Organic Acid Disorders (Those with these disorders are unable to remove certain waste products from their blood)						
Medical Condition	**Testing Platform/ Analyte**	**Limitations and Interference**	**Normal Range**	**Symptoms *if not treated***	**Common Medical Treatment**	**Confirmatory Test**
Propionic acidemia (PA)	Tandem mass spectrometry (MS/MS) C3, C3/C2	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Breathing problems, seizures, swelling of the brain, stroke, coma/death.	Protein-restricted diet; medical formula; no fasting; carnitine and biotin therapy	Referral to metabolic center for urine organic acids analysis, specific enzyme analysis, and/or mutation analysis
Methylmalonic acid (MMA)	Tandem mass spectrometry (MS/MS) C3, C3/C2	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Breathing problems, seizures, swelling of the brain, stroke, coma/death.	Protein/fat-restricted diet; medical formula; no fasting; carnitine therapy and possibly B-12 therapy	Referral to metabolic center for urine organic acids analysis, specific enzyme analysis, and/or mutation analysis
Isovaleric acidemia (IVA)	Tandem mass spectrometry (MS/MS) C5	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Brain damage resulting in life-long learning problems or intellectual disabilities	Protein-restricted diet; no fasting; carnitine and glycine therapy	Referral to metabolic center for urine organic acids analysis, specific enzyme analysis, and/or mutation analysis
3-methylcrotonyl CoA carboxylase deficiency (3MCC)	Tandem mass spectrometry (MS/MS) C5OH	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Breathing problems, seizures, swelling of the brain, stroke, coma/death. Liver failure and brain damage resulting in life-long learning problems or intellectual disabilities	No fasting, protein restricted diet, medical formula, carnitine therapy if deficient	Referral to metabolic center for urine organic acids analysis, specific enzyme analysis, and/or mutation analysis

3-hydroxy-3- methylglutaryl CoA lyase deficiency (HMG)	Tandem mass spectrometry (MS/MS) C5OH, C6DC	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Breathing problems, seizures, coma/death	Protein restriction medical formula, no fasting	Referral to metabolic center for urine organic acids analysis, specific enzyme analysis, and/or mutation analysis
Multiple carboxylase deficiency (MCD)	Tandem mass spectrometry (MS/MS) C50H	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Difficulty breathing, motor skill delay, hearing loss, speech loss, lack of coordination, seizures, brain damage, death	Biotin therapy	Referral to metabolic center for urine organic acids analysis, specific enzyme analysis, and/or mutation analysis
Beta-ketothiolase deficiency (BKT)	Tandem mass spectrometry (MS/MS) C5:1, C5OH	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Intellectual disability, enlarged heart, poor growth, abnormal muscle tone, jerky movement, low white blood cells and platelets.	Protein restricted diet, no fasting, carnitine therapy, bicitra supplement	Referral to metabolic center for urine organic acids analysis, specific enzyme analysis, and/or mutation analysis
Glutaric acidemia, type 1 (GA-1)	Tandem mass spectrometry (MS/MS) C5DC	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Muscle contractions and spasms, poor coordination and balance, metabolic acidosis, seizures, swelling of the brain, coma/death	Protein restriction; carnitine therapy, riboflavin supplement	Referral to metabolic center for urine organic acids analysis, specific enzyme analysis, and/or mutation analysis
Fatty Acid Oxidation Disorders (People affected with these disorders are difficulty burning fat for energy)						
Medical Condition	**Testing Platform/ Analyte**	**Limitations and Interference**	**Normal Range**	**Symptoms *if not treated***	**Common Medical Treatment**	**Confirmatory Test**

