Definitions of medical intervention and diagnosis, by the disorder for core conditions.

The purpose of this document is to serve as a guide for defining the notification of the newborn screening results, medical intervention, and the date of diagnosis. Each definition correlates to Quality Indicator metrics and aims to provide standardization for Newborn Screening programs.

Amino Acid Disorders	Notification of abnormal NBS result [i]	Medical Intervention[ii]	Date of Diagnosis
Argininosuccinic Aciduria (ASA)	The notification of an out-of-range result, such as Citrulline or Arginosuccinate acid, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of ASA. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Diet change, drug, or supplement therapy. • Collection or testing for plasma ammonia and amino acids, urine amino acids, and arginosuccinate lyase enzyme. • Investigating poor feeding, vomiting, lethargy, tachypnea, or seizures.	The date the clinical report reflects a confirmed diagnosis: • Amino acid and enzyme profile results +/- genotyping/sequencing of the *ASL* gene.
Citrullinemia, Type I (CIT)	The notification of an out-of-range result, such as Citrulline or Arginosuccinate acid, by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of CIT.	The date of the clinical report reflects a confirmed diagnosis: • Amino acid and enzyme profile results +/- genotyping/sequencing of

Amino Acid Disorders	Notification of abnormal NBS result [i]	Medical Intervention[ii]	Date of Diagnosis
	Time-critical disorder.	Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Diet change, drug, or supplement therapy. • Collection or testing for plasma ammonia and amino acids, urine amino acids, and arginosuccinate lyase enzyme. • Investigating poor feeding, vomiting, lethargy, tachypnea, or seizures.	the *ASS1* gene and *SLC25A13* gene.
Classic Phenylketonuria (PKU)	The notification of an out-of-range result, such as Phenylalanine and/or Tyrosine, by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of PKU. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Diet change, drug, or supplement therapy.	The date of the clinical report reflects a confirmed diagnosis: • Amino acid and enzyme profile results +/- genotyping/sequencing of the *PAH* gene.

Amino Acid Disorders	Notification of abnormal NBS result [i]	Medical Intervention[ii]	Date of Diagnosis
		• Collection or testing for plasma amino acids, urine pterins, or DHPR activity. *Note:* Newborns with PKU are asymptomatic.	
Homocystinuria (HCY)	The notification of an out-of-range result, such as Methionine or Homocysteine, by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of HCY. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Diet change, drug, or supplement therapy. • Collection or testing plasma and urine amino acids.	The date of the clinical report reflects a confirmed diagnosis: • Amino acids and total homocysteine profile results + genotyping/sequencing of the *CBS* gene.
Maple Syrup Urine Disease (MSUD)	The notification of an out-of-range result, such as Leucine, Isoleucine, and Valine, by the NBS Program to the appropriate medical professional. **Time-critical disorder**.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of MSUD. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening	The date of the clinical report reflects a confirmed diagnosis: • Plasma amino acids and urine organic acid profile results +/ genotyping/sequencing of the *BCKDHA, BCKDHB, or DBT* genes.

Amino Acid Disorders	Notification of abnormal NBS result [i]	Medical Intervention[ii]	Date of Diagnosis
		result is reported and may include any of the following: • Diet change, drug, or supplement therapy. • Collection or testing for plasma amino acids and urine organic acid analysis. • Investigating poor feeding, lethargy, tachypnea seizures, or other symptoms.	
Tyrosinemia, Type I (TYR I)	The notification of an out-of-range result, such as SUAC and Tyrosine, by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of TYR I. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Diet change or drug therapy. • Collection or testing for liver function tests, Alpha-fetoprotein, electrolytes, plasma amino acids, or urine organic acids.	The date of the clinical report reflects a confirmed diagnosis: • Plasma amino acids and urine organic acid profile results +/- genotyping/sequencing of the *FAH* gene.

Amino Acid Disorders	Notification of abnormal NBS result [i]	Medical Intervention[ii]	Date of Diagnosis
		• Investigating failure to thrive, jaundice, diarrhea, or vomiting.	

