Washington State Newborn Screening
Screening Tests, Result Classifications and Corresponding Follow-Up Actions

This document briefly explains the tests for the disorders screened for by the Washington State Newborn Screening Program. It also contains cutoff tables for the disorders, results classifications and corresponding follow-up actions. Follow-up actions described in this document are general guidelines and are sometimes modified based on individual test results, consultation with specialists, and the child's clinical status. The table below serves as a key relating the classification of results in this document to the comments found in Newborn Screening Reports.

Classification of results within this document	Corresponding comments found on NBS mailer report
Normal	NORMAL FINDINGS
Borderline, Presumptive, Partial, Profound or Elevated	Abnormal
Interfering Substances	Unsuitable

Disorders

Amino acid disorders argininosuccinic acidemia (ASA) citrullinemia (CIT) homocystinuria (HCY) maple syrup urine disease (MSUD) phenylketonuria (PKU) tyrosinemia type 1 (TYR I)	**Endocrine Disorders** congenital adrenal hyperplasia (CAH) congenital hypothyroidism (CH)
Fatty acid disorders carnitine uptake deficiency (CUD) long-chain L-3-hydroxy acyl-CoA dehydrogenase (LCHAD) deficiency medium-chain acyl-CoA dehydrogenase MCAD) deficiency trifunctional protein (TFP) deficiency very-long chain acyl-CoA dehydrogenase (VLCAD) deficiency	**Lysosomal Storage Disorders** mucopolysaccharidosis type I (MPS-I) glycogen storage disorder type II (Pompe)
Organic acid disorders 3-hydroxy-3-methylglutaric aciduria (HMG) beta-ketothiolase deficiency (BKT) glutaric acidemia type 1 (GA-I) isovaleric acidemia (IVA) methylmalonic acidemias (CblA,B and MUT) multiple carboxylase deficiency (MCD) propionic acidemia (PROP)	**Other disorders** biotinidase deficiency cystic fibrosis (CF) galactosemia hemoglobinopathies severe combined immunodeficiency (SCID) X-linked adrenoleukodystrophy (X-ALD) spinal muscular atrophy (SMA)

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Argininosuccinic acidemia (ASA) / Citrullinemia (CIT) – 08/07/2023

Screening Test

Screening for these disorders is performed by tandem mass spectrometry (MS/MS) measuring *citrulline (cit), argininosuccinic acid (asa)* and *arginine (arg)*. If CIT is elevated, secondary markers are analyzed. Results are classified in the tables below.

Screening Result Classifications and Corresponding Follow-up Actions for ASA and CIT

Citrulline µmol/L blood	Age at collection ≤ 6 days	Age at collection > 6 days
< 35.7	Normal	Normal
35.7 – 110.9	Borderline	Normal
≥ 111	Borderline or Presumptive†	Borderline or Presumptive†
Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	Health care provider is contacted by phone to recommend repeat newborn screening specimen or *diagnostic testing*. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend immediate follow-up specimen or *diagnostic testing*. Newborn screening results are also mailed to submitter.

†Final results depend on secondary markers (normal ranges for ASA secondary markers: cit/arg < 5.56, asa < 0.77 and asa/arg < 0.15; normal ranges for CIT secondary markers: cit/arg < 5.56)

Note: If baby is on HA/TPN prior to specimen collection, results are considered unsuitable due to interfering substances and the health care provider is contacted to recommend a repeat newborn screening specimen.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include: poor feeding, vomiting, lethargy, hypotonia, tachypnea, seizures and signs of liver disease.

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Homocystinuria (HCYS) – 08/07/2023

Screening Test
Homocystinuria screening is done using tandem mass spectrometry (MS/MS) to measure the level of *methionine (met)* and *phenylalanine (phe)* in the blood. Results are classified as in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for HCYS

Methionine µmol/L blood	Classification	
	met/phe <1.0	met/phe ≥1.0
< 59.00	Normal	Normal
59.00 – 76.79	Normal	Borderline
76.80 – 99.19	Borderline	Borderline
≥ 99.20	Borderline	Presumptive
Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to specimen submitter. No follow-up is required	If first specimen on LBW baby or collected early (1-6 hours) NBS waits for the routine second specimen, otherwise health care provider is contacted to request second specimen. If second screen and previous normal, health care provider is contacted to request third specimen. If second screen and previous abnormal, health care provider is contacted to recommend *diagnostic testing*. Results are also mailed to submitter.	If first screen, health care provider is contacted by phone to recommend immediate second screen. If second screen, immediate *diagnostic testing* is recommended if non-NICU baby and third screen if NICU baby. Results are also mailed to submitter.

Note: If baby is on HA/TPN prior to specimen collection, results are considered unsuitable due to interfering substances and the health care provider is contacted to recommend a repeat newborn screening specimen.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. HCY is usually asymptomatic in the newborn period, in older children symptoms may include: developmental delay, ectopia lentis, skeletal deformities and thromboembolism.

