



# Nevada Newborn Screening Guide

NEVADA STATE PUBLIC HEALTH LABORATORY

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University of Nevada, Reno  
School of Medicine

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# NBS CONSULTANT CONTACT INFORMATION

## **Metabolic Consultant:**

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## **LABORATORY DAYS/HOURS OF OPERATION:**

**MONDAY-FRIDAY 8:00AM-5:00PM**

## **LAB CLOSURE/HOLIDAY OBSERVANCES:**

New Year's Day  
Martin Luther King Day  
Presidents' Day  
Memorial Day  
Independence Day  
Labor Day  
Nevada Day  
Veterans Day  
Thanksgiving Day  
Day after Thanksgiving  
Christmas Day

## **Mail/receiving services:**

The University has a central mail/receiving service center that is open Monday-Friday from 8:00am-5:00pm. All newborn screen specimens mailed to the laboratory is processed and delivered through the mail center.

## **Newborn Screening Staff:**

Laboratory: 3 FTE, 4 PTE

Follow-Up: 1 PTE

# **OVERVIEW OF NEVADA NEWBORN SCREENING PROGRAM**

## **Newborn Blood Spot Screening:**

Newborn Blood Spot Screening is an essential preventative public health system recognized in the US and internationally. It is comprised of ***screening, follow-up, diagnosis, management, evaluation, and education.*** The primary goal of newborn screening is the early identification of infants at risk for selected metabolic and inherited disorders so treatment may commence before permanent neurological and developmental damage has occurred thus improving outcomes for the newborn. The national standard of care to identify the infant, complete confirmatory testing, and begin treatment is prior to 21 days of age. In Nevada, newborn blood spot screening began in 1978 with Phenylketonuria (PKU) as the first disorder on the panel. Screening for Congenital Hypothyroidism, Hemoglobinopathies, Biotinidase, Galactosemia, Maple Syrup Urine Disorder were subsequently added to the panel. In 2003, Congenital Adrenal Hyperplasia was added and Tandem Mass Spectrometer testing started. In 2008, Cystic Fibrosis screening was added. In 2011, Tyrosinemia screening test was improved. Currently, there is no standard statewide newborn screening panel and each state's program differ. Many states, including Nevada have increased their screening panel to include all tests recommended by the American College of Medical Genetics (ACMG). Nevada currently screens for over 30 conditions that include metabolic disorders, endocrine disorders, hematological disorders, and cystic fibrosis. In 2013, the Nevada State Legislature passed Senate Bill 92 to include the examination of newborns to determine whether the infant may have Critical Congenital Heart Disease (CCHD). Effective July 1, 2015, birth hospitals must submit a monthly report of positive cases to the Department of Public and Behavioral Health. In April 2015, Nevada State Public Health Laboratory (NSPHL) applied for the Severe Combined Immunodeficiency (SCID) grant and awarded a two-year grant from CDC for set-up of SCID screening. The first year is to purchase equipment for validation and train personnel and second year is to purchase additional equipment to implement statewide screening. Anticipated start date for SCID testing is January 2018. **From 7/1/2014 to 11/30/2017, there was 161 confirmed disorder cases.** Nevada statutes detailed in NAC 442.020-442.050 mandates newborn blood spot screening for all infants born in Nevada. Nevada is a two-screen state meaning a first blood spot specimen is collected between 24-48 hours of life ideally before discharge and a second blood spot specimen collected between 10-14 days of age on all infants.

Since 1978, Nevada through the competitive process has contracted with Oregon Public Health Laboratory to perform analytical testing of newborn specimens. In 2011, the Nevada State Legislature passed Senate Bill 131 an initiative to perform Newborn Screening in the State of Nevada as part of the State's economic mission to diversify its economy. The Nevada State Public Health Laboratory (NSPHL) is the first priority to perform newborn screening analyses and implement the program statewide. To start the transition, NSPHL collaborated with the University of Nevada School of Medicine (UN SOM) Department of Pediatrics and the School of Community Health Sciences, and Department of Health & Human Services to develop a framework and operational plan to implement both Newborn Screening analytical and follow-up case management through the University system. The analytical component is located at the NSPHL in Reno and officially started on 7/1/2014. The benefits of having the laboratory services done within state include improved transit, improved turn-around time for test results, improved communication/teamwork, and facilitate prompt treatment for affected infants. The case management/follow-up component is managed statewide by the Follow-Up Coordinator in Las Vegas. Metabolic consultant is contracted out of state from Utah and provides metabolic clinic follow-up through Nevada Early Intervention Services and consultation to the NBS laboratory. The Newborn Screening Program officially transitioned from the state health division to NSPHL on 1/1/2015. NSPHL is one of five laboratories in the U.S. that is part of the university rather than a state health division.

In preparation for the 7/1/2014 official start date, a planning meeting occurred on 2/27/2014 to re-activate the newborn screening advisory committee and consensus on standing agenda items.

The first official meeting occurred on 4/15/2014 and subsequent meetings held quarterly via teleconference and/or videoconference. The purpose of the newborn screening advisory committee are as follows: to provide program review for dried blood spot and hearing screenings, discuss quality review, provide a voice for consumers, discuss newborn screening best practices, promote an active role in advocacy, provide guidance, review proposals for addition of tests in the screening panel and provide recommendations to appropriate parties. Committee members include practicing pediatricians; specialty physicians in metabolic, hemoglobinopathies, cystic fibrosis, endocrine disorders; dietician; neonatologist; birth hospital newborn screening coordinator, families, laboratory manager, follow-up coordinator; March of Dimes coordinator; hearing coordinator, representatives from state public and behavioral health; and additional membership to include legislative, Medicaid, and Nevada Hospital Association (NHA) representatives.

The newborn screening program utilizes a systems approach and requires successful collaboration with community partners such as primary care providers, families, birthing facilities, specialists, mail/courier groups, treatment centers, public health officials, legislators, and other stakeholders.

**Newborn Early Hearing Detection and Intervention Program (EDHI):**

The mission of EDHI is to ensure ***universal newborn hearing screening, diagnostic follow up for infants who do not pass, and early intervention for those infants identified with hearing loss.*** Every day, 33 babies are born in the United States with permanent hearing loss. With three of every 1000 newborns having hearing loss, it is the most frequently occurring congenital condition. When a child's hearing loss is identified soon after birth, families and professionals can make sure the child receives intervention services at an early age. Studies have shown that children who receive appropriate early intervention services in the first 6 months of life can improve language, social, and academic development to levels comparable to their normally hearing peers by 3-5 years of age.

In 2002, Nevada passed legislation requiring that all hospitals with more than 500 births per year screen the hearing of newborn babies. Prior to passage of this legislation, it was estimated that only 40% of Nevada's newborns received a hearing screening. Through a cooperative grant from the Centers for Disease Control and Prevention (CDC), Nevada is implementing an EHDI tracking and monitoring system to build upon the success of newborn hearing screenings.

Nevada statutes detailed in NRS 442.500-442.590 require that every infant undergo a hearing screening prior to discharge from a hospital or birthing center or referred for a hearing screening at least by one month of age. Before three months of age, all infants who do not pass the hearing screen should receive a complete hearing evaluation by an audiologist. Infants with confirmed hearing loss should be referred for intervention services by six months of age.

EHDI website: <http://dpbh.nv.gov/Programs/EHDI/EHDI-Home/>



# The Nevada Early Hearing Detection and Intervention (EHDI) Program

## 2013 Statewide Annual Performance Summary

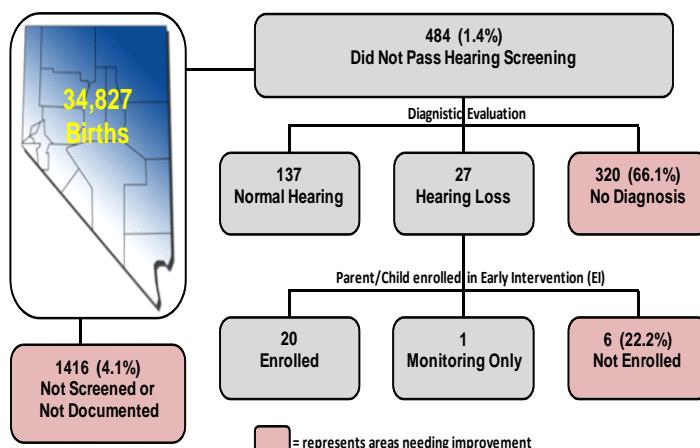
**Newborn Hearing Screening is just the first step.** The purpose of screening is to identify those babies who might have hearing loss and are in need of a more thorough hearing evaluation. Nevada supports the national best practice 1 - 3 - 6 goals outlined by the Joint Committee on Infant Hearing and the Centers for Disease Control and Prevention:  
<http://www.cdc.gov/ncbdd/hearingloss/documents/goals.pdf>

**1—Hearing Screening by 1 Month of Age**

**3—Diagnostic Audiology by 3 Months of Age**

**6—Enrollment in Early Intervention by 6 Months of Age**

The success of a hearing screening program is measured not only by the percent of babies screened but also the percent of referred babies that access diagnostic hearing testing. Since the program began in 2010, it has demonstrated steady improvements in the rate of follow-up hearing testing. With a continued focus on provider education & documentation and use of the strategies listed below, the goal is to see more and more babies receive quality and comprehensive care.



### Hospital Strategies That Improve Follow-Up

- Screening staff complete web-based training curriculum
- Nurses and hearing screeners use EHDI-approved scripts to report screen results to parents
- Discharge nurses schedule an out-patient rescreen or audiology appointment prior to hospital discharge
- Provide families with EHDI brochures and follow-up guidelines including a list of pediatric audiologists
- Ensure hearing screen results are recorded on newborn exam report
- Include accurate family contact information and Primary Care Providers (PCPs) name on monthly report to EHDI Program



### Parent Quote

"I didn't know. My friends didn't know either. Moms should be aware and need to know what the next steps are and the importance of following up. Our lack of education made it scary at first. Once we got educated it was so much more manageable."

- Amy (mother of Owen who was diagnosed at 1 month and fitted with hearing aids at 2 months.)