Endocrine Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Congenital Adrenal Hyperplasia (CAH)	The notifications of an out-of-range result, such as 17-OHP or steroid profile, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or endocrine consultation to evaluate the potential diagnosis of CAH. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Date of oral glucocorticoid replacement therapy, or IV fluids, IM/IV hydrocortisone. • Collection or testing of serum 17-OHP, ACTH, urinary steroid profile, electrolyte panel, and plasma renin activity (PRA). • Investigating poor feeding, vomiting, lethargy, ambiguous genitalia, or non-palpable testes.	The date of the clinical report reflects a confirmed diagnosis, with or without other abnormal adrenal hormone abnormalities, and evaluation by an endocrinologist. • Serum and urine results + genotyping/sequencing of the *CYP21A2* gene

Endocrine Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Primary Congenital Hypothyroidism (CH)	The notifications of an out-of-range result, such as TSH, Total, and Free T4, by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or endocrine consultation to evaluate the potential diagnosis of CH. Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • Serology evaluation of TSH, Free T4, and Total T4. • Initiates therapy like levothyroxine. • Investigating poor growth, prolonged jaundice, puffy facies, large fontanels, macroglossia, or umbilical hernia.	The date of the clinical report reflects a confirmed diagnosis: • Serology testing +/- imaging,

Fatty Acid Oxidation Disorder	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Carnitine Uptake Defect/Carnitine Transport Defect (CUD)	The notification of an out-of-range result, such as C0 and other acylcarnitines, by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of CUD. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Carnitine therapy • Collection or testing of plasma and urine carnitine. • Investigating poor feeding, lethargy, tachypnea, hepatomegaly, or hypotonia.	The date of the clinical report reflects a confirmed diagnosis: • Acylcarnitine profile results +/- genotyping/sequencing of the *SLC22A5* gene.
Long-chain L-3 Hydroxyacyl- CoA Dehydrogenase Deficiency (LCHAD)	The notification of an out-of-range result, such as C16-OH and other long-chain acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of LCHAD. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following:	The date of the clinical report reflects a confirmed diagnosis: • Acylcarnitine and enzyme profile results +/- genotyping/sequencing of the *HADHA* gene.

Fatty Acid Oxidation Disorder	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		• Advisement to avoid fasting or initiation of IV glucose. • Collection or testing of plasma acylcarnitines and urine organic acids. • Investigating poor feeding, lethargy, vomiting, hypotonia, hepatomegaly, hypoglycemia, arrhythmias, or cardiac insufficiency.	
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)	The notification of an out-of-range result, such as C8, with or without C6 and C10, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of MCAD. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Advisement to avoid fasting or initiation of IV glucose. • Collection or testing of plasma acylcarnitines and urine organic acids.	The date of the clinical report reflects a confirmed diagnosis: • Acylcarnitine and enzyme profile results +/- genotyping/sequencing of the *ACADM* gene.

Fatty Acid Oxidation Disorder	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		• Investigating poor feeding, vomiting, lethargy, hypotonia, or hypoglycemia.	
Trifunctional Protein Deficiency (TFP)	The notification of an out-of-range result, such as C16-OH and other long-chain acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of TFP. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Advisement to avoid fasting or initiating IV glucose. • Collection or testing of plasma acylcarnitines and urine organic acids. • Investigating poor feeding, lethargy, vomiting, hypotonia, hepatomegaly, hypoglycemia, arrhythmias, or cardiac insufficiency.	The date of the clinical report reflects a confirmed diagnosis: • Acylcarnitine and enzyme profile results +/- genotyping/sequencing of the *HADHA* and *HADHB* genes.

