FOOTNOTES

South Carolina DPH Newborn Screening Newsletter

ISSUE 12 DEC 24

CELEBRATE!

September was Newborn Screening Awareness Month & Sickle Cell Awareness Month

New Media Release! *DPH Highlights Success Stories for Newborn Screening Awareness Month.*

The media release can be accessed on our website or by utilizing this link:

https://dph.sc.gov/news/dph-highlights-success-stories-newborn-screening-awareness-month

OUR BEST FOOT FORWARD

The South Carolina (SC) Public Health Laboratory (PHL) began screening newborns for two additional disorders, X-linked Adrenoleukodystrophy (X-ALD) and Argininemia, on April 22, 2024. The South Carolina Newborn Screening panel now screens for more than 58 primary and secondary conditions.

What to expect as South Carolina continues screening newborns for Argininemia and X-Linked Adrenoleukodystrophy?

Argininemia is contained within the amino acid panel on the laboratory report. X-ALD is displayed in an additional row on the laboratory report.

An example of the report is shown below, where both argininemia and X-ALD are normal:

X-ALD

- More common/severe in males
- Frequency of disease is < 200 new cases annually in the U.S.
- Most affected newborns show no symptoms, but some may experience vomiting, fatigue, and/or muscle weakness
- Treatment includes stem cell transplantation

Argininemia

- Also known as Arginase Deficiency
- Frequency of disease is < 15 new cases annually in the U.S.
- Symptoms may include problems with feeding, vomiting, poor growth, seizures, and stiff muscles with increased reflexes
- Treatment includes dietary restrictions, medications, and other therapies.

Screening Test	Screening Results	Value	Expected Ranges	Units	Note
X-linked Adrenoleukodystrophy (X-ALD)	Within Acceptable Limits		Within Acceptable Limits		
Amino Acid (AA) Panel (Includes SA)	Within Acceptable Limits		Panel Within Acceptable Limits		
Acylcarnitine (AC) Panel	Within Acceptable Limits		Panel Within Acceptable Limits		
Pompe					
GAA (acid-a-glucosidase)	Within Acceptable Limits		> 20% of Daily Median	%	
Mucopolysaccharidosis Type I (MPSI)					
IDUA (a-L-iduronidase)	Within Acceptable Limits		> 10% of Daily Median	%	
Krabbe					
GALC (β-galactocerebrosidase)	Within Acceptable Limits		> 15% of Daily Median	%	

The table below shows the analytes for argininemia and X-ALD as well as the expected ranges.

Analyte	Target Disorder	Expected Range (µmol/L)	
C26:0-LPC (C26:0 lysophosphatidylcholine)	X-ALD	1st tier	2nd tier*
		< 0.40	< 0.20
Arginine (ARG)	Argininemia	< 80.00	

**All specimens that are abnormal for 2nd tier C26:0-LPC are sent to Greenwood Genetic Center (GGC) for 3rd tier targeted gene sequencing of the ABCD1 gene, which is specific for X-linked adrenoleukodystrophy.*

What terms should you be familiar with?

Argininemia (Arginase Deficiency) is an autosomal recessive disorder causing hyperammonemia secondary to arginine deficiency. It is a disorder first noticed in children with growth reduction, slowing cognition, and missed milestone developments. Affected newborns are found to have elevated levels (up to four times) of arginine. Arginase deficiency is the most uncommon urea cycle disorder. The estimated incidence ranges from 0.5 to 1 per 1,000,000 people worldwide.

Leukodystrophy is a group of inherited genetic diseases that damage the myelin, or white matter, of the brain.

Myelin, also known as white matter, forms a protective coating around nerves. It helps them quickly carry information from one part of the brain and spinal cord to another.

X-linked adrenoleukodystrophy is a genetic disorder connected to the X chromosome. It mainly affects the nervous system and adrenal glands, which are located on top of each kidney. In this disorder, the fatty covering (myelin) that insulates nerves in the brain and spinal cord deteriorates over time. The loss of myelin reduces the ability of the nerves to relay information to the brain.

There are four types of X-ALD: a childhood cerebral form, an adrenomyeloneuropathy type (AMN), an adrenal insufficiency only form, and a type called asymptomatic. ALD is a progressive disease, which affects males more than females. The estimated incidence is around 1 per 15,000 people worldwide.

What will an outside of acceptable limit screening result look like on the lab report?

First tier screening for ARG and X-ALD will be performed at the SC PHL using a quantitative biochemical test. An abnormal ARG (> 80 µmol/L) will be reported as **"Outside Acceptable Limits"** and will show the concentration of ARG, as shown below. Since arginine is contained within the amino acid panel, the panel will also say **"Outside Acceptable Limits"** and all analytes within the panel will display on the report.