### "The Kudos Korner"

**Kudos to our smallest birthing hospitals: Banner Churchill, Humboldt General, Mesa View and William Bee Ririe, which provide newborn hearing screening although they are not mandated to screen due to their low birth numbers. This is a testament to their desire to follow best practice guidelines and provide quality care.**

**Responsibilities of the Nevada State Newborn Screening Program are:**

- Ensuring that newborn screening occurs for all newborn babies in the state for the disorders mandated by state regulation NAC 442.020-442.050
- Verifying that each newborn has had access to screening and if not, taking action to assure screening is available
- Providing appropriate follow up and referrals to health care providers for newborns with abnormal screening results to facilitate time sensitive repeat/confirmatory testing and treatment services
- Consulting with health care providers and sub-specialists regarding test implications and appropriate follow up actions
- Providing consultation, technical assistance, and education about the newborn screening program to hospitals, health care providers, parents/families of affected newborns, and community partners
- Collecting, analyzing, and disseminating data on newborn screening requirements, including cost effectiveness of the system and health outcome
- Evaluating outcomes of the program, ongoing quality improvement, and promoting continued access to appropriate specialty health care

**Responsibilities of the primary health care providers and facilities are:**

- Ensuring that newborn screening occurs and those results are known
- Serving as the linkage between the NBS Program and the affected newborn and family
- Being the first contact in transmitting out-of-range or invalid screening results
- Communicating the results in a knowledgeable and sensitive fashion to the families
- Serving as a resource for the families and the NBS Program
- Assisting with appropriate actions
- Facilitating repeat or confirmatory testing and appropriate sub-specialty care
- Reporting the results of the confirmatory tests and the diagnosis to the NBS Program

**Responsibilities of the families are:**

- Identifying a primary health provider (if appropriate) for result reporting by the time the newborn is discharged from the birth facility
- Providing accurate, complete demographic information, in order to facilitate follow up
- Verifying that newborn screening occurs and those results are known
- Assisting with appropriate actions taken in response to out-of-range results or invalid screening
- Participating in decision-making around possible interventions and ensuring adherence to the decided course of action

**Responsibilities of the pediatric sub-specialty providers in newborn screening follow up are:**

- Assisting with development of confirmatory and diagnostic protocols
- Assisting with confirmatory and diagnostic evaluations and other interventions
- Providing clinical/medical advice to the newborn screening program
- Collecting and sharing information for effective patient management and system evaluation
- Collaborating with primary healthcare providers to establish shared management plans in partnership with the child and family

### **Confidentiality of Newborn Screening Records:**

All personal information on the NBS forms and in the database are protected from unwarranted or unauthorized disclosure of personal information. Records are available only to persons who are authorized access by State law and supporting rules.

### **Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule:**

The HIPAA Privacy Rule recognizes the need for public health programs to access protected health information (PHI) to conduct public health activities to prevent or control disease, injury or disability. The Privacy Rule\* expressly permits release of PHI relating to newborn screening, without individual authorization, from a covered entity to state public health departments or agencies contacted, by public health departments, to provide newborn screening follow-up.

[www.cdc.gov/mmwr/preview/mmwrhtml/m2e411a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/m2e411a1.htm)

The Office of Civil Rights has oversight and enforcement responsibility of the Privacy Rule.

<http://www.hhs.gov/ocr>

### **New Rule Effective 2/3/2014- Patient's Access to Completed Laboratory Test Reports:**

The final rule announced today amends the Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulations to allow laboratories to give a patient, or a person designated by the patient, his or her “personal representative,” access to the patient’s completed test reports on the patient’s or patient’s personal representative’s request. At the same time, the final rule eliminates the exception under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule to an individual’s right to access his or her protected health information when it is held by a CLIA-certified or CLIA-exempt laboratory. While patients can continue to get access to their laboratory test reports from their doctors, these changes give patients a new option to obtain their test reports directly from the laboratory while maintaining strong protections for patients’ privacy.

<http://www.hhs.gov/news/press/2014pres/02/20140203a.html#.U020rddFDS8.email>

## **10 important points to remember about NBS:**

- 1- Please use the term “**Newborn Screening**” or “**Newborn Blood Spot Screening**”. The term “**PKU test**” is outdated and confusing to parents. The screening panel now includes markers for approximately 30 + separate disorders, the most recently added being cystic fibrosis.
- 2- Incidence of all the blood spot conditions is now one infant in 1000 or 50-70 new cases each year in Nevada (~one infant/week identified).
- 3- Screen every normal infant **TWICE**.
  - 1<sup>st</sup> screen: 24-48 hours of age or at discharge, whichever comes first;
  - 2<sup>nd</sup> screen: 10-14 days of age
- 4- Screen every **NICU infant THREE TIMES**.
  - 1<sup>st</sup>: on admission regardless of age;
  - 2<sup>nd</sup>: 48-72 hours of age;
  - 3<sup>rd</sup>: 28 days of age or at discharge, whichever comes first
- 5- Validity of screening specimens.
  - 1<sup>st</sup> screen identifies 90% of all conditions (1<sup>st</sup> and 2<sup>nd</sup> for NICU);
  - 2<sup>nd</sup>/3<sup>rd</sup> screen identifies 10% of all conditions
- 6- Goal of NBS-diagnose and treat in the first two weeks of life since:
  - ~20 disorders can kill or maim in the first week or two of life
  - 10-20% of infants will be symptomatic in the first week
  - 5-10% may die in the first week
  - Infants with hypothyroidism and PKU lose significant IQ points if thyroid stimulating hormone (TSH) and phenylalanine are not under control by 2 weeks of age
- 7- Maintain high index of suspicion for early presentation of emergent conditions:
  - Symptoms: lethargy, poor feeding, weight loss or sudden cardiopulmonary arrest
  - Five infants have died before 10 days of age in our region even with NBS. None of the diagnoses was suspected despite symptoms.
  - 1-2% of affected infants may have false positive results.
  - Screening tests are not diagnostic and affected infants may be missed. Practitioners should remain alert for signs of these conditions in infants and children regardless of the screening result.
- 8- Primary blood markers in emergent conditions:
  - Hypoketotic hypoglycemia, sudden cardiopulmonary arrest (fatty acid oxidation disorders)
  - Hyperammonemia (urea cycle disorders)
  - Acidosis (organic acidemia)
  - Abnormal electrolytes and sodium (congenital adrenal hyperplasia)
  - Reducing substances in urine, liver dysfunction (galactosemia)
- 9- If parents refuse testing, complete Newborn Screening Test Refusal Form and counsel parents.
- 10- Visit the NSPHL website: [www.med.unr.edu/nsphl](http://www.med.unr.edu/nsphl) to download information.

## **Common newborn screening misconceptions of practitioners:**

- **The diseases are so rare practitioners may advise parents not to have the screening done.**

FACT: NBS identifies 1:1,000 infants with one of the conditions included in the screening panel. Nationally, this represents 5,000 infants/year that would otherwise die or become irreversibly harmed by a late or missed diagnosis. In Nevada, 45-50 infants are identified each year, or about one infant per week.

- **Practitioners may believe the first test is of no value if obtained before 24-48 hours of age or before the infant has ingested protein or milk.**

FACT: 90 percent of affected infants have abnormal results on the first test regardless of age or food ingestion. The ability to identify infants relates to a combination of the severity of their genetic disorder, physiologic and environmental factors, the quality of their screening specimen, and the rapidity of the entire screening system to find them before they become symptomatic. There is nothing magic about a specific age cutoff as each disorder has its own “best screening window” and they are all different. Dietary intake dose make a difference in galactosemia, in that a galactosemic infant on a soy-based or other non-lactose formula would not be ingesting galactose and may have false positive results although newer laboratory assays make that less likely. Infants who are well fed may have normal acylcarnitines for fatty acid disorders. Dietary information is helpful to evaluate the significance of certain abnormal results.

- **Practitioners may believe the second screen is unnecessary.**

FACT: Approximately 11 states mandate a second screen for every infant and virtually all states recommend it if the first screen is drawn before 24 hours of age. In Nevada and other states with repeat screens, 10 percent of all infants affected are routinely found on the second screen.

Approximately four of the conditions on the screening panel may take a week or more to manifest themselves, long after an infant has been discharged and screened the first time. The efficacy of a second screen is controversial and under study by the U.S. Centers for Disease Control and Prevention.

- **Practitioners may believe the second screen is unnecessary if the first screen is collected when the infant is 5-7 days of age.**

FACT: More than 20 conditions on the screening panel can kill or maim in the first week to 10 days of life. To delay screening would mean almost certain death or disability for these infants and a test at 5-7 days is too early to pick up many of the later onset disorders. A test at the end of the first week of life is better than no test, but is probably the worst time to collect it in terms of saving infant’s lives and mental capacity.

- **Some practitioners believe the pain of specimen collection is so great for the infant that screening is not “worth it”, or that the infant will suffer permanent psychological damage.**

FACT: The pain of a heel stick can be minimized if not eliminated by using a scalpel bladed lancet device and by feeding the infant a small amount of sucrose water or breast milk before and during the procedure. Many families can attest that it is far more painful to have the infant die or to spend one’s life permanently damaged because a few drops of blood were not collected at birth.

- **Practitioners may believe newborn screening is “just a piece of paperwork” to be gotten out of the way.**  
FACT: Newborn screening represents one of the most successful public health programs ever undertaken in terms of prevention and cost savings, surpassing even immunizations. It is true that most programs do not do enough to alert practitioners to their importance and value to the screening process and to the number of infants identified.
- **Some practitioners tell parents that newborn screening is a test for “intellectual disabilities”.**  
FACT: Newborn screening tests for certain conditions that in some cases can lead to intellectual disabilities. It is by no means a test for all sources of intellectual disabilities and a normal screening result does not mean an infant will have intellectual disabilities due to other causes.
- **Many practitioners use the antiquated term “PKU test” which implies to parents that PKU is the only condition screened.**  
FACT: More than 30 separate disorders (including PKU) can now be screened for in the newborn period. PKU has not been the only disorder on most screening batteries since the mid-70s when hypothyroidism was added. The correct term is newborn screening (NBS).

## **Common misconceptions about hearing screening:**

- **Parents will know if their child has a hearing loss by the time their child is 2-3 months of age.**

FACT: Prior to the universal screening, the average age at which children were found to have a hearing loss is 2-3 years of age. Children with mild to moderate hearing loss were often not identified until 4 years of age.

- **Parents can identify a hearing loss by clapping their hands behind the child's head.**

FACT: Children can compensate for a hearing loss. They use visual cues, such as shadows or parental expressions and reactions, or they may feel the breeze caused by the motion of the hands.

- **The High-Risk Register (HRR) is all that is needed to identify children with hearing loss.**

FACT: The HRR misses approximately 50% of all children with hearing loss.

- **Hearing loss does not occur often enough to justify the use of universal screening programs.**

FACT: Hearing loss affects approximately 2-4 per 1000 live births and it has been estimated to be one of the most common congenital anomalies.

- **Tests are not reliable and cause too many infants to be referred to specialists.**

FACT: Referral rates are as low as 5-7%.

- **There is no rush to identify a hearing loss. The loss does not to be identified until a child is aged 2-3 years.**

FACT: Children identified when they are older than 6 months can have speech and language delays. Children identified when they are younger than 6 months do not have these delays and are equal to their hearing peers in terms of speech and language.

- **Children younger than 12 months cannot be fitted with hearing aids.**

FACT: Children as young as one month of age can be fit and benefit with hearing aids.