Fatty Acid Oxidation Disorder	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)	The notification of an out-of-range result, such as C14, C14:1, and other long-chain acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of VLCAD. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Advisement to avoid fasting or initiating IV glucose. • Collection or testing of plasma acylcarnitines, • Investigating poor feeding, vomiting, lethargy, hypotonia, hepatomegaly, arrhythmias, or cardiac complications.	The date of the clinical report reflects a confirmed diagnosis: • Acylcarnitine enzyme profile results +/- genotyping/sequencing of the *ACADVL* gene.

Hemoglobinopathies	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Presence of Hb S [S, Beta-Thalassemia, S,C Disease, S,S Disease (Sickle Cell Anemia)]	The notification of an out-of-range result by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or hematologist consultation to evaluate the possible diagnosis of Sickle Cell Anemia (FS), SC disease (FSC), Sickle Beta + Thalassemia (FSA), Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • The collection or testing of a complete blood count (CDC) with or without a manual smear and a hemoglobin electrophoresis analysis. • Investigating splenomegaly or jaundice. • Decision to initiate antibiotics, or not to initiate antibiotics.	The date of the clinical report reflects a confirmed diagnosis: • Confirmation testing by alternative method (e.g., secondary electrophoresis) +/- DNA studies. ○ Hemoglobin S

Lysosomal Storage Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Glycogen Storage Disease Type II (Pompe) *New disorder*	The notification of an out-of-range result, such as GAA, by the NBS Program to the appropriate medical professional.	Date of the clinic or hospital consultation to evaluate the potential diagnosis of Pompe.	The date of the clinical report reflects a confirmed diagnosis: • Alpha-glucosidase enzyme analysis results +

Lysosomal Storage Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • Chest X-ray, EKG, ECHO, or other examination of cardiac status. • Collection or testing for urine glucose tetrasaccharide (HEX4), muscle enzymes CK, LDH, AST, ALT).	genotyping/sequencing of the *GAA* gene.
Infantile Krabbe Disease *New Disorder* **Draft- Public health surveillance algorithm in development**	The notification of an out-of-range result, such as GALC, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the clinic or hospital consultation to evaluate the potential diagnosis of Krabbe. Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • Collection or testing of biochemical or molecular for galactosylceramidase enzyme, psychosine analysis, or GALC gene sequencing. • Investigating irritability, spasticity, poor feeding, and muscle weakness.	The date of the clinical report reflects a confirmed diagnosis: • Leukocyte galactocerebrosidase enzyme assay and erythrocyte psychosine concentration +/- genotyping/sequencing of the *GALC* gene.

Lysosomal Storage Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		Note: Newborns with Krabbe are asymptomatic.	
Metachromatic Leukodystrophy (MLD) *New Disorder*	The notification of an out-of-range result, such as C16:0-sulfatide, C16:1-OH-sulfatide, or arylsulfatase A enzyme (ARSA), by the NBS Program to the appropriate medical professional.	Date of the first clinic or hospital consultation to evaluate the potential diagnosis of MLD. Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • Testing for ARSA leukocyte enzyme assay, urine sulfatides, or urine glycosaminoglycans analysis (GAGs). • Investigating neurologic decline in motor and cognitive function.	The date of the clinical report reflects a confirmed diagnosis: • Arylsulfatase A enzyme analysis results, genotyping/sequencing of *ARSA* gene, and GAG results.
Mucopolysaccharidosis Type I (MPS I) *New disorder*	The notification of an out-of-range result, such as IDUA enzyme or GAGs, by the NBS Program to the appropriate medical professional.	Date of the first clinic or hospital consultation to evaluate the potential diagnosis of MPS I. Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • Urine testing for glycosaminoglycans analysis (GAGs) like dermatan sulfate, heparan sulfate, keratan	The date of the clinical report reflects a confirmed diagnosis: • Alpha-L-iduronidase enzyme analysis results, genotyping/sequencing of the *IDUA* gene, and GAG results.

