHAD)
- Short-Chain Acyl-CoA Dehydrogenase (SCAD) Deficiency
- Trifunctional Protein (TFP) Deficiency
- Very Long-Chain Acyl-CoA Dehydrogenase (VLCAD) Deficiency

**Hemoglobin Disorders**

- Hemoglobinopathies (Var Hb)
- S, Beta-Thalassemia (Hb S/ßTh)
- S, C Disease (Hb S/C)
- Sickle Cell Anemia (Hb SS)

**Organic Acid Conditions**

- 2-Methyl-3-Hydroxybutyric Acidemia (2M3HBA)
- 2-Methylbutyrylglycinuria (2MBG)
- 3-Hydroxy-3-Methylglutaric Aciduria (HMG)
- 3-Methylcrotonyl-CoA Carboxylase (3-MCC) Deficiency
- 3-Methylglutaconic Aciduria (3MGA)
- Beta-Ketothiolase (BKT) Deficiency
- Ethylmalonic Encephalopathy (EME)
- Glutaric Acidemia, Type I (GA-1)
- Holocarboxylase Synthetase Deficiency (MCD)
- Isobutyrylglycinuria (IBG)
- Isovaleric Acidemia (IVA)
- Malonic Acidemia (MAL)
- Methylmalonic Acidemia (Cobalamin Disorders) (Cbl A,B)
- Methylmalonic Acidemia (Methymalonyl-CoA Mutase Deficiency) (MUT)
- Methylmalonic Acidemia with Homocystinuria (Cbl C, D, F)
- Propionic Acidemia (PROP)

**Lysosomal Storage Disorders**

- Glycogen Storage Disease Type II (Pompe Disease)
- Mucopolysaccharidosis Type 1 (MPS-1)

**Other Genetic Disorders**

- Adrenoleukodystrophy (ALD)
- Biotinidase Deficiency (BIOT) (Spanish version)
- Classic Galactosemia (GALT) (Spanish version)
- Galactoepimerase Deficiency (GALE)
- Galactokinase Deficiency (GALK)
- Spinal Muscular Atrophy (SMA)

**Immunology**

- Severe Combined Immunodeficiency (SCID)
- Adenosine deaminasedeficient severe combined immunodeficiency (ADA-SCID)
- T-cell Related Lymphocyte Deficiencies

**May be identified by NBS**

- Duarte Galactosemia
- Carrier Identification

**Coming Soon**

- Mucopolysaccharidosis Type 2 (MPS-2)

***Please note: Cystic Fibrosis, Critical Congenital Heart Disease, Cytomegalovirus (CMV) and Hearing Loss ARE screened for in CT. However, they ARE NOT addressed by the Network.***

## APPENDIX 2: HOW CAN A GENETIC COUNSELOR SUPPORT YOUR PRACTICE & FAMILIES?

Genetic counselors (GCs) are healthcare professionals who have specialized education in genomics/genetics and counseling. GCs can work with families and their healthcare providers to understand complex genomic/genetic information and help them make informed decisions on their healthcare based on genetic testing and family history.

The GC role is to help patients and their families understand and make decisions about genetic testing, genetic conditions, and related issues. These may include medical and emotional concerns for you and your family. Genetic counselors can provide information and answer questions about:

- The science behind genetic conditions
- The chance for genetic disease in you or other family members
- Genetic testing (benefits and limitations)
- Management and prevention of genetic conditions
- Available resources/support

To schedule a telehealth visit with a NBS genetic counselor, families should call (860) 837-5759 and request "a visit with the newborn screening genetic counselor". Visits with the NBS GC are available at no cost to families who live in CT when the baby was identified through NBS.

## APPENDIX 3: INITIAL INTAKE CONVERSATION BETWEEN NETWORK AND PCP PRACTICE

During the initial conversation, the Network will notify you of the condition the baby flagged for, ask follow-up questions about the baby's status, recommend next steps, and notify you of what specialty care team the baby has been referred to (Connecticut Children's Genetics, Connecticut Children's Endocrinology, Yale Hematology, Yale Immunology, etc.)

Based on the condition and initial intake conversation, potential questions asked:

- Have you seen the newborn? (yes/no)
- Where is the newborn now? (home/hospital/emergency room/clinic/other)
- Are the parent(s) aware of the screening result yet? (yes/no/unknown)
- Does the newborn have any family history relevant to the condition for which they had a positive screen? (yes/no/unknown)
- Has the newborn regained birth weight? (yes/no/unknown)
- Were there any delivery concerns? (yes/no/unknown)
- Does the newborn have any feeding issues? (yes/no/unknown)
- Does the newborn have vomiting concerns? (yes/no/unknown)
- Is the newborn breastfeeding? (yes/no/unknown)
- Are any social services like DCF involved with this family? (yes/no/unknown)
- Does patient have difficulty accessing or affording transportation? (yes/no/unknown)
- Who lives at home with the newborn?
- Preferred follow-up location? (Connecticut Children's/Yale New Haven Hospital/other)
- Preferred lab for confirmatory blood work?

