ATTACHMENT A - Delaware

Disorders **Included in the StepOne® Newborn Screening Panel**

DISORDERS DETECTED BY TANDEM MASS SPECTROMETRY

Fatty Acid Oxidation Disorders

Carnitine/Acylcarnitine Translocase Deficiency (Translocase)
Carnitine/Acylcarnitine Transferase Deficiency Type I[1]
3-Hydroxy Long Chain Acyl-CoA Dehydrogenase Deficiency (LCHAD)
2,4-Dienoyl-CoA Reductase Deficiency[1]
Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD)
Multiple Acyl-CoA Dehydrogenase Deficiency (MADD or Glutaric Acidemia-Type II)
Neonatal Carnitine Palmitoyl Transferase Deficiency Type II (CPT-II)
Short Chain Acyl-CoA Dehydrogenase Deficiency (SCAD)
Short Chain Hydroxy Acyl-CoA Dehydrogenase Deficiency (SCHAD)
Trifunctional Protein Deficiency (TFP Deficiency)
Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)

Organic Acid Disorders

3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG)
Glutaric Acidemia Type I (GA 1)
Isobutyryl-CoA Dehydrogenase Deficiency
Isovaleric Acidemia (IVA)
- Acute onset
- Chronic

2-Methylbutyryl-CoA Dehydrogenase Deficiency
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC Def.)
3-Methylglutaconyl-CoA Hydratase Deficiency
Mitochondrial Acetoacetyl-CoA Thiolase Deficiency (3-Ketothiolase Def.)
Propionic Acidemia (PA)
- Acute onset
- Late onset

Malonic Aciduria
Methylmalonic Acidemias
- Methylmalonyl-CoA Mutase Deficiency 0
- Methylmalonyl-CoA Mutase Deficiency +
- Some Adenosylcobalamin Synthesis Defects
- Maternal Vitamin B12 Deficiency

Multiple CoA Carboxylase Deficiency

X-Adrenoleukodystrophy (X-ALD)

Amino Acid Disorders

Argininemia
Argininosuccinic Aciduria (ASA Lyase Deficiency)
- Acute onset
- Late onset

Carbamoylphosphate Synthetase Deficiency[1]
Citrullinemia (ASA Synthetase Deficiency)
- Acute onset
- Late onset

Homocystinuria
Hypermethioninemia
Hyperammonemia, Hyperornithinemia, Homocitrullinuria Syndrome (HHH)[1]
Hyperornithinemia with Gyral Atrophy[1]
Maple Syrup Urine Disease (MSUD)
- Classical MSUD
- Intermediate MSUD

5-Oxoprolinuria (Pyroglutamic Aciduria)[1]
Phenylketonuria (PKU)
- Classical PKU
- Hyperphenylalaninemia
- Biopterin Cofactor Deficiencies

Tyrosinemia
- Transient Neonatal Tyrosinemia
- Tyrosinemia Type I (Tyr I)[2]
- Tyrosinemia Type II (Tyr II)
- Tyrosinemia Type III (Tyr III)

OTHER OBSERVATIONS

Hyperalimentation
Liver Disease
Medium Chain Triglyceride Oil Administration
Presence of EDTA Anticoagulants in blood specimen
Treatment with Benzoate, Pyvalic Acid, or Valproic Acid
Carnitine Uptake Deficiency[1]

Lysosomal Storage Disorders
- Mucopolysaccharidosis Type I (MPS-I) and Pompe

Diet Screening
- Monitoring for PKU, Hyperphenylalanemia, and Tyrosinemia

Disorders Detected by Other Technologies

Biotinidase Deficiency
- Complete Deficiency
- Partial Deficiency

Congenital Adrenal Hyperplasia**
- Salt Wasting 21-Hydroxylase Deficiency
- Simple Verilizing 21-Hydroxylase Deficiency

Congenital Hypothyroidism**
Cystic Fibrosis (not valid after 90 days of age)*
Galactosemia**
- Galactokinase Deficiency
- Galactose-1-Phosphate Uridyltransferase Deficiency
- Galactose-4-Epimerase Deficiency

Severe Combined Immunodeficiency (SCID)
Sickle Cell & other Hemoglobinopathies
- Hemoglobin S, S/C, S/Beta-Thalassemia, C, & E Diseases

Spinal Muscular Atrophy (SMA)

The analyses conducted by PerkinElmer Genetics produce results that can be used by qualified physicians in the diagnosis of disorders described herein. Evidence of these conditions will be detected in the vast majority of affected individuals; however, due to genetic variability, age of the patient at time of specimen collection, quality of the specimen, health status of the patient, and other variables, such conditions may not be detected in all affected patients.

[1]There is a lower probability of detection of this condition during the immediate newborn period.

[2]Succinylacetone (SUAC) is the primary marker for Tyrosinemia Type 1.

*For information on DNA Carrier Testing for children over 90 days of age, please call 866-463-6436.
** 2nd Sample

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ATTACHMENT B
PerkinElmer Genetics Second Tier Reflex Testing Menu

PerkinElmer Genetics uses combinations of assays in a multi-tier approach that optimizes detection of abnormal results. Positive DNA identification for many disorders further speeds definitive diagnosis and implementation of critical therapies.

Biochemical Second Tier Testing

Disorder	Testing Approach
Congenital Adrenal Hyperplasia	First Tier; 17-OH P Second Tier; Extracted 17-OH P on all elevated.
Congenital Hypothyroidism	First Tier; either T4 or TSH. Second Tier TSH with a primary T4.
Galactosemia	First Tier; Total Galactose plus quantitative Uridyltransferase. Second Tier; Fractionated Galactose.

DNA Second Tier Testing

Disorder	Mutations Detected
Galactosemia	N314D (Duarte) Q188R, S135L, K285N, and L195P (Classical)
Hemoglobinopathies	Hb S (173A>T), Hb C (172G>A), Hb E (232G>A), Hb D (121G>C) and Hb O (121G>A) β Thalassaemias -29A>G, -88C>T, and IVS1+6T>C
Cystic Fibrosis	This chart contains the 23 mutations recommended by the ACOG/ACMG:

ΔF508	1717-1G>A	W1282X	2307insA
ΔI507	R560T	N1303K	Y1092X
G542X	R553X	394delTT	M1101K
G85E	G551D	Y122X	S1255X
R117H	1898+1G>A	R347H	3876delA
621+1G>T	2184delA	V520F	3905insT
711+1G>T	2789+5G>A	A559T	*5/7/9T*
1078delT	3120+1G>A	S549N	*F508C*
R334W	R1162X	S549R	*I507V*
R347P	3659delC	1898+5G>T	*I506V*
A455E	3849+10kbC>T	2183AA>G	

Biotinidase Deficiency	G98:d7i3, Q456H, R157H, R538C, D252G and D444H; D444H;A171T, D444H; F403V, D444H;R157H
MCAD	A985A>G, 199T>C
LCHAD	1528G>C
Glutaric Acidemia 1	A421V (Amish) R402W (Caucasian)
Propionic Acidemia	E168K (Spanish) 1218del14/ins12 (Caucasian) 1170insT
Methylmalonic Acidemia	N219Y (Caucasian) G717V (African American)
3-Methylcrotonyl-CoA Carboxylase Def.	518insT (Mennonite)
Maple Syrup Urine Disease	Y438N (previously known as Y393N)
Isovaleric Acidemia	A282V