Reference: Delaney, A. M., Meyers, A. D., Ruth, R. A., Faust, R. A., & Talavera, F. (Jan 31, 2012). Newborn Hearing Screening. Retrieved from emedicine.medscape.com/article/836646-overview.

# **NEWBORN SCREENING PRACTICES AND PROCEDURES:**

## **Responsibilities for obtaining a newborn screening specimen:**

Nevada statutes detailed in NAC 442.020-442.050 require that every infant be tested, and designates that every hospital, obstetric center or person responsible for registering the birth of the child shall be responsible for specimen collection. The hospital or obstetric center must require the parent or guardian of the infant to sign a statement that he/she will take the infant to a hospital, physician, public health nurse or the State Hygienic Laboratory for the second specimen. Practitioners and midwives that deliver infants out of hospital should follow the same guidelines as hospital births.

All birthing facilities and birthing centers in Nevada are required to practice uniform discharge screening regardless of the age or feeding status. This process is done because some infants do not return for routine post-natal care and most of the tests are valid at any age. Failure to collect a specimen before discharge may result in a significant liability on both the facility and responsible practitioner if an affected infant is missed.

## **Parent refusal to have the infant screened:**

A parent may refuse screening for personal and/or religious beliefs. Parents may be influenced by the attitude of their practitioner toward newborn screening, and the majority agrees to screening if properly counseled about the importance of early detection. Infants have been harmed as a result of practitioners who have advised against screening as "the conditions were too rare", or "we don't want to poke the infant", or "the second test is not really necessary". In the event that parents are adamantly opposed to screening, it is the responsibility of the practitioner to inform them about the process and all screening conditions and to obtain a signed Newborn Screening Test Refusal (Informed Dissent) document. This document is placed in the infant's medical record with a copy given to the parents, and copies forwarded to the laboratory/follow-up and the primary care provider. Failure to do so may result in significant practitioner and facility liability if an affected infant is not screened and subsequently harmed. Unfortunately, informed dissent does not confer protection from liability, but can limit damage in some cases.

## **Infants who are never tested:**

It is estimated that approximately 1-2 percent of births are not screened because of either parental refusal or practitioner oversight or omission. For every 1 percent of newborns not screened in the United States, approximately 45-50 infants will be missed each year. These infants represent a major medical and legal liability to the program and to practitioners involved in their care. The legal awards for missed cases have been as high as \$30 million per case. Hospitals must develop a fail-safe system to ensure screening of every infant before discharge.

## **Timing of screening or proper time for specimen collection:**

There are over 20 conditions on the screening panel that can kill or maim in the first week or two of life; however, another three or four may not show any abnormal results until the second or third week of life. Improved technology in the laboratory makes the issue of milk ingestion less important than it was in the past. Specimens obtained prior to 48 hours of age are valid for most of the conditions covered on the newborn screening panel. There is, however, a statistical chance that certain amino acid and endocrine disorders, urea cycle defects and FAO disorders may be missed.

### **Normal Newborns:**

In Nevada, all infants must have two specimens. For normal, non-premature infants, the first specimen should be collected before discharge, ideally between 24-48 hours and no later than five days of age. These recommendations are earlier than the Nevada Administrative Rules currently specify, but due to the number and severity of emergency metabolic conditions and CAH, an earlier specimen is preferable. A second specimen must be collected between 10-14 days of age on all infants.

### **Premature, Low Birth Weight or Sick Infants:**

All Neonatal Intensive Care Units (NICU) in Nevada are strongly urged to practice “admission screening” before any non-respiratory therapy is started. In some cases, the infants may only be minutes or a few hours old. This is followed by a second specimen between 48-72 hours of age and a third specimen at 28 days or at discharge, whichever comes first. A special three-part kit is available for NICU infants.

### **Dying Infants:**

If an infant is likely to die, especially if there is no apparent cause for death, it is appropriate to collect a newborn screening specimen. In addition, collect a urine specimen, which should be frozen immediately. While dying infants may have abnormal amino acids as a normal response to organ failure, the blood may also provide a diagnosis of an early onset screening disorder or be a source of DNA for future diagnostic studies. In many cases, the blood spots have been the only source of DNA available for that infant and have been a valuable resource for families.

### **Older Infants:**

The American Academy of Pediatrics recommends that physicians know the screening status of every child in their care. Older infants and children may enter the practice without evidence of screening, or the physician may be suspicious of a screenable condition. Unfortunately, laboratories have established standards and cutoffs for newborns and infants only up to six months of age. Hence, these values are neither applicable nor reliable for older infants and children. In these cases, it is best to proceed directly to diagnostic testing if there are signs or symptoms of a metabolic disorder present in the child.

# **Recommendations for Timeliness in Newborn Screening**

## **(March 2015)**

The following recommendations were approved in February by the Advisory Committee for Heritable Disorders in Newborns and Children (ACHDNC) Laboratory Standards and Procedures Subcommittee.

1. Presumptive positive results for time-critical conditions should immediately be reported to the child's healthcare provider and no later than 5 days of life.
2. All presumptive positive results for time-sensitive conditions should be reported to the healthcare provider as soon as possible but no later than 7 days of life.
3. All NBS results should be reported within 7 days of life ("Normal" screening results).
4. In order to achieve these goals (and reduce delays in newborn screening):
  - Initial NBS specimens should be collected in the appropriate time frame for the baby's condition but no later than 48 hours after birth.
  - NBS specimens should be sent to the Laboratory as soon as possible; ideally within 24 hours of collection.

<https://www.newsteps.org/news-and-education/news/update>

## **NSPHL workflow:**

- All specimens with normal results are reported within 24 hours
- Specimens with abnormal results are repeated the next day and reported within 36-48 hours
- For critical results, submitters and PCPs are notified as soon as results are available
- Average TAT for all specimens: 1.83 working days

# DOUBLE KIT

 <b>EXPIRATION</b> <b>2018-80</b> <b>LOT</b> <b>104588 / 315135</b>	<p style="text-align: center;"><b>Original Kit Number</b></p> <p style="text-align: right;"><b>Affix Contact Label Here</b></p> <p><b>Collection/Reporting Information</b></p> <p>Birth Hospital: _____ Code: _____      Collection Facility: _____ Code: _____      Collection Address: _____      Report To Physician/Clinic: _____ Code: _____      Physician's Address: _____      City, State, Zip: _____</p> <p><b>Mother/Guardian's Information</b></p> <p>Name: _____ Last: _____ First: _____      Date of Birth: _____ / _____ / _____ Maiden: _____      Street Address: _____      City, State, Zip: _____      Phone: (_____) _____      Emergency Contact Phone: (_____) _____      Father's Name/Phone: _____</p>	<p style="text-align: right;"><b>Affix Accession Label Here</b></p> <p style="text-align: right;"><b>State Lab Use Only</b></p>
<p><b>Newborn Screening Supplemental Element Screening Form</b></p> <p>New York State Public Health Laboratory, Albany, NY 12204-3655      New York State Department of Health, Albany, NY 12204-3655</p> <p style="text-align: center;"><b>NV</b></p>		
 <b>EXPIRATION</b> <b>2018-80</b> <b>LOT</b> <b>104588 / 315135</b>	<p style="text-align: center;"><b>Original Kit Number</b></p> <p style="text-align: right;"><b>Affix Contact Label Here</b></p> <p><b>Collection/Reporting Information</b></p> <p>Birth Hospital: _____ Code: _____      Collection Facility: _____ Code: _____      Collection Address: _____      Report To Physician/Clinic: _____ Code: _____      Physician's Address: _____      City, State, Zip: _____</p> <p><b>Mother/Guardian's Information</b></p> <p>Name: _____ Last: _____ First: _____      Date of Birth: _____ / _____ / _____ Maiden: _____      Street Address: _____      City, State, Zip: _____      Phone: (_____) _____      Emergency Contact Phone: (_____) _____      Father's Name/Phone: _____</p>	<p style="text-align: right;"><b>Affix Accession Label Here</b></p> <p style="text-align: right;"><b>State Lab Use Only</b></p>
<p><b>Newborn Screening Supplemental Element Screening Form</b></p> <p>New York State Public Health Laboratory, Albany, NY 12204-3655      New York State Department of Health, Albany, NY 12204-3655</p> <p style="text-align: center;"><b>NV</b></p>		

## **Completing the blood spot specimen card:**

The requested information on the newborn screening specimen card is critical to interpreting test results and follow up therefore **ALL fields must be filled out completely and accurately**. Demographic data should be completed before the blood is drawn to avoid contamination of the specimen. Print legibly in capital letters and neatly using black ink.

**QUALITY ASSURANCE TIP: Double check that ALL fields are complete, accurate, legible, and quality of the blood spots prior to being sent to testing laboratory.**

### **STEP-BY-STEP INSTRUCTIONS:**

- 1- **KIT ID#:** This is a unique identifier number used to identify infant and to link first and second specimens in the data system.
- 2- **PARENT REFUSED TESTING:** Check the box if a parent/guardian refuses the newborn screening test. Have the parent/guardian sign the Newborn Screening Test Refusal Form (Informed Dissent) and give them a copy. Reason for refusal field must be completed on the form. The original should be placed in the infant's medical record and copies forwarded to the NV NBS Program and infant's primary care provider. Proceed with completing the demographic information on the card as you would if blood had been collected. Submit the card along with the signed refusal form to the laboratory.
- 3- **ADOPTED:** Check the box if infant is being adopted and record the adoption agency or guardian's contact info on the newborn screening card. Record the infant's adoptive name (if known) on the card. This expedites follow up in case of abnormal screening results and avoids calling the birth mother if she is no longer responsible for the infant.
- 4- **DECEASED:** Check the box if the baby is deceased. Proceed with completing the demographic information on the card as much as possible and submit the card to the laboratory. Notify NBS FU Coordinator or laboratory if an infant death occurs to prevent unnecessary notification of parents regarding subsequent screening or confirmatory testing.
- 5- **FIRST SCREEN, SECOND SCREEN, OTHER:** Check appropriate box to indicate if newborn screening specimen is a first or second screen. Check OTHER in situations such as 3<sup>rd</sup> screen, NICU, etc.
- 6- **INFANT'S NAME:** Record infant's last name followed by first name. If no name is available at the time of specimen collection, the last name followed by "boy" or "girl" should be used. **DO NOT LEAVE BLANK.**
- 7- **INFANT'S BIRTH DATE:** Use an eight-digit number (mm/dd/yyyy) for date of birth. For example, a birth on March 20, 2014 would be recorded as 03/20/2014. This information along with the infant's time of birth is used for accurate interpretation of screening results.
- 8- **INFANT'S BIRTH TIME:** Record time of birth in military time. For example, a birth at 1:30 pm is recorded as 1330. This information is used to determine if the newborn specimen was collected within the appropriate collection timeframe and in conjunction with #7.

