



STATE OF TENNESSEE
DEPARTMENT OF HEALTH
DIVISION OF LABORATORY SERVICES
NEWBORN SCREENING PROGRAM
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To: All Providers of Newborn Screening Specimens

From: Christine D. McKeever
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Date: February 24, 2011

Subject: Tandem Mass Spectrometry Reagent Change

With specimens received on March 5, 2011 (Julian date 064), the Tennessee Department of Health Newborn Screening laboratory will begin screening for Aminoacidopathies, Organic Acidopathies and Beta Fatty Acid Oxidation disorders by Tandem Mass Spectrometry with a new tandem mass spectrometry reagent kit. This kit allows for addition of the analyte Succinylacetone (SA). SA is the primary analyte that may be indicative of Hepatorenal Tyrosinemia Type 1 (HTT-1) when elevated. This kit also allows us to screen for the disorder 3-Hydroxyacyl CoA dehydrogenase deficiency (M/SCHAD).

Reference ranges for all analytes will change, once screening with the new kit commences. Enclosed with this letter is a listing of analytes, normal values, and their respective disorders associated when elevated. Reference ranges will be continually monitored through population statistics, and cutoffs adjusted as necessary.

This new tandem mass spectrometry reagent kit cannot differentiate between certain analytes because some of the analytes have identical masses. For instance, C3-DC and C4-OH have the same mass of 248. Therefore, when there is an elevation in either or both of these analytes, the instrument cannot differentiate whether the elevation is due to C3-DC or C4-OH. In this instance, we report the cumulative concentration of both analytes. This also occurs for the analytes C4-DC and C5-OH, as well as C5-DC and C6-OH. When elevated, these also are reported as cumulative concentrations.

We are truly excited about this reagent kit change and the addition of two new diseases to our screening panel. Please be patient with us during this transition. If you have any questions, you may contact Christine McKeever (615-262-6352 or Chris.McKeever@tn.gov) or Thomas Childs (615-262-6446 or Thomas.Childs@tn.gov).

