NEWBORN BLOOD SCREENING

I. DEFINITION:

Newborn screening consists of screening tests performed on blood specimen spots collected on filter paper to identify rare hidden disorders and a point of care screen performed by the birthing facility to identify 7 primary critical congenital heart disease (CCHD) utilizing pulse oximetry screening. According to Oklahoma law 63 O.S.1981, Sections 1-533 and 1-534 and the Oklahoma State Department of Health (OSDH) Newborn Screening Program Regulations (2004), all infants born in Oklahoma are required to be screened for phenylketonuria (PKU) and other Amino Acid disorders, congenital hypothyroidism, classic galactosemia, sickle cell diseases, congenital adrenal hyperplasia, cystic fibrosis, medium chain acyl coenzyme A dehydrogenase deficiency, and other Fatty acid disorders, Organic acid disorders, Biotinidase deficiency, Severe Combined Immunodeficiency (SCID) and CCHD via pulse oximetry screening. Due to the time sensitivity for pulse oximetry screening for Critical Congenital Heart Disease (CCHD), the county health departments are not responsible for screening or providing follow-up measures related to CCHD. For information regarding time of screening, please review Time of Screening & Follow-up Fact Sheet.

II. ETIOLOGY AND EPIDEMIOLOGY:

A. Amino Acid Disorders

1. Screening for PKU began in 1963 and expanded to other Amino Acid disorders in May 2008. Other Amino Acid disorders include Argininemia (ARG), Arginosuccinic aciduria (ASA), Citrullinemia type 1 (CIT), Citrullinemia type II (CIT II), Homocystinuria (HCY), Hypermethioninemia (MET), Maple Syrup Urine Disease (MSUD), Tyrosinemia type I, Tyrosinemia type II, and Tyrosinemia type III. (see attach follow-up sheet)

2. Amino acid disorders are caused by the body’s inability to breakdown or metabolize certain amino acids in proteins, or by the inability to detoxify the by-product of amino acids (ammonia) through the urea cycle. The buildup of amino acids and/or by-products of amino acid metabolism in the blood cause severe medical complications.

3. The most common found amino acid disorder is phenylketonuria (PKU). PKU screening began in 1963 and became law in 1967. PKU occurs at rates of 1 in 23,244 among Oklahoma live births. The disease is characterized by the body’s failure to convert the amino acid phenylalanine to tyrosine due to a deficiency or lack of the enzyme phenylalanine hydroxylase. This disorder can lead to cognitive and intellectual disabilities if not treated with a low phenylalanine diet beginning within the first month of life.

4. Amino acid disorders are autosomal recessive, which means an amino acid disorder is inherited when both parents pass an abnormal (non-working) amino acid gene to their child. This means that both parents are carriers of a particular amino acid disorder for the child to be affected by the disease. A carrier typically does not have signs or symptoms of the disease since they have one normal (working) gene.

5. When two carriers of a particular amino acid disorder have children together, there is a 1 in 4 (25%) chance for each baby to have the amino acid disorder.

6. There is usually no family history of affected family members since autosomal recessive conditions are most likely to occur in siblings rather than in preceding generations.
7. The aggregate incidence of amino acid disorders is approximately 1/10,500 with some disorders that are rarer in the population. Newborns with these disorders often appear normal initially but can rapidly develop life threatening symptoms.

B. Congenital Hypothyroidism (CH)

1. Screening for CH began in 1979. (see attached follow-up sheet)
2. CH is a condition characterized by a lowered rate of metabolism due to deficiency of thyroid hormone (thyroxine) production.
3. CH occurs in 1 out of 3,000 infants born in Oklahoma. This disorder can lead to cognitive and intellectual disabilities and growth delays if not treated with daily thyroid hormone replacement within the first month of life.

C. Classic Galactosemia

1. Screening began in 1991. (see attached follow-up sheet)
2. Galactosemia is an inherited disorder characterized by the body’s failure to break down galactose due to a deficiency or lack of the enzyme galactose-1-phosphate uridyl transferase. This defect in carbohydrate metabolism can lead to failure to thrive, liver disease, cataracts, cognitive and intellectual disabilities and death if not treated with a lactose-free diet beginning within the first month of life.
3. Galactosemia is autosomal recessive, which means galactosemia is inherited when both parents pass an abnormal (non-working) galactosemia gene to their child. This means that both parents are carriers of galactosemia for the child to be affected by the disease. A carrier typically does not have signs or symptoms of the disease since they have one normal (working) gene.
4. When two carriers of galactosemia have children together, there is a 1 in 4 (25%) chance for each baby to have galactosemia.
5. There is usually no family history of affected family members since autosomal recessive conditions are most likely to occur in siblings rather than in preceding generations.
6. Classic Galactosemia occurs in 1 in 40,000 among Oklahoma live births.

D. Sickle Cell Disease and Hemoglobinopathies

1. Screening for sickle cell disease and other hemoglobinopathies began in 1991. (see PHYSICIAN APPROVED PROTOCOL: HEMOGLOBINOPATHY SCREENING)
2. Hemoglobinopathies refers to trait conditions, sickle cell diseases, or hemoglobin diseases.
3. Sickle cell disease is the term used to identify disorders in which the red blood cells sickle under stress. Sickle cell diseases are a group of genetic disorders that are autosomal recessive. For disease to occur, the individual must receive a non-working hemoglobin gene from each parent.
4. Sickle cell disease is autosomal recessive, which means sickle cell disease is inherited when both parents pass an abnormal (non-working) sickle cell gene to
their child. This means that both parents are carriers of sickle cell disease for the child to be affected by the disease. A carrier typically does not have signs or symptoms of the disease since they have one normal (working) gene. The most common trait conditions are sickle cell trait and hemoglobin C trait, which occur at rates of 1:16 and 1:47 respectively among the African-American population in Oklahoma.

5. If the patient inherits non-working genes from both parents, he or she is not able to make any normal hemoglobin and has a disease state. Sickle cell diseases vary in severity, but can result in sepsis and death if treatment with prophylactic penicillin is not started within the first two months of life.

6. When two carriers of a hemoglobin trait have children together, there is a 1 in 4 (25%) chance for each baby to have a hemoglobin disease.

7. The most common forms are sickle cell anemia (hemoglobin SS disease) and hemoglobin SC disease, which occur in 1:400 and 1:900 among African-American births in Oklahoma.

E. Cystic Fibrosis (CF)

1. Screening for Cystic Fibrosis began February 14, 2005. (see attached follow-up sheet)

2. Genetic alterations in both CF genes (CFTR) affect the normal passage of chloride in certain cells. This produces thick, sticky mucus that clogs the lungs and leads to breathing problems and frequent lung infections. It may also obstruct the pancreas preventing digestive enzymes from reaching the intestines causing malnutrition.

3. CF is an inherited disorder that occurs in approximately 1 in every 3,200 Caucasian births (1 in 3,900 live births of all Americans).

4. Cystic fibrosis is autosomal recessive, which means CF is inherited when both parents pass an abnormal (non-working) CF gene to their child. This means that both parents are carriers of CF for the child to be affected by the disease. A carrier typically does not have signs or symptoms of the disease since they have one normal (working) gene.

   When two carriers of cystic fibrosis have children together, there is a 1 in 4 (25%) chance for each baby to have cystic fibrosis.

5. There is usually no family history of affected family members since autosomal recessive conditions are most likely to occur in siblings rather than in preceding generations.

F. Congenital Adrenal Hyperplasia (CAH)

1. Screening for Congenital Adrenal Hyperplasia began February 14, 2005. (see attached follow-up sheet)

2. CAH is a group of inherited disorders that affects the adrenal glands.
3. CAH is caused by a deficiency of an enzyme needed for the adrenal glands to function properly. There are two main forms of CAH: Classical CAH and Non-Classical.

4. Screening is designed to detect classical CAH due to 21-hydroxylase enzyme deficiency. In Classic CAH 21-hydroxylase deficiency, newborns have excessive adrenal androgen biosynthesis which results in genital virilization (enlargement of the clitoris/ambiguous genitalia) and some will have salt-wasting. Classical CAH (severe enzyme deficiency) occurs in approximately 1 in 15,000 births and is a potentially life-threatening disorder that requires life-long management.