Carnitine uptake defect (CUD)	Tandem mass spectrometry (MS/MS) Free Carnitine	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Breathing problems, swelling of the brain, seizures, coma/death, enlarged heart or liver, muscle weakness, anemia	Avoid fasting; low fat diet; Carnitine therapy	Plasma and urine carnitine analysis Referral to metabolic center for specific enzyme analysis, metabolite analysis, and/or mutation analysis
Medium chain acyl- CoA dehydrogenase deficiency (MCAD)	Tandem mass spectrometry (MS/MS) C6, C8, C10, C8/C10	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Breathing problems, seizures, coma/death	Avoid fasting; low fat diet; Carnitine therapy	Quantitative plasma acetylcarnitine profile, urine acylglycine, urine organic acids, DNA analysis Referral to metabolic center for specific enzyme analysis, metabolite analysis, and/or mutation analysis
Very long chain acyl- CoA dehydrogenase deficiency (VLCAD)	Tandem mass spectrometry (MS/MS) C14, C14:1, C14:2, C14:1/C16	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Breathing problems, seizures, coma/death	Avoid fasting; low fat diet with medium chain triglyceride (MCT) oil supplement; carnitine therapy	Quantitative plasma acetylcarnitine profile, urine organic acids, mutation analysis of the VLCAD gene, genetic testing Referral to metabolic center for specific enzyme analysis, metabolite analysis, and/or mutation analysis

Long chain 3 hydroxyacyl-CoA dehydrogenase deficiency {LCHAD) Trifunctional protein deficiency (TFP)	Tandem mass spectrometry (MS/MS) C16:1OH, C16OH, C18:1OH, C18:2OH	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	Normal	Breathing problems, swelling of the brain, seizures, coma/death,	Avoid fasting; low fat diet; Long chain fatty acid restriction; medium chain triglycerides (MCT) oil supplement; carnitine therapy	Quantitative plasma acylcarnitine profile, urine organic acid analysis, free e-OH-fatty acids, biochemical and molecular genetic testing to differentiate LCHAD from TFP Referral to metabolic center for specific enzyme analysis, metabolite analysis, and/or mutation analysis
Amino Acid Disorders						
Medical Condition	**Testing Platform/ Analyte**	**Limitations and Interference**	**Normal Range**	**Symptoms *if not treated***	**Common Medical Treatment**	**Confirmatory Test**
Argininosuccinic aciduria (ASA) Characterized by ammonia build-up in the blood	Tandem mass spectrometry (MS/MS) Citrulline	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	<55 umol/L	Muscle weakness and decreased tone, breathing problems, seizures, swelling of the brain, coma/death Poor growth, enlarged liver, learning/intellectual disability	High-calorie, protein-restricted diet; arginine supplementation	Quantitative plasma ammonia and amino acid analysis, urine orotic acid. Immediate consult with a metabolic specialist at a metabolic treatment center
Citrullinemia, type I, (classic form) (CIT) Characterized by ammonia build-up in the blood	Tandem mass spectrometry (MS/MS) Citrulline	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	<55 umol/L	Muscle weakness and decreased tone, breathing problems, seizures, swelling of the brain, coma/death Poor growth, enlarged liver, learning/intellectual disability	High-calorie, protein-restricted diet; arginine supplementation, sometimes dialysis	Quantitative plasma ammonia and amino acid analysis; urine for orotic acid. Immediate consult with metabolic specialist at a metabolic treatment center