Enclosure

Metabolites	Normal Values	Disorder(s) Related
Amino Acid Disorders		
Arginine	Arg < 95 $\mu\text{mol/L}$	Argininemia (Arginase Deficiency)
Citrulline	Cit > 3 $\mu\text{mol/L}$	Carbamoylphosphate Synthetase Deficiency
Citrulline	Cit < 42 $\mu\text{mol/L}$	Citrullinemia Type I (Arginosuccinate Synthetase Deficiency) Citrullinemia Type II (Citrin Deficiency) Argininosuccinate Lyase Deficiency (Arginosuccinic Aciduria)
Cit/Arg Ratio	Cit/Arg < 6.00	Citrullinemia Type I (Arginosuccinate Synthetase Deficiency) Citrullinemia Type II (Citrin Deficiency) Argininosuccinate Lyase Deficiency (Arginosuccinic Aciduria)
Argininosuccinic Acid	Asa < 0.18 $\mu\text{mol/L}$	Argininosuccinate Lyase Deficiency (Arginosuccinic Aciduria)
Asa/Arg Ratio	Asa/Arg < 0.13	Argininosuccinate Lyase Deficiency (Arginosuccinic Aciduria)
Glycine	Gly < 774 $\mu\text{mol/L}$	Nonketotic Hyperglycinemia
Methionine	Met < 61 $\mu\text{mol/L}$	Homocystinuria or variant forms of Hypermethioninemia
*Methionine (under validation)	Met > 7 $\mu\text{mol/L}$	Methylenetetrahydrofolate Reductase Deficiency
Ornithine	Orn < 377 $\mu\text{mol/L}$	Hyperornithinemia-Hyperammonemia-Homocitrullinuria (HHH) Hyperornithinemia with Gyral Atrophy
Orn/Cit Ratio	Orn/Cit < 18.9	Hyperornithinemia-Hyperammonemia-Homocitrullinuria (HHH) Hyperornithinemia with Gyral Atrophy
Phenylalanine	Phe < 152 $\mu\text{mol/L}$	Phenylketonuria Hyperphenylalaninemia due to: Phenylalanine Hydroxylase Deficiency GTP Cyclohydrolase I Deficiency Pterin-4-Alpha Carbinolamine Dehydratase Deficiency 6-Pyruboyltetrahydropterin Synthase Deficiency Defects of biopterin co factor biosynthesis Defects of biopterin co factor regeneration
Phe/Tyr Ratio	Phe/Tyr < 2.01	Phenylketonuria Hyperphenylalaninemia due to: Phenylalanine Hydroxylase Deficiency GTP Cyclohydrolase I Deficiency Pterin-4-Alpha Carbinolamine Dehydratase Deficiency 6-Pyruboyltetrahydropterin Synthase Deficiency Defects of biopterin co factor biosynthesis Defects of biopterin co factor regeneration
Tyrosine	Tyr < 330 $\mu\text{mol/L}$	Transient Tyrosinemia Tyrosinemia Types II and III
Valine	Val < 250 $\mu\text{mol/L}$	Maple Syrup Urine Disease Types IA, IB, II
Val/Phe Ratio	Val/Phe < 4.13	Maple Syrup Urine Disease Types IA, IB, II
Leucine	Leu < 288 $\mu\text{mol/L}$	Maple Syrup Urine Disease Types IA, IB, II
Leu/Phe Ratio	Leu/Phe < 5.53	Maple Syrup Urine Disease Types IA, IB, II
Succinylacetone	SA < 1.56 $\mu\text{mol/L}$	Hepatorenal Tyrosinemia Type I
Organic Acid Disorders		
C3	C3 < 6.35 $\mu\text{mol/L}$	Propionic Acidemia Methylmalonic Acidemia due to: Methylmalonyl-CoA Mutase Deficiency Deficient Synthesis of 5-Prime Deoxyadenosylcobalamin Defects in the MMAA gene Methylmalonic Acidemia with B12 defect and Homocystinuria Multiple CoA Carboxylase Deficiency
C3-DC + C4-OH	C3-DC + C4-OH < 0.31 $\mu\text{mol/L}$	Malonic Aciduria (MA) 3-Hydroxyacyl CoA Dehydrogenase Deficiency (M/SCHAD)
C4	C4 < 1.33 $\mu\text{mol/L}$	Isobutyryl CoA Dehydrogenase Deficiency (IBCD)
C5	C5 < 0.62 $\mu\text{mol/L}$	Isovaleric Acidemia (IVA) 2 Methylbutyryl CoA Dehydrogenase Deficiency (2MBCD) 2 Methyl 3 Hydroxybutyric Aciduria (2M3HBA)
C5:1	C5:1 < 0.08 $\mu\text{mol/L}$	2 Methyl 3 Hydroxybutyric Aciduria (2M3HBA)
C4-DC + C5-OH	C4-DC + C5-OH < 0.52 $\mu\text{mol/L}$	Multiple CoA Carboxylase Deficiency 2 Methyl 3 Hydroxybutyric Aciduria (2M3HBA) 3 Hydroxy 3 Methylglutaryl CoA Lyase Deficiency (HMG) 3 Methyl Crotonyl CoA Carboxylase Deficiency (3 MCC) 3 Methylglutaconyl CoA Hydratase Deficiency (3MGA) Methylmalonic Acidemia(MMA)
C4-DC + C5-OH/C8 Ratio	C4-DC + C5-OH/C8 < 7.49	Multiple CoA Carboxylase Deficiency 2 Methyl 3 Hydroxybutyric Aciduria (2M3HBA) 3 Hydroxy 3 Methylglutaryl CoA Lyase Deficiency (HMG) 3 Methyl Crotonyl CoA Carboxylase Deficiency (3 MCC) 3 Methylglutaconyl CoA Hydratase Deficiency (3MGA) Methylmalonic Acidemia(MMA)
C5-DC + C6-OH	C5-DC + C6-OH < 0.37 $\mu\text{mol/L}$	Glutaric Acidemia Type I (GAI) 3-Hydroxyacyl CoA Dehydrogenase Deficiency (M/SCHAD)
C6-DC	C6-DC < 0.28 $\mu\text{mol/L}$	3 Hydroxy 3 Methylglutaryl CoA Lyase Deficiency (HMG)