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Maple Syrup Urine Disease (MSUD) - 08/07/2023

Screening Test
The MSUD screening is done using tandem mass spectrometry (MS/MS) to measure the levels of *leucine/isoleucine (leu)*, *valine (val)*, *phenylalanine (phe)* and *alanine (ala)* in the blood. Results are classified as in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for MSUD

Leucine µmol/L blood	Age at collection ≤ 6 days		Age at collection > 6 days	
	not all secondary markers† elevated	all secondary markers† elevated	not all secondary markers† elevated	all secondary markers† elevated
< 273.70	Normal	Normal	Normal	Normal
273.70 – 358.79	Borderline	Presumptive	Normal	Normal
358.80 – 434.79	Borderline	Presumptive	Borderline	Presumptive
≥ 434.80	Presumptive	Presumptive	Borderline	Presumptive
Typical Follow-up Actions				
Normal Results	**Borderline Results**		**Presumptive Results**	
Results are mailed to submitter. No follow-up is required.	If age at collection ≤ 6 days, NBS waits for routine second specimen. If Age at collection > 6 days, a repeat NBS is requested. If previous abnormal, health care provider is contacted to recommend *diagnostic testing*. Results are also mailed to submitter.		Health care provider is contacted and immediate *diagnostic testing* is recommended. If leucine is ≥ 466, not all secondary markers are elevated and baby is ≤6 days at time of collection, a metabolic specialist is consulted. Results are also mailed to submitter.	

†Final results depend on secondary markers (normal ranges: val < 200, leu/ala < 1.0, leu/phe < 3.65 and val/phe < 3.0)

Note: If baby is on HA/TPN prior to specimen collection, results are considered unsuitable due to interfering substances and the health care provider is contacted to recommend a repeat newborn screening specimen.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include: poor feeding, vomiting, lethargy, tachypnea, seizures and alternating hypertonia/hypotonia.

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Phenylketonuria (PKU) – 08/07/2023

Screening Test

The PKU screening is no longer performed by the bacterial inhibition assay developed by Dr. Robert Guthrie, commonly known as the "Guthrie test." Screening is now done using a technology called tandem mass spectrometry (MS/MS). The levels of *phenylalanine (phe)* and *tyrosine (tyr)* in the blood spot are measured by a tandem mass spectrometer. Results are classified as in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for PKU

Phenylalanine µmol/L blood	Age ≤ 24 hrs		Age > 24 hrs	
	phe/tyr ratio < 2	phe/tyr ratio ≥ 2	phe/tyr ratio < 2	phe/tyr ratio ≥ 2
< 164.40	Normal	Normal	Normal	Normal
164.40 – 193.99	Normal	Borderline	Normal	Borderline
194.00 – 262.69	Borderline	Presumptive	Borderline	Borderline
≥ 262.70	Presumptive	Presumptive	Presumptive	Presumptive

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	Health care provider is contacted by phone to recommend a repeat newborn screening specimen. If baby is in the NICU, NBS waits for routine second specimen. Results are also mailed to submitter.	Health care provider is contacted by phone to recommend an immediate repeat newborn screening specimen or *diagnostic testing* per PKU Clinic staff recommendations. Results are also mailed to submitter.

Note: If baby is on HA/TPN prior to specimen collection, results are considered unsuitable due to interfering substances and the health care provider is contacted to recommend a repeat newborn screening specimen.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. PKU is usually asymptomatic in the newborn period, in older children symptoms may include: developmental delay, hyperactivity, eczema, autistic-like features, seizures and a musty odor.

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Tyrosinemia type I (TYR-I) - 08/07/2023

Screening Test
Screening for these disorders is performed by tandem mass spectrometry (MS/MS). The most sensitive (and specific) primary marker for TYR-I is *succinylacetone* (SUAC). If this is elevated, *tyrosine (tyr)* is analyzed. Results are classified as in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for TYR-I

SUAC µmol/L blood	Classification
< 2.48	Normal
≥ 2.48	Presumptive
Typical Follow-up Actions	
Normal Results	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	Health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. TYR-I is usually asymptomatic in the newborn period, in older children symptoms may include: liver disease with cirrhosis, renal disease, rickets and neurologic crises.

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Congenital Adrenal Hyperplasia (CAH) – 04/29/2020

Screening Tests

CAH screening, is done by fluoroimmunoassay. The test measures hormone levels of *17-hydroxyprogesterone (17-OHP)*, which is elevated in infants with CAH. Due to variability of the disorder and the age of the infant, the level of 17-OHP may not correlate with the clinical severity of the disease. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for CAH

	Weight <1500 grams		
17-OHP ng/mL serum	**Age < 6 days**	**Age: 6-29 days**	**Age ≥ 30 days**
< 50	Normal	Normal	Normal
50 to 79.9	Normal	Normal	Borderline
80 to 99.9	Borderline	Borderline	Borderline
100 to 149.9	Borderline	Borderline	Presumptive
≥ 150	Presumptive	Presumptive	Presumptive
	Weight 1500-2499 grams		
	Age < 6 days	**Age: 6-29 days**	**Age ≥ 30 days**
< 40	Normal	Normal	Normal
40 to 79.9	Normal	Borderline	Borderline
80 to 99.9	Borderline	Borderline	Borderline
100 to 149.9	Borderline	Borderline	Presumptive
≥ 150	Presumptive	Presumptive	Presumptive
	Weight ≥ 2500 grams		
	Age ≤ 6 hours	**7 hours to 6 days**	**Age ≥ 6 days**
< 40	Normal	Normal	Normal
40 to 59.9	Normal	Normal	Borderline
60 to 79.9	Borderline	Borderline	Borderline
80 to 99.9	Borderline	Borderline	Presumptive
≥ 100	Presumptive	Presumptive	Presumptive

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	If first screen, wait for routine second screen. If previous abnormal, health care provider is contacted by phone to recommend repeat newborn screen or immediate *diagnostic testing*. Results are also mailed to submitter.	Health care provider is contacted by phone to recommend a repeat newborn screening specimen and/or *diagnostic testing* as soon as possible. Results are also mailed to submitter.