Screening Test	Screening Results	Value	Expected Ranges	Units	Note
Amino Acid (AA) Panel (Includes SA)	Outside Acceptable Limits		Panel Within Acceptable Limits		
Arginine	Outside Acceptable Limits	88.83	<80.00	µmol/L	
ASA	Within Acceptable Limits	0.65	<1.00	µmol/L	
Citrulline	Within Acceptable Limits	20.80	<60.00	µmol/L	
Leucine + Isoleucine	Within Acceptable Limits	273.23	<325.00	µmol/L	
Methionine	Within Acceptable Limits	62.23	<75.00	µmol/L	
Phenylalanine	Within Acceptable Limits	68.32	<120.00	µmol/L	
Tyrosine	Within Acceptable Limits	61.55	<300.00	µmol/L	
Valine	Within Acceptable Limits	232.03	<250.00	µmol/L	

An abnormal X-ALD (> 0.4 µmol/L) will reflex to 2nd tier testing. The 2nd tier screening for X-ALD will also be performed at the SC PHL. If this test is abnormal (> 0.2 µmol/L), it will be reported as **"Outside Acceptable Limits"** and will show the concentration of C26:0-LPC as shown below.

Screening Test	Screening Results	Value	Expected Ranges	Units	Note
C26:0-LPC	Outside Acceptable Limits	0.400	<2.00	µmol/L	1
Amino Acid (AA) Panel (Includes SA)	Within Acceptable Limits		Panel Within Acceptable Limits		
Acylcarnitine (AC) Panel	Within Acceptable Limits		Panel Within Acceptable Limits		
Pompe					
GAA (acid-a-glucosidase)	Within Acceptable Limits		> 20% of Daily Median	%	
Mucopolysaccharidosis Type I (MPSI)					
IDUA (a-L-iduronidase)	Within Acceptable Limits		> 10% of Daily Median	%	
Krabbe					
GALC (β-galactocerebrosidase)	Within Acceptable Limits		> 15% of Daily Median	%	

A specimen will then be sent to the Greenwood Genetic Center (GGC) Laboratory for 3rd tier genetic sequencing of the *ABCD1* gene. A snippit above shows an example of what an abnormal X-ALD screening result will look like on the report when it is abnormal by both 1st and 2nd tier analysis.

What is the notification process for abnormal results?

The SC Department of Public Health (DPH) NBS follow up staff will provide notification of abnormal ARG and X-ALD screening results to the primary care provider and/or physician indicated on the NBS specimen collection form by phone, fax, and/or mail, when results are indicative of potential disease.

What are the next steps that should be taken?

When results are indicative of potential disease, verbal and written clinical instructions will be provided via a phone call and notification letter. Notification may also include coordination with a medical specialist as needed.

Are there resources available?

Yes! See links below:

- South Carolina Department of Public Health (DPH) Newborn Screening website: https://dph.sc.gov/professionals/health-professionals/health-services-facilities/newborn-screening
- ACMG Newborn Screening ACT sheets: acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx

STORY TIME!

Do you or someone you know have a newborn screening story they would like to share?

Please send an email to NBSQI@dph.sc.gov.

We would love to hear more about your story!

UP-AND-COMING

- **Newborn Screening** electronic test orders and results (NBS ETOR)
- **Next disorders to be added to the test panel:** Mucopolysaccharidosis Type II (MPS-II) and Fabry disease
- **Updated Collection Forms** to include new DPH logo

WELCOME NEW STAFF!

- **Susan D'Agostino, BSN, RN**
  Newborn Screening Follow-up Coordinator
- **Katrina L. Davis**
  Newborn Screening Follow-up Coordinator
- **Erik Lewis**
  Newborn Screening Laboratory Technologist
- **Khushbu Patel**
  Newborn Screening Laboratory Technologist

ONE STEP AT A TIME

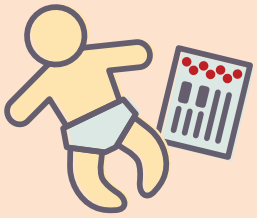
Newborn screening blood spot testing begins shortly after birth, with the blood being collected from the baby's heel between 24 – 48 hours after birth. The blood is collected on a specialized filter paper. Each pre-printed circle on the card should be filled with one large drop of blood. The blood should soak through to the other side of the filter card. After the blood has been allowed to dry (between 3 – 4 hours), the filter paper collection card is packaged and sent (ideally same day) to the SC PHL for testing. The blood spot testing involves highly complex testing methodologies and instrumentation and can take a few days to complete. Currently, there are 58 disorders tested on the SC newborn screening panel and more are being added every year.