## APPENDIX 4: SIGNS AND SYMPTOMS TO WATCH FOR

Some babies with metabolic disorders never have serious signs or symptoms. Sometimes signs and symptoms may not happen until later in life. Each disorder has different signs and symptoms. In general, we recommend asking the family to call the baby's doctor if there are any changes from typical behavior, such as: lethargy (being very tired/unable to wake the baby), new fussiness, not eating well, having trouble gaining weight, diarrhea, vomiting or infection. For some of the conditions screened, a newborn's condition can deteriorate rapidly. **If your patient is exhibiting one or several of these signs or symptoms, care treatment might need to be expedited.** Please reach out to the Network or specialty care team currently working with the newborn. If it is the weekend and you are concerned about the baby's condition, it may be appropriate to send the patient to the emergency department for evaluation. It would be helpful to notify parents and/or staff of the condition the baby screened for.

## APPENDIX 5: RESPONSE TO SICKLE CELL TRAIT RESULTS

If you are notified that a newborn screen has identified a sickle cell trait, confirmatory testing is necessary. The following actions are recommended:

1) Document the result in the newborns' medical record

2) Discuss the result with the family

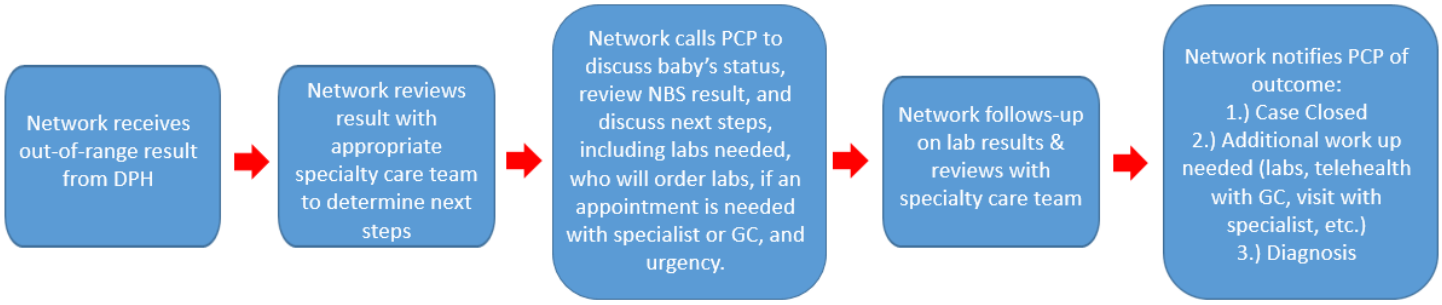
3) Order hemoglobin electrophoresis at 6 months of age to confirm carrier status

4) Fax results to the DPH Newborn Screening Program at (860)730-8385

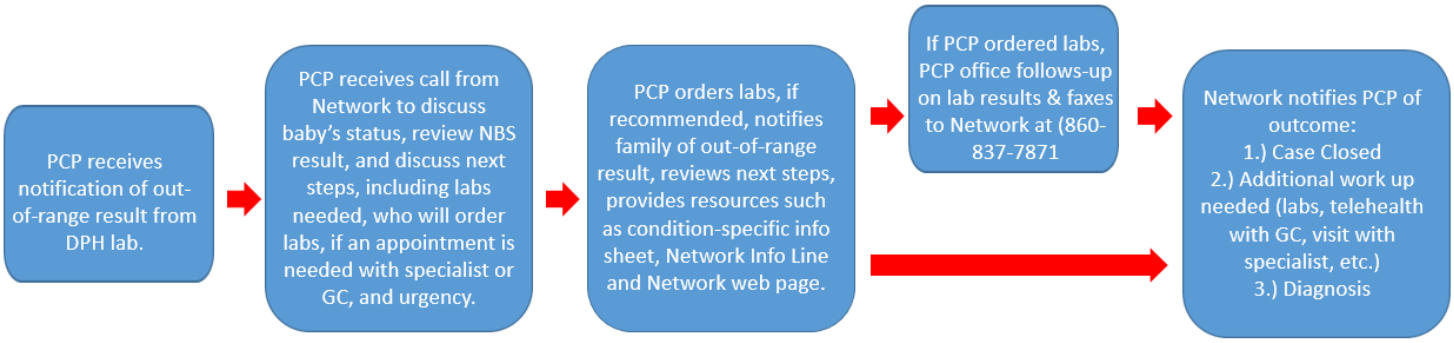
5) If Hgb trait is confirmed by electrophoresis, genetic counseling is indicated for this family. To schedule a telehealth visit with a NBS genetic counselor, families should call (860) 837-5759 and request "a visit with the newborn screening genetic counselor". Visits with the NBS genetic counselor are available at no cost to families who live in CT when the baby was identified through NBS.