Note: If baby is on steroids prior to specimen collection, results are considered unsuitable due to interfering substances and the health care provider is contacted to recommend a repeat newborn screening specimen.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include electrolyte imbalance (low sodium and high potassium), ambiguous genitalia, lethargy, vomiting, poor feeding and precocious puberty.

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Screening Tests

The newborn screening test for CH measures the infant's *thyroid stimulating hormone (TSH)* level using a fluoroimmunoassay technique. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for CH

Age at Collection	Borderline Passive TSHμIU/mL serum≥	Borderline Active TSHμIU/mL serum≥	Presumptive TSHμIU/mL serum≥	Presumptive TSHμIU/mL serum≥	Urgent Presumptive TSHμIU/mL serum≥
1 hr	115	175	n/a	190	300
2-7 hr	100	150	n/a	180	300
8-17 hr	60	100	n/a	125	300
18-22 hrs	40	75	n/a	80	300
23-25 hrs	35	75	n/a	80	300
26-35 hrs	30	50	n/a	80	300
36-47 hrs	26	50	n/a	60	100
48-72 hrs	20	50	n/a	60	100
73-144 hrs	18	40	n/a	50	100
145-504hrs	n/a	n/a	16	35	100
505 hrs - 6 mos	n/a	n/a	13	30	100

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	For ***Borderline Passive*** results NBS waits for the routine second specimen. For ***Borderline Active*** results NBS contacts health care provider to recommend newborn screening specimen as soon as possible. If previous abnormal, health care provider is contacted by phone to recommend *diagnostic testing*. Results are also mailed to submitter.	Health care provider is immediately contacted by phone to recommend *diagnostic testing* as soon as possible. Results are also mailed to submitter. For ***Urgent Presumptive*** results, treatment should be initiated immediately after specimen collection, unless mother is on antithyroid medication.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Congenital hypothyroidism is usually asymptomatic in the first few months, in older children symptoms may include prolonged jaundice, constipation, lethargy, poor muscle tone, feeding problems, a large tongue, mottled and dry skin, distended abdomen, umbilical hernia, stunted growth and developmental disability.

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Carnitine Uptake Deficiency (CUD) – 08/07/2023

Screening Test
Screening for CUD is performed by tandem mass spectrometry (MS/MS). The primary marker is *free carnitine* (*C0*). If *C0* is low, secondary markers are analyzed. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for CUD

C0 µmol/L blood	Classification	
	not all secondary markers† low	all secondary markers† low
> 8.35	Normal	Normal
≤ 8.35	Abnormal	Abnormal
Typical Follow-up Actions		
Normal Results	**Abnormal (not all 2º markers low)**	**Abnormal (all 2º markers low)**
Results are mailed to submitter. No follow-up is required.	If first specimen, NBS waits for routine second specimen. If second specimen with a normal first, collected at ≥18 hours of age, and birth weight >2500 grams) no further testing is needed. If previous specimen does not meet the above criteria the health care provider is contacted to request a third screen, if baby is in the NICU NBS waits for routine third specimen. If second specimen with a borderline first, NBS contacts health care provider to recommend *diagnostic testing*, including maternal samples. Newborn screening results are also mailed to submitter.	If first specimen for a non-NICU baby, NBS contacts health care provider to recommend an immediate repeat newborn screening specimen. If second specimen, , and linked with a normal first, health care provider is contacted to request a third specimen. If linked to an abnormal first screen, health care provider is contacted to recommend immediate *diagnostic testing* including maternal samplesNewborn screening results are also mailed to submitter.

† Final results depend on secondary markers (C3+C16 < 2.0 and (C0+C2+C3+C16+C18+C18:1)/CIT < 3.0)

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include: poor feeding, lethargy, tachypnea, tachycardia, hepatomegaly and reduced muscle tone.

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Long-chain L-3-hydroxy acyl-CoA dehydrogenase (LCHAD)deficiency/ Trifunctional Protein (TFP) deficiency - 08/07/2023

Screening Test
Screening for these disorders is performed by tandem mass spectrometry (MS/MS). The primary marker for LCHAD and TFP deficiencies is *3 hydroxy-hexadecanoylcarnitine (C16OH)*. If *C16OH* is elevated, secondary markers are analyzed. Results are classified as in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for LCHAD/TFP

C16OH µmol/L blood	Classification	
	not all secondary markers† elevated	all secondary markers† elevated
< 0.12	Normal	Normal
≥ 0.12	Borderline	Presumptive
Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	Health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.	