Lysosomal Storage Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		sulfate, and chondroitin 6-sulfate.	
Mucopolysaccharidosis Type II (MPS II) *New disorder* ***Draft- Public health surveillance algorithm in development.***	The notifications of an out-of-range result, such as I2S enzyme or GAGs, by the NBS Program to the appropriate medical professional.	Date of the first clinic or hospital consultation to evaluate the potential diagnosis of MPS II. Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • Urine testing for glycosaminoglycans analysis (GAGs) like dermatan sulfate, heparan sulfate, keratan sulfate, and chondroitin 6-sulfate.	The date of the clinical report reflects a confirmed diagnosis: • Iduronate-2-Sulfatase enzyme analysis results, genotyping/sequencing of the *IDS gene*, and GAG results.

Organic Acid Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
3-Hydroxy-3-Methyglutaric Aciduria (HMG) ***Draft- Public health surveillance algorithm in development.***	The notification of an out-of-range result, such as C5-OH, C6-DC, and other acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of HMG. Medical intervention should be the **first date** that alters the child's care. This date may be	The date of the clinical report reflects a confirmed diagnosis: • Urine organic acid and plasma acylcarnitine profile results +/- genotyping/sequencing of the *HMGCL* gene.

Organic Acid Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		before the newborn screening result is reported and may include any of the following: • Date of diet change, drug, or supplement therapy. • Collection or testing of plasma acylcarnitines and urine organic acids. • Investigating poor feeding, vomiting, lethargy, hypoglycemia, ketonuria, or metabolic acidosis.	
3-Methylcrotonyl-CoA Carboxylase Deficiency (3-MCC)	The notification of an out-of-range result, such as C5-OH and other acylcarnitines, by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of MCC. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Date of diet change, drug, or supplement therapy. • Collection or testing of plasma acylcarnitines and urine organic acids. • Investigating poor feeding, vomiting, lethargy, hypoglycemia,	The date of the clinical report reflects a confirmed diagnosis: • Urine organic acids, plasma amino acids, and plasma acylcarnitine profile results +/- genotyping/sequencing of the *MCCC1* and MCCC2 gene.

Organic Acid Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		ketonuria, or metabolic acidosis.	
β-Ketothiolase Deficiency (BKT) ***Draft- Public health surveillance algorithm in development.***	The notification of the out-of-range result, such as C5:1, C5-OH, and other acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of BKT:. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Date of diet change, drug, or supplement therapy. • Collection or testing of plasma acylcarnitines and urine organic acids. • Investigating poor feeding, vomiting, lethargy, hypoglycemia, ketonuria, or metabolic acidosis.	The date of the clinical report reflects a confirmed diagnosis: • Urine organic acids, plasma amino acids, and plasma acylcarnitine profile results +/- genotyping/sequencing of the *ACAT1* gene.
Glutaric Acidemia Type I (GA1)	The notification of the out-of-range result, such as C5-DC and other acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of GA 1. Medical intervention should be the **first date** that alters the child's care. This date may be	The date of the clinical report reflects a confirmed diagnosis: • Urine and plasma organic acids and acylcarnitine profile results +/- genotyping/sequencing of the *GCDH* gene.

Organic Acid Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		before the newborn screening result is reported and may include any of the following: • Date of diet change, drug, or supplement therapy. • Collection or testing of urine and plasma organic acids and acylcarnitines. • Investigating poor feeding, macrocephaly, or hypotonia.	
Holocarboxylase Synthase Deficiency (MCD)	The notification of the out-of-range result, C3, C5-OH, and other acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of MCD. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Date of diet change, drug, or supplement therapy. • Collection or testing of plasma acylcarnitines and urine organic acids. • Investigating poor feeding, vomiting, lethargy, hypoglycemia, ketonuria, or metabolic acidosis.	The date of the clinical report reflects a confirmed diagnosis: • Urine organic acids, plasma amino acids, and plasma acylcarnitine profile results +/- genotyping/sequencing of the *HLCS* gene.