Have you ever wondered what happens after the testing has been completed? Newborn screening laboratory staff communicate the testing results to the Newborn Screening Follow-up team. The Follow-up team coordinates with pediatric medical consultants and medical specialists throughout the state to notify pediatricians and parents of the results of their baby's newborn screen. In addition to communicating NBS results, they also follow-up with an infant's care team to ensure they have received treatment and verify whether or not a baby has been diagnosed with a newborn screening disorder. In addition, some disorders qualify for extended care services and those cases are passed along to the SC DPH long-term follow-up team (Children & Youth with Special Healthcare Needs Program) once short-term follow-up has been completed.

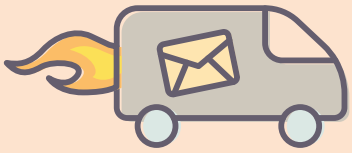
Back in the laboratory, newborn screening laboratory staff store the newborn screening collection forms in a secure –20 C freezer where they remain for up to one year. After one year in storage, the blood collection cards are properly destroyed and disposed of. If a parent would like to have their baby's collection form returned before it is destroyed, they may reach out to the Newborn Screening Laboratory for instructions.

The Newborn Screening Program (lab + follow up) works hard every day to detect babies with rare but treatable conditions. The goal is to help provide early intervention, improve lifelong health, and promote positive outcomes for the babies born in the state of South Carolina. Medical providers can help ensure the Newborn Screening program is providing quality testing by sharing newborn screening diagnosed case information with the Newborn Screening team. In addition to the information assisting the program with tracking cases, it assists the laboratory with selecting appropriate, data driven reference ranges – making sure that babies with conditions are detected early.

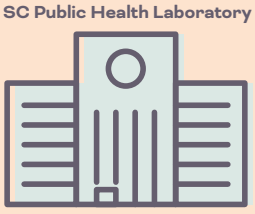
The Process



Collected shortly after birth

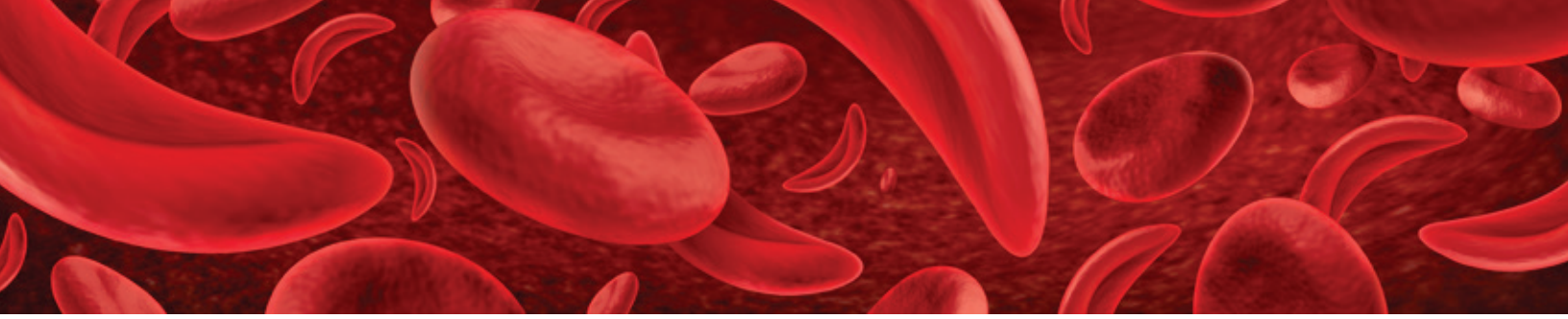


Transported quickly!



Testing completed

Results sent to pediatrician



SPOTLIGHT ON SICKLE CELL ANEMIA

September is Sickle Cell Awareness Month! Approximately 250 million people worldwide carry the gene for sickle cell disease.

Sickle cell anemia is one of a group of inherited disorders known as sickle cell disease (SCD). It is the most common inherited blood disorder in the U.S. SCD affects 1 in 400 blacks and 1 in 19,000 Latinos and has a carrier rate of 1 in 12 and 1 in 100 for black and Latino populations in the U.S., respectively. SCD affects the shape of red blood cells, which carry oxygen to all parts of the body. Red blood cells are usually round and flexible, so they move easily through blood vessels. In sickle cell anemia, some red blood cells are shaped like sickles or crescent moons. These sickle cells also become rigid and sticky, which can slow or block blood flow. Sickled cells die early, which results in a constant shortage of red blood cells. This can cause pain, damage to body organs and anemia.