5. The classic form is further divided into the simple virilizing form (25% of affected) and the salt-wasting form in which aldosterone production is inadequate (75% of affected). Screening may detect non-classical CAH (moderate enzyme deficiency), a milder form of CAH that is not life-threatening. Females with the non-classic form are not virilized at birth.

6. CAH is autosomal recessive, which means CAH is inherited when both parents pass an abnormal (non-working) CAH gene to their child. This means that both parents are carriers of CAH for the child to be affected by the disease. A carrier typically does not have signs or symptoms of the disease since they have one normal (working) gene.

7. When two carriers of CAH have children together, there is a 1 in 4 (25%) chance for each baby to have CAH.

8. There is usually no family history of affected family members since autosomal recessive conditions are most likely to occur in siblings rather than in preceding generations.

G. Fatty Acid Oxidation Disorders

1. Screening for MCAD began in 2006 and then expanded to other fatty acid oxidation disorders in September 2008. Other fatty acid oxidation disorders include Carnitine Uptake Defect (CUD), Short-chain acyl-Co-A dehydrogenase Deficiency (SCAD), Glutaric Acidemia Type II (GAII), Medium-chain Ketoacyl-Co-A thiolase deficiency (MCAT), Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD), Carnitine acylcarnitine translocase deficiency (CACT). Carnitine palmitoyltransferase I deficiency (CPT IA), Carnitine palmitoyltransferase II deficiency (CPT II), Long chain L-3-hydroxyacyl- CoA dehydrogenase deficiency (LCHAD), and Trifunctional protein deficiency (TFP). (see attached follow-up sheet)

2. Fatty acid oxidation disorders including Medium chain acyl coenzyme A dehydrogenase deficiency (MCAD) prevent the body from using certain fats for energy, particularly during periods without food (fasting).

3. The most common found fatty acid oxidation disorder is medium chain acyl coenzyme A dehydrogenase deficiency (MCAD). MCAD is an inherited disorder that occurs at rates of 1 in 15,000 to 1 in 20,000 live births. The disease is characterized by the body’s failure to convert medium chain fatty acids into energy due to a lack of the enzyme medium chain acyl coenzyme A dehydrogenase.

4. Fatty acid oxidation disorders can lead to metabolic crisis, respiratory failure, cardiac arrest and death if not treated.
5. Fatty acid disorders are autosomal recessive, which means a fatty acid disorder is inherited when both parents pass an abnormal (non-working) fatty acid gene to their child. This means that both parents are carriers of a particular fatty acid disorder for the child to be affected by the disease. A carrier typically does not have signs or symptoms of the disease since they have one normal (working) gene.

6. When two carriers of a particular fatty acid disorder have children together, there is a 1 in 4 (25%) chance for each baby to have the fatty acid disorder.

7. There is usually no family history of affected family members since autosomal recessive conditions are most likely to occur in siblings rather than in preceding generations.

H. Organic Acid Disorders

1. Screening for Organic Acid disorders began in October 2008. They include Propionic Acidemia (PROP), Methylmalonic academia (MUT), Malonic Acidemia (MAL), Isobutyrylglycinuria (Isobutyrylglycinuria CoA dehydrogenase deficiency (IBG), Isovaleric Acidemia (IVA), 2-Methylbutrylglycinuria (2MBG), 3-Methylcrotonyl-CoA carboxylase deficiency (3MCC), 3-Methylglutaconic aciduria (3MGA), 3-Hydroxy-3-methylglutaric aciduria (HMG), Holocarboxylase synthetase deficiency (multiple carboxylase deficiency) (MCD), 2-Methyl-3-hydroxybutyric aciduria (2M3HBA), Beta ketothiolase deficiency (βKT), and Glutaric acidemia type 1 (GA1). (see attached follow-up sheet)

2. Organic acid disorders are caused by the body’s inability to process certain proteins and/or fats properly.

3. These disorders can lead to metabolic crisis, respiratory failure, cardiac arrest and death if not treated.

4. Organic acid disorders are autosomal recessive, which means an organic acid disorder is inherited when both parents pass an abnormal (non-working) organic acid gene to their child. This means that both parents are carriers of a particular organic acid disorder for the child to be affected by the disease. A carrier typically does not have signs or symptoms of the disease since they have one normal (working) gene.

5. When two carriers of a particular organic acid disorder have children together, there is a 1 in 4 (25%) chance for each baby to have the organic acid disorder.

6. There is usually no family history of affected family members since autosomal recessive conditions are most likely to occur in siblings rather than in preceding generations. The aggregate incidence of organic acid disorders is approximately 1/11,500 with some disorders that are rarer in the population.

I. Biotinidase Deficiency

1. Screening for Biotinidase deficiency began November 1, 2010. (see attached follow-up sheet)

2. Biotinidase deficiency is an inherited disorder that occurs in approximately 1 in 60,000 newborns.

3. Biotinidase deficiency is characterized by the body’s inability to reuse and recycle the vitamin biotin.
4. Biotinidase deficiency is also known as late-onset multiple carboxylase deficiency. Partial biotinidase deficiency is a milder form of this condition.

5. Biotinidase deficiency disorder is autosomal recessive, which means biotinidase deficiency is inherited when both parents pass an abnormal (non-working) biotinidase deficiency gene to their child. This means that both parents are carriers of biotinidase deficiency for the child to be affected by the disease. A carrier typically does not have signs or symptoms of the disease since they have one normal (working) gene.

6. When two carriers of biotinidase deficiency have children together, there is a 1 in 4 (25%) chance for each baby to have the biotinidase deficiency disorder.

7. There is usually no family history of affected family members since autosomal recessive conditions are most likely to occur in siblings rather than in preceding generations.

J. Severe Combined Immunodeficiency (SCID)

1. Screening for SCID began January 27, 2015. (see attached follow-up sheet)

2. SCID includes a group of rare but serious and potentially fatal, inherited immune disorders in which T lymphocytes fail to develop and B lymphocytes are either absent or compromised. This prevents the immune system from maturing.

3. Infants with SCID have an increased risk to develop serious infections.

4. Prematurity or other less serious immune disorders may result in an infant screening positive for SCID.

K. Critical Congenital Heart Disease (CCHD)

1. Screening for Critical Congenital Heart Disease began January 2014.

2. Critical congenital heart disease is characterized by an abnormal structure to the heart which creates abnormal blood flow patterns.

3. CCHD screening targets seven primary and five secondary types of CCHDs. The primary conditions targeted include hypoplastic left heart syndrome, pulmonary atresia (with intact septum), tetralogy of fallot, total anomalous pulmonary venous return, transposition of the great arteries, tricuspid atresia, and truncus arteriosus. Not every baby with a CCHD will have low levels of oxygen in the blood during the newborn CCHD screening, therefore a baby who passes the screen can still have a heart defect.

4. CCHD occurs in approximately 8 out of every 1,000 babies born.

III. CLINICAL FEATURES:

A. Amino Acid Disorders including Phenylketonuria (PKU)

1. The affected infant may have no signs or symptoms.

2. The presentation of the various aminoacidopathies varies from no obvious clinical symptoms for months (phenylketonuria), to acute encephalopathy (maple syrup urine disease, citrullinemia, argininosuccinic aciduria) within days following
3. Symptoms of an untreated infant or child may include failure to thrive, irritability, urine with a musty odor, developmental delay, and impaired postnatal physical growth affecting head circumference (microcephaly) and height.

4. Dermatology symptoms include eczema, hypopigmentation, and scleroderma.

5. Older males have reduced semen volume and sperm count.

6. Untreated or inadequately treated patients may present with developmental delay, behavioral disorders, hyperactivity, impaired thinking, altered perception, memory problems, depression, agoraphobia, anxiety, aggression, self-abuse, and cognitive and intellectual disabilities.

7. An affected patient who never received treatment from infancy to adulthood will suffer profound cognitive and intellectual disabilities.

8. Amino acid disorders that affect the urea cycle may exhibit the following symptoms: hyperammonemia, tachypnea, vomiting, and respiratory alkalosis. Severe hyperammonemia in a newborn is a medical emergency.

9. If symptoms present after neonatal period they are like that of Reye Syndrome.

10. Lack of early identification and treatment may result in serious medical consequences, including cognitive and intellectual disabilities, developmental delays, failure to thrive, and/or death.

