NEVADA STATE PUBLIC HEALTH LABORATORY NEWBORN SCREENING PROGRAM

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NEVADA RARE DISEASE ADVISORY COUNCIL

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NEWBORN SCREENING HISTORICAL BACKGROUND

- In 1961, Dr. Robert Guthrie introduced the collection of blood on filter paper to detect PKU in newborns.
- This combination of easily transportable specimens and an inexpensive test made large-scale testing for PKU possible.
- The first case of PKU was detected using this procedure in a pilot study of 800 newborns who had been screened.
- As a result of these efforts, the successful introduction of DBS as a source of PKU screening eventually led to a population-based screening of newborns using a few blood drops collected from a heel stick and absorbed into special filter paper.
- Today, NBS is the largest population-based genetic screening effort in developed countries, and its expansion is considered one of the 10 great public health achievements of the first 10 years of the 21st century.

- Newborn Screening is an essential preventative public health system recognized in the US and internationally comprised of **screening**, **follow-up**, **diagnosis**, **management**, **evaluation**, and **education**.

- Newborn screening represents one of the most successful public health programs ever undertaken in terms of prevention and cost savings, surpassing even immunizations.

- The primary goal is to ensure early identification of metabolic and inherited conditions that can affect a child's long- term health or survival. Early detection, diagnosis, and intervention helps prevent death or disability and improve outcomes for infants/children.

- The national standard of care to identify the infant, complete confirmatory testing, and begin treatment is prior to **21 days** of age.

- 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 SCREENING

The Three Parts to Newborn Screening

Did you know?

All babies in the United States receive newborn screening.

Blood test or heel stick

A small blood sample is taken from your baby's heel and placed on a newborn screening card. This card is mailed to a state laboratory for analysis.

Hearing screen

One of two tests may be used to screen for hearing loss in your baby. Both tests are simple and safe and can be done while your baby is asleep.

Pulse oximetry

Pulse oximetry is a test that measures the amount of oxygen in your baby's blood and can detect some heart problems called Critical Congenital Heart Disease (CCHD).