Maple syrup urine disorder (MSUD) Characterized by the inability to digest leuicine, isoleucine, and valine	Tandem mass spectrometry (MS/MS) Leucine	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	<305 umol/L	Rigid/floppy muscles, brain swelling, seizures, metabolic acidosis, coma	Protein-restricted diet; medical formula	Immediate consult with metabolic specialist at a metabolic treatment center
Homocystinuria (HCY) Characterized by the inability to digest methionine in food	Tandem mass spectrometry (MS/MS) Methionine, C3, and/or C3/C2	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	<75 umol/L	Intellectual and developmental disability; delays in crawling/walking/talking; poor growth; poor vision; behavior and emotional problems	Protein- restricted diet; medical formula; vitamin B6, betaine, and folic acid supplements; vitamin b12 injections or L-cysteine supplements	Quantitative plasma amino acid analysis, total plasma homocysteine
Phenylketonuria (PKU) Characterized by the inability to digest phenylalanine in food.	Fluorescence assay Phenylalanine	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	<188 umol	Intellectual disabilities, behavior problems, hyperactivity, restlessness or irritability, seizures, eczema	Protein-restricted diet; medical formula	Repeat newborn screen; consult metabolic clinic; Quantitative plasma amino acid analysis, red blood cell DHPR assay, urine neopterin, DNA testing for PAH gene mutation
Tyrosinemia, type I Characterized by the build-up of tyrosine in the blood	Tandem mass spectrometry (MS/MS) Succinylacetone (SUAC)	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after seven days may limit the ability of the assay to detect disease states	<5.42 umol/L	Rickets, delays in walking, severe liver and kidney problems, death	Protein-restricted diet; medical formula; medication and vitamin D supplement	Immediate consult with metabolic specialist at a metabolic treatment center
Tyrosemia, type II and III Characterized by the build-up of tyrosine in the blood	Tandem mass spectrometry (MS/MS) Tyrosine	Total parenteral nutrition (TPN and blood transfusions Unsatisfactory specimens or specimens collected before 24 hours of age or received after	<360 umol/L	Intellectual disabilities	Protein-restricted diet; medical formula; medication	Immediate consult with metabolic specialist at a metabolic treatment center

		seven days may limit the ability of the assay to detect disease states				
Endocrine Disorders						
Medical Condition	**Testing Platform/ Analyte**	**Limitations and Interference**	**Normal Range**	**Symptoms *if not treated***	**Common Medical Treatment**	**Confirmatory Test**
Primary congenital hypothyroidism Characterized by an Insufficient thyroid hormone	Time resolved fluorescence assay Thyroid hormone T4 and Second tier TSH	Maternal medications, EDTA or sodium citrate anticoagulant interference, iodine exposure, cardiac medications	>6.0 ug/dL	Breathing problems, delays in sitting/crawling/walking/talking, poor weight gain and growth, goiter, anemia, slow heart rate, hearing loss	Oral intake of throxine upon consultation of pediatric endocrinologist	Thyroid stimulating hormone (TSH)
Congenital adrenal hyperplasia (CAH) Characterized by a lack of 21-hydroxylase	Solid phase, time-released fluoroimmunoassay 17-hydroxyprogesterone (17-OHP)	Treatment with dexamethasone, hydrocortisone, or prednisone may result in false-negative results Preterm or low weight newborns, and samples collected before 24 hours of age may result in false positive results. Some congenital enzyme defects of the steroid biosynthesis, which cause CAH do not cause in increase in 17 αOHP, resulting in false negative results. Anomalous results can also be caused by uneven saturation, poorly collected or improperly dried specimens, or contamination of the blood spot with fecal material	Weight dependent: Birth weight (grams) / 17-OHP (ng/mL) <1500 / <125 1500-2499 / <63 >2500 / <32	Confusion, irritability, rapid heart rate, coma	Hydrocortisone pills, treatment for salt-wasting	Repeat newborn screen; Serum 17-OHP; sodium, potassium and plasma renin if salt wasting is suspected.