†Final results depend on secondary markers (normal ranges: C14 < 0.60, C14:1< 0.60, C16 < 5.69, C16OH/C16 < 0.062, C18 < 1.73 and C18:1 < 2.48)

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include: poor feeding, vomiting, lethargy, hepatomegaly, cardiac insufficiency, hypoglycemia, maternal liver disease during pregnancy and a history of sudden unexpected death in a sibling.

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Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency – 08/07/2023

Screening Test
The MCAD deficiency screening is done using tandem mass spectrometry (MS/MS) to measure the levels of *octanoyl carnitine (C8)* and *(C10)* in the blood. If C8 is elevated, and C8/C10 ratio is ≥0.5, secondary markers are analyzed. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for MCAD

C8 µmol/L blood	Classification	
	not all secondary markers† elevated	all secondary markers† elevated
< 0.51	Normal	Normal
0.51 – 1.07	Borderline	Borderline
≥ 1.08	Borderline	Presumptive
Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	Health care provider is contacted by phone to recommend *diagnostic testing*. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend immediate *diagnostic testing*. Results are also mailed to submitter.

†Final results depend on secondary markers (normal ranges: C8/C2 < 0.02, C8/C10 <0.92 and C10:1 < 0.18 µmol/L).

Note: If baby is on HA/TPN prior to specimen collection, results are considered unsuitable due to interfering substances and the health care provider is contacted to recommend a repeat newborn screening specimen.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include: poor feeding, vomiting, lethargy, hypotonia and hepatomegaly.

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Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency – 08/07/2023

Screening Test
Screening for VLCAD deficiency is performed by tandem mass spectrometry (MS/MS). The primary marker for VLCAD deficiency is *tetradecenoylcarnitine (C14:1)*. If *C14:1* is elevated, secondary markers are analyzed. Results are classified as in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for VLCAD

C14:1 µmol/L blood	Age at collection ≤ 6 days	Age at collection > 6 days
< 0.49	Normal	Normal
0.49 – 0.68	Normal	Borderline
0.69 – 0.74	Borderline or Presumptive†	Borderline
≥ 0.75	Presumptive	Presumptive
Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	Post-analytical tools and/or specialist consult are used to assess appropriate follow-up. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.

† Final results depend on secondary markers (normal ranges: C14:1/C2 < 0.07, C14 < 0.6, C14:1/C16 < 0.2, C12:1 < 0.15, and C14:2 < 0.09)

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include: poor feeding, vomiting, lethargy, hypotonia, hepatomegaly, arrhythmia, and evidence of cardiac decompensation.

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Mucopolysaccharidosis type-I (MPS-I) – 7/3/2023

Screening Test
Screening for MPS-I is performed by digital microfluidics. Activity of the enzyme alpha-L-iduronidase (IDUA), which is reduced in infants with this disorder, is measured. A diminished enzyme activity indicates that the infant may have MPS-I. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for MPS-I

IDUA (µmol/L/hr)	Low Enzyme Activity		
	First Specimen	Linked to Normal	Linked to Abnormal (None Normal)
> 3.94	Normal	Normal	Normal
1.5 – 3.94	Borderline	Normal	Persistently Low
< 1.5	Borderline	Normal	Persistently Low

Typical Follow-up Actions		
Normal or Linked to Normal	Borderline	Persistently Low
Results are mailed to specimen submitter. No follow-up is required.	Depending on level of result, NBS will wait for routine second specimen or NBS will call the healthcare provider to recommend a subsequent specimen. Results are also mailed to submitter.	NBS will call the healthcare provider to recommend second specimen, check clinical status of newborn and inform them of next steps, which may include second tier screening or diagnostic testing. Results are also mailed to submitter.

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Glycogen Storage Disorder Type II (Pompe disease) – 7/3/2023

Screening Test
Screening for Pompe disease is performed by digital microfluidics. Activity of the enzyme acid alpha glucosidase (GAA), which is reduced in infants with this disorder, is measured. A diminished enzyme activity indicates that the infant may have Pompe disease. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for Pompe disease

GAA (µmol/L/hr)	Classification	
	Age at collection ≤ 6 days	**Age at collection > 6 days**
> 8.70	Normal	Normal
7.83-8.70	Low enzyme activity	Normal
4.69-7.82	Low enzyme activity	Normal
< 4.69	Low enzyme activity	Low enzyme activity
Typical Follow-up Actions		
Normal Results	**Low enzyme activity**	
Results are mailed to specimen submitter. No follow-up is required.	NBS will call the health care provider to check clinical status of newborn and inform them of next steps, which may include a subsequent NBS specimen, second tier screening, third tier screening, and/or diagnostic testing. If linked with a normal specimen, no follow-up is required unless there are clinical concerns. Results are also mailed to submitter.	

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses below. Symptoms include: cardiomegaly, hypotonia, failure to thrive, breathing problems. This recommendation includes abnormal results linked to a previous normal result.