9- **INFANT'S BIRTH WEIGHT:** Record the birth weight preferably in grams or alternatively in pounds and ounces. This information is necessary in determining testing cutoff values and interpreting the screening results.

10- **GENDER:** Check the appropriate box to designate newborn's gender as male or female. This information is used for accurate interpretation of screening results.

11- **DATE OF SPECIMEN COLLECTION:** Use an eight-digit number (mm/dd/yyyy) representing the date on which the specimen was obtained. This date establishes the parameter determining whether the specimen was received within the acceptable timeframe for testing. Enzymes and metabolites begin to break down as soon as the specimen is drawn. The older the specimen when received for testing, the less likely the level of enzymes and metabolites will be accurate.

12- **SPECIMEN COLLECTION TIME:** Record time of specimen collection in military time. Screening results are based on the age of the infant at the time of specimen collection.

13- **INFANT'S CURRENT WEIGHT:** Record the current weight at the time of collection preferably in grams or alternatively in pounds and ounce. This information is necessary in determining testing cutoff values and interpreting the screening results.

14- **PERSON RESPONSIBLE FOR SPECIMEN COLLECTION:** The card is a legal document hence record name or initials of person collecting the specimen. In addition, this information may be used for quality assurance activities such as staff re-training in proper specimen collection especially in unsatisfactory specimens resulting in repeat specimen collection.

15- **MEDICAL RECORD NUMBER:** Record the infant's medical record number established by the birth hospital. This information is used for identification and reference purposes.

16- **SINGLE BIRTH:** Check appropriate box to indicate single birth. **MULTIPLE BIRTHS:** Check appropriate box for multiple births, circle A, B, C, D, etc. to record birth order. For example, birth order is important if baby is one of a set of multiples such as twins, triplets, etc. Names alone may not be enough to link multiple specimens in the data system.

17- **RACE:** Check all that applies for one or more of the five racial categories. As well, check box to indicate Hispanic or Non-Hispanic. This information is used for accurate interpretation of testing results and is useful for profiling disorders and gene variations by ethnicity.

18- **FOOD SOURCE:** Check appropriate box for infant's food source in the last 24 hours. Some testing methodologies are impacted by feeding time.

19- **GESTATIONAL WEEKS:** Record weeks of gestation at time of birth and **NOT** the current age. Gestation is the period between conception and birth and measured in weeks. This information is important as it directly affects the medical treatment plan for example- infants born premature.

**MECONIUM ILEUS:** Check appropriate box for Meconium Ileus or other bowel obstruction.

**NICU/SPECIAL CARE NURSERY:** Check appropriate box if NICU baby.

**TRANSFUSION:** If the infant has had a transfusion, check the box and record the date of the most recent transfusion. Transfusions may require repeat testing and can invalidate tests results in hemoglobinopathies, galactosemia, and biotinidase.

- 20- **BIRTH HOSPITAL NAME/CODE:** Record full name of birth hospital and assigned hospital code. This information is used to determine where the first screening results are to be sent, helps identify a baby from another born on the same day with the same last name, and as a reference source for additional information as needed.
- HOME BIRTHS-** Midwives or others in attendance of a home birth are responsible for specimen collection or alternatively arrange for specimen collection within the appropriate period. Record "HOME" in this field on the specimen card.
- 21- **COLLECTION/SUBMITTER FACILITY:** Record the full name and address of the collection facility or submitter (this should be the birth hospital or midwife on all initial newborn screens) and assigned code. Same principle as stated in #20.
- 22- **PROVIDER/CLINIC NAME:** Record full name (last, first) or clinic name and address of the primary care physician that will be responsible for the infant **AFTER** discharge. This information distinguishes providers with the same name and the clinic where provider is located. Do **NOT** list the physicians such as Hospitalist or Neonatologist who cared for the infant in the hospital. If the infant is in NICU, the hospitalist/birth unit may be listed as the physician-of-record and assumes that responsibility until a provider accepts care of the infant. Please ensure that the provider's information is accurate and complete for rapid follow up of abnormal screening result(s).

- 23- **MOTHER/GUARDIAN'S INFORMATION:** Record mother's last name followed by first name. As well, record mother's maiden name. For single mothers, the last name and maiden name may be the same. This information is used for identification/linking purposes. Record mother's date of birth (mm/dd/yyyy), current address, phone number including area code, and emergency contact number including area code. Record father's full name and phone number including area code. If infant is going to be released at birth to adoptive parents or guardian, provide contact information for them- full name, phone number including area code, and address. This information is important and critical for prompt follow up on infants in need of retesting or diagnostic testing.

**Completing the miscellaneous or single blood spot specimen card:**

Miscellaneous or single specimen cards are used as replacement for inadequate specimens, recall specimens, or when the second part of a double or original kit issued to the parent at the hospital/birthplace has been lost.

- 1- All data fields must be completed. Refer to step-by-step instructions.
- 2- Check the box to indicate if this is a first or second screen.
- 3- Keep in mind the kit number on the single specimen card will not be the same as the original kit number. For linking purposes, enter the original kit number of the baby's initial screen if known under OTHER or on the left edge of the card. If need be, call the hospital nursery to ask for the original kit number.

## **Instructions for proper specimen collection:**

1. To prevent specimen contamination, do not touch any part of the filter paper circles before, during, or after collection. Multiple agents can contaminate filter paper.
2. Identify infant and match with correct screening kit. Make sure to collect the correct kit part (1, 2, and 3) depending on which specimen is being collected.
3. Complete all demographic data before proceeding to collection.
4. Observe universal precautions.
5. Capillary blood obtained from a heel lance is the preferred specimen. Cord blood is not a satisfactory specimen as the infant's biochemistry will not be reflected. Specimens obtained from peripheral or central lines are acceptable if they are flushed of parenteral nutrition or antibiotics. Blood from an intravenous stick is acceptable as long as it does not clot and can be applied to the filter paper directly.
6. It is essential to open a capillary bed to obtain sufficient blood. The most effective method is to use scalpel bladed lancets manufactured specifically for heel sticks in infants. Pointed lancets are painful to the infant and make a hole rather than a small slit, greatly reducing blood flow. Under no circumstances should a lancet longer than 2.0 mm be used on infants weighing less than 2,500 grams.
7. As per your institution's protocol, heat infant's foot if necessary in warm water, towel, or chemical pack. Heat source should not exceed 42 degrees centigrade and should not be left in contact with skin for a prolonged period.
8. Select a lance site on the infant's heel (see diagram), cleanse with alcohol and air dry. Hold infant's limb lower than the heart.
9. Lance the heel with the sterile scalpel bladed lancet. Wipe away the first drop of blood to remove tissue fluids. Do not milk the heel. If blood flow is insufficient, it is better to stop and re-lance the heel.
10. Allow sufficient blood to collect on the heel to fill each circle by a single application to the filter paper. Do not use capillary tubes or other collection devices. Apply blood only to one side of the filter paper (it does not matter which side is used). Blood should soak all the way through the filter paper so that the blood spots look similar on both sides. Complete, even saturation of the entire circle is essential for accurate testing. Neatness does not count.
11. It is important not to superimpose blood drops on top of each other. Let each drop touch the paper about 1/8 inch away from each other. This may prevent layering and uneven saturation, one cause of false results.
12. Collect the blood in all five circles. A minimum of three circles is necessary to complete the screening battery. If there are problems with sufficient blood flow, it is better to fill three circles completely than to fill five circles inadequately.
13. After circles are filled, the foot should be elevated above the heart and a sterile gauze pad or cotton swab pressed against the puncture site until the bleeding stops. Bandages should be avoided as they may irritate sensitive skin.
14. Air-dry specimens at room temperature for 2-4 hours in a horizontal position with the blood spots exposed. A CD holder works well. Hanging wet specimens will cause heavier red cells to migrate to the dependent end of the circle resulting in uneven saturation.
15. Do not expose the specimen to heat or humidity at any time. Do not dry on a heater, in a microwave, with a hair dryer or in sunlight. Do not place in plastic bags, leave in a hot mailbox or in a hot car; proteins and enzymes will be destroyed. Ensure that each specimen is completely dry before mailing. In hot weather, desiccant packets may be added to reduce humidity during transit.

16. Do **NOT** batch specimens collected over several days as infants affected with emergent disorders may die before results can be made available. Specimens can be sent in the same package, but there must be a daily mail or courier pick up for all specimens.
17. Insert dried specimens into an envelope (do not use plastic), seal and mail within 4-12 hours of collection and no later than 24 hours after collection. Weekend and holiday specimens should be stored at room temperature and sent by overnight mail or courier at the earliest opportunity. All specimens should be sent by first class or overnight mail or by courier. Specimens should be received by the Lab within 12-48 hours of collection.
18. Specimens should be documented as sent. If by a courier, a packing list should be kept and the courier should sign for pickup and delivery of specimens. This step protects the hospital from liability in the event the specimen is lost in transit.

\*These recommendations conform to the CLSI publication LA4-A5.

#### **Importance of linking specimens:**

The Newborn Screening Kit ID number is a single unique number assigned to each infant at time of birth. This number is used to identify each infant and serves as a linking mechanism for the newborn screening data. Linking issues occur when information provided is different on the two specimen cards. This may result in unnecessary collection of an additional specimen, delay in testing and results reporting, and treatment for affected infants when there are abnormal results.

#### **Proper storage of newborn screen specimen cards (prior to use) and expiration date:**

Storage area should be cool, clean, and dry. Specimen cards should be placed in an upright or vertical position **NOT** horizontal and stacked on top of each other. Improper storage can result in compression of the filter paper fibers that can interfere with the absorption of the blood and test results. Likewise, the absorption of ambient moisture in the air can affect the filter paper. The newborn screening specimen card is a Food and Drug Administration (FDA) regulated form and has a shelf life of 3 years after printing. Pls. note expiration dates and do **NOT** use after expiration date.

#### **Specimen transport:**

If lives are to be saved, it is critically important that the NSPHL receive newborn screening specimens as soon as possible after collection. Ideally, specimens should be mailed or transported as soon as they are dried (2-4 hours) and no later than 24 hours after collection. Consideration should be given to the use of overnight courier or mail services if specimens are taking longer than 2-3 days to arrive at the laboratory. If a courier is used, it is advisable to establish a list of specimens sent and to document the time of specimen pick-up and delivery. This protects the submitter if specimens are lost in transit.

Specimens collected on Saturday, Sunday or Monday or Friday holidays are best stored in a cool room and sent express or overnight mail at the first opportunity as NSPHL is not open on weekends or observed holidays.

The importance of early sample collection and prompt transit is illustrated by the fact the infants with galactosemia, organic acidemias and fatty acid oxidation disorders may die within a week or two of birth. Enzyme activity and hemoglobin may be destroyed or diminished in specimens that are older than 10 days or exposed heat and humidity.