11. Lifelong treatment includes a special diet and special care during times of illness or stress.

B. Congenital Hypothyroidism

1. The affected infant appears normal at birth and may not present clinically with symptoms until the hypothyroidism is severe and long standing.

2. Clinical symptoms include a large posterior fontanel, prolonged jaundice, macroglossia, hoarse cry, distended abdomen, umbilical hernia, puffy face, cold extremities, persistent constipation, and hypotonia.

3. Inadequate or delayed treatment can result in developmental disability. Not treating an affected infant will result in mental and growth retardation.

C. Classic Galactosemia

1. The affected infant may have no signs or symptoms, but frequently have vomiting and formula intolerance.

2. Without treatment, affected infants will exhibit failure to thrive, jaundice, enlarged liver, liver failure, kidney failure, sepsis, and cataracts.

3. Although children with galactosemia are started on diet restriction at birth, there continues to be a high incidence of long term complications involving speech and language, fine and gross motor skill delays, and specific learning disabilities. Ovarian failure may occur in girls.

4. Not treating the affected infant may result in cognitive and intellectual disabilities.
D. Sickle Cell Disease and Hemoglobinopathies

1. The affected infant with sickle cell disease usually has no signs or symptoms at birth.

2. The first manifestations of the disease usually include anemia, colic-like symptoms, and feeding difficulties.

3. Painful episodes in young children are often precipitated by an acute febrile illness.

4. Without newborn screening, presentation of symptoms commonly occurs at one to three years of age. The affected child may present with acute anemia, hand-foot syndrome, splenic sequestration, pain or devastating infection.

5. No treatment may result in severe illness or death.

**Note:** Penicillin prophylaxis for sickle cell disease should begin at 1 or 2 months of age.

**Fever Alert:** If a child with sickle cell disease has a fever of 101°F or greater immediate medical intervention is required. The child must be referred promptly to an emergency room for a septic workup and IV antibiotics. For a copy of the Fever Management Guidelines for Infants with Sickle Cell Disease, please contact the newborn screening program at (405) 271-6617 or Sickle Cell Program at (405) 271-5311.

E. Cystic Fibrosis (CF)

1. Approximately 10-20% of newborns with CF have meconium ileus.

2. Symptoms can vary greatly with the most common clinical symptoms including recurrent cough, wheezing, frequent lung infections, chronic abdominal pain, loose stools and failure to thrive. Often, infants have very salty-tasting skin.

3. Early treatment with special formulas, supplemental feedings, pancreatic enzymes and vitamins prevents or ameliorates malnutrition and improves growth.

4. Failure to treat an affected infant can result in severe malnutrition and impaired growth.

F. Congenital Adrenal Hyperplasia (CAH)

1. The affected infant may have no signs or symptoms at birth, however adrenal crisis can occur as early as one to four weeks of age.

2. Salt wasting (Classical CAH) symptoms include poor feeding, weight loss, failure to thrive, vomiting, dehydration, hypotension, hyponatremia, and hyperkalemia progressing to adrenal crisis (azotemia, vascular collapse, shock and death).

3. Simple virilizing (Classical CAH) has prenatal virilization of external genitalia without salt-wasting.

4. Without newborn screening, males are at greatest risk for being discharged home without a diagnosis and experience a salt-wasting crisis at home. Females are usually identified due to the clinical presentation of ambiguous genitalia; however, screening has prevented missed sex assignment.
5. Non-classical CAH (mild form of CAH) symptoms can occur at any time from infancy through adulthood and include premature puberty, rapid growth in childhood with ultimate short stature, hirsutism, oily hair and skin, severe cystic acne, polycystic ovary syndrome and infertility.

6. Treatment with hormones prevents death due to salt wasting crisis and in girls prevents incorrect sex assignment.

7. Failure to treat an affected infant can result in adrenal crisis and possible death.

G. Fatty Acid Oxidation Disorders including Medium chain acyl coenzyme A dehydrogenase deficiency (MCAD)

1. The affected infant appears normal at birth.

2. Infants are typically asymptomatic until the infant is weaned from nighttime feeds and experiences a period of fasting (in an infant defined as more than 3 to 4 hours without feeding).

3. Clinical symptoms are notable during periods of acute illness or fasting and include hypoglycemia (often hypoketotic hypoglycemia), lethargy, hepatomegaly and hyperammonemia.

4. During the intervals between episodes of illness, patients typically appear completely well. There is no muscle weakness, however some patients are impressively hypotonic and display a reluctance to exercise or poor muscle strength.

5. Inadequate or delayed treatment can result in metabolic crisis resulting is developmental disability or death.

6. Not treating an affected infant will result in metabolic crisis causing severe brain damage, developmental delay, respiratory failure, cardiac arrest and death.

7. Newborns with these disorders often appear normal initially but can rapidly develop life threatening symptoms.

8. Lifelong treatment includes a special diet and special care during times of illness or stress.

H. Organic Acid Disorders

1. The affected infant appears normal at birth.

2. Organic acid disorders can manifest as a life-threatening sepsis-like picture of feeding difficulties, lethargy, vomiting, and seizures.

3. Metabolic acidosis almost always accompanies this presentation and hyperammonemia is common.

4. Newborns with these disorders often appear normal initially but can rapidly develop life threatening symptoms.

5. Lifelong treatment includes strict dietary management of a special diet, possible medication, and special care during times of illness or stress.
I. Biotinidase Deficiency
   1. The affected infant appears normal at birth.
   2. Clinical symptoms begin over a few weeks to several years and may vary depending on the amount of dietary biotin intake.
   3. Children with profound biotinidase deficiency may exhibit ataxia, hypotonia, developmental delay, conjunctivitis, skin rash, alopecia, seizures, hearing loss, breathing problems and optic atrophy.
   4. Not treating an affected infant will lead to metabolic ketoacidosis and organic aciduria.
   5. Treatment includes oral biotin supplementation.

J. Severe Combined Immunodeficiency (SCID)
   1. The affected infant appears normal at birth.
   2. Clinical symptoms can begin as early as 2-4 months of life and include diarrhea, failure to thrive, otitis media, serious infections (pneumonia, meningitis and/or sepsis), opportunistic infections, and oral thrush.
   3. Bone marrow hematopoietic cell transplantation may be curative, and outcomes are best if performed within the first 3 months of life or before infections occur.
   4. A newborn or individual diagnosed with SCID should not ever receive a live vaccine. A live vaccine may cause severe, life threatening infections for patients affected by SCID.
   5. For newborns presenting for their initial Rotavirus vaccine, verify the SCID testing portion of the newborn screen is normal prior to administering the vaccine.
   6. For newborns who have an abnormal or out-of-range result for SCID on the newborn screen: verify with the Newborn Screening Program that follow-up for the abnormal screen has been completed and obtain permission to administer the Rotavirus vaccine before administering the vaccine. Administer all other vaccines which are not live vaccines as scheduled.
   7. For newborns presenting for their initial Rotavirus vaccine who were not born in Oklahoma, verify question #8 on the ODH Screening Checklist for Contraindications to Vaccines for Children and Teens was marked “No” prior to administering the Rotavirus vaccine.
   8. Treatment may include enzyme replacement, gene therapy, prophylactic antibiotics and bone marrow hematopoietic cell transplantation.
   9. Not treating an affected infant will lead to death.

K. Critical Congenital Heart Disease (CCHD)
   1. The affected infant may appear normal at birth.
   2. Clinical symptoms begin over a few days to weeks and may include breathing problems, pounding heart, weak pulse, very pale or blue skin color, poor feeding
or very sleepy.

3. Children with a critical congenital heart disease have an abnormal structure to their heart which creates abnormal blood flow patterns.

4. Treatment may include surgical repair or cardiac catheterization.

5. Not treating an affected infant may lead to developmental delays, neurologic injury, cardiogenic shock, or death.

IV. MANAGEMENT PLAN:

A. Laboratory Studies:

1. All infants seen by a health care provider in the first 3 months of life should have results of the newborn dried blood spot screen documented in the medical record. If unable to verify that a screen occurred, a specimen should be obtained immediately.

   a. Ideally screen results should be documented in the medical record by one - two weeks of age. This may require the infant to be entered into a tracking system.

   b. To obtain screening results access the Newborn Screening Results website at [http://nbsresults.health.ok.gov](http://nbsresults.health.ok.gov) 24 hours a day, 7 day a week. To access the NBSR, a user name and password are required. To access individual test results, the infant’s filter paper serial number or other search criteria are required.

   c. To obtain a user name and password, please call the Newborn Screening Laboratory 405-271-5070.

   d. To obtain information about newborn screening on babies born out of state, use the web site below to determine contact information: [https://data.newsteps.org/newsteps-web/stateProfile/input.action](https://data.newsteps.org/newsteps-web/stateProfile/input.action)

2. All infants with unsatisfactory initial filter paper screen must have a repeat test done within 48 hours.

3. All infants tested prior to 24 hours of age should have a repeat test done at 3 to 5 days of age. For premature or sick infant testing, please review the Time of Screening & Follow-up Fact Sheet.