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HMG deficiency and Multiple Carboxylase deficiency (MCD) – 07/22/2019

Screening Test

Screening for HMG deficiency is performed by tandem mass spectrometry (MS/MS). The primary marker for HMG deficiency is *3-hydroxy-isovaleryl carnitine (C5-OH)*. If *C5OH* is elevated, a secondary marker is analyzed. Results are classified as in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for HMG and MCD

C5OH µmol/L blood	Classification	
	C5OH/C8 < 10	C5OH/C8 ≥ 10
< 0.77	Normal	Normal
0.77 – 3.89	Borderline	Presumptive
≥ 3.90	Borderline	Borderline

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	If first specimen, health care provider is contacted by phone to recommend a repeat newborn screening specimen as soon as possible. If second specimen, health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter. **Special Circumstance:** If C5OH is greater than 4.33 µmol/L, the likelihood of HMG is very low. The probable reason for the elevation in C5OH is 3-methylcrotonyl carboxylase (3MCC) deficiency in the newborn or the mother.	If first specimen, health care provider is contacted by phone to recommend a repeat newborn screening specimen as soon as possible or immediate *diagnostic testing* (if symptomatic). If second specimen, health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses below. Symptoms may include: poor feeding, vomiting and lethargy.

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Beta-ketothiolase deficiency (BKT) - 07/22/2019

Screening Test
Screening for BKT deficiency is performed by tandem mass spectrometry (MS/MS). The primary marker for BKT deficiency is *3-methylcrotonyl carnitine (C5:1),* also known as *tiglyl carnitine*. If *C5:1* is elevated, secondary markers are analyzed. Results are classified as in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for BKT

C5:1 µmol/L blood	Classification	
	not all secondary markers† elevated	all secondary markers† elevated
< 0.11	Normal	Normal
≥ 0.11	Borderline	Presumptive

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	If first specimen, health care provider is contacted by phone to recommend an immediate repeat newborn screening specimen. If second specimen, health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.

† Final results depend on secondary markers (normal ranges: C5OH < 1.00 and C5OH/C8 < 10.0)

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses below. Symptoms may include: poor feeding, vomiting and lethargy.

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Glutaric acidemia type I (GA-I) - 08/07/2023

Screening Test
Screening for GA-I is performed by tandem mass spectrometry to measure the levels of *glutarylcarnitine (C5DC)* in the blood. If *C5DC* is elevated, secondary markers are analyzed. Results are classified as in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for GA-I

C5DC µmol/L blood	Classification	
	not all secondary markers† elevated	all secondary markers† elevated
< 0.14	Normal	Normal
0.14 - 0.16	Borderline	Presumptive
≥ 0.17	Borderline	Presumptive
Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	If first specimen, wait for routine 2nd or health care provider is contacted by phone to recommend immediate second newborn screening specimen. If second specimen and NICU baby with birth weight ≤1500 grams NBS requests a third specimen otherwise health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.

† Final results depend on secondary markers (normal ranges: C5DC/C5OH < 1.0, C5DC/C8 < 1.0 and C5DC/C16 < 0.055

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses below. Symptoms may include: macrocephaly, muscle hypotonia, dystonia, poor feeding and irritability.

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Isovaleric acidemia (IVA) – 04/29/2020

Screening Test
Screening for IVA is performed using tandem mass spectrometry (MS/MS). The primary marker for IVA is *isovalerylcarnitine (C5)*. If *C5* is elevated, secondary markers are analyzed. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for IVA

C5 µmol/L blood	Birth weight ≤ 1500g		Birth weight > 1500g	
	Age at collection ≤ 6 days	Age at collection > 6 days	Age at collection ≤ 6 days	Age at collection > 6 days
< 0.62	Normal	Normal	Normal	Normal
0.62 – 0.80	Interfering substances	Normal	Borderline	Normal
0.81 – 1.25	Interfering substances	Interfering substances	Borderline or Presumptive†	Borderline
≥ 1.26	Presumptive	Presumptive	Presumptive	Presumptive

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	Health care provider is contacted to inquire about antibiotic use (antibiotics may interfere with results). If first specimen and no antibiotics, an immediate second newborn screening specimen is recommended. If second specimen, health care provider is contacted by phone to recommend third screen or *diagnostic testing*. If baby is in the NICU, NBS waits for routine subsequent specimen. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.

† Final results depend on secondary markers (normal ranges: C5/C0 < 0.02, C5/C2 < 0.02 and C5/C3 < 0.33)

Note: If baby is on antibiotics prior to specimen collection, results are considered unsuitable due to interfering substances and the health care provider is contacted to recommend a repeat newborn screening specimen.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses below. Symptoms may include: poor feeding, vomiting, lethargy, tachypnea and an odor of sweaty feet.

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Methylmalonic and Propionic acidemias (MMAs and PROP) - 08/07/2023

Screening Test
Screening for these disorders is performed by tandem mass spectrometry (MS/MS). The primary marker for methylmalonic acidemia and propionic acidemia is *propionylcarnitine (C3)*. If *C3* is elevated, secondary markers are analyzed. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for MMAs/PROP

C3 µmol/L blood	Age at collection ≤ 6 days		Age at collection > 6 days	
	not all secondary markers† elevated	all secondary markers† elevated	not all secondary markers† elevated	all secondary markers† elevated
< 4.08	Normal	Normal	Normal	Normal
4.08 – 4.68	Normal	Normal	Borderline	Presumptive
4.69 – 6.10	Normal	Borderline	Borderline	Presumptive
6.11 – 8.02	Borderline	Presumptive	Borderline	Presumptive
8.03 – 10.97	Borderline	Presumptive	Borderline	Presumptive
≥ 10.98	Presumptive	Presumptive	Presumptive	Presumptive

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	If first screen, wait for routine second screen. If previous abnormal, health care provider is contacted by phone to recommend repeat newborn screen or immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.