**Retention of blood spots:**

The newborn screening specimen card is kept between 6-12 months from the date of submission to NSPHL then destroyed. The newborn screening specimen card and health records are protected by law (NRS 629.101-110, Genetic Information) and as such cannot be used for purposes other than newborn screening except as allowed by law.

**NBS fee:**

Nevada's NBS Program historically is funded through birth registration fees as detailed in NAC 440.210. Nevada's birthing facilities submit these fees monthly to the Nevada State Health Division for each child born at their facility. As of 3/1/2014, the birth registration fees was increased to \$81.00 if paid or on before the 30<sup>th</sup> day after the infant's date of birth or \$83.00 if paid later. These fees support 100% of the cost of the NBS Program that includes program staff, laboratory testing, short-term follow- up, and medical consultation to Nevada's primary care physicians. In addition, these fees fund specialty clinics for children with metabolic disorders. Regulation amendment proposal to redact the NBS fee from the birth registry fee was submitted to State Board of Health and adopted at a public hearing held on 9/9/2016. Effective 11/2/2016, NSPHL has authority over the NBS program and fee implementation and currently exploring financial alternative(s) for long-term sustainability of the NBS program.

**Quality Assurance/CQI:**

A quality assurance surveillance program is currently in place for ongoing quality improvement of the screening practices within the state. Screening Practice Profiles are provided on a monthly basis to hospitals and birth facilities in Nevada that monitors transit time, inadequate specimens, demographic omissions, and timing errors. It is recommended that hospitals/birthing facilities consider an in-house coordinator for NBS quality assurance activities and point-of-contact with the NBS program. Hospital quality assurance activities may include maintaining inventory of NBS supplies, educating staff in areas that need improvement based on monthly practice profile report, maintain tracking logs for specimens, and courier pick-up logs.

It is recommended that facilities provide orientation sessions about newborn screening to all new employees that include review of this newborn screening guide as well as individual refreshers as needed. In addition, the NBS staff upon request can provide in-service presentations for specific topics. Likewise, NSPHL staff and Follow-Up Coordinator are available by phone and/or e-mail for assistance.

# Laboratory Testing Methods:

**National Newborn Screening and Genetics Resource Center's 29 Core Conditions Recommended for Newborn Screening**

<u>Disorder</u>	<u>Method of Testing</u>
<b>Endocrine Disorders</b>	
1. Congenital Adrenal Hyperplasia	Fluorometric
2. Congenital Hypothyroidism	Fluorometric
<b>Hemoglobin Disorders</b>	
3. Sickle Cell Disease S/S	HPLC
4. Sickle Cell Disease S/C	HPLC
5. Thalassemia Major	HPLC
<b>Metabolic Disorders</b>	
6. Biotinidase Deficiency	Colorometric
7. Galactosemia	Beutler &Hills
<b>Amino Acid Disorders</b>	
8. Argininosuccinate Lyase Deficiency (ASA)	TMS
9. Citrullinemia	TMS
A. Classic Citrullinemia	TMS
B. Citrullinemia Type II	TMS
10. Homocystinuria	TMS
12. Hyperphenylalanemia, including Phenylketonuria	TMS
13. Tyrosinemia	TMS
A. Tyrosinemia, Type 1	TMS
B. Tyrosinemia, Type 2	TMS
<b>Organic Acid Disorders</b>	
14. Beta-Ketothiolase Deficiency	TMS
15. Glutaric Aciduria, Type I (Glutaryl-CoA Dehydrogenase Deficiency)	TMS
16. Isovaleryl-CoA Dehydrogenase Deficiency (Isovaleric Acidemia)	TMS
17. Maple Syrup Urine Disease	TMS
18. Methylmalonic Acidemia (MMA; 8 types)	TMS
19. A. Methylmalonic Aciduria, Vitamin B-12 Responsive	TMS
20.	
B. Methylmalonic Aciduria, Vitamin B-12 Nonresponsive	TMS
C. Vitamin B12 Metabolic Defect with Methylmalonicacidemia and Homocystinuria	TMS
D. Propionic Acidemia (PA)	TMS
21.	
3-methylglutaconyl-CoA Hydratase Deficiency	TMS
A. 3-methylglutaconyl-CoA Aciduria Type I	TMS
B. 3-methylglutaconyl-CoA Aciduria Type II	TMS
C. 3-methylglutaconyl-CoA Aciduria Type III	TMS
D. 3-methylglutaconyl-CoA aciduria Type IV	TMS

22. Multiple Carboxylase Deficiency	TMS
<b>Fatty Acid Oxidation Disorders</b>	
23. Carnitine Uptake/Transporter Defects	TMS
A. Carnitine-Acylcarnitine Translocase Deficiency	TMS
B. Carnitine Transporter Defect	TMS
C. Carnitine Palmitoyl Transferase I Deficiency (CPT I)	TMS
D. Carnitine Palmitoyl Transferase II Deficiency (CPT II)	TMS
24. Glutaric Aciduria, Type II (Multiple Acyl-CoA Dehydrogenase Deficiency (MADD))	TMS
25. Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD)	TMS
26. Long Chain L-3 Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHADD)	TMS
27. Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD)	TMS
28. Short Chain Acyl-CoA Dehydrogenase Deficiency (SCADD)	TMS
29. Cystic Fibrosis	IRT

\*TMS = Tandem Mass Spectrophotometer

\*HPLC = High Pressure Liquid Chromatography

\*IRT = Immunotrypsinogen Testing

**Laboratory Information Systems Used:**

Perkin Elmer Specimen Gate and Patient Care

Hemoglobinopathies- IEF

T4/TSH/IRT/17-OHP- Delfia Fluorometry

Galt/Biotinidase- Victor Fluorometry

Metabolic Disorders- Tandem MS/MS

## MENU: SUPPLEMENTAL TESTING FROM PKI GENETICS (JUN 2014)

DISORDER	1° MARKER	2° MARKER	METHODOLOGY	TAT	Notes:
<b>CAH</b>	17-OHP	Extracted 17-OHP	Immuno fluourescence	72 hours	Eliminates interferences; reduces false positives.
<b>Galactosemia</b>	Total Galactose	Gal-1-Phosphate	Colorimetric	48 hours	Useful to differentiate epimerase & kinase deficiency from UT def.; Total Gal. >15 ug/dL
<b>Galactosemia</b>	Uridyltransferase	UT Mutations	DNA	48 hours	Q188R, S135L, K285N, L195P, N314D
<b>Cystic Fibrosis</b>	IRT	CFTR Mutations	DNA - Luminex	72 hours	39 mutation panel that includes the 23 recommended by ACOG/ACMG
<b>Hemoglobinopathies</b>	IEF Pattern	Hgb Mutations	DNA	48 hours	Hb S, Hb C, Hb E, Hb D & Hb O $\beta$ Thal. - 29A>G,-88C>T & IVS1+6T>C
<b>Biotinidase Deficiency</b>	Biotinidase	Biotinidase Mutations	DNA	48 hours	G98:d7i3, Q456H, R157H, R538C, D252G, D444H, D444H;A171T, D444H;F403V, D444H;R157H
<b>MCAD</b>	C8	MCAD Mutations	DNA	48 hours	A985A>G, 199T>C
<b>LCHAD</b>	C18;1OH, C16OH, C18OH	LCHAD Mutation	DNA	48 hours	1528G>C
<b>Glutaric Acidemia 1</b>	C5 DC	GA1 Mutations	DNA	48 hours	A421V, R402W
<b>Propionic Acidemia</b>	C3	PPA Mutations	DNA	48 hours	E168K, 1218del14/ins 12, 1170insT
<b>Methylmalonic Acidemia</b>	C3	MMA Mutations	DNA	48 hours	N219Y, G717V
<b>MSUD</b>	Leucine	MSUD Mutation	DNA	48 hours	Y438N
<b>Isovaleric Acidemia</b>	C5	IVA Mutation	DNA	48 hours	A282V
<b>3-Methylcrotonyl-CoA Carboxylase Deficiency</b>	C5OH	3-MCC Mutation	DNA	48 hours	518insT

- TAT Estimates do not include weekends and Holidays

# Conditions included in the Nevada screening panel:

Nevada newborns are screened for the following 31 core and 29 secondary conditions recommended by the College of Medical Genetics and the March of Dimes. The purpose of newborn screening is to identify infants at risk that require more definitive testing. As with any laboratory test, both false negatives and false positive results are possible.

**Screening test results are insufficient information on which to base diagnosis or treatment.**

- Cystic Fibrosis\*

**Endocrine Conditions:**

- Congenital adrenal hyperplasia (CAH)\*±
- Congenital hypothyroidism\*

**Hemoglobin Conditions:**

- Sickle cell disease and other hemoglobinopathies\*

**Metabolic Conditions:**

**Amino Acid Conditions:**

- Homocystinuria\*
- Hyperphenylalanemia including phenylketonuria (PKU)
- Tyrosinemia\*

**Fatty Acid Oxidation Conditions:**

- Carnitine uptake defect
- Carnitine palmitoyl transferase I deficiency (CPT I)\*
- Carnitine palmitoyl transferase II deficiency (CPT II)
- Multiple acyl-CoA dehydrogenase deficiency (MADD)
- Short chain acyl-CoA dehydrogenase deficiency (SCAD)
- Medium chain acyl-CoA dehydrogenase deficiency (MCAD)±
- Long chain 3 hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)\*±
- Very long chain acyl-CoA dehydrogenase deficiency (VLCAD)\*±

**Organic Acid Conditions:**

- Beta-ketothiolase deficiency (BKD)±
- Glutaric acidemia, Type I (GA I)\*
- Isobutyryl CoA dehydrogenase deficiency (IBD)±
- Isovaleric acidemia (IVA)\*±
- Malonic aciduria
- Maple syrup urine disease (MSUD)±
- Methylmalonic acidemias (MMA/8 types)±
- Propionic acidemia (PA)\*±
- 3-Hydroxy-3-methylglutaryl CoA lyase deficiency (HMG)\*
- 2-Methyl-3-hydroxybutyryl CoA dehydrogenase deficiency (MBHD)\*
- 2-Methylbutyryl CoA dehydrogenase deficiency (2MBC)\*
- 3-Methylcrotonyl CoA carboxylase deficiency (3MCC)
- 3-Methylglutaconyl CoA hydratase deficiency (3MGH)
- Multiple carboxylase deficiency