4. All newborns must be tested for amino acid disorders including phenylketonuria, congenital hypothyroidism, galactosemia, sickle cell disease, congenital adrenal hyperplasia, cystic fibrosis, and fatty acid disorders including medium- chain acyl coenzyme A dehydrogenase deficiency, organic acid disorders, biotinidase deficiency and SCID. For time of testing, reference Time of Screening & Follow-up Fact Sheet.

5. The OSDH Public Health Lab will provide hemoglobin trait testing for parents of newborns identified with a hemoglobin trait or disease.

6. Testing is done using the Newborn Screening Kit ODH #450. To order kits, please contact the Public Health Laboratory Service, Oklahoma State Department of Health, P.O. Box 24106, Oklahoma City, Oklahoma 73124, by phone at (405) 271-5070, or utilize the OSDH website.
7. It is essential that all information on the Newborn Screening Kit laboratory requisition be completed. Omitted information may cause the specimen to be discarded or may delay testing. Fill out all demographic information completely and accurately.

8. Instructions on how to draw, handle and mail is listed on the filter paper laboratory requisition. It is important that the specimen be horizontally air dried for 3 hours. Do not place the specimen in a plastic bag. Specimens must be sent within 24 hours of collection. For an in-service on how to collect specimens or a parent education video, please contact the Follow-Up Program at (405) 271-6617 or 1-800-766-2223.

9. Blood transfusions affect all screen results. Ideally, all newborns should have an initial screen collected prior to a blood transfusion. See Time of Screening and Follow-up Fact Sheet for more information.

B. Abnormal Laboratory Results:

1. Contact short term follow up at (405) 271-6617.

2. For follow-up of abnormal test results see Follow-up Procedures for Amino Acid Disorders including PKU, Hypothyroidism, Galactosemia, Sickle Cell Disease, Congenital Adrenal Hyperplasia, Cystic Fibrosis, and Fatty Acid Disorders including MCAD, Organic Acid Disorders, Biotinidase Deficiency, and Severe Combined Immunodeficiency.

3. The OSDH Public Health Lab will provide routine monitoring of phenylalanine levels for all cases identified with phenylketonuria (PKU).

4. All infants who have a positive pulse oximetry screen for CCHD must have additional testing and an evaluation performed by a physician prior to being discharged from the birthing facility.

C. A parent or guardian may refuse newborn screening or the pulse oximetry screening for their infant on the grounds that such examination conflicts with their religious tenets and practices. The refusal (see attached form) should be in writing and documented in the newborn's medical record with a copy sent to the OSDH Newborn Screening Program at (405) 271-4892.

D. County Health Departments are not responsible for performing pulse oximetry screening or obtaining refusal for CCHD screening.

V. RESOURCES:

A. Contact the Newborn Screening Short-term Follow-up Program for information regarding follow-up, formula program, publications, statistics and test results:
B. Contact the Newborn Screening Laboratory for information regarding testing methods, filter paper orders, specimen collection, mailing instructions, submitted information and test results:

Oklahoma State Department of Health
Public Health Laboratory Service
Metabolic Disease Screening (MDS)
P.O. Box 24106
Oklahoma City, Oklahoma 73124-0106

Tonya McCallister, MS, MPH  Soheila Haddad, MS
Laboratory Scientist IV  Laboratory Scientist IV
(405) 271-5070  (405) 271-5070
Fax: (405) 271-4850  Fax: (405) 271-4850
Email: TonyaJ@health.ok.gov  Email: SoheilaH@health.ok.gov

C. For Fact Sheets on diseases, see OSDH website (http://nsp.health.ok.gov)

VI. TREATMENT:

A. Amino Acid Disorders including Phenylketonuria (PKU)

1. Treatment for Amino Acid disorders includes strict dietary management and may include medication. The diet needs to be managed by a metabolic specialist and a metabolic dietician. Special care may be required during times of stress or illness.
2. Urea cycle disorders (ARG, CIT) and MSUD are life threatening. Immediate intervention is warranted to prevent hyperammonemia, neurological deterioration, and death.

3. For PKU a low-phenylalanine diet is required for life. The PKU diet consists of limited amounts of certain fruits, vegetables, specially formulated low-protein food products and a medical formula that supplies the essential protein needed for normal growth and good health. A low-phenylalanine diet should begin before the infant is one to four weeks of age and continue for life. Treatment for other amino acid disorders should begin immediately after identifying a possible disorder and continue throughout life once the disorder has been confirmed.

4. Affected women of childbearing age must be on treatment prior to conception and during pregnancy to prevent cognitive and intellectual disabilities of the fetus.

5. Life-long comprehensive care by a metabolic specialist and nutritionist is essential for optimal neurological health.

B. Congenital Hypothyroidism

1. Daily thyroid hormone replacement is required. Treatment for CH should begin by one to four weeks of age and continue for life. Once on therapy, these children will require regular monitoring to ensure that they remain euthyroid during the rapid growth and development of infancy.

2. Please be aware that L-thyroxine (synthroid) should not be mixed with soy formula as this product interferes with absorption.

3. Life-long comprehensive medical care in collaboration with a pediatric endocrinologist is necessary to ensure adequate treatment for normal growth and development.

C. Classic Galactosemia

1. Treatment for Classic Galactosemia requires strict exclusion of lactose/galactose from the diet.

2. Treatment for the affected newborn should begin by two to four weeks of age and continue for life.

3. Life-long comprehensive care by a metabolic specialist and nutritionist is essential to ensure optimal health.

D. Sickle Cell Disease

1. To avoid sepsis and possible death, children with confirmed or suspected sickle cell disease must be on prophylactic penicillin within the first two months of life.

2. Life-long comprehensive care by a pediatric hematologist is essential to ensure optimal health.

E. Cystic fibrosis (CF)

1. Treatment for CF should begin by 14 days of age and continue for life.

2. Nutritional therapies to treat and prevent malnutrition include special formulas,
supplemental feedings and fat-soluble vitamins.

3. Pancreatic enzyme replacement may be required and is used to treat pancreatic insufficiency.

4. Current therapies to treat and prevent pulmonary complications may include chest physiotherapy and use of antibiotics, bronchodilators, anti-inflammatory drugs and mucolytic agents.

5. Life-long comprehensive care provided by a CF Care Center is essential to ensure optimal health.

F. Congenital Adrenal Hyperplasia (CAH)

1. Treatment of CAH depends on the age of diagnosis and the clinical form of CAH and must be continued for life.

2. An affected female fetus can avoid virilization of genitalia with prenatal administration of dexamethasone to the mother. Newborns with either the salt wasting or simple virilizing forms may require plastic surgery to restore the external genitalia to normal.

3. A multidisciplinary team of specialist in pediatric endocrinology, pediatric urology/surgery, medical genetics and psychology is essential for the diagnosis and management of the newborn with ambiguous genitalia.

4. The salt-wasting forms are treated with mineralocorticoid replacement (fludrocortisone) and sodium chloride to retain sodium and glucocorticosteroids to stop the effects of androgen overproduction.

5. The simple virilizing forms are treated with glucocorticoids.

6. For the non-classical forms, treatment addresses pseudoprecocious puberty and growth acceleration.

7. In adult females the symptoms of concern are hirsutism, menstrual disorder and infertility.

8. Life-long comprehensive care in collaboration with a pediatric endocrinologist is needed for optimal health outcomes.

G. Fatty Acid Oxidation Disorder including Medium chain acyl coenzyme A dehydrogenase deficiency (MCAD)

1. Treatment for fatty acid disorders should begin immediately after identifying a possible disorder and continue throughout life once the disorder has been confirmed.