† Final results depend on secondary markers (normal ranges: C3/C2 < 0.21 and C3/C16 < 2.4)

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses below. Symptoms may include: poor feeding, vomiting, lethargy and tachypnea.

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Biotinidase deficiency – 04/29/2020

Screening Tests

Biotinidase deficiency screening is done by a colorimetric assay. Activity of the enzyme biotinidase, which is reduced in infants with this disorder, is measured. A diminished color in the processed blood specimen indicates that the infant may have biotinidase deficiency. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for Biotinidase Deficiency

Biotinidase (% activity)	Classification
> 20%	Normal
10% – 20%	Partial
< 10%	Profound

Typical Follow-up Actions		
Normal Results	**Partial Results**	**Profound Results**
Results are mailed to specimen submitter. No follow-up is required.	If first specimen, NBS waits for routine second specimen. If second specimen with a normal first, no further follow-up is needed. If second specimen with an abnormal first, contact health care provider to recommend *diagnostic testing*. Results are also mailed to submitter.	If first screen, health care provider is contacted by phone to recommend immediate second specimen. If second screen linked to a previous abnormal, immediate diagnostic testing is recommended. Results are also mailed to submitter.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include seizures, ataxia, hypotonia, developmental delay, hearing loss, decreased vision, rash, conjunctivitis, hair loss and fungal infections.

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Cystic Fibrosis (CF) - 07/01/2023 - Washington State Cutoffs

Screening Tests
The cystic fibrosis screening is performed using a fluoroimmunoassay to measure the level of *immunoreactive trypsinogen (IRT)* which is elevated in infants with this disorder. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for CF

First Tier: IRT/IRT - Age at Collection ≤144 hours					
IRT Value (ng/mL)	Previous Normal IRT	No Previous Specimen	Previous Abnormal IRT		
			No Previous DNA	Previous DNA: Zero Variants	Previous Abnormal DNA
<56.7	Normal	Normal	Normal	Normal	Normal
56.7 – 200.0	Normal	Second tier	Second tier	Elevated	Elevated
>200.0	Normal	Second tier	Second tier	Elevated	Elevated

First Tier: IRT/IRT - Age at Collection >144 hours					
IRT Value (ng/mL)	Previous Normal IRT	No Previous Specimen	Previous Abnormal IRT		
			No Previous DNA	Previous DNA: Zero Variants	Previous Abnormal DNA
<43.3	Normal	Normal	Normal	Normal	Normal
43.3 – 200.0	Normal	Second tier	Second tier	Elevated	Elevated
>200.0	Normal	Second tier	Second tier	Elevated	Elevated

Typical Follow-up		
Normal Results	Elevated Results	Second Tier
Results are mailed to submitter. No follow-up is required.	If second specimen is elevated and linked to previous normal, a subsequent specimen may be requested. If second tier CFTR DNA panel was run on a previous specimen, see report from previous specimen. Results are also mailed to submitter.	CFTR DNA panel is run off the dried blood spot. If no variants are detected, no follow-up needed unless there are clinical concerns or a subsequent specimen has an IRT >200. If one variant detected, health care provider is called to recommend a sweat test. Babies with one variant can have CF. If two variants are detected, health care provider is called to recommend referral to an accredited cystic fibrosis care center. Results are also mailed to submitter.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include meconium ileus, persistent cough, wheezing, repeated or prolonged bouts of pneumonia, failure to thrive, frequent greasy stools and persistent abdominal pain.

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Cystic Fibrosis (CF) – 07/01/2023 – Idaho cutoffs

Screening Tests
The cystic fibrosis screening is performed using a fluoroimmunoassay to measure the level of *immunoreactive trypsinogen (IRT)* which is elevated in infants with this disorder. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for CF

First Tier: IRT/IRT – Age at Collection ≤144 hours			
IRT Value (ng/mL)	Age at Collection ≤2 hours	Age at Collection 3-144 hours	
		BW <2500g	BW ≥2500g
<70.00	Normal	Normal	Normal
70.00 – 99.99	Normal	Normal	Borderline
100.00 – 149.99	Borderline	Borderline	Borderline
150.00 – 199.99	Borderline	Second tier	Second tier
200.00 - 400.00	Second tier	Second tier	Second tier
>400.00	Borderline	Borderline	Borderline

First Tier: IRT/IRT - Age at Collection >144 hours				
IRT Value (ng/mL)	Previous Normal IRT	Previous Abnormal IRT		
		No Previous DNA	Previous Normal DNA	Previous Abnormal DNA
<60.00	Normal	Normal	Normal	Normal
60.00-85.00	Elevated	Second tier	Elevated	Elevated
>85.00	Elevated	Second tier	Elevated	Elevated

Typical Follow-up		
Normal Results	Elevated Results	Second Tier
Results are mailed to submitter. No follow-up is required.	If second specimen is elevated and linked to previous normal, a subsequent specimen may be requested. If second tier CFTR DNA panel was run on a previous specimen, see report from previous specimen. Results are also mailed to submitter.	CFTR DNA panel is run off the dried blood spot. If no variants are detected, no follow-up needed unless there are clinical concerns or a subsequent specimen has an IRT >200. If one variant detected, health care provider is called to recommend a sweat test. Babies with one variant can have CF. If two variants are detected, health care provider is called to recommend referral to an accredited cystic fibrosis care center. Results are also mailed to submitter.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include meconium ileus, persistent cough, wheezing, repeated or prolonged bouts of pneumonia, failure to thrive, frequent greasy stools and persistent abdominal pain.