**Urea Cycle Conditions:**

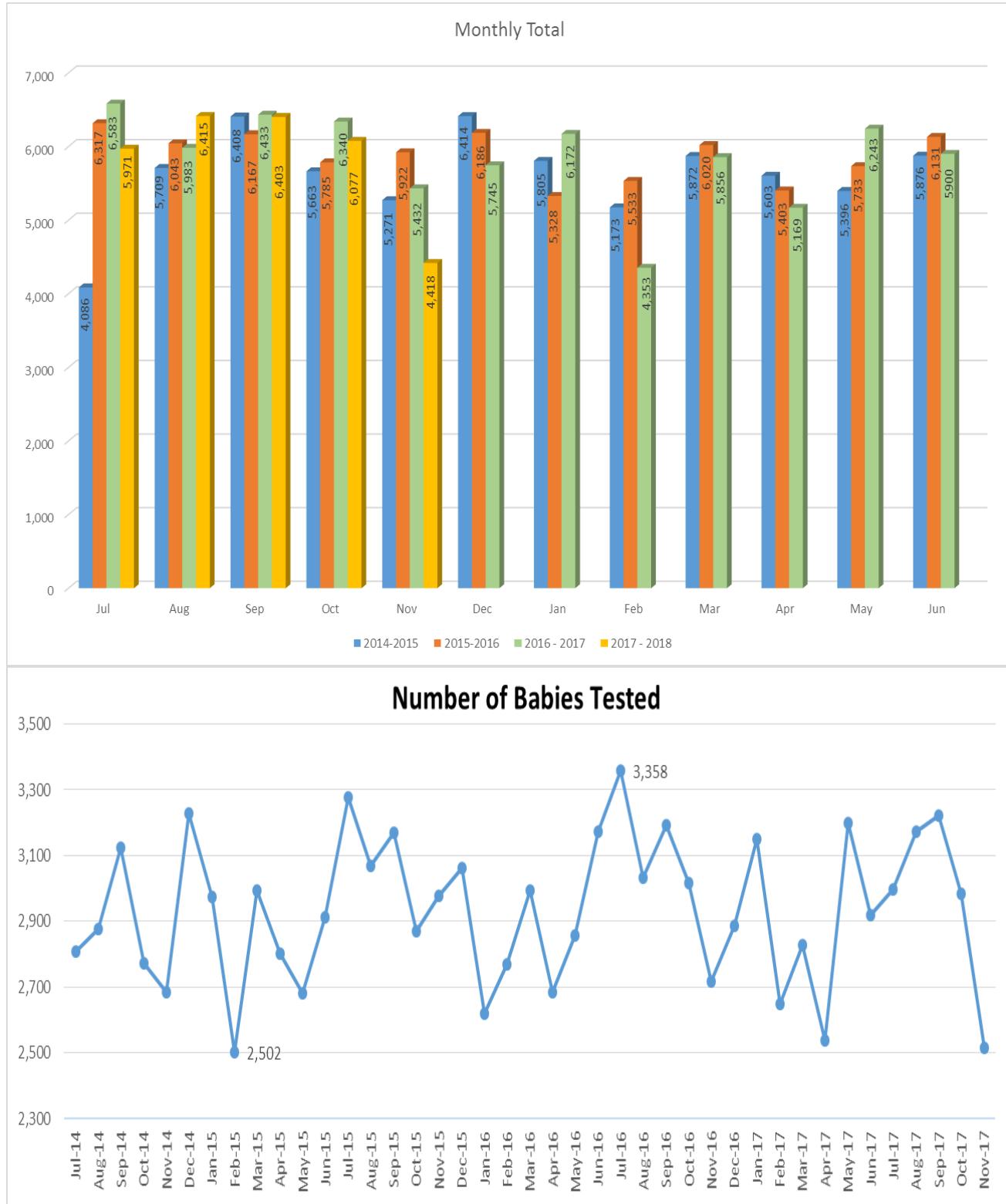
- Arginase deficiency
- Argininosuccinate lyase deficiency (ASA)±
- Citrullinemia±

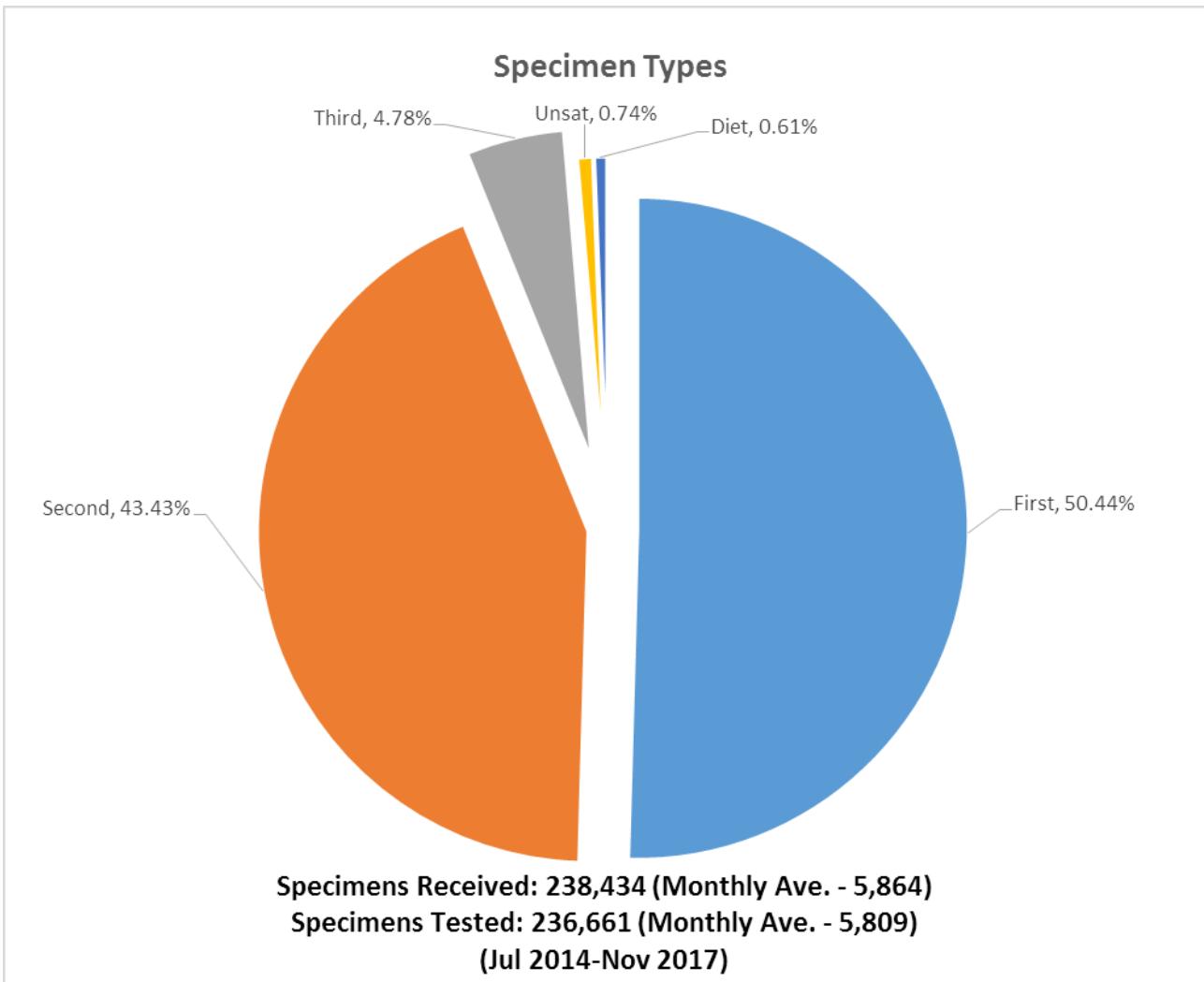
**Other Conditions:**

- Biotinidase deficiency
- Galactosemia±
- Newborn hearing loss
- Critical Congenital Heart Disease (CCHD)- started 7/1/2015
- Severe Combined Immunodeficiency (SCID)- to start January 2018

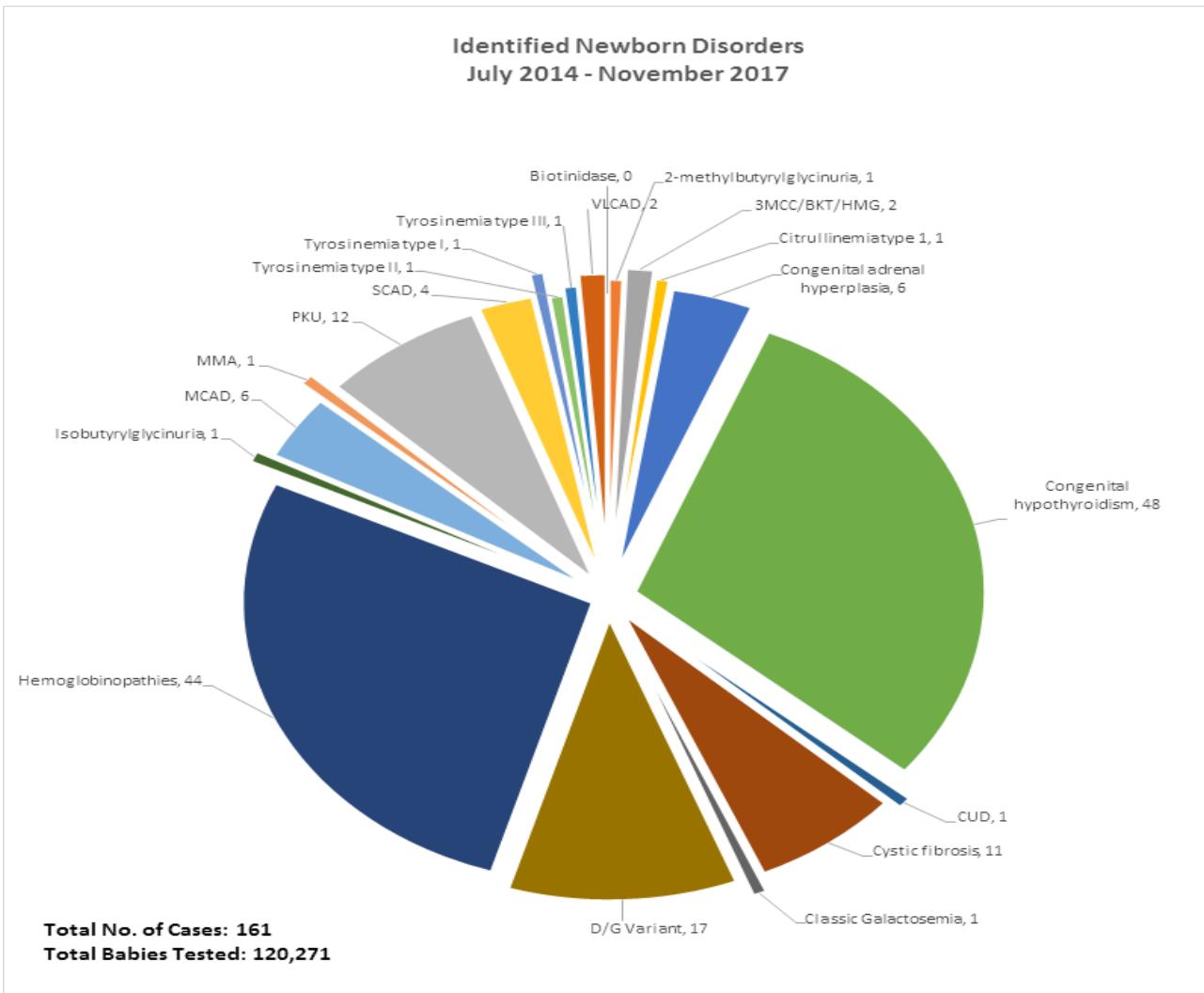
\* The screening test will not detect 100 percent of affected infants. ± Represent emergent conditions, infants are at risk of illness or death in the first week of life or two.