Organic Acid Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Isovaleric Acidemia (IVA)	The notification of the out-of-range result, C5 and other acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of IVA Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Date of diet change, drug, or supplement therapy. • Collection or testing of plasma and urine acylcarnitines, and urine organic acids. • Investigating poor feeding, vomiting, lethargy, tachypnea, or odor of sweaty feet.	The date of the clinical report reflects a confirmed diagnosis: • Plasma acylcarnitines, and urine acylcarnitines and organic acids profile results +/- Genotyping/sequencing of the *IVD* gene.
Methylmalonic Acidemia Cbl A, B (cobalamin disorders) (MMA)	The notification of the out-of-range result, such as C3, C3/C2, and other acylcarnitines, by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of MMA. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following:	The date of the clinical report reflects a confirmed diagnosis: • Plasma and urine organic acid profile results + genotyping/sequencing of the *MMAA* and *MMAB* gene.

Organic Acid Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		• Date of diet, drug, or supplement therapy. • Collection or testing of plasma and urine organic acids, and vitamin B12 analysis. • Investigating poor feeding, vomiting, lethargy, tachypnea, ketonuria, hypoglycemia, or failure to thrive.	
Methylmalonic Acidemia (methylmalonyl-CoA mutase) (MUT)	The notification of the out-of-range, C3, C3/C2, and other acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder**.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of MUT. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Date of diet, drug, or supplement therapy. • Collection or testing of plasma and urine organic acids, and vitamin B12 analysis. • Investigating poor feeding, vomiting, lethargy, tachypnea, ketonuria, hypoglycemia, or failure to thrive.	The date of the clinical report reflects a confirmed diagnosis: • Plasma and urine organic acid profile results + genotyping/sequencing of the *MMUT* gene.

Organic Acid Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Propionic Acidemia (PROP)	The notification of the out-of-range result, C3, C3/C2, and other acylcarnitines, by the NBS Program to the appropriate medical professional. **Time-critical disorder**.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of PROP. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Date of diet, drug, or supplement therapy. • Collection or testing of plasma and urine organic acids, and vitamin B12 analysis. • Investigating poor feeding, vomiting, lethargy, tachypnea, ketonuria, hypoglycemia, or failure to thrive.	The date of the clinical report reflects a confirmed diagnosis: • Plasma and urine organic acid profile results +/- genotyping/sequencing of the *PCCA* and *PCCB* gene.

Other Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Biotinidase Deficiency (BIOT)	The notification of an out-of-range result, such as Biotinidase, by the NBS Program to the appropriate medical professional.	Date of the first clinic, hospital, or metabolic specialist consultation to evaluate the potential diagnosis of BIOT.	The date of the clinical report reflects a confirmed diagnosis: • Serum biotinidase and urine organic acids, +/-

Other Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • Biotin supplements. • Collection or testing of serum Biotinidase assay. • Investigation of seizures, hypotonia, ataxia, skin rash, etc.	genotyping/sequencing of the *BTD* gene.
Classic Galactosemia (GALT)	The notification of an out-of-range result, such as Galactose-1-phosphate and Total Galactose, by the NBS Program to the appropriate medical professional. **Time-critical disorder.**	Date of the first clinic, hospital, or metabolic consultation with a metabolic specialist to evaluate the potential diagnosis of GALT. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Date of diet change. • Urine reducing substances.	The date of the clinical report reflects a confirmed diagnosis: • Red blood cell GALT activity and/or galactose-1-phosphate (gal-1-P), +/ *GALT* mutation analysis.
Cystic Fibrosis (CF)	The notifications of an out-of-range result, such as immunoreactive trypsinogen (IRT), by the NBS Program to the appropriate medical professional.	Date of the first clinic or hospital consultation to evaluate the potential diagnosis of CF or initiate therapy. Medical intervention should be the **first date** that alters the child's care. This date may be	The date of the clinical report reflects a confirmed diagnosis: • Positive sweat chloride test. • Genotype/sequencing identifying variants in the *CFTR* gene.