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Cystic Fibrosis (CF) – 07/01/2023 - Hawaii cutoffs

Screening Tests
The cystic fibrosis screening is performed using a fluoroimmunoassay to measure the level of *immunoreactive trypsinogen (IRT)* which is elevated in infants with this disorder. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for CF

First Tier: IRT/IRT - Age at Collection ≤144 hours					
IRT Value (ng/mL)	Previous Normal IRT	No Previous Specimen	Previous Abnormal IRT		
			No Previous DNA	Previous DNA: Zero Variants	Previous Abnormal DNA
<56.7	Normal	Normal	Normal	Normal	Normal
56.07 – 200.0	Normal	Second tier	Second tier	Elevated	Elevated
>200.0	Normal	Second tier	Second tier	Elevated	Elevated

First Tier: IRT/IRT - Age at Collection >144 hours					
IRT Value (ng/mL)	Previous Normal IRT	No Previous Specimen	Previous Abnormal IRT		
			No Previous DNA	Previous DNA: Zero Variants	Previous Abnormal DNA
<43.3	Normal	Normal	Normal	Normal	Normal
43.03 – 200.0	Normal	Second tier	Second tier	Elevated	Elevated
>200.0	Normal	Second tier	Second tier	Elevated	Elevated

Typical Follow-up		
Normal Results	Elevated Results	Second Tier
Results are mailed to submitter. No follow-up is required.	If second specimen is elevated and linked to previous normal, a subsequent specimen may be requested. If second tier CFTR DNA panel was run on a previous specimen, see report from previous specimen. Results are also mailed to submitter.	CFTR DNA panel is run off the dried blood spot. If no variants are detected, no follow-up needed unless there are clinical concerns or a subsequent specimen has an IRT >200. If one variant detected, health care provider is called to recommend a sweat test. Babies with one variant can have CF. If two variants are detected, health care provider is called to recommend referral to an accredited cystic fibrosis care center. Results are also mailed to submitter.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include meconium ileus, persistent cough, wheezing, repeated or prolonged bouts of pneumonia, failure to thrive, frequent greasy stools and persistent abdominal pain.

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Galactosemia – 08/08/2023

Screening Tests
Galactosemia screening is done by a fluorometric assay that measures activity of the GALT enzyme. Diminished fluorescence in the processed blood specimen indicates that the infant may have galactosemia. A second-tier test will be performed on screen positive specimens if needed to further clarify the significance of the initial test results. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for Galactosemia

GALT (Units/gHb)	Age at collection ≤ 144 hours		Age at collection >144 hours	
	Counts Ratio <2*	Counts Ratio ≥2*	Previous Specimen(s) Normal	Previous Specimen Abnormal or No Previous Specimen
> 3.09	Normal	Normal	Normal	Normal
2.71 – 3.09	Borderline	Borderline	Borderline	Presumptive
< 2.71	Presumptive	Borderline	Borderline	Presumptive

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	If first screen, health care provider is contacted by phone to request routine second specimen. If second screen, NBS calls health care provider to check clinical status. Results are mailed to submitter.	Health care provider is immediately contacted by phone to recommend substitution of soy formula for breast milk or commercial based formula and prompt diagnostic testing. Results are mailed to submitter.

* Final results depend on the raw counts ratio (patient/positive control) - normal range: counts ratio ≥ 2

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms may include hepatomegaly, jaundice, vomiting, failure to thrive, diarrhea, lethargy, *E.coli* sepsis, kidney damage, cataracts and mental disability.

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Hemoglobin Disorders – 1/14/2011

Screening Result Classifications and Follow-up Actions for Common Abnormal Hemoglobins

Hemoglobin Phenotype	Likely Genotype	Classification	NBS Typical Follow-up Action
FA	Normal	Normal	None
AF	Infant >10 days		
AA	Transfusion	Normal	Recommend rescreening 4-6 weeks after last transfusion.
FSS	Sickle cell anemia	Severe Disease	Contact health care provider (HCP) by phone and recommend immediate referral to a pediatric hematologist.
FS- or FS2A	Sickle beta thalassemia		
FSC	Sickle C disease		
FSD	Sickle D disease		
F only	Beta thalassemia major	Severe Disease	Contact HCP by phone and recommend immediate referral to a pediatric hematologist.
FE-	Hemoglobin E beta-zero thalassemia	Severe Disease	Contact HCP by phone to recommend referral to a pediatric hematologist.
FA + high Bart's	Hemoglobin H disease		
FEE	Hemoglobin E disease	Mild/Moderate Disease	Contact HCP by phone to recommend referral to a pediatric hematologist.
FCC	Hemoglobin C disease		
FDD	Hemoglobin D disease		
FAS	Hemoglobin S trait	Trait	Report by letter to HCP recommending family studies and genetic counseling.
FAE	Hemoglobin E trait		
FAC	Hemoglobin C trait		
FAD	Hemoglobin D trait		
FA + moderate Bart's	Bart's hemoglobin, marker for alpha thalassemia and Constant Spring	Trait	Report by letter to HCP recommending follow-up testing to determine clinical significance for child and reproductive implications for family.
FA + Variant	Unidentified variant hemoglobin trait	Trait	Report by letter to HCP recommending follow-up only if accompanied by clinical signs or *family history* of hemoglobinopathy.