2. Treatment of Fatty Acid disorders consists primarily of the avoidance of fasting. Feeding precautions are required and include scheduled feeding throughout the day and night. Parents are educated to keep a plentiful supply of readily accepted and tolerated oral carbohydrates in the home and to set an alarm during the night to ensure periods of fasting are avoided.

3. To prevent metabolic crisis and death, admission to a hospital and parenteral glucose are mandatory to manage vomiting or anorexia that prevents oral intake.
4. In some cases carnitine supplementation is recommended.

5. Life-long comprehensive care in collaboration with a metabolic specialist and nutritionist is needed for optimal health outcomes.

H. Organic Acid Disorders

1. Treatment for organic acid disorders should begin immediately after identifying a possible disorder and continue throughout life once the disorder has been confirmed.

2. Treatment of Organic Acid disorders consist primarily of carnitine and/or glycine supplementation, protein restriction, and a disorder appropriate formula. Feeding precautions are required and include scheduled feeding throughout the day and night. Parents are educated to set an alarm during the night to ensure periods of fasting are avoided. Life-long comprehensive care in collaboration with a metabolic specialist and nutritionist is needed for optimal health outcomes.

3. To prevent metabolic crisis affected infants need to have frequent feedings and special care during times of stress or illness.

4. Life-long comprehensive care in collaboration with a metabolic specialist and nutritionist is needed for optimal health outcomes.

I. Biotinidase Deficiency

1. Treatment for Biotinidase deficiency consists primarily of biotin supplementation. Treatment for the affected newborn should begin by two weeks of age.

2. Life-long comprehensive care in collaboration with a metabolic specialist and nutritionist is needed for optimal health outcomes.

J. Severe Combined Immunodeficiency (SCID)

1. Bone marrow hematopoietic cell transplantation may be curative, and outcomes are best if performed within the first 3 months of life or before infections occur.

2. Not treating an affected infant will lead to death.

3. Comprehensive care by a pediatric immunologist is needed for optimal health outcome.

K. Critical Congenital Heart Disease (CCHD)

1. Treatment may include surgical repair or cardiac catheterization.

VII. NEWBORN BLOOD SCREENING FOLLOW-UP PROGRAMS:

A. The primary function of the follow-up component is to locate infants with screening results that are screen positive and to facilitate the entry of those infants into the diagnostic and management components of the newborn screening system in a timely fashion.

B. The newborn screening system consists of short-term and long-term follow-up.

C. To enhance effectiveness of the programs, the short and long-term follow-up programs require evaluation components including tracking and reporting of outcomes.
D. **Short-term follow-up** begins when the laboratory obtains an initial result that is screen out-of-range and ends with a definitive diagnosis and documentation that appropriate treatment has been initiated.

E. **Long-term follow-up** begins with treatment and continues throughout life. Long-Term tracking and outcome evaluation are the responsibilities of the newborn screening program.

F. **Short-term Follow-Up Program Staff**

Oklahoma State Department of Health
Prevention & Preparedness Services
Screening & Special Services
1000 N.E. 10th Street – Room 709
Oklahoma City, Oklahoma 73117-1299

Lisa Caton, MS, RN
Director of Screening & Special Services
(405) 271-6617
Fax (405) 271-4892
Voicemail: (405) 271-9444 ext. 56750
E-mail: LisaRC@health.ok.gov

Debbie Hines, RN
Newborn Screening Nurse Coordinator
(405) 271-6617
Fax: (405) 271-4892
Voicemail: (405) 271-9444 ext. 56822
E-mail: DeborahLH@health.ok.gov

Vacant
Special Populations Nurse
(405) 271-6617
Fax (405) 271-4892
Voicemail: (405) 271-9444 ext. 56752
E-mail:

Vacant
Newborn Screening – Administrative Program Manager
(405) 271-6617
Fax (405) 271-4892
Voicemail: (405) 271-9444 ext. 56737
E-mail:

Rachel Hunter, BSN, RN
Newborn Screening Education Coordinator
(405) 271-6617
Fax (405) 271-4892
Voicemail: (405) 271-9444 ext. 56744
E-mail: RachelH@health.ok.gov

Susan Wegrzynski, MS, RN
Nurse Manager
(405) 271-6617
Fax (405) 271-4892
Voicemail: (405) 271-9444 ext. 56752
E-mail: Susanmw@health.ok.gov

G. **Long Term Follow-Up Program Staff**

Metabolic Nurse, Coordinator
Julie Boyd, MS, RN
(405) 271-8001, ext. 42074
(405) 271-8685

Metabolic Dietician
Ashley Ethridge, RD, LD
(405) 271-8001, ext 42450
(405) 271-8685

Endocrine Newborn Screening, Coordinator
Amanda Patterson, BSN, RN
(405) 271-8001, ext. 43051
Pager-(405) 575-8228

Sickle Cell Disease Nurse, Coordinator (OKC)
Joyce Clytus, BSN,RN
(405) 271-5311

Sickle Cell Disease Nurse, Coordinator (Tulsa)
Joyce Clytus, BSN,RN
(405) 271-5311

Healthy & Ready to Work, Sickle Cell Disease Coordinator
Vacant
(405) 271-8001, ext. 42527
(405) 271-5311

VIII. **PHYSICIAN REFERRALS:**
The Newborn Screening Program Regulations, 2004, states all confirmed cases (congenital hypothyroidism, galactosemia, amino acid disorders including phenylketonuria, sickle cell disease, congenital adrenal hyperplasia, cystic fibrosis fatty acid disorders including medium-chain acyl coenzyme A dehydrogenase deficiency, organic acid disorders, biotinidase deficiency, and severe combined immunodeficiency) should have a referral to a pediatric sub-specialist. The following pediatric sub-specialists and staff are available for consultation:

A. Pediatric Endocrinologists
   Oklahoma City:  
   David Domek, M.D.  (405) 945-4525  
   Steven Chernausek, M.D.  (405) 271-6764
   Minu George, M.D.  (405) 271-6764
   Sowmya Krishnan, M.D.  (405) 271-6764
   Jeanie Tryggestad, M.D.  (405) 271-6764
   Monica Marin, M.D.  (405) 271-6764
   David Sparling, M.D.  (405) 271-6764
   Paul Dasari, M.D.  (405) 271-4417
   Tulsa:  
   David Jelley, M.D.  (918) 619-4803
   Laura Chalmers, M.D.  (918) 619-4803

B. Metabolic Specialists
   Specialist:  
   Klaas Wierenga, M.D.  (405) 271-8685
   Michelle Polan, M.D.  (405) 271-8685
   Dietician:  
   Ashley Ethriedge, R.D., L.D.  (405) 271-8001 Ext. 42450

C. Pediatric Hematologists
   Oklahoma City:  
   Arpan Sinha, M.D.  (405) 271-5311
   Ashley Baker, M.D.  (405) 271-5311
   Tulsa:  
   Ashraf Mohamed, M.D.  (918) 502-6720

D. Pediatric Pulmonologist
   Oklahoma City:  
   Nighat Mehdi, M.D.  (405) 271-6390
   Tulsa:  
   Joseph Walter, M.D.  (918) 502-2000
   Lee Droemer, M.D.  (918) 502-2000

E. Pediatric Immunologist
   Oklahoma City:  
   Timothy D. Trojan, M.D.  (405) 607-4333
   Tulsa:  
   James T. Love, M.D.  (918) 307-1613

IX. COUNSELING:

A. A newborn screening parent pamphlet has general information about the newborn screening blood test and the filter paper kit’s detachable parent education slip has a brief description of each disorder. To order pamphlets send a request in writing (order form ODH 15) to OSDH, Shipping and Receiving, 1000 N.E. Tenth, Oklahoma City, OK, 73117-1299. (Catalog Number: P-652-English and P652A-Spanish).

B. For assistance in counseling health professionals or parents, utilize program educational materials located on the OSDH website or contact the Newborn Screening Program. Also refer to the PHYSICIAN APPROVED PROTOCOL: HEMOGLOBINOPATHY SCREENING.
C. Consultation regarding newborn screening results or follow-up can be obtained by contacting the Short-Term Follow-Up Program Staff at (405) 271-6617 or 1-800-766-2223.