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NBS Sample Collection

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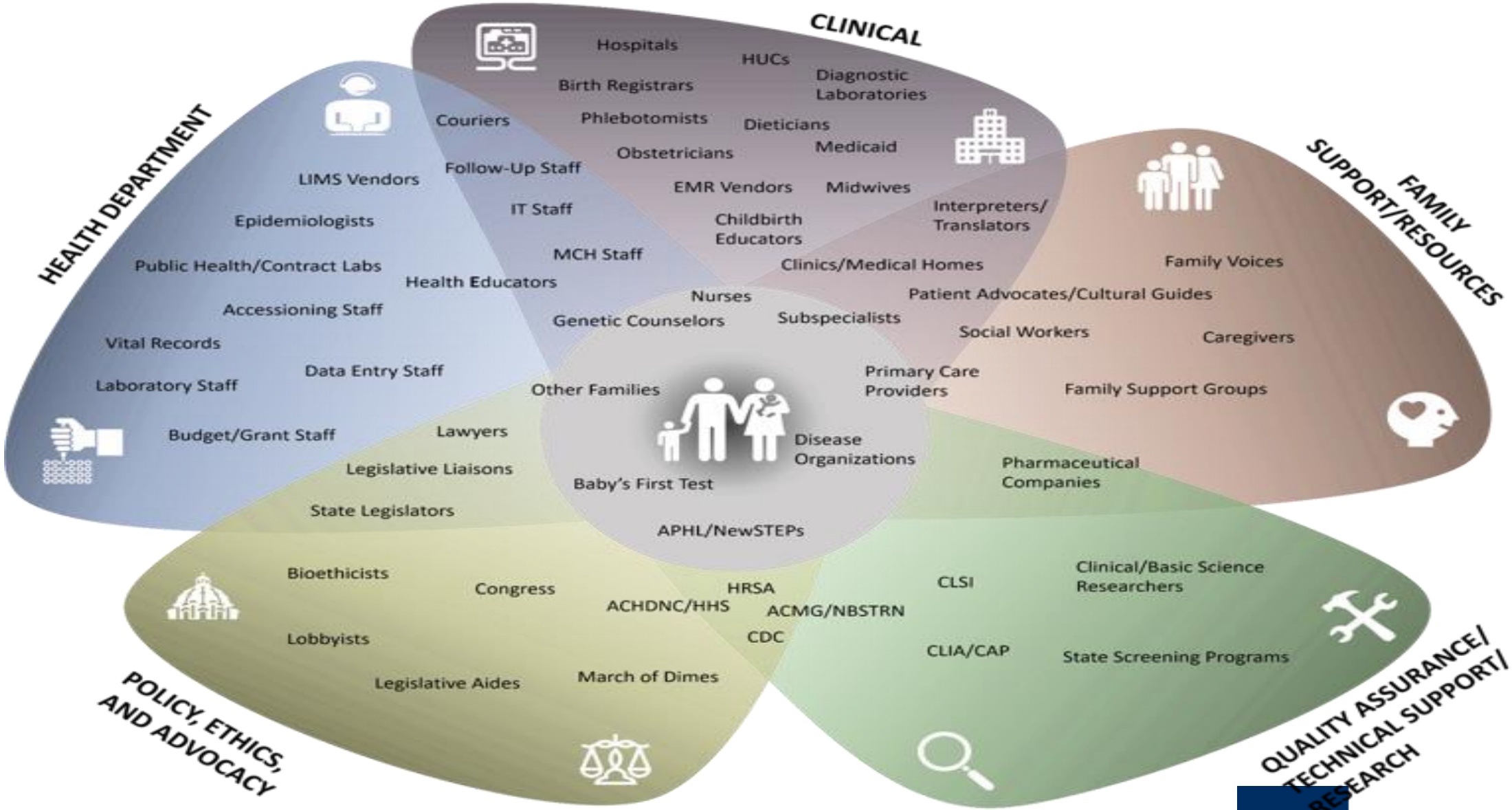

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HISTORY OF NEWBORN BLOOD SPOT SCREENING IN NEVADA

- Newborn screening has been performed on Nevada infants since **1978**; however, Nevada was sending the testing to the Oregon Public Health Laboratory for analyses
- Phenylketonuria (PKU)-first disorder on the panel in **1978**
- Congenital Hypothyroidism, Hemoglobinopathies, Biotinidase, Galactosemia, Maple Syrup Urine Disorder-subsequently added to the panel
- Congenital Adrenal Hyperplasia-added in **2003**
- Tandem Mass Spectrometer testing-started in **2003**
- Cystic Fibrosis-added in **2008**
- Tyrosinemia screening test improved- **2011**
- In **2011**, legislation was modified to have the testing preferably done in Nevada. The Nevada State Public Health Laboratory was chosen to perform the testing
- On **July 1, 2014**, the Nevada State Public Health Laboratory began screening all Nevada newborns
- Severe Combined Immunodeficiency (SCID)-added in **2018**
- Spinal Muscular Atrophy-added in **2024**
- X-linked Adrenoleukodystrophy (ALD), Pompe, Mucopolysaccharidosis Type 1 (MPS 1) Mucopolysaccharidosis Type 2 (MPS 2)-to be added/implemented **2024-2025**

IMPLEMENTATION OF NEWBORN SCREENING IN NEVADA

- **No funding** was provided to the NSPHL to implement newborn screening. Existing staff validated and implemented the new methodologies and technologies associated with newborn screening
- The NSPHL was fortunate to have a donor, Mick Hitchcock PhD, provide over **$1 million dollars** to purchase the highly complex and technical mass spectrometry instrumentation for the newborn metabolic testing
- Experienced staff were hired as the NSPHL approached the July 1, 2014 live date to perform the daily testing and follow-up duties that would be required
- On **July 1, 2014**, the Nevada State Public Health Laboratory began screening all Nevada newborns for 29 core conditions (hearing loss and CCHD screenings done independently) and 26 secondary conditions
- On **January 1, 2015**, the Newborn Screening Program officially transitioned from the state health division to NSPHL. NSPHL is one of five laboratories in the U.S. that is part of the university rather than a state health division.