Symptoms of sickle cell disease usually appear around 6 months of age and include anemia, pain crises, swelling of the hands and feet and frequent infections. Management of sickle cell anemia focuses on relieving symptoms, preventing complications and avoiding pain episodes. Recently, the U.S. Food and Drug Administration approved two cell-based gene therapies for the treatment of sickle cell disease in patients 12 years and older. For a child to have sickle cell anemia, both parents must carry one copy of the sickle cell gene and pass both copies to the child. If only one parent passes the sickle cell gene to the child, that child will have sickle cell trait. People with sickle cell trait are carriers of the disease and make both typical hemoglobin and sickle cell hemoglobin. Their blood may contain some sickle cells, but they generally don't have symptoms.

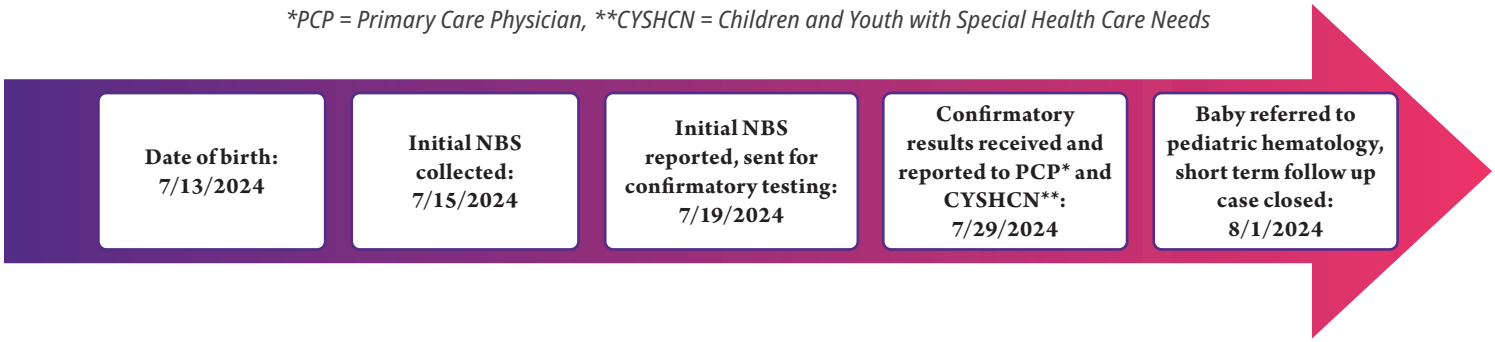
Fortunately, every baby in the United States is screened for sickle cell disease as part of their newborn screen. In 2022 and 2023 there were 36 and 32 diagnosed cases of sickle cell disease, respectively, in South Carolina. These patients were identified through newborn screening.

Sickle cell trait is not a disease, but it can be passed on to children. When a person has sickle cell trait (SCT), they are a carrier of the sickle cell gene. This means a person with SCT could pass the trait on to their children. Someone who has SCT will not get SCD; sickle cell trait does not change into sickle cell disease.

For more information on sickle cell disease, please visit: https://dph.sc.gov/health-wellness/child-teen-health/services-children-and-youth-special-health-care-needs/sickle-cell

Typical timeline for one newborn screening specimen, from birth to referral to pediatric hematology for sickle cell disease

**PCP = Primary Care Physician, **CYSHCN = Children and Youth with Special Health Care Needs*



ON THE RUN

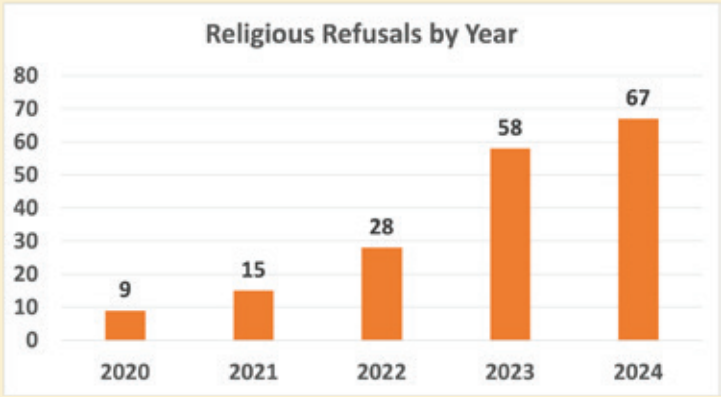
Health Department Courier Boxes

In July 2024, new newborn screening courier boxes (pictured here) started being rolled out to county health departments. The boxes are being implemented in conjunction with an optional service update that was sent out to medical providers on July 18th regarding the newborn screening specimen drop offs at SC health departments. Newborn screening specimens dropped off at county health departments will be transported via a courier to the Public Health Laboratory. The optional service can help speed up specimen transport from midwives, pediatricians, and PKU specimen submitters at no cost to the submitter. The specialized courier boxes are very recognizable and will help speed up the transport process from health departments to the laboratory for testing.