D. All infants confirmed with trait or a disorder identified through newborn screening should be referred for counseling:

1. OUHSC Genetics Program (405) 271-8685 (Oklahoma City area)
2. The Children’s Hospital at Saint Francis (918) 502-8365 (Tulsa area)

E. For further information on hemoglobinopathies, please refer to the PHYSICIAN APPROVED PROTOCOL: HEMOGLOBINOPATHY SCREENING. The following are hemoglobinopathy pamphlets that can be utilized as counseling guides:

   Hemoglobin C Trait: Catalog Number P-545
   Sickle Cell Trait: Catalog Number P-547
   About Sickle Cell Disease and Sickle Cell Trait: Catalog Number P-562

F. To order pamphlets send a request in writing (order form ODH 15) to OSDH, Shipping and Receiving, 1000 N.E. Tenth, Oklahoma City, OK, 73117-1299 or fax request to (405) 271-4892.

REFERENCES:

When should a HEALTHY NEWBORN be screened?
- **Ideal**: 24 hours plus one minute OR
- Immediately prior to discharge, whichever comes first.

What if baby is discharged prior to 24 hours of age?
- Collect specimen immediately prior to discharge.
- Notify parent/guardian that a repeat screen is required at 3-5 days of age.
- Distribute the blood collection kit’s blue information sheet to the parent/guardian.

When should the PREMATURE or SICK newborn be screened? (Includes blood transfusion recipients)
- **Ideal**: 24 hours of age plus one minute
- **Maximum**: 3-7 days of age
- Prior to red blood cell transfusion if possible
- If screened prior to 24 hours of age a repeat screen is required at 7-14 days of life.
- **Repeat screen** is also recommended at 14 days of age for all premature or sick infants.

What if baby is transfused prior to the collection of an Initial Screen? Ideally, all newborns should have an initial screen collected prior to a blood transfusion even if they are less than 24 hours old.
- Collect initial screen by the 7th day of life.
- Collect TWO Repeat screens:
  1. **7 days post transfusion** (recommended by Newborn Screening Program (NSP) consultants because plasma and/or red cells will again reflect the infant’s own metabolic processes)
  2. **90 to 120 days of life** (recommended by NSP consultants to evaluate Sickle Cell Disease)

- **Blood transfusions affect ALL screen results**

FOLLOW-UP REQUIREMENTS
- Record screen result in infant’s chart (pertains to any infant examined in the first 3 months of life).
- If infant was on soy or a lactose-free formula at time of testing, the galactosemia screen is invalid:
  - Contact the NSP and request a GALT enzyme on initial specimen. (Specimens are destroyed 42 days after collection. If you suspect galactosemia DO NOT place the infant back on regular formula).
- Upon notification by the NSP, obtain required repeat testing in the timeframe specified so that therapy, when indicated, can be initiated expeditiously:
  - Report laboratory results not performed by the Public Health Laboratory, diagnosis, treatment date (if applicable), and referral information to the NSP within 7 days after completion of the medical evaluation.
  - Refer diagnosed cases to a pediatric sub-specialist and to the designated newborn screening long-term follow-up services.
  - If the parents cannot be contacted after a reasonable search, the NSP must be notified.

The Newborn Screening Program Blood Test Screens for congenital hypothyroidism, classic galactosemia, phenylketonuria (PKU) and other amino acid disorders, sickle cell disease, cystic fibrosis, congenital adrenal hyperplasia, medium-chain acyl coenzyme A dehydrogenase deficiency (MCAD) and other fatty acid disorders, organic acid disorders, biotinidase deficiency and severe combined immunodeficiency (SCID). Screening can detect healthy carriers of cystic fibrosis and sickle cell disease. Screening test are not diagnostic, false positives are expected and false negatives may occur.
Amino Acid Disorder (AA) Screening Fact Sheet for Health Care Providers
Newborn Screening Program of the Oklahoma State Department of Health

What are the characteristics of Amino Acid Disorders (AA)?
- Amino acid disorders are caused by the body’s inability to breakdown or metabolize certain amino acids in proteins, or by the inability to detoxify the by-products of amino acids (ammonia) through the urea cycle.
- The buildup of amino acids and/or by-products of amino acid metabolism in the blood causes severe medical complications.
- Autosomal recessive genetic conditions. Most infants are born to parents who are both unknowingly asymptomatic carriers and have NO known history of an Amino Acid disorder in the family.
- The incidence of all AAs are approximately 1/8000 live births with some disorders (PKU) occurring more frequently than others.
- Symptoms vary by disorder. Clinical symptoms vary from no clinical symptoms for months (phenylketonuria), to acute encephalopathy (maple syrup urine disease, citrullinemia, argininosuccinic aciduria) within hours/days following birth. In each of these disorders, the lack of early identification and treatment may result in serious medical consequences, including mental retardation, developmental delays, failure to thrive and/or death.
- Treatment involves a special diet managed by a metabolic specialist and a metabolic dietitian, frequent feedings, and special care during times of illness or stress.

What is the screening methodology for Amino Acid disorders?
An amino acid profile by Tandem Mass Spectrometry (MS/MS) is performed on each filter paper. Analytes are simultaneously tested on each filter paper. Analyte results are used to establish results requiring follow-up. All out-of-range analyte results require follow-up.

What are the follow-up needs?
The follow-up program will provide detailed guidance on needed actions. The following metabolic specialists have approved all recommendations:
- Klasa Warenga, M.D. (405) 271-8885
- Michelle Polan, M.D. (405) 271-8885

Metabolic Nurse Specialist – Julie Boyd, RN-phone (405) 271-8001 ext. 42074

What is my role in screening?
If you are listed as the infant’s planned health care provider on the filter paper requisition, you are required by the Newborn Screening Program Regulations to initiate follow-up activities.

<table>
<thead>
<tr>
<th>Primary Marker (µmol/L)</th>
<th>Secondary Marker (µmol/L)</th>
<th>Potential Disorder</th>
<th>Risk*</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arginine 100 - &lt;200</td>
<td>NA</td>
<td>ARGIN</td>
<td>LR</td>
<td>Repeat Filter paper. Consult metabolic specialist as needed.</td>
</tr>
<tr>
<td>Arginine ≥ 200</td>
<td>NA</td>
<td>ARGIN</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>Citrulline ≥ 55</td>
<td>Citrulline/Arg ratio ≥ 6.5</td>
<td>CIT-I &amp; CIT-II &amp; A9A</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>Methionine 100 - &lt;160</td>
<td>NA</td>
<td>HOY &amp; MET</td>
<td>LR</td>
<td>Repeat Filter paper. Consult metabolic specialist as needed.</td>
</tr>
<tr>
<td>Methionine ≥ 160</td>
<td>NA</td>
<td>HOY &amp; MET</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>Leucine ≥ 355</td>
<td>Valine ≥ 330</td>
<td>MSUD</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>Leucine ≥ 355</td>
<td>Leucine/Valine ratio ≥ 4.8</td>
<td>MSUD</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>Phenylalanine 150 - &lt;182</td>
<td>NA</td>
<td>PKU &amp; H.Pri&amp; BIOPT</td>
<td>LR</td>
<td>Repeat Filter paper. Consult metabolic specialist as needed.</td>
</tr>
<tr>
<td>Phenylalanine &gt;182</td>
<td>NA</td>
<td>PKU &amp; H.Pri&amp; BIOPT</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>Tyrosine ≥ 400 &amp; infant &lt;14 days of age</td>
<td>NA</td>
<td>TYR-I &amp; TYR-II &amp; TYR-III</td>
<td>LR</td>
<td>Repeat Filter paper. Consult metabolic specialist as needed.</td>
</tr>
<tr>
<td>Tyrosine ≥ 400 &amp; infant &gt;14 days of age</td>
<td>NA</td>
<td>TYR-I &amp; TYR-II &amp; TYR-III</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
</tbody>
</table>

Cut-off values may change. Please contact the OK NSS Program for clarification if needed. More information is available on OSDH website or call (405) 271-6617.

*HR: High Risk
*LR: Low Risk

Newborn Screening Program (405) 271-8817 or 1-800-766-2223
Metabolic Nurse Specialist (405) 271-8885
http://nsp.health.ok.gov
Revised August 3, 2017
AA General Info 1.1.1
AA Screen

Out-of-Range (abnormal)

Not consistent with
No further action needed.