BENEFITS OF HAVING LABORATORY SERVICES DONE WITHIN STATE

- Improved transit
- Improved turn-around-time for test results
- Improved communication/teamwork
- Facilitate prompt treatment for affected infants

NSPHL WORKFLOW

The NSPHL processes **200-600** specimens per day (Monday-Friday)

NBS cards are punched and tested on the day received

Normal results are faxed (preferred) or mailed within **24 hours** by regular postal service

Abnormal results are called and faxed to the hospital and Attending Physician within **48 hours** of sample receipt

Average turn-around-time (TAT) for all specimens-**1.83** working days

NEVADA REGULATIONS

- **NAC 442.020-442.050** mandates newborn blood spot screening for all infants born in Nevada

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- Nevada is 1 of 14 states currently requiring 2 NBS tests per infant. Many states recommend a 2nd NBS test; but do not require it.

For well babies

- First screen at 24-48 hours or before leaving hospital, whichever is first
- Second screen at 10-14 days of age

For premature and low birth weight babies (Neonatal Intensive Care [NICU])

- First screen at NICU admission before any medical treatment, TPN feeding or transfusion
- Second screen between 48-72 hours
- Third screen at 28 days or at discharge

- **OPT OUT** for parents who refuse newborn screening testing

NEWBORN SCREENING FEE

Historically, Nevada's fee for NBS laboratory testing was part of the birth registry fee defined in NAC 440.210.

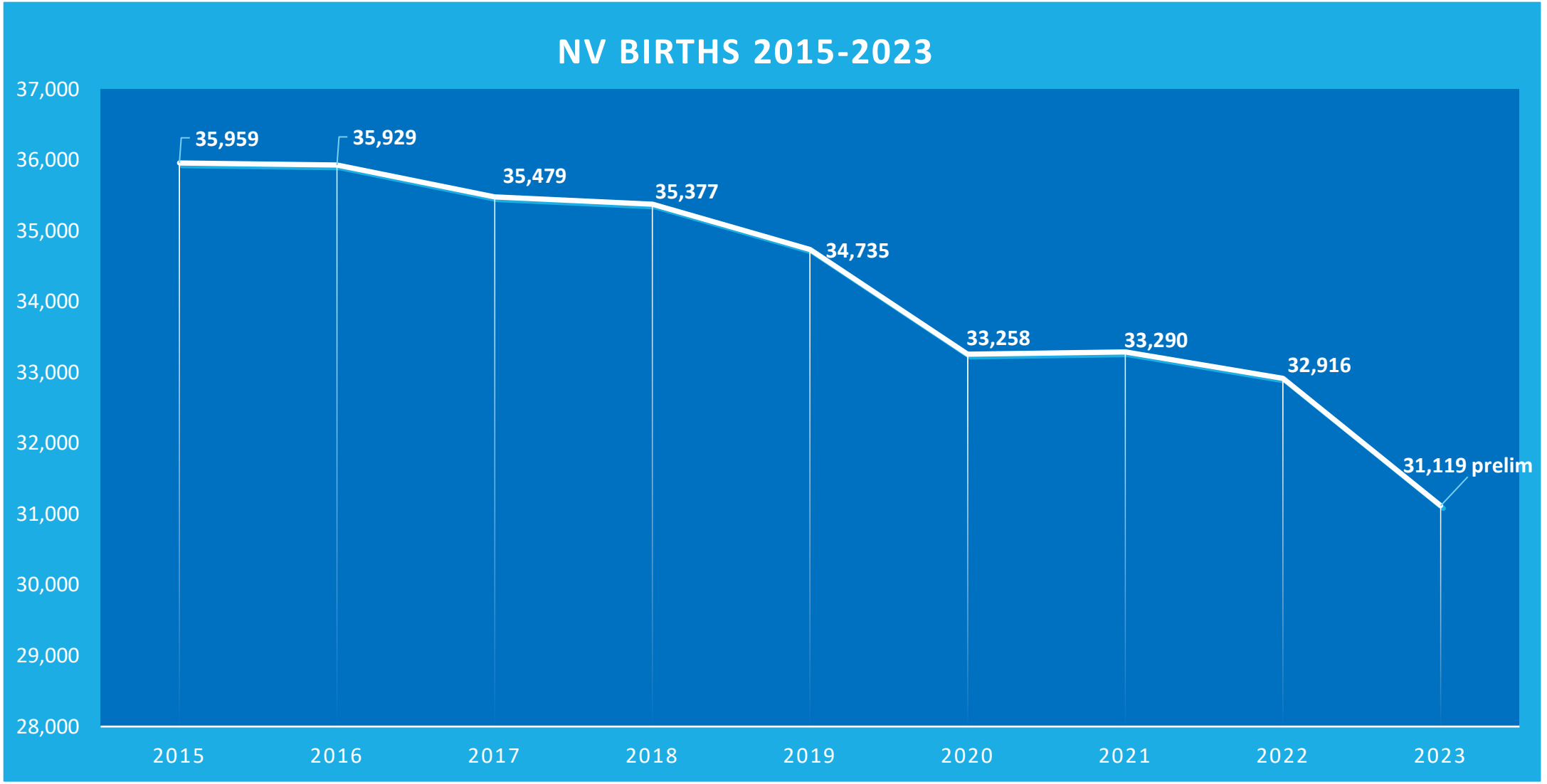
Nevada State Board of Health adopted regulation amendments to NAC 440.020-442.050 on 9/9/2016. Effective 11/2/2016, NSPHL has authority over the NBS program and fee implementation.