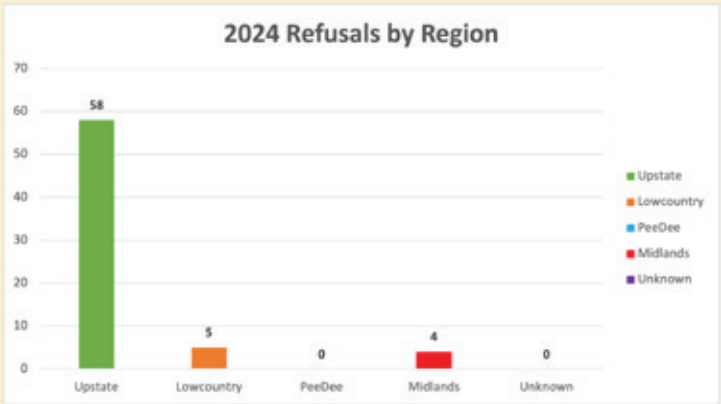
Religious Objections to Date

Newborn screening may only be refused by religious objection from a baby's parents. The newborn screening program keeps track of religious objection forms received from health care providers. The Parental Religious Objection Form (DPH 1804) is currently available in English, Spanish, Ukrainian, and Russian. The two graphs below show the religious refusals received by the newborn screening program from 2020 to 2024 (Graph 1) and the refusals received thus far in 2024 by geographic region (Graph 2). As shown in Graph 1, the SC NBS program continues to see an increase in NBS refusals each year.

Graph 1: Total number of newborn screening refusals received each year beginning in 2020.



Graph 2: Total number of refusals through December 2024 by geographic region in South Carolina.



Unsatisfactory Specimen Trends

Unsatisfactory newborn screening specimens negatively impact newborns because they hinder the ability to provide timely and accurate diagnosis and intervention for potentially serious health conditions. This adversely impacts both individual health outcomes and public health efforts.

The high number of unsatisfactory specimens in South Carolina in January 2022, where 6.6% of overall specimens were deemed unsatisfactory, is significant for several reasons:

Impact on Screening Accuracy: Unsatisfactory specimens compromise the accuracy of newborn screening tests. When a specimen is unsatisfactory, it often means the specimen was inadequate or compromised in some way, which could lead to false-negative or inconclusive results. This can delay the diagnosis and timely intervention for newborns who may have conditions that require early detection and treatment. The images below show examples of a satisfactory specimen (Figure 1) and unsatisfactory specimen (Figure 2). The unsatisfactory specimen shown in Figure 2 is a good example of blood spot layering.

Figure 1. Satisfactory newborn screening specimen showing one drop of blood per circle.

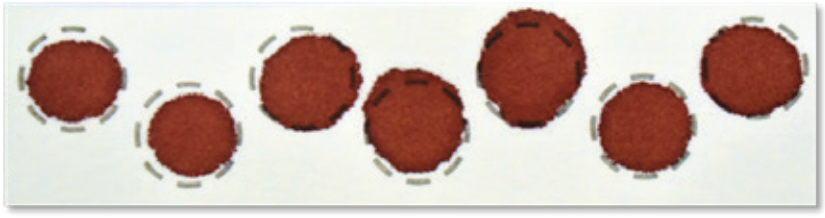


Figure 2. Unsatisfactory newborn screening specimen showing multiple drops of blood per circle.

Potential for Missed Diagnoses: If a newborn screening result is based on an unsatisfactory specimen, there is a risk of missing important diagnoses. Certain genetic, metabolic, and congenital disorders may not be detected promptly, potentially leading to adverse health outcomes for affected infants.