NO

YES

Elevation in Leucine and Citrulline are MEDICAL EMERGENCIES and require IMMEDIATE FOLLOWUP

Low Risk

1. Contact family within 24 hours to assess infant's clinical status and consider initiating feeding precautions.
2. Repeat filter paper within 48 hours.

Tyrosine elevation and less than 14 days of age. Repeat filter paper at 14 days of age.

High Risk for ARG, METH, PKU, TYR

High Risk for Leucine (MSUD) and Citrulline

From the time of report the contacted provider will:
1. Contact family within one hour of notification.
2. Immediate consultation with metabolic specialist.
4. Refer for immediate evaluation and diagnostic work-up in consultation with Metabolic Specialist. Evaluation by Metabolic Specialist must occur within hours.

Appointment with metabolic specialist for diagnostic testing (testing must be coordinated by the specialist or newborn screening program):
1. Acyclovir Profile (plasma)
2. Cystine (plasma)
3. Urine Organic Acids
4. Other lab and/or DNA may be indicated

Diagnostic Testing
Inconclusive:
Monitoring and medical management as advised by Metabolic Specialist within 24 to 48 hours.

Diagnostic Testing
Consistent with:
Refer to metabolic specialist for medical evaluation.

Diagnostic Testing
Within Normal Limits:
Not consistent with AA

Table 1: In-range AA Screen Results

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Primary Analyte (umol/L)</th>
<th>Secondary Analyte (umol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARG</td>
<td>Arginine &lt; 100</td>
<td>NA</td>
</tr>
<tr>
<td>CIT-I, CIT-II, ASA</td>
<td>Cit &lt; 55</td>
<td>Cit/Arg ratio &lt; 6.5</td>
</tr>
<tr>
<td>HCY &amp; METH</td>
<td>Methionine &lt; 100</td>
<td>Met/Phe ratio &lt; 1.2</td>
</tr>
<tr>
<td>MSUD</td>
<td>Leucine &lt; 300</td>
<td>Valine &lt; 280 &amp; Leu/Phe ratio &lt; 4.8</td>
</tr>
<tr>
<td>PKU, H-Phe, &amp; BIOPT</td>
<td>Phenylalanine &lt; 150</td>
<td>NA</td>
</tr>
<tr>
<td>TYR-I, TYR-II, TYR-III</td>
<td>Tyrosine &lt; 400</td>
<td>NA</td>
</tr>
</tbody>
</table>

1. These values are utilized for newborns less than 60 days old.
2. Elevations of the secondary analytes are reported as "not consistent with AA" if primary analyte is in range.
Amino Acid Disorders FOLLOW-UP

FILTER PAPER RESULTS | INDICATED PROCEDURES
---|---
**Amino Acid Screen - Normal Result**<br> If specimen was collected before the infant was 24 hours of age, a specimen should be collected and submitted to the Oklahoma State Department of Health (OSDH) Laboratory for testing when the infant is 3 to 5 days of age. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.

**Amino Acid Screen – Low Risk Result**<br> Repeat Filter Paper specimen should be collected and sent to the OSDH laboratory within 48 hours. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.

**Amino Acid Screen – High Risk Result**
Immediate referral to a metabolic specialist is indicated.

**Two Abnormal Amino Acid Screen Results on Filter Paper**
Immediate referral to a metabolic specialist is indicated.

LABORATORY PROCEDURE
1. Amino Acid analytes are tested on each filter paper.

<table>
<thead>
<tr>
<th>Primary Analyte (µmol/L)</th>
<th>Secondary Analyte (µmol/L)</th>
<th>Potential Disorder</th>
<th>Risk</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arginine 100-200</td>
<td>NA</td>
<td>ARG</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>Arginine ≥ 200</td>
<td>NA</td>
<td>ARG</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>Citrulline ≥ 55</td>
<td>Cit/Arg ratio ≥ 6.5</td>
<td>CIT-I &amp; CIT-II &amp; ASA</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>Methionine 100-&lt; 160</td>
<td>NA</td>
<td>HYC &amp; MET</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>Methionine ≥ 160</td>
<td>Met/Phe ratio ≥ 1.2</td>
<td>HYC &amp; MET</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>Leucine ≥ 355</td>
<td>Valine ≥ 330</td>
<td>MSUD</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>Leucine ≥ 355</td>
<td>Leu/Phe ratio ≥ 4.8</td>
<td>MSUD</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>Phenylalanine 150-&lt; 182</td>
<td>NA</td>
<td>PKU &amp; H-PHE &amp; BIOPT</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>Phenylalanine ≥ 182</td>
<td>NA</td>
<td>PKU &amp; H-PHE &amp; BIOPT</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>Tyrosine ≥ 400 &amp; infant &lt; 14 days of age</td>
<td>NA</td>
<td>TYR-I &amp; TYR-II &amp; TYR-III</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>Tyrosine ≥ 400 &amp; infant ≥ 14 days of age</td>
<td>NA</td>
<td>TYR-I &amp; TYR-II &amp; TYR-III</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
</tbody>
</table>

A filter paper specimen refers to the Newborn Screening Kit ODH #450. Filter paper kits may be ordered from the: Public Health Laboratory Service, OSDH, P.O. Box 24106, Oklahoma City, OK, 73124-0106, call (405) 271-5070, or utilize the OSDH website.

For a Metabolic Specialist:
Klaas Wierenga, M.D.    (405) 271-8685
Michelle Polan, M.D.    (405) 271-8685

Questions regarding follow-up, please contact the Newborn Screening Short-term Follow-up Program at (405) 271-6617 or 1-800-766-2223 or fax to (405) 271-4892. Questions regarding laboratory procedure should be directed to the OSDH Lab at (405) 271-5070 or fax to (405) 271-4850.
CONGENITAL HYPOTHYROIDISM FOLLOW-UP PROCEDURES

<table>
<thead>
<tr>
<th>FILTER PAPER RESULTS</th>
<th>INDICATED PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH – Normal Range</td>
<td>If specimen was collected before the infant was 24 hours of age, a Repeat Filter Paper (FP) specimen should be collected and submitted to the Oklahoma State Department of Health (OSDH) Laboratory for testing when the infant is 3 to 5 days of age. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td>Abnormal TSH 30 - &lt; 50 μIU/ml</td>
<td>Repeat Filter Paper specimen should be collected and sent to the OSDH laboratory within 48 hours OR Serum Free T4 &amp; TSH should be drawn at 14 days of life. This test cannot be done at the OSDH Laboratory. If serum results are abnormal, immediate referral to a pediatric endocrinologist is indicated.</td>
</tr>
<tr>
<td>Abnormal TSH ≥ 50 μIU/ml</td>
<td>Serum Free T4 &amp; TSH should be drawn within 48 hours. This test cannot be done at the OSDH Laboratory. If serum results are abnormal, immediate referral to a pediatric endocrinologist is indicated.</td>
</tr>
<tr>
<td>Two Abnormal TSH Results on Filter Paper</td>
<td>Serum Free T4 &amp; TSH should be drawn within 48 hours. This test cannot be done at the OSDH Laboratory. If serum results are abnormal, evaluation by a pediatric endocrinologist is indicated.</td>
</tr>
</tbody>
</table>

LABORATORY PROCEDURE:

Normal Filter Paper Result: TSH < 30 μIU/ml

A filter paper specimen refers to the Newborn Screening Kit ODH #450. Filter Paper Kits may be ordered from the Public Health Laboratory Service, OSDH, P.O. Box 24106, Oklahoma City, OK 73124-0106, call (405) 271-5070, or the OSDH website.

If a Serum Free T4 and TSH is indicated, a reference or hospital laboratory will have to be utilized. Serum Free T4 & TSH testing is not a service provided by the OSDH Laboratory.