The fee is currently $81 for both the 1st and 2nd sample testing, repeats

NOTE: Additional disorders will require more equipment, space, and personnel therefore a fee increase will be required to implement and support the testing long-term

RESPONSIBILITIES OF THE NEWBORN SCREENING PROGRAM

- 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



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NEWBORN SCREENING ESSENTIALS

- The correct term is “Newborn Screening” or “Newborn Blood Spot Screening”. The term “PKU test” is outdated and confusing-the screening panel now includes markers for approximately 30+ separate disorders

- Incidence of all the blood spot conditions is ~one infant in 1000 or 50-70 new cases each year in Nevada (~one infant/week identified)

- 1st screen identifies approximately 90% of all conditions (1st and 2nd for NICU)

- 2nd/3rd screen identifies approximately 10% of all conditions

- 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

This is a screen. There are presumptive positives reported that are “true positives” & some “false positives” - Confirmation is required to distinguish

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.

The newborn screen is designed to detect babies at risk before they have signs and symptoms

Early detection and treatment results in prevention of irreversible complications

There is often no family history. Siblings may not have history of any screened disorders

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NV NEWBORN SCREENING PANEL

Nevada newborns are screened for the following 32 core and 29 secondary conditions recommended by the College of Medical Genetics, March of Dimes, and Recommended Uniform Screening Panel (RUSP).

Genetic
- Cystic Fibrosis*

Endocrine Conditions
- Congenital Adrenal Hyperplasia (CAH)*±
- Congenital Hypothyroidism*

Hemoglobin Conditions
- Sickle Cell Disease and other Hemoglobinopathies*

Metabolic Conditions
- Biotinidase Deficiency
- Galactosemia±

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± (via confirmatory testing for elevated CIT)
- Citrullinemia±

Other Conditions
- Newborn Hearing Loss
- Critical Congenital Heart Disease-started 7/1/2015
- Severe Combined Immunodeficiency (SCID)-started 1/29/2018
- Spinal Muscular Atrophy (SMA)-started 1/2/2024

*** 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.

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BIOTINIDASE

Deficiency of Biotin, part of the Vitamin B complex. Impact without early treatment- seizures, damage to immune system, intellectual disabilities, hearing loss. Benefits of early treatment- prevent all adverse consequences.