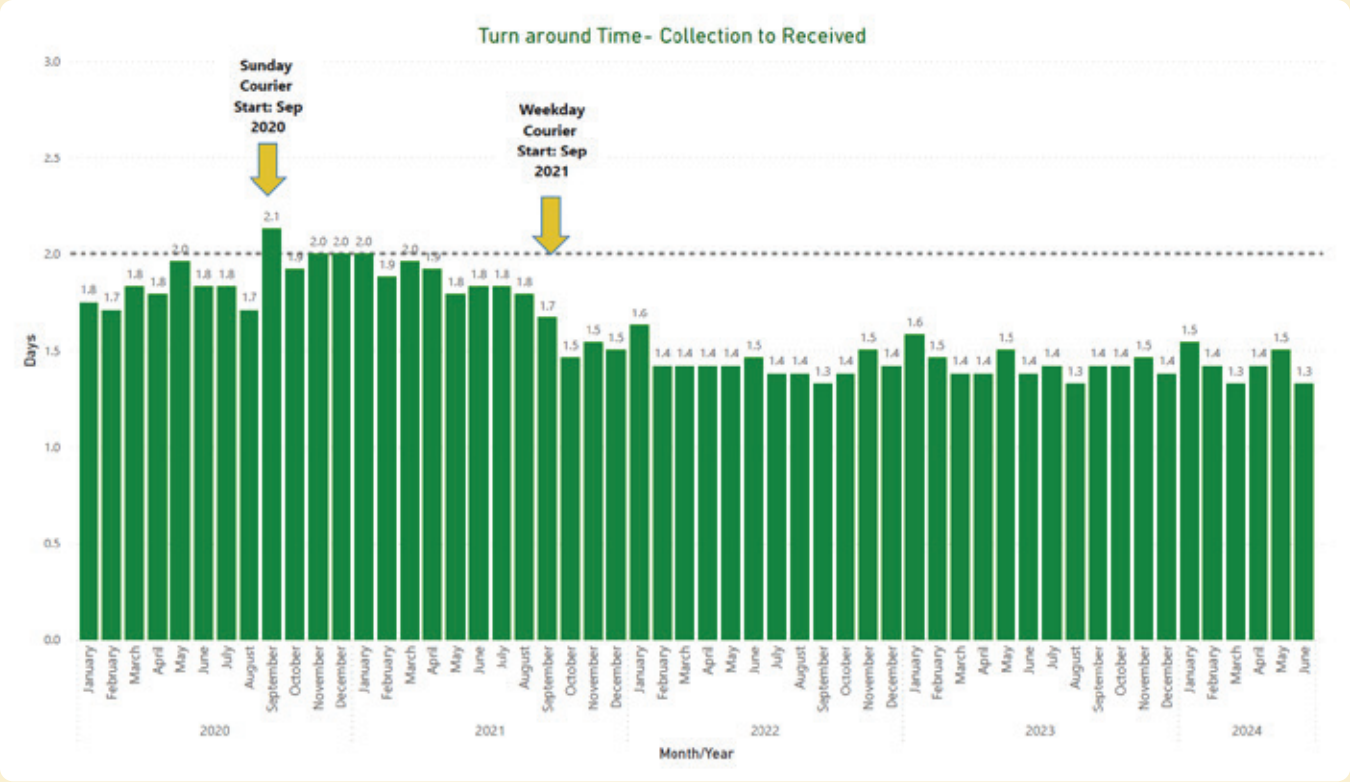
Impact on Families: Families of newborns with unsatisfactory screening results may experience heightened anxiety and uncertainty. They may need to undergo additional testing or resubmission of specimens, which can prolong the period of uncertainty and delay necessary medical interventions or treatments.