## APPENDIX 6: NETWORK WORKFLOW

**Of note, the NBS Network will inform the PCP of any next steps, including need for follow up labs, specialist referral, and who is responsible for making these referrals and ordering the labs.*




## APPENDIX 7: PCP WORKFLOW



## APPENDIX 8: GUIDANCE ON HEEL-STICK SPECIMEN COLLECTION FOR PCP OFFICES

https://portal.ct.gov/-/media/DPH/NBS-Forms-and-Documents/Heel-stick-specimens-for-PCPs.pdf?la=en

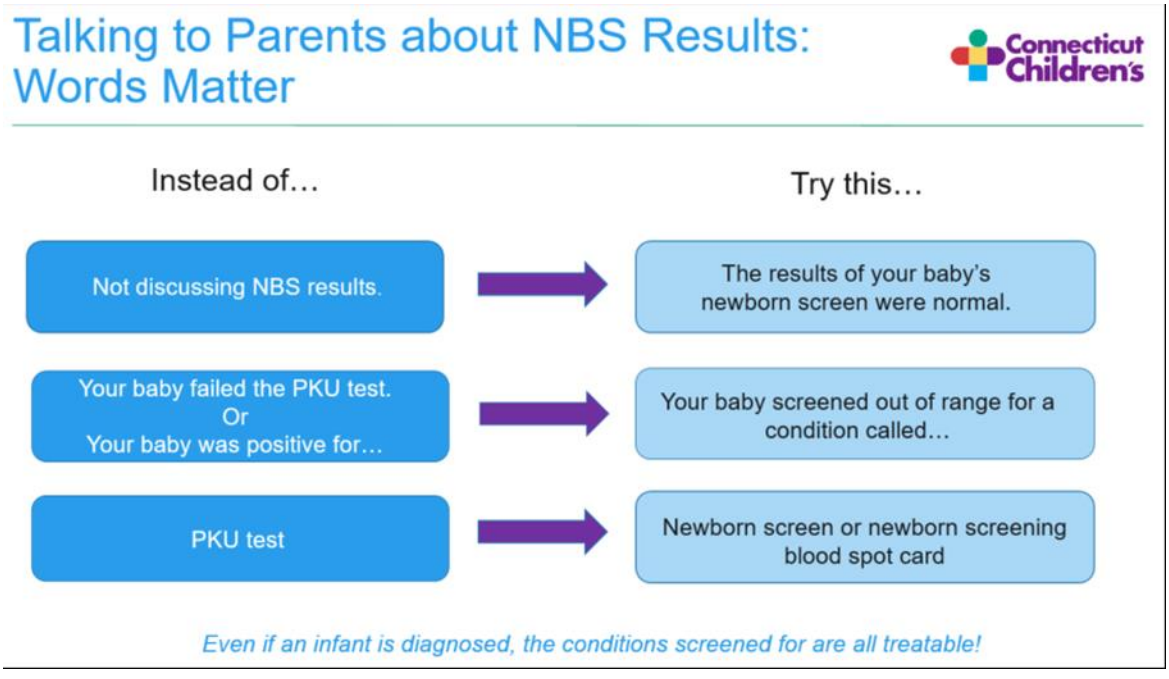
## APPENDIX 9: COMMUNICATION OF NBS RESULTS TO FAMILIES

Notify the family as soon as possible about their NBS result. For many conditions, it is not safe to wait until the next visit. At the time of the referral, the Network will fax you a condition-specific info sheet that will provide basic information about the condition the baby flagged for, signs and symptoms to watch for, appropriate resources, and the Network Info Line. If parents have additional questions or concerns, you can refer them to the Network NBS Info Line at (860) 837-7870.

You will be notified of ALL NBS results. It is important to document these results in the patient's record. A conversation about NBS should occur no matter what the results are.
**If the NBS is WNL:** Ensure screening results are documented in the medical record. Communicate results to family.
**If the DPH NBS Program requests a repeat:** Obtain a repeat specimen and send to Dr. Katherine A Kelley State Public Health Laboratory in Rocky Hill.
**If the result is out of range:** the DPH NBS Program will notify you of the out-of-range result. The Network will contact you to guide you through next steps.

Initial PCP contact with the family:

1) State the name of the condition. "*Johnny's newborn screen was out of range for a condition called XXX*."
2) Emphasize that NBS is a SCREENING, not a DIAGNOSIS.
3) Explain that all conditions screened for are TREATABLE.
4) Review NEXT STEPS. "*Please make an appointment for Johnny to have labs drawn at Quest at Connecticut Children's in Hartford tomorrow.*"
5) Provide resources. (Condition-specific info sheet, Connecticut Children's website, Baby's First Test)



## APPENDIX 10: PARTICIPATION IN MOC QI PROJECT

Connecticut Children's offers a Maintenance of Certification (MOC) Project with the goals of (1) improving documentation of NBS results in the child's chart and (2) improving documentation of a conversation with parents regarding their child's NBS results. This includes both in and out-of-range NBS results. If you are interested in participating in the MOC Project, please contact Debra Ellis at dellis@connecticutchildrens.org

## APPENDIX 11: SHOULD I CALL THE NETWORK OR THE PROGRAM?