GALACTOSEMIA

Inability to break down galactose, a major sugar found in milk. Impact without early treatment- galactose accumulates in vital organs, leading to severe intellectual disabilities, liver disease, blindness, overwhelming infections, and death. Benefits of early treatment- prevent death, improve mental function and reduce other morbidity.

CONGENITAL ADRENAL HYPERPLASIA

Impaired production of cortisol and other adrenal hormones. Impact without early treatment- salt loss and shock may result in early sudden death, virilization, and abnormal growth. Benefits of early treatment- prevent death, reduce virilization and abnormal growth.

CONGENITAL HYPOTHYROIDISM

Inadequate production of thyroid hormone. Impact without early treatment- intellectual disabilities, growth failure. Benefits of early treatment- normal growth and mental development.

CYSTIC FIBROSIS

Defect in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Impact without early treatment- thick, sticky mucus build up in the lungs and digestive system. Benefits of early treatment- improve physical growth, cognitive function, and possibly lung function.

SICKLE CELL/HEMOGLOBINOPATHIES

Primary objective is to identify those infants with sickle cell disease because these infants will experience far less illness and death if they are promptly entered into a comprehensive health care program that includes prophylactic treatment with penicillin.

AMINO ACIDEMIAS

Inability to break down amino acids, found in all foods containing protein. Impact without early treatment- intellectual disabilities, seizures, coma, and death. Benefits of early treatment- prevent intellectual disabilities and other neurological damage.

FATTY ACID OXIDATION

Inability to process or break down fats in the body due to missing or dysfunctional enzymes. Impact without early treatment- serious damage to brain, liver, heart, eyes, and muscles. Benefits of early treatment- prevent intellectual disabilities and other neurological damage.

ORGANIC ACIDEMIAS

Inability to process or break down organic acids, by-products of protein and fatty acid metabolism. Impact without treatment- severe nerve/physical damage and death. Benefits of early treatment- prevent intellectual disabilities and other neurological damage.

IMMUNO-DEFICIENCY (SCID)

Complete lack of immune system in the baby. Screening test- DNA test: measure number of T-cell excision circles (TRECs) by real time PCR. Impact without early treatment-severe life-threatening infections that complicate treatment and possible death. Benefits of early treatment-prevent death and cure the condition.

SPINAL MUSCULAR ATROPHY

Progressive neuromuscular disorder that destroys muscle-controlling nerve cells called motor neurons. In SMA, motor neurons in the spinal cord are affected. SMA affects many parts of the body, most notably the skeletal and respiratory (breathing) muscles. Medical and scientific advances show quality of life is improving for individuals with SMA, and life expectancy is increasing.

CONFIRMED CASES (TOTAL=507)

Biotinidase	4	1 profound; 16 Partial deficiency (1 deceased and 6 compound heterozygous)
2-methylbutyrylglycinuria	1	Detected on confirmatory test
3MCC/BKT/HMG	2	1 Carrier, 1 Mild variant
Citrullinemia type 1	2	plus 2 carriers, 2 Mild variants
Congenital adrenal hyperplasia	13	1 Mild deficiency; 3 Salt-wasting
Congenital hypothyroidism	98	80 Confirmed
CPT type 2	1	1st case
CUD	2	Borderline CUD (Primary carnitine deficiency)
Cystic fibrosis	31	and 21 heterozygous (One copy of CFTR mutation); 3 compound heterozygous
Classic Galactosemia	5	plus 1 carrier
D/G Variant	22	
GA1	1	This is GA Type 1
GA2	1	