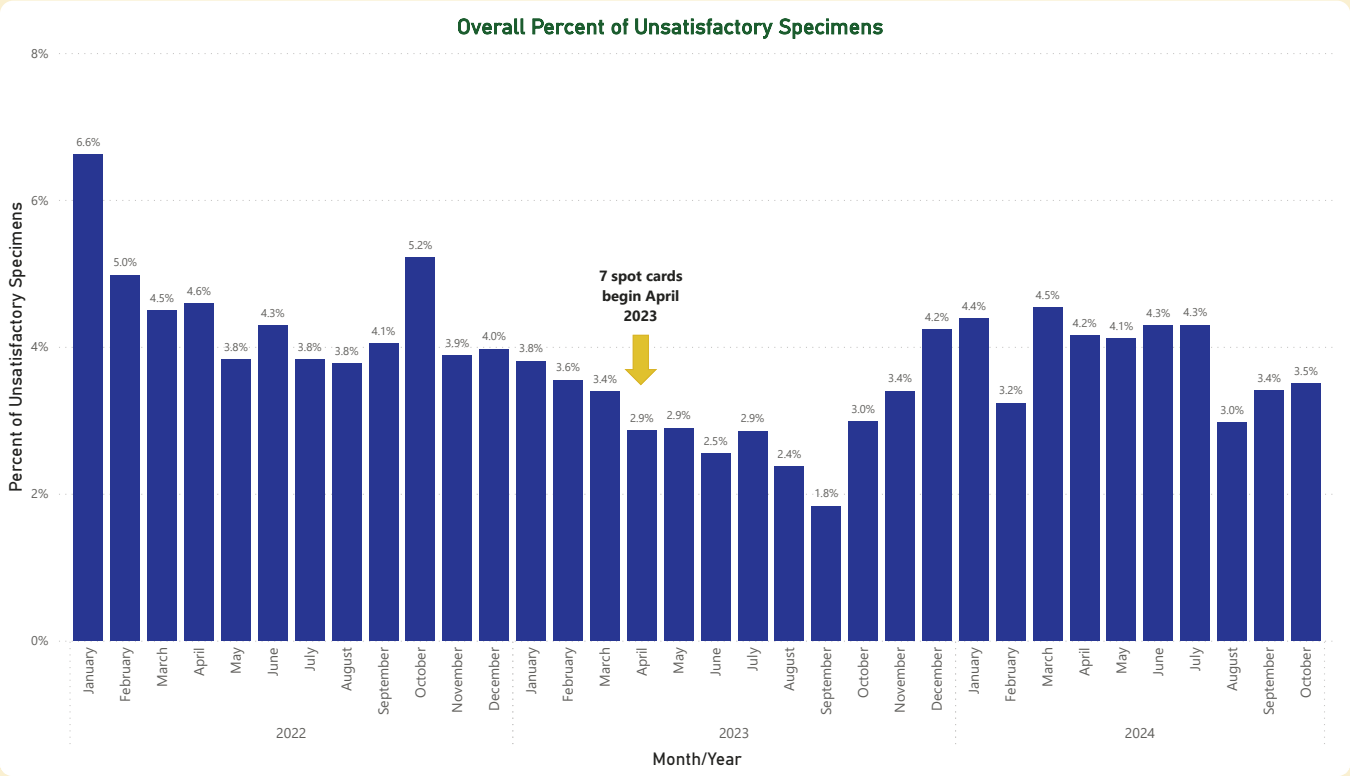
Public Health Concerns: High rates of unsatisfactory specimens can indicate issues within the newborn screening process, such as problems with specimen collection, transportation, or laboratory handling. Addressing these issues is crucial to maintaining the effectiveness of the newborn screening program and ensuring that all infants receive the best possible start in life.

Identifying and addressing the reasons behind a high rate of unsatisfactory specimens has led South Carolina to implement two quality improvement initiatives, and overall, see a reduction in the number of unsatisfactory specimens received.

1) Increasing the number of blood spots from five to seven.

2) Training healthcare providers on proper specimen collection techniques and improving transportation methods for specimens. This involves reducing the time it takes to receive the specimen once it has been collected.





NEWBORN SCREENING DIAGNOSED CASES IN 2023

Congenital Hypothyroidism

AnMed Health
Lexington Medical Center
McLeod Health Florence
McLeod Health Clarendon
MUSC Health Florence
MUSC Shawn Jenkins
Prisma Health Baptist
Prisma Health Greenville
Prisma Health Tuomey
Saint Francis Eastside
Self Regional Health care
Summerville Medical Center

Cystic Fibrosis

Prisma Health Baptist
Aiken Regional Medical
MUSC Shawn Jenkins
Prisma Health Baptist
Prisma Health Greer

Spinal Muscular Atrophy

Birth Choice Midwifery
McLeod Health Florence
MUSC Shawn Jenkins
Prisma Health Greer
Spartanburg Medical Center

Hemoglobin Disorders

AnMed Health
Bon Secours St Francis Hospital
Carolina Pines Regional Medical
Colleton Medical Center
Conway Medical Center
Lexington Medical Center
McLeod Health Florence
MUSC Health Florence
MUSC Orangeburg
MUSC Shawn Jenkins
Prisma Health Baptist Hospital
Prisma Health Baptist Parkridge
Prisma Health Patewood
Prisma Health Richland
Saint Francis Eastside
Summerville Medical Center

Congenital Adrenal Hyperplasia

Aiken Regional Medical
Moncrief Army Hospital
Spartanburg Medical Center

Galactosemia

Piedmont Medical Center
Prisma Health Patewood
Roper St Francis Berkely

Metabolic Disorders

Phenylketonuria (PKU)

Prisma Health Greer
Spartanburg Medical Center

Fatty Acid Oxidation Disorders

Very long-chain acyl-CoA dehydrogenase (VLCAD)