Hemoglobin traits, with the exception of alpha thalassemia trait and variant trait, are only reported after receipt of two concurring specimens. For traits only, the second specimen eliminates the need for further confirmatory testing.

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Severe Combined Immunodeficiency (SCID) - 04/29/2020

Screening Test
SCID screening, is done by DNA testing. The test measures T-cell receptor excision circle (TREC) levels, which are low or absent in infants with SCID. Results are classified in the table below.

TREC/µL blood	Classification	
	ß-actin < 28 Cq	ß-actin ≥ 28 Cq
> 80	Normal	Normal
61 – 80	Borderline	Inconclusive*
< 61	Presumptive	Inconclusive*

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	If first specimen, or second screen linked to a previous normal, health care provider is contacted by phone to recommend immediate second newborn screening specimen. If second specimen and previous abnormal, health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend immediate *diagnostic testing*. Newborn screening results are also mailed to submitter.

* Inconclusive results mean that no DNA amplification occurred in the reference gene (ß-actin). Follow-up for inconclusive results is: if first screen, DOH waits for routine second specimen; if second screen and previous borderline, DOH calls health care provider and recommend diagnostic testing; if second screen and previous inconclusive or normal, DOH calls health care provider immediately to request subsequent specimen; if persistently inconclusive, DOH reviews with NBS SCID consultant.

IMPORTANT: if clinical signs of the disorder are present, immediate diagnostic referral should supersede follow-up responses above. SCID is usually asymptomatic in the newborn period, in older infants symptoms may include multiple infections, diarrhea, oral thrush and failure to thrive.

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X-linked Adrenoleukodystrophy (X-ALD) – 12/14/2022

Screening Test

X-ALD screening is performed by tandem mass spectrometry. The test measures lysophosphatidylcholine (C26:0 LPC) levels, which are elevated in infants with X-ALD and other peroxisomal disorders. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for X-ALD

C26:0 LPC μmol/L blood	Age at Collection ≤144 hours		
	MALES, WASHINGTON FEMALES or SEX UNKNOWN	IDAHO FEMALES	
		Non-NICU	NICU
<0.220	NORM	NORM	NORM
0.220 – 0.729	Presumptive	Borderline	Borderline
≥0.730	Presumptive	Borderline	High Borderline
C26:0 LPC μmol/L blood	**Age at Collection >144 hours**		
	MALES or WASHINGTON FEMALES or SEX UNKNOWN	**IDAHO FEMALES**	
		Non-NICU	**NICU**
<0.160	NORM	NORM	NORM
0.160 – 0.409	Borderline or Presumptive	Borderline	Borderline
≥0.410	Presumptive	Borderline	High Borderline

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to submitter. No follow-up is required.	If born in Washington or males born in Idaho, health care provider is contacted by phone to recommend a subsequent newborn screening specimen. If Idaho female, educational materials are sent to the Provider. If high borderline, NICU is contacted to check for symptoms of Zellweger Syndrome. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend *diagnostic testing*. Newborn screening results are also mailed to submitter.

IMPORTANT: Newborns with X-ALD are typically asymptomatic; if clinical signs of Zellwegger syndrome are present, immediate diagnostic referral should supersede follow-up responses above. Symptoms include: profound hypotonia (can lead to secondary feeding issues); facial features (tall forehead, large fontanelle). Less common symptoms include: seizures; cataracts; x-ray findings (calcifications, stippling, especially around the knee).

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Spinal Muscular Atrophy (SMA) – 02/01/2022

Screening Test
SMA screening is done by DNA testing. The test detects exon 7 of the survival motor neuron 1 gene (SMN1), which is absent in infants with SMA. Results are classified in the table below.

Screening Result Classifications and Corresponding Follow-up Actions for SMA

SMN1	β-actin < 28 Cq	β-actin ≥ 28 Cq
Present	Normal	Normal
Absent	Presumptive	Inconclusive

Typical Follow-up Actions		
Normal Results	Inconclusive Results	Presumptive Results
Results are mailed to submitter. No follow-up is required.	Health care provider is contacted by phone to request an immediate subsequent specimen. Newborn screening results are also mailed to submitter.	Health care provider is contacted by phone to recommend immediate *referral to a specialty clinic*. Newborn screening results are also mailed to submitter.

* Inconclusive results mean that sufficient DNA amplification did not occurr in the reference gene (ß-actin).

IMPORTANT: if clinical signs of the disorder are present, immediate referral to a specialty clinic should supersede follow-up responses above. SMA is usually asymptomatic in the newborn period, in older infants symptoms may include muscle weakness that can cause difficulty swallowing, poor feeding, and breathing problems.

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