Hemoglobinopathies	128	FS(67), FSC(37), FSA(7), FC(8), FCA(2), FD(1), FE(2), FSE(1), FE/Beta thal(2), Hydrops fet(1)
Isobutyrylglycinuria (IBG)/Isobutyryl-CoA dehydrogenase (IBD) def.	2	1 IBD
IVA	2	1 pending DNA test
MCAD	19	1 carrier and 2 Mild variants
MMA	2	
Methionine adenosyltransferase def. (MAT)	1	
MSUD	1	
PA	1	This is a mild variant
PKU	18	and 6 Hyperphenylalaninemia
SCAD	8	All Benign; No tx needed
SCID (Low TREC)	10	1 Edward's Syndrome (Deceased), 6 Di George, 1 Jak 1 Wiskott Aldrich Synd., 1 partial DiGeorge and 2 T-cell lymphopenia;
Tyrosinemia type I	1	
Tyrosinemia type II	2	
Tyrosinemia type III	1	
VLCAD	4	and 12 Carriers

Hemoglobin Traits	Total
FA+Other	1,128
FAB	2,662
FAC	1,254
FAC/Barts	60
FAS	4,319
FAS/Barts	204
FA+Other/Barts	36
FAS+Other	9
Total	**9,672**

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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.

REQUESTS FOR INFORMATION

Follow-up services include contacting the provider to confirm infant information, obtain important information, notification of test results, additional instructions, facilitate confirmatory testing, and other related newborn screening services.

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 Newborn Screening Program is a public health program and is exempt from the Privacy Rule of the Health and Insurance Portability and Accountability Act (HIPAA). Request for protected health information to provide newborn screening services is allowed and information is kept confidential.

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

PRACTICE PROFILE REPORTS

(Continuous Quality Improvement Surveillance)

Monthly reports are provided to submitters reporting on:

Sample Card Transit Times

Demographic Errors

Specimen Collection Errors

Unsatisfactory Samples Submitted for Testing

Card Management

NEVADA NBS ADVISORY COMMITTEE

Meet every 4 months via Zoom

- Provides program review for dried blood spot and hearing screenings
- Discuss quality review
- Provides a voice for consumers
- Discuss newborn screening best practices
- Promotes advocacy
- Review proposals for addition of NBS tests
- Provide recommendations

FINAL WORDS ABOUT COST-PKU

A treated person with PKU lives a normal productive life. They work and pay taxes. Without treatment they are severely brain damaged, can't work, and require costly care. The treatment is simple: specially modified food and formula for the rest of their lives. The treatment is preventative care and cost effective chronic disease management. It costs $10,000 or less per year to provide the medical food and formula for a PKU patient. It costs $200,000 or more per year to care for a brain damaged person with PKU or at least $60,000/year for residential treatment. It is a 95% savings in medical expenses to treat a PKU patient with food and formula. There are ~20,000 Americans with inborn errors of metabolism who need this treatment. 38 states have mandates to provide the food and formula for PKU, but many patients are denied access to health insurance and treatment. Most state mandates expire, at age 6 or 18, even though the diet is required for life. As a result, patients can suffer brain damage and cost the Health care system and tax payers an additional 1-2 Billion dollars per year. In states with treatment provisions, many self-insured plans deny treatment under ERISA.

The costs of treating an individual with untreated PKU can be up to 13 times the cost of providing proper treatment. Therefore, screening for PKU and maintaining lifelong care for affected individuals will result in a net gain to taxpayers and a cost-savings to the government.

https://www.npkua.org/portals/0/pdfs/talking_points.pdf

Nevada Statewide Medical Consultants

NICOLA LONGO, MD, PHD
University of Utah Genetics/Pediatrics
Metabolic Consultant (Biotinidase Deficiency, Galactosemia, Organic Acidemias, Urea Cycle, Amino Acid, Fatty Acid Oxidation Disorders)

ALEXANDRA AGUILAR, MD
Endocrinology Consultant (Hypothyroidism, Congenital Adrenal Hyperplasia)

SUMIT GUPTA, MD
Cure 4 The Kids
Hemoglobinopathy Consultant (Sickle cell diseases)

CRAIG NAKAMURA, MD
Children's Lung Specialists, LTD
Pulmonary Consultant (Cystic Fibrosis)

AHMAD RAYES, MD
Immunology Consultant (SCID)

Neurologist Consultant (SMA) TBD

NEVADA STATE PUBLIC HEALTH LABORATORY

FOLLOW-UP

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Thank you! Questions?

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