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

Fatty acid disorders

Organic acid disorders

Other disorders

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To submit a request, please call 1-800-525-0127 (TDD/TTY 1-800-833-6388).

Argininosuccinic acidemia (ASA) / Citrullinemia (CIT) – 4/21/2015

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
< 36	Normal	Normal
36 – 110.9	Borderline or Presumptive†	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) – 7/1/2016

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
< 55	Normal	Normal
55 – 71	Normal	Borderline
71 – 89	Borderline	Borderline
≥ 90	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 non-NICU baby, health care provider is contacted to request second specimen. If first specimen on LBW baby or collected early (1-6 hours) NBS waits for the routine second specimen. If second screen and previous normal, health care provider is contacted to request third specimen. If second screen and previous abnormal, 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 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) – 10/24/2013

Screening Test

The MSUD screening is done using a 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
< 236	Normal	Normal	Normal	Normal
236 – 321	Borderline	Borderline	Normal	Normal
322 – 465	Borderline	Presumptive	Borderline	Presumptive
≥ 466	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 first screen on non-NICU baby, health care provider is contacted by phone to request a repeat newborn screening specimen. If first specimen on LBW baby or collected early (1-6 hours) NBS waits for routine second specimen. If second screen and previous normal, a repeat NBS is requested. If second screen and LEU ≥ 400 NBS consults with metabolic specialists, 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. Results are also mailed to submitter.	

†Final results depend on secondary markers (normal ranges: val < 220, leu/ala < 1.5, 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) – 7/28/2016

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
< 152	Normal	Normal	Normal	Normal
152 – 179	Normal	Borderline	Normal	Borderline
180 – 239	Borderline	Presumptive	Borderline	Borderline
≥ 240	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) – 5/8/2015

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	
	tyr < 209	tyr ≥ 209
< 3.0	Normal	Normal
≥ 3.0	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 to recommend an immediate second newborn screen. If second specimen, health care provider is contacted 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.

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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Carnitine Uptake Deficiency (CUD) – 10/19/2016

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
> 11.4	Normal	Normal
7.5 – 11.4	Normal	Borderline
< 7.5	Presumptive	Presumptive
Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
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 (C0>13.6, 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, contact health care provider to recommend *diagnostic testing* including maternal samples. Newborn screening results are also mailed to submitter.	If first specimen, health care provider is contacted by phone to recommend an immediate repeat newborn screening specimen. If second specimen, 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 samples. If baby is in the NICU, a subsequent specimen is requested. Newborn 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 – 4/21/2015

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
< 0.13	Normal	Normal
≥ 0.13	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 – 10/24/2013

Screening Test

The MCAD deficiency screening is done using tandem mass spectrometry (MS/MS) to measure the levels of *octanoyl carnitine (C8)* and *acyl carnitine (C2)* in the blood.

Screening Result Classifications and Corresponding Follow-up Actions for MCAD

C8 µmol/L blood	Classification	
	not all secondary markers† elevated	all secondary markers† elevated
< 0.50	Normal	Normal
0.50 – 0.99	Borderline	Borderline
≥ 1.0	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 – 12/7/2016

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
< 0.50	Normal	Normal
0.50 – 0.58	Normal	Borderline or Presumptive[†]
0.59 – 0.74	Normal or Borderline[†]	Presumptive
≥ 0.75	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 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: 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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HMG deficiency and Multiple Carboxylase deficiency (MCD) – 7/1/2016

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
< 0.87	Normal	Normal
0.87 – 4.33	Borderline	Presumptive
≥ 4.34	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 5.0 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) – 4/21/2015

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
< 0.14	Normal	Normal
≥ 0.14	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) – 9/6/2013

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
< 0.13	Normal	Normal
≥ 0.13	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 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) – 4/21/2015

Screening Test

Screening for IVA is performed by 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
< 0.77	Normal	Normal	Normal	Normal
0.77 – 0.98	Interfering substances	Normal	Borderline	Normal
0.99 – 1.79	Interfering substances	Interfering substances	Borderline or Presumptive†	Borderline
≥ 1.80	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) – 7/1/2016

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
< 4.0	Normal	Normal	Normal	Normal
4.0 – 4.59	Normal	Normal	Borderline	Presumptive
4.6 – 5.89	Normal	Borderline	Borderline	Presumptive
5.9 – 7.99	Borderline	Presumptive	Borderline	Presumptive
8.0 – 11.29	Borderline	Presumptive	Borderline	Presumptive
≥ 11.3	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 – 10/14/2008

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 in 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, immediate diagnostic testing is recommended. Results are mailed to specimen 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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Congenital Adrenal Hyperplasia (CAH) – 2/24/2015

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 specimen 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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Congenital Hypothyroidism (CH) – 2/15/2012

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

Typical Follow-up Actions		
Normal Results	**Borderline Results**	**Presumptive Results**
Results are mailed to specimen submitter. No follow-up is required.	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 a repeat newborn screening specimen and/or *diagnostic testing* as soon as possible. Results are also mailed to submitter. For ***Urgent Presumptive*** results, treatment should be initiated immediately.

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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Cystic Fibrosis (CF) – 2/7/2014

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. No referrals will be made on the basis of a single specimen; elevation on two consecutive newborn screening specimens is the criteria for referral. Results are classified in the table below.

Laboratory Result Classifications and Corresponding Follow-up Actions for CF

	Birth weight < 1500g		Birth weight ≥ 1500g	
IRT (ng/mL)	**Age at collection < 6 days**	**Age at collection ≥ 6 days**	**Age at collection < 6 days**	**Age at collection ≥ 6 days**
< 70	Normal	Normal	Normal	Normal
70 - 99	Normal	Elevated	Normal	Elevated
≥ 100	Elevated	Elevated	Elevated	Elevated

Typical Follow-up Actions		
Normal Results	**Elevated Results**	**Persistent Elevated Results**
Results are mailed to specimen submitter. No follow-up is required.	NBS waits for the routine second specimen. If not received within 2 to 4 weeks, health care provider is contacted to recommend newborn screening specimen as soon as possible. Results are also mailed to submitter.	If previous screen was elevated, health care provider is contacted by phone to refer for diagnostic testing (sweat test) as soon as possible.

Note: Two specimens with elevated IRT drawn prior to six days of age or within three days of each other do not meet our criteria for persistent elevation. DOH will request a 3rd specimen for newborns when both specimens demonstrating an elevated IRT are drawn prior to six days of age or within three days of each other.
A second-tier protocol, implemented in late 2007 to improve sensitivity, calls for a third newborn screening specimen if the IRT on the first screen is greater than 50 ng/mL AND the IRT on the second screen is greater than 85 ng/mL.

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 – 6/14/2016

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)	Classification
> 3.11	Normal
2.52 – 3.11	Normal or Partial†
< 2.52	Profound

Typical Follow-up Actions		
Normal Results	**Partial Results**	**Profound Results**
Results are mailed to specimen submitter. No follow-up is required.	If first screen, health care provider is contacted by phone to request routine second specimen. If two abnormal screens, diagnostic testing is recommended. Results are mailed to specimen 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 specimen 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

Laboratory 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	Report by phone or letter recommending a diagnostic work-up.
FCC	Hemoglobin C 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) – 6/13/2014

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	
	β-actin < 28 Cq	β-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 (β-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.