## MONTHLY SAMPLES RECEIVED FROM JULY/2014 TO NOVEMBER/2017





	<b>First</b>	<b>Second</b>	<b>Third</b>	<b>Unsat</b>	<b>Diet</b>	<b>Total</b>
<b>Jul-2014 to Jun-2015</b>	<b>34,363</b>	<b>28,507</b>	<b>3,146</b>	<b>875</b>	<b>368</b>	<b>67,259</b>
	51.09%	42.38%	4.68%	1.30%	0.55%	
<b>Jul-2015 to Jun-2016</b>	<b>35,525</b>	<b>30,640</b>	<b>3,472</b>	<b>406</b>	<b>465</b>	<b>70,508</b>
	50.38%	43.46%	4.92%	0.58%	0.66%	
<b>Jul 2016 to Jun 2017</b>	<b>35,490</b>	<b>31,136</b>	<b>3,355</b>	<b>343</b>	<b>453</b>	<b>70,777</b>
	50.14%	43.99%	4.74%	0.48%	0.64%	
<b>Jul 2017 to Nov 2017</b>	<b>14,893</b>	<b>13,258</b>	<b>1,424</b>	<b>149</b>	<b>166</b>	<b>29,890</b>
	49.83%	44.36%	4.76%	0.50%	0.56%	



Confirmed Cases	
Biotinidase	0
2-methylbutyrylglycinuria	1
3MCC/BKT/HMG	2
Citrullinemia type 1	1
Congenital adrenal hyperplasia	6
Congenital hypothyroidism	48
CUD	1
Cystic fibrosis	11
Classic Galactosemia	1
D/G Variant	17
Hemoglobinopathies	44
Isobutyryl glycinuria	1
MCAD	6
MMA	1
PKU	12
SCAD	4
Tyrosinemia type I	1
Tyrosinemia type II	1
Tyrosinemia type III	1
VLCAD	2
<b>Total</b>	<b>161</b>

## Ordering NBS specimen kits:

Fax kit order to: Nevada State Public Health Laboratory  
1660 N. Virginia Street, MS 0385  
Reno, NV 89557  
Phone: 775-682-6238  
**Fax: 775-327-5117**

TWO-PART KIT<sup>a</sup> (first and second screen kit) is the initial form used by hospitals/birthing centers where baby was born and issued to the parent at the hospital/birthplace.

THREE-PART KIT<sup>b</sup> (Triple kit or NICU kit) is used by hospitals/birthing centers' NICU for Pre-term, Low Birth Weight, and Sick Newborns.

SINGLE<sup>c</sup> (miscellaneous kit) is used as replacements for inadequate specimens, recall specimens, or for use when the second part of a double or original kit is lost

**Color codes:**

- <sup>a</sup> blue/green, canary-submitter's copy
- <sup>b</sup> blue/green/purple, canary-submitter's copy
- <sup>c</sup> red, canary-submitter's copy

Facilities should submit kit orders at least two weeks in advance before they run out of kits. Orders are shipped by ground or next business day. Make sure your facility has a system for receiving and maintaining inventory of cards.

**Note: All kits are pre-coded for the specific individual/facility and must not be loaned to or borrowed from other facilities. Three-part kits are available only to NICU's.**

## **NEWBORN SCREENING PROGRAM FOLLOW- UP PROCEDURES:**

### **Reporting of results:**

Screening test results are sent to the submitter of the specimen card and filed in the infant's medical chart. If the infant has been discharged, the hospital/birthing center/midwife shall forward the screening results to the infant's PCP promptly especially in abnormal/unsuitable results. As well, the NBS Follow-Up Coordinator shall contact the PCP regarding abnormal result(s) and recommendations for further action.

### **Normal results:**

Normal results are reported within 24 hours and auto-faxed Monday-Friday to hospitals and to the physician-of-record.

### **Presumptive positive results:**

Presumptive positive results are considered urgent and reported to the Newborn Screening Follow-Up Coordinator who will immediately phone the submitting hospital or practitioner with recommendations for further action. The appropriate sub-specialty provider is simultaneously contacted as well for further instructions. Such action is followed by fax to the primary care provider to assure prompt receipt and include NBS results, action required, condition specific information, instructions for confirmatory testing, and sub-specialist contact information and additional instruction as needed. These cases are followed to ensure confirmatory testing is completed, diagnosis confirmed or ruled out, and affected infants referred to appropriate disorder specialist for treatment.

### **Borderline results and repeats:**

Borderline abnormalities are reported immediately by phone or fax to the submitting hospital and/or practitioner with a request for retesting. It is the practitioner's responsibility to ensure that all infants with abnormal results are retested; all such infants are also tracked by the laboratory and/or the NBS Follow-Up coordinator until a resolution or diagnosis is confirmed. State health agencies are notified for assistance when there are problems in obtaining repeat tests for infants with abnormal results.

### **Unsatisfactory results and repeats:**

Unsatisfactory specimens such as uneven saturation, quantity not sufficient, early, or contaminated specimens represent unscreened babies and legal liability risk for the hospital/provider. Unsatisfactory specimens will generate an automatic fax or phone request for a retest. As well, hard copies are mailed to the practitioner. It is important for providers to respond promptly upon notification to ensure no further delay in screening.

### **Request for information:**

Missing key data in the specimen card and/or illegible handwriting will require a follow up phone call to submitter to obtain the necessary information. This is time consuming and delays results therefore it is important to submit specimen cards with all data fields completed.

For long-term follow-up/tracking purposes, the NBS program may contact the health care provider/hospitals over time for additional information. The request for information is not subject to limitations of HIPAA.

### **Physician-of-record:**

Before discharge, hospital and birth unit personnel may be designated and listed on the specimen card as the physician-of-record. In the event of an abnormal test result, the screening laboratory will refer to the physician-of-record although the infant is no longer under his or her care and may not even be known to him or her. Responsibility for follow-up remains with the physician-of-record until another practitioner actively accepts it. It is essential to list the practitioner who will be providing direct care after discharge.

### **Practitioner responsibility for documentation:**

It is the responsibility of the practitioner to ensure every infant is tested and that the result is received and filed in the medical record. Practitioners should know the screening status of every infant in their care, regardless of age. Specific care should be paid to infants/children adopted from overseas as not all countries have newborn screening programs.

Specimen collection must be documented in the infant's chart and if preferred in a separate logbook. Information should include name of infant, hospital ID number, screening kit ID number, date collected, date mailed, and the name of the person who collected the specimen. When screening results are returned to the submitter, they should be noted in the logbook and the report filed in the medical records. Community practitioners must also ensure that the second specimen is obtained at the appropriate time and that documentation is completed.

In the event the results of an infant's screening tests are not received from the screening laboratory within two weeks of collection, the hospital and practitioner should assume responsibility for follow up. We recommend the following procedure:

- 1-Contact the Lab to determine if specimen was received and to request a report be mailed or faxed.
- 2-If the specimen was not received, it must be presumed lost. Notify the infant's private physician and/or parents by phone and letter that the specimen may have been lost and another specimen should be obtained without delay.
- 3-Document these actions in the infant's medical record.
- 4-Request a copy of the repeated screening results is sent to your facility for the medical record.
- 5-If these steps do not result in the infant being screened, notify the NBS Follow-Up Coordinator at 702-671-2224, the infant's health care provider and consider a public health referral.

### **Practitioner access to newborn screening results:**

Results are obtained by faxing a request on primary care provider letterhead to NSPHL. The request should include baby's name/birth date, mother's full name, address and phone number.

Electronic reports (e-reports) and automatic faxing of newborn screening results went live on 8/1/2016 with providers receiving reports on the same day results are approved and released. As well, NSPHL is currently exploring e-report access via the Health Information Exchange (HIE).

## **SPECIAL CONSIDERATIONS:**

### **Transfusions:**

A specimen should be obtained before the transfusion as donor cells provide normal levels of enzymes and hemoglobins and may temporarily normalize certain metabolites. Metabolite tests (e.g., phenylalanine, carnitine, and galactosemia) will become abnormal after a few days regardless of the transfusion. It may take as long as 120 days for infants to develop abnormal enzyme levels and hemoglobins after a transfusion, significantly delaying diagnosis and treatment. This is the rationale for admission screening for every NICU infant. An early screening test, before these interventions are begun, has been life saving for affected infants in the past. While only a small percentage of infants receive red cell transfusions, it has been impossible to establish policies and procedures in NICUs that ensure specimen collection before transfusion. Furthermore, even with aggressive follow up and the assistance of local physicians we are able to obtain a valid screening test on less than 40 percent of the transfused infants three months after the last transfusion. For affected infants, damage may have accrued during this time, increasing the liability to the physician, hospital, state, and program.

### **Premature infants and sick infants:**

While NICU admission screening is strongly recommended, some premature/sick infants tested in the first few hours of life may have an increased chance of false positive results from elevated thyroid stimulating hormone (TSH) and/or 17-OH-progesterone. These levels are generally elevated in the first 24 hours after birth as a reaction to stress, falling into normal range a day or two later. In addition, a very early specimen is not valid for many of the amino acids, such as phenylalanine or leucine, but these metabolites rise independent of transfusions and should be identified on the second test. We believe NICU admission screening improves screening for infants who will receive transfusions without creating an undue number of false positives.

### **Transferred infants:**

The receiving hospital or birthing center is responsible for taking the first blood sample from the infant during the first 2 days of life. The hospital or birthing center that transfers the infant is responsible for taking the first blood sample after the first 2 days of life. As appropriate, the hospital or birthing center should notify the receiving facility of the newborn screen status and include verification of screening in the transport paperwork. The receiving hospital or birthing center should verify the screen status of all transferred newborns. If screening cannot be verified, the receiving hospital should obtain the newborn blood sample.

### **Parents who do not reside in NV State:**

The same newborn screening guidelines apply. If an infant will not reside in NV State, it is important to obtain and list the name and contact information of the follow up health care provider.

### **Adoptions:**

For babies being adopted, the infant's adoptive name (if known) or the guardian or adoptive agency and contact information should be noted on the newborn screening specimen card for linking and follow up purposes.