Other Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
		before the newborn screening result is reported and may include any of the following: • Pancreatic enzymes/Salt supplements. • Antibiotics or other medication to support or manage symptoms. • Appointment for sweat chloride testing.	• Nasal Potential Difference (NPD) results.
Duchenne Muscular Dystrophy (DMD) *New disorder*	The notification of an out-of-range result, such as CK-MM, by the NBS Program to the appropriate medical professional.	Date of the first clinic or hospital consultation to evaluate the potential diagnosis of DMD or initiate therapy. Medical intervention should be the **first date** that alters the child's case. This may include any of the following: • Physical examination including physical, cardiac, and neurological. • Neuromuscular investigation includes, but is not limited to, proximal leg weakness, late walking, frequent falls, waddling gait, delayed growth, and muscle pain. • Collection of cord blood or whole blood for molecular testing.	The date of the clinical report reflects a confirmed diagnosis: • Genotyping/sequencing of the *DMD* gene.

Other Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Guanidinoacetate Methyltransferase Deficiency (GAMT) *New disorder* ***Draft- Public health surveillance algorithm in development.***	The notification of an out-of-range result, such as GUAC and Creatine, by the NBS Program to the appropriate medical professional.	Date of the first clinic or hospital consultation to evaluate the potential diagnosis of GAMT. Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • Neurological investigation for hypotonia, epilepsy, etc. • Urine/plasma testing for creatine.	The date of the clinical report reflects a confirmed diagnosis: • Plasma and urine GUAC and creatine analysis, + genotyping/sequencing of the *GAMT* gene. • Rule out arginase deficiency.
Severe Combined Immunodeficiencies (SCID)	The notification of an out-of-range result, such as TREC, by the NBS Program to the appropriate medical professional.	Date of the first clinic or hospital consultation with an immunologist or infectious disease specialists to evaluate the potential diagnosis for SCID: Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • Includes testing (but not limited to) CBC with differential and Flow Cytometry. • Maternal T-cell engraftment • Proliferation of PHA • Antibiotic therapy or isolation protocol.	The date of the clinical report reflects a confirmed diagnosis: • Flow cytometry and CD4 results + genotyping/sequencing for *IL2RG* or other gene mutations known to cause SCID.

Other Disorders	Notification of abnormal NBS result	Medical Intervention	Date of Diagnosis
Spinal Muscular Atrophy (SMA)	The notification of an out-of-range result, such as SMN1 and SMN2, by the NBS Program to the appropriate medical professional.	Date of the first clinic or hospital consultation to evaluate the potential diagnosis for SMA. Medical intervention should be the **first date** that alters the child's care. This may include any of the following: • The neuromuscular investigation includes but is not limited to, hypotonia, weakness, poor feeding, or respiratory difficulties.	The date of the clinical report reflects a confirmed diagnosis: • *SMN1* sequencing/ SMN1 and *SMN2* dosage analysis.
X-linked Adrenoleukodystrophy (X-ALD) *New disorder*	The notification of an out-of-range result, such as C24:0 and C26:0, by the NBS Program to the appropriate medical professional.	Date of the first clinic or hospital consultation to evaluate the potential diagnosis for X-ALD. Medical intervention should be the **first date** that alters the child's care. This date may be before the newborn screening result is reported and may include any of the following: • Adrenal insufficiency investigation. • Adrenal steroid replacement. • Specimen collection for very long chain fatty acids (VLCFA)/Plasmalogens.	The date of the clinical report reflects a confirmed diagnosis: • Serum fatty acid profile and imaging + genotyping/sequencing *ABCD1* gene.

[i] The notification of an abnormal result(s) may be communicated by phone, fax, mailer, or other method deemed acceptable by the program's policy.

[ii] Medical intervention is any interaction between a medical professional and the newborn/infant's family that alters the care of the child based on abnormal newborn screening results. The intervention will be the earliest date that clinical action was rendered. Medical intervention includes a medical professional advising against fasting or the date therapy was initiated. This may also include the date additional samples were collected for confirmation testing. See Quality Indicator Source Document for further explanation.