Prisma Health Greenville

Organic Acid Metabolism Disorders

3-Methylcrotonyl-CoA carboxylase deficiency (3-MCC)

Prisma Health Greenville

Isovaleric Acidemia (IVA)

AnMed Health

Propionic Acidemia

Spartanburg Medical Center

ON THE SPOT

Here are the top 5 performing birthing hospitals who achieved the lowest average percentage of unsatisfactory newborn screening specimens for 2023:

Hospital Name	Total Specimens Submitted	Number of Unsatisfactory Specimens	Percent of Unsatisfactory Specimens
Hilton Head Hospital	216	0	0.00%
Prisma Health: Oconee Memorial Hospital	448	2	0.45%
Aiken Regional Medical Center	1046	5	0.48%
AnMed Health Women and Children's Hospital	1389	10	0.72%
Prisma Health: Greenville Memorial Hospital: Newborn Nursery	3770	29	0.77%

FIRST TIME EVERY TIME!

The Newborn Screening Quality Improvement (QI) team provides in-person training. As of December 2024, the program has provided 3 lunch & learn sessions and 39 training courses to various medical professionals. The training has received very positive feedback and provides an opportunity to practice blood spot collection using our simulated baby feet.

Email NBSQI@dph.sc.gov to sign up for training or request our helpful training materials on everything from adequate specimen types to the courier processes. We are always ready to assist.

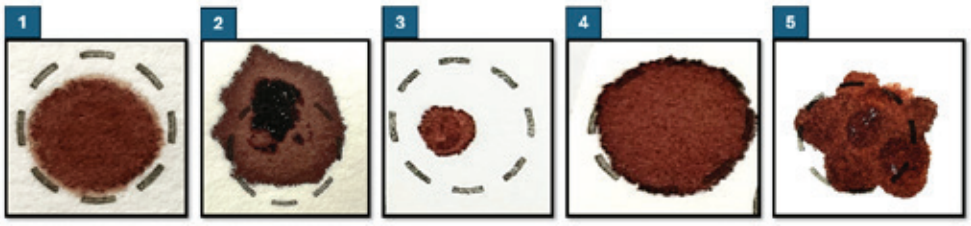
Comments from training:

"Learned so much, staff made it comfortable, felt like a discussion with round table input and improvements."

"Awesome training! We loved hearing our site location stats and ways we can improve our collections!"

"It was an excellent presentation with interactive education for staff. It was the right length and excellent material presented."

Check your spot knowledge:



1. **Contaminated**—Notice the pink halo around the blood spot. Prevent this by wiping away the first drop of blood and not applying too much pressure to the heel during collection.
2. **Clotted**—The dark section of the spot is a clot from another blood drop being added overtop an existing blood spot. Apply only one drop of blood per circle.
3. **Quantity Insufficient**—The blood drop is too small for testing. Blood drops should fill the preprinted circles completely. Applying a heel warmer before collection may help.
4. **Satisfactory for testing**—The blood drop meets the laboratory's standards for testing.
5. **Layered**—Multiple drops of blood layer the circle. Apply only one drop of blood per circle. The blood drop should fill the circle completely.

EDUCATIONAL INFORMATION:

Are you educating parents about Newborn Screening?

Visit dph.sc.gov/professionals/health-professionals/health-services-facilities/newborn-screening to find our updated newborn screening brochure and educational handouts for parents and providers.

Are you in need of NBS brochures?

Please go to dph.sc.gov/professionals/health-professionals/educational-materials

Brochures are currently offered in English, Spanish, Russian, and Ukrainian. If you do not see your preferred language, please reach out to our program for more information.

Are you in need of NBS collection forms?

Email PHL-supply@dph.sc.gov or call 803-896-0913 to receive collection forms.

Time to check your collection forms! The next batches of filter paper expire on: 9/30/2024 & 5/31/2024!

Are you in need of drying racks or laminated flyer booklets?

You can email the Newborn Screening Quality Improvement team at NBSQI@dph.sc.gov to place your request.

WE ENJOY HELPING OUR PARTNERS PUT THEIR BEST FOOT FORWARD!

CONTACT US. WE'RE HERE TO HELP!

DPH Newborn Screening Program:
(803) 898-3192

DPH Newborn Screening Lab:
(803) 896-0891

Keep us on our toes.
Please give us feedback on what you would like to see in our next Footnotes Edition.

Email NBSQI@dph.sc.gov with your suggestions.

SOUTH CAROLINA DEPARTMENT OF PUBLIC HEALTH
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