Pulmonary Disorders						
Medical Condition	**Testing Platform/ Analyte**	**Limitations and Interference**	**Normal Range**	**Symptoms *if not treated***	**Common Medical Treatment**	**Confirmatory Test**
Cystic fibrosis (CF) Characterized by a buildup of thick mucus in the lungs	Fluorescence assay Immunoreactive Trypsinogen (IRT) Second tier genotyping	Meconium ileus, heat degradation, contamination with EDTA or heparain	<80.1 ng/mL	Bronchitis/pneumonia, poor growth, chronic diarrhea, impaired learning ability	Pulmonary therapy; prevent infection; replace digestive enzymes	Sweat chloride (gold standard) and/or DNA mutation analysis
Other Metabolic Disorders						
Medical Condition	**Testing Platform/ Analyte**	**Limitations and Interference**	**Normal Range**	**Symptoms *if not treated***	**Common Medical Treatment**	**Confirmatory Test**
Biotinidase deficiency Characterized by insufficient biotin	Colorimetric assay Biotinidase	Sulfonamides sulfisoxazole or trimethoprim and sulfamethoxazole can cause a false negative Enzyme destruction by heat, humidity, or delay between collection and testing (false positive); transfusion (false negative)	Enzyme Present	Intellectual and developmental disability; seizures; skin rash; alopecia; hearing loss; death	Biotin therapy	Repeat newborn screen; Quantitative enzyme assay; consultation with a metabolic clinic
Classic galactosemia (GALT) Characterized by the inability to digest galactose	Fluorescence assay Galactose-1 Phosphate Uridyl-1-Transferase (GALT)	Enzyme destruction by heat, humidity, or delay between collection and testing (false positive); transfusion (false negative)	>3.00 u/gHb	Hypoglycemia, seizures, enlarged liver, jaundice, bleeding, blood infections, cataracts	Galactose and lactose-restricted diet, Vitamin C and K supplement	Galactose-1 phosphate uridyltransferase enzyme and galactosemia DNA panel
Hemoglobin Disorders						
Medical Condition	**Testing Platform/ Analyte**	**Limitations and Interference**	**Normal Range**	**Symptoms *if not treated***	**Common Medical Treatment**	**Confirmatory Test**
Hemoglobinopathy Hemoglobin disease or trait	Isoelectric focusing (IEF) with high-performance liquid chromatography (HPLC) reflex Hemoglobin fractions: Fetal (F), Adult (A), Sickle (S), C-Hemoglobin (C), E-Hemoglobin (E), D-Hemoglobin (D) Hemoglobin patterns:	Red blood cell transfusion—repeat screen 90-120 days post transfusion	Normal (F+A)	In sickle cell disease: death by sepsis or splenic sequestration anemia; sickling crisis	Fluids, pain killers, blood transfusion Hemoglobin disease: prophylactic penicillin until age five	High performance liquid chromatography (HPLC) reflex, DNA testing

	FA=Normal FS-Hemoglobin S disease/Sickle Beta Thalassemia FSC=Hemoglobin SC disease FSA=Sickle Beta Thalassemia FE=Hemoglobin E disease/Hemoglobin E-Beta Thalassemia FSD=Hemoglobin SD disease FSE=Hemoglobin SE disease F only=Beta Thalassemia Major					
Immunology Disorders						
Medical Condition	**Testing Platform/ Analyte**	**Limitations and Interference**	**Normal Range**	**Symptoms *if not treated***	**Common Medical Treatment**	**Confirmatory Test**
Severe combined immunodeficiency (SCID) Characterized by the baby's lack of T-cells and severely reduced B-cell function	Real-Time qPCR T-cell receptor excision circles (TRECs)	Specimen contamination can cause false negative	<=1.079 MoM	Death in infancy or early childhood	Bone marrow transplant. Prophylactic antibiotics, antiviral and antifungal agents, and intravenous gamma globulin are given until bone marrow transplant is performed.	Complete Blood Count (CBC) with differential and flow cytometry to determine the extent of cell lymphopenia
Other Disorders						
Medical Condition	**Testing Platform/ Analyte**	**Limitations and Interference**	**Normal Range**	**Symptoms *if not treated***	**Common Medical Treatment**	**Confirmatory Test**
Spinal Muscular Atrophy Characterized by pathogenic variants in the SMN1 gene	Real-Time qPCR *SMN1* gene		Presence of *SMN1* Exon 7	Increasingly lilted mobility	Injections, physical and occupational therapy, rehabilitation	SMN1 Exon 7 absence and SMN2 copy number assessment

*Information included in this table was taken from the Medical Home Portal (Medical Home Portal, n.d.)and the Wisconsin Newborn Screening Program (Wisconsin State Laboratory Newborn Screening Program, 2020) (Association of Public Health Laboratories); (Clinical and Laboratory Standards Institute, 2019); (Wisconsin State Laboratory Newborn Screening Program, 2020)