### **Infants with clinical signs or family history:**

The newborn screening test, like any laboratory test, may have false positives and false negatives. If signs and symptoms of one of the newborn screening conditions are clinically evident, the physician should proceed to

the diagnostic testing, pending the results of the screen or in spite of the results of the screen. It may be necessary to treat as if the infant has the condition. Medical consultation is available 24-hours, 7 days a week for assistance for rapid diagnosis and institution of treatment for infants suspected to have the disease. Common laboratory tests available locally may help distinguish conditions. These include CAH-electrolytes, FAO disorders-glucose, OA disorders-arterial blood gas, complete metabolic panel, Urea cycle disorders-ammonia, glucose.

**If the results of the newborn screening are pending:**

For any of the screened conditions, but especially those in which the metabolite accumulation can be life threatening such as adrenal hyperplasia or many of the metabolic conditions, contact a consultant specialist for instructions on further evaluation of the infant.

**If the newborn screening test result was “normal”:**

If clinical symptoms suggest one of the screened conditions despite a “normal” screening result, the physician should proceed as if the infant has the condition and immediately contact a consultant specialist for instructions further evaluation of the infant. If the infant is found to be affected, notify the NSPHL lab as soon as possible.

**Infants with family history such as affected sibling or other close relative:**

As many of the conditions tested for by newborn screening are genetic, it is possible that multiple family members may be affected. Prenatal diagnosis is possible for many of these conditions; if prenatal diagnosis determines that the infant is affected, any appropriate treatment (e.g., special diet) should be initiated immediately after birth. If prenatal diagnosis predicts an unaffected infant, practitioners should bear in mind that no prenatal diagnostic test is 100 percent accurate. Neonates who are siblings or close relatives of an affected individual have a 25 percent risk of having the condition themselves. They are, therefore, not part of the “general population” for whom newborn screening is designed. For any infant with a positive family history, providers should contact appropriate consultant specialists, ideally prenatally, or immediately at birth, to determine the proper diagnostic tests and proper timing of those tests and whether supportive therapy is needed.

**Screening siblings or an infant older than 6 months of age:**

The NSPHL will not screen infants older than 6 months due to the lack of appropriate cutoffs. Infants and children older than 6 months can be “screened” using a filter paper specimen, but sent to a diagnostic laboratory with age appropriate cutoffs.

**Screening for disorders not on the NV state panel:**

Contact local laboratories for more information.

## **MATERNAL CONDITIONS AND TREATMENTS AFFECTING NBS RESULTS**

### **MATERNAL CONDITIONS:**

- Thyroid dysfunction: Hypothyroid mothers on adequate replacement therapy during pregnancy deliver infants with normal thyroid function. Maternal hyperthyroidism treated with propylthiouracil (PTU) during pregnancy may result in transient hypothyroidism in the infant. Inadvertent treatment with radioactive iodine after 8 weeks gestation may result in permanent hypothyroidism in the infant. Mothers who ingest megadoses of iodine during pregnancy may have infants with hypothyroidism.
- Steroids: These are frequently given to mothers during pregnancy and may suppress fetal adrenal function resulting in false negative 17-OH progesterone in the infant affected with congenital adrenal hyperplasia.
- Fatty liver of pregnancy or HELLP syndrome (hemolysis, elevated liver enzymes, low platelets): Increased risk of fetus with fatty acid oxidation disorder or a normal fetus with transiently elevated acylcarnitines.
- Maternal CAH, PKU and 3-MCC deficiencies may result in transient elevations of respective analytes in infant.
- Maternal carnitine deficiency: may result in low carnitine levels in the infant.
- Maternal B12 deficiency: may result in elevated propionylcarnitine (C3).

### **TRANSIENT HYPOTHYROIDISM OF PREMATURITY (THOP):**

The hypothalamic-pituitary-thyroid (HPT) axis is not functioning properly in premature infants and it is positively correlated with gestational age. In addition, sick and premature infants have a greater need for thyroxine and topical iodine skin cleansers depress T4. As a result T4 levels can be quite low for a week or more; TSH levels are usually normal. The significance of THOP on later development is still unknown due to the lack of well-controlled long-term outcome studies, but is thought to be somewhat benign. While a low T4 and an elevated TSH are the classic hallmarks of congenital hypothyroidism, some infants with CH have a delayed rise in their TSH, so practitioners cannot assume a premature or sick infant with a low T4 only has THOP and not CH. Serial screening specimens for T4/TSH are required until the T4 normalizes.

### **ANTIBIOTIC THERAPY:**

Antibiotics containing pivalic acid (for example: pirampicillin, pivmecillinan, cedidorempivoxil) given to mothers during labor or to newborns may cause false elevation of isovaleryl/2-methyl butyryl carnitine. Be sure to specify this antibiotic on the request slip if it has been used.

### **PARENTERAL NUTRITION AND CARNITINE THERAPY:**

These are not contraindications to screening, but samples should not be taken from the line that is used to deliver the nutrition or drugs. High levels of several amino acids can occur during parenteral nutrition and are the most common reason for "mixed elevations." Carnitine, added to intravenous solutions or formulas, may mask the biochemical markers for carnitine acylcarnitine translocase deficiency or carnitine palmitoyl transferase deficiency, type II. Screening specimens must be repeated after these therapies are discontinued.

### **RED CELL TRANSFUSIONS:**

A specimen should be obtained before the transfusion as donor cells provide normal levels of enzymes and hemoglobins and may temporarily normalize certain metabolites. Metabolite tests (e.g., phenylalanine, carnitine, galactosemia) will become abnormal after a few days regardless of the transfusion. It may take as long as 120 days for infants to develop abnormal enzyme levels and hemoglobins after a transfusion, significantly delaying diagnosis and treatment. This is the rationale for admission screening for every NICU infant.

### **TRANSIENT ABNORMALITIES:**

While NICU admission screening is strongly recommended, some premature/sick infants tested in the first few hours of life may have an increased chance of false positive results from elevated thyroid stimulating hormone (TSH) and/or 17-OH-progesterone. These levels are generally elevated in the first 24 hours after birth as a reaction to stress, falling into normal range a day or two after. A recent study of infants in the NWRNSP tested on admission showed that an additional 4 percent of NICU infants has elevated TSH on these early specimens, but 99 percent resolved on the second test. As well, a very early specimen is not valid for many of the amino acids, such as phenylalanine or leucine, but these metabolites rise independent of transfusions and should be identified on the second test. We believe NICU admission screening improves screening for infants who will receive transfusions without creating an undue number of false positives.

### **TREATMENTS USED IN SPECIAL CARE BABY UNIT AND EFFECTS ON NBS RESULTS:**

**Total Parenteral Nutrition (TPN)-** can cause elevation of multiple amino acids and duration of effect is 4-24 hours after TPN discontinued.

**Carnitine supplementation-** can cause elevations of acylcarnitines and can mask carnitine transport disorders for the duration of supplementation and weeks later.

**Red cell transfusion and Extra Corporeal Life Support (ECLS) (pre-and postnatal transfusions)-** can mask the absence of enzymes and proteins intrinsic to the red blood cell (RBC), thereby negating results for hemoglobinopathies and galactosemia (when testing is for galactose 1 phosphate uridyl transferase (GALT) enzyme activity. Duration of effect is 120 days after last transfusion and ECLS invalidates all NBS results for analyte-specific periods of time.

**Dopamine-** can cause false-negative testing for CH because levels of TSH are suppressed. Duration of effect is until drug therapy is stopped.

**Steroids-** can cause suppressed TSH and T4 and possible false-negative results for CH; may also suppress 17-OHP resulting in false-negative testing for CAH. Duration of effect is unknown-depends on class of steroid and dose; estimate 1-2 weeks.

**Iodine exposure with povidone/iodine preps-** can cause transient hypothyroidism, low T4 and elevated TSH. Once exposure to topical iodine is discontinued, resolution may take 2-6 weeks depending on dose absorbed and other factors.

**Pivalic acid antibiotic therapy-** may cause elevated isovaleryl 2-methylbutyryl carnitine and duration of effect is unknown.

## **CONDITIONS OF THE INFANT AFFECTING NEWBORN SCREENING TESTS:**

**Immature hypothalamic-pituitary thyroid axis**-can cause low T4, normal TSH and infants with congenital hypothyroidism (CH) can be missed. Duration of effect is up to 6 weeks of age.

**Hypoxyxinemia of preterm birth**- can cause transient hypothyroidism, low T4; normal TSH followed by elevated TSH. Duration of effect is up to 6 weeks of age.

**Liver enzyme immaturity**- can cause transient elevations of tyrosine, methionine, and galactose, occasionally other amino acids. Duration of effect is a few weeks.

**Iodine deficiency**- can cause transient hypothyroidism low T4 and elevated TSH. Duration of effect is until supplemented.

**Acute illness**- can cause transient hypothyroidism; low T4, elevated TSH, elevated immunoreactive trypsinogen (IRT). Duration of effect is until recovered.

**Hypoxia**- can cause elevated IRT and duration of effect is until recovered.

**Liver disease**- can cause elevated tyrosine, methionine, galactose and depression of biotinidase enzyme. Duration of effect is until recovered.

**Renal immaturity**- can cause elevated 17-OHP, amino acids and duration of effect is until recovered.

**Preterm**- can cause lower biotinidase levels inversely related to gestational age. Duration of effect is 40 weeks gestational age.

**REFERENCES:**

- NW Regional Newborn Screening Program: Nevada Practitioner Manual, 9<sup>th</sup> Edition, 2011  
Delaney, A. M., Meyers, A. D., Ruth, R. A., Faust, R. A., & Talavera, F. (Jan 31, 2012). Newborn Hearing Screening. Retrieved from emedicine.medscape.com/article/836646-overview.  
CLSI

**RESOURCE LIST:**

Genetics Home Reference  
<http://ghr.nlm.nih.gov/>

National Newborn Screening and Genetics Resource Center  
<http://genes-r-us.uthscsa.edu/>

American Academy of Pediatrics  
[www.aap.org](http://www.aap.org)

March of Dimes  
[www.marchofdimes.org](http://www.marchofdimes.org)

Sickle Cell/Hemoglobinopathies  
[www.cdc.gov/.../sicklecell/](http://www.cdc.gov/.../sicklecell/)

Cystic Fibrosis Foundation  
[www.cff.org/AboutCF/Testing/](http://www.cff.org/AboutCF/Testing/)

Centers for Disease Control Early Hearing Detection and Intervention  
[www.CDC.GOV/ncbddd/ehdi](http://www.CDC.GOV/ncbddd/ehdi)

National Institute on Deafness and Other Communication Disorders  
[www.nidcd.nih.gov](http://www.nidcd.nih.gov)

Hands and Voices  
[www.handsandvoices.org](http://www.handsandvoices.org)