Fatty Acid Disorders		
C0	C0 >8.0 $\mu\text{mol/L}$	Carnitine Uptake Deficiency (CUD)
C0	C0 < 75 $\mu\text{mol/L}$	Carnitine Palmitoyl Transferase Deficiency Type I (CPT I)
C4	C4 < 1.33 $\mu\text{mol/L}$	Short Chain AcylCoA Dehydrogenase Deficiency (SCAD) Multiple AcylCoA Dehydrogenase Deficiency (MADD or GAI)
C5	C5 < 0.62 $\mu\text{mol/L}$	Multiple AcylCoA Dehydrogenase Deficiency (MADD or GAI)
C5:1	C5:1 < 0.08 $\mu\text{mol/L}$	Mitochondrial Acetoacetyl CoA Thiolase (Beta Ketothiolase/SKAT) Deficiency
C4-DC + C5-OH	C4-DC + C5-OH < 0.52 $\mu\text{mol/L}$	Mitochondrial Acetoacetyl CoA Thiolase (Beta Ketothiolase/SKAT) Deficiency
C5-DC + C6-OH	C5-DC + C6-OH < 0.37 $\mu\text{mol/L}$	Multiple AcylCoA Dehydrogenase Deficiency (MADD or GAI)
C6	C6 < 0.29 $\mu\text{mol/L}$	Medium Chain AcylCoA Dehydrogenase Deficiency (MCAD)
C8	C8 < 0.41 $\mu\text{mol/L}$	Medium Chain AcylCoA Dehydrogenase Deficiency (MCAD)
C8/C10 Ratio	C8/C10 < 2.1	Medium Chain AcylCoA Dehydrogenase Deficiency (MCAD)
C10	C10 < 0.22 $\mu\text{mol/L}$	Multiple AcylCoA Dehydrogenase Deficiency (MADD or GAI)
C10:1	C10:1 < 0.15 $\mu\text{mol/L}$	Medium Chain AcylCoA Dehydrogenase Deficiency (MCAD)
C10:2	C10:2 < 0.07 $\mu\text{mol/L}$	2,4 Dienyl CoA Reductase Deficiency
C14	C14 < 0.58 $\mu\text{mol/L}$	Very Long Chain AcylCoA Dehydrogenase Deficiency (VLCAD)
C14:1	C14:1 < 0.42 $\mu\text{mol/L}$	Very Long Chain AcylCoA Dehydrogenase Deficiency (VLCAD) Multiple AcylCoA Dehydrogenase Deficiency (MADD or GAI)
C14-OH	C14-OH < 0.05 $\mu\text{mol/L}$	Long Chain Hydroxyl AcylCoA Dehydrogenase Deficiency (LCHAD)
C16	C16 > 0.43	Carnitine Palmitoyl Transferase Deficiency Type I (CPT I)
C16	C16 < 6.33 $\mu\text{mol/L}$	Multiple AcylCoA Dehydrogenase Deficiency (MADD or GAI) Very Long Chain AcylCoA Dehydrogenase Deficiency (VLCAD) Long Chain Hydroxyl AcylCoA Dehydrogenase Deficiency (LCHAD) Trifunctional Protein Deficiency Carnitine/Acylcarnitine Translocase Deficiency (CACTD) Carnitine Palmitoyl Transferase Deficiency Type II
C16:1	C16:1 < 0.50 $\mu\text{mol/L}$	Carnitine /Acylcarnitine Translocase Deficiency(CACTD) Carnitine Palmitoyl Transferase Deficiency Type II
C16-OH	C16-OH < 0.07 $\mu\text{mol/L}$	Long Chain Hydroxyl AcylCoA Dehydrogenase Deficiency (LCHAD) Trifunctional Protein Deficiency
C18	C18 < 1.55 $\mu\text{mol/L}$	Carnitine /Acylcarnitine Translocase Deficiency(CACTD) Carnitine Palmitoyl Transferase Deficiency Type II Long Chain Hydroxyl AcylCoA Dehydrogenase Deficiency (LCHAD) Trifunctional Protein Deficiency Very Long Chain AcylCoA Dehydrogenase Deficiency (VLCAD)
C18:1	C18:1 < 2.27 $\mu\text{mol/L}$	Carnitine /Acylcarnitine Translocase Deficiency(CACTD) Carnitine Palmitoyl Transferase Deficiency Type II
C18:2	C18:2 < 0.99 $\mu\text{mol/L}$	Carnitine /Acylcarnitine Translocase Deficiency(CACTD) Carnitine Palmitoyl Transferase Deficiency Type II
C18:1-OH	C18:1-OH < 0.05 $\mu\text{mol/L}$	Long Chain Hydroxyl AcylCoA Dehydrogenase Deficiency (LCHAD) Trifunctional Protein Deficiency