For a Pediatric Endocrinologist:

Oklahoma City
David Domek, M.D. (405) 945-4525
Laura Chalmers, M.D. (918) 619-4803
Minu George, M.D. (405) 271-6764
Sowmya Krishnan, M.D. (405) 271-6764
Jeanie Tryggestad, M.D. (405) 271-6764
Monica Marin, M.D. (405) 271-6764
Steven Chernausek, M.D. (405) 271-6764
David Sparling, M.D. (405) 271-6764
Paul Dasari, M.D. (405) 271-4417

Tulsa
David Jelley, M.D. (918) 619-4803

Questions regarding follow-up, please contact the Newborn Screening Short-term Follow-up Program at (405) 271-6617 or 1-800-766-2223 or fax to (405) 271-4892. Questions regarding laboratory procedure should be directed to the OSDH Lab at (405) 271-5070 or fax to (405) 271-4850.
GALACTOSEMIA FOLLOW-UP

<table>
<thead>
<tr>
<th>FILTER PAPER RESULTS</th>
<th>INDICATED PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Galactose – Normal Range</strong></td>
<td>If specimen was collected before the infant was 24 hours of age, a specimen should be collected and submitted to the Oklahoma State Department of Health (OSDH) Laboratory for testing when the infant is 3 to 5 days of age. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td><strong>Total Galactose ≥ 10 mg/dl Enzyme Present</strong></td>
<td>Not consistent with classic galactosemia. May indicate a variant form of galactosemia, carrier, or normal genotype. Repeat testing is at the discretion of the provider. Options may include a repeat filter paper or confirmation testing through a metabolic specialist. Free confirmation Galactose-a-Phosphate Uridyl Transferase (GAL-1-PUT) testing through OSDH is no longer available for this test result.</td>
</tr>
<tr>
<td><strong>Galactose ≥ 17 mg/dl Enzyme Present</strong></td>
<td>Not consistent with classic galactosemia. May indicate a variant form of galactosemia, carrier, or normal genotype. Since the galactose is significantly elevated, treatment (soy formula/lactose free-diet) and further testing may be indicated. Referral to a metabolic specialist indicated. Free confirmation GAL-1-PUT testing through OSDH is no longer available for this test result.</td>
</tr>
<tr>
<td><strong>Total Galactose ≥ 7 mg/dl Low Enzyme</strong></td>
<td>A repeat filter paper within 48 hours is recommended; however, if clinically indicated (i.e., a family history of classic or Duarte galactosemia and/or infant is symptomatic) treatment with soy formula and confirmatory testing may be needed. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td><strong>Total Galactose ≥ 7 mg/dl No Enzyme</strong></td>
<td>Start infant on a soy formula within 48 hours. Immediate referral to a metabolic specialist is indicated.</td>
</tr>
<tr>
<td><strong>Two Abnormal Total Galactose Results on Filter Paper With Enzyme Low or Absent on Repeat</strong></td>
<td>Start infant on a soy formula within 48 hours. Immediate referral to a metabolic specialist is indicated.</td>
</tr>
</tbody>
</table>

LABORATORY PROCEDURE
A two-tier screen is utilized:
1. Total Galactose level is tested on each filter paper.
2. If the Total Galactose level is elevated (i.e., ≥ 7 mg/dl) then GALT (enzyme testing) is performed.

Normal Filter Paper Result: Total Galactose < 7 mg/dl or Total Galactose < 10 mg/dl with Enzyme Present

Note: If infant was on soy or a lactose-free formula at time of testing, a two-tier screen is required. To request an enzyme screen on an initial specimen, contact the Newborn Screening Program (NSP).

A filter paper specimen refers to the Newborn Screening Kit ODH #450. Filter paper kits may be ordered from the: Public Health Laboratory Service, OSDH, P.O. Box 24106, Oklahoma City, OK, 73124-0106, call (405) 271-5070, or the OSDH website.

For free GAL-1-PUT testing: Contact the Newborn Screening Program for free testing (405) 271-6617 or 1-800-766-2223. The Newborn Screening Nurse Coordinator must be contacted for arrangements and approval. This is not a service routinely offered.

For a Metabolic Specialist:
Klass Wierenga, M.D. (405) 271-8685
Michelle Polan, M.D. (405) 271-8685

Questions regarding follow-up, please contact the Newborn Screening Short-term Follow-up Program at (405) 271-6617 or 1-800-766-2223 or fax to (405) 271-4892. Questions regarding laboratory procedure should be directed to the OSDH Lab at (405) 271-5070 or fax to (405) 271-4850.
# CYSTIC FIBROSIS FOLLOW-UP

<table>
<thead>
<tr>
<th>FILTER PAPER RESULTS</th>
<th>INDICATED PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoreactive Trypsinogen (IRT) Normal Range</td>
<td>If specimen was collected before the infant was 24 hours of age, a specimen should be collected and submitted to the Oklahoma State Department of Health (OSDH) Laboratory for testing when the infant is 3 to 5 days of age. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td>IRT ≥ 65 ng/ml &amp; no (0) mutations*</td>
<td>Not consistent with cystic fibrosis (CF) unless symptomatic or if there is a family history of Cystic Fibrosis. Most consistent with a normal genotype. Approximately 1% of newborns with this type of test result will have CF. Confirmatory newborn sweat testing and genetic counseling indicated within 1 to 2 weeks only if symptomatic or if there is a family history of Cystic Fibrosis.</td>
</tr>
<tr>
<td>IRT ≥ 65 ng/ml &amp; one (1) mutation</td>
<td>Probable Carrier for CF or possible CF. Confirmatory newborn sweat testing and genetic counseling indicated within 1 to 2 weeks. Confirmation testing and genetic counseling must be performed at a designated Newborn Screening Program (NSP) sweat testing site: OU Medical Center Sweat Testing Laboratory (405) 271-6161 Saint Francis Laboratory (918) 494-6572 To meet the special needs of newborns, these sites have an assigned day to perform the testing. Newborns should only be tested on the designated sweat test day for newborns.</td>
</tr>
<tr>
<td>IRT &gt; 65 ng/ml &amp; two (2) mutations</td>
<td>Consistent with CF. Confirmatory newborn sweat testing and genetic counseling indicated within 1 to 2 weeks. Confirmation testing and genetic counseling must be performed at a designated Newborn Screening Program (NSP) sweat testing site: - OU Medical Center Sweat Testing Laboratory (405) 271-6161 Saint Francis Laboratory (918) 494-6572 To meet the special needs of newborns, these sites have an assigned day to perform the testing. Newborns should only be tested on the designated sweat test day for newborns.</td>
</tr>
</tbody>
</table>

* There are over 1,200 CF mutations. The newborn screening program screens for 39+4 CF mutations. To view DNA testing panel, visit OSDH Web site [www://gp.health.ok.gov](http://www://gp.health.ok.gov). Please note, only newborns with an elevated IRT (i.e., ≥ 65 ng/ml) or if special request is made receive DNA testing.

## LABORATORY PROCEDURE:

A two-tier screen is utilized: (1) Immunoreactive Trypsinogen (IRT) level is tested on each filter paper. (2) If the IRT level is elevated, DNA testing is performed. This test is performed on the same sample by a contract laboratory.

Normal Filter Paper Result: IRT < 65 ng/ml OR IRT ≥ 65 ng/ml to < 170 ng/ml with no (zero) mutations.

A filter paper specimen refers to the Newborn Screening Kit ODH #450. Filter paper kits may be ordered from the: Public Health Laboratory Service, OSDH, P.O. Box 24106, Oklahoma City, OK, 73124-0106, call (405) 271-5070, utilize the OSDH website.

Free confirmatory sweat testing and genetic counseling, call Follow-up Program: (405) 271-6617 or 1-800-766-2223

For a Sweat Test Center:

<table>
<thead>
<tr>
<th>Oklahoma City</th>
<th>Tulsa</th>
</tr>
</thead>
<tbody>
<tr>
<td>OU Medical Center Laboratory Client Services (405) 271-6161</td>
<td>The Children’s Hospital at Saint Francis (918) 502-8365</td>
</tr>
</tbody>
</table>

Newborn Screening Short-term Follow-up Program: (405) 271-6617 or 1-800-766-2223 or fax to (405) 271-4892

Public Health Laboratory: (405) 271-5070 or fax to (405) 271-4850
## CONGENITAL ADRENAL HYPERPLASIA DUE TO 21-HYDROXYLASE DEFICIENCY FOLLOW-UP

<table>
<thead>
<tr>
<th>FILTER PAPER RESULTS</th>
<th>INDICATED PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Birth Weight &gt; 2500 grams:</strong></td>
<td>If specimen was collected before the infant was 24 hours of age, a specimen should be collected and submitted to the Oklahoma State Department of Health (OSDH) Laboratory for testing when the infant is 3 to 5 days of age. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td><strong>17 OHP ng/ml</strong></td>
<td><strong>Steroid Profile</strong></td>
</tr>
<tr>
<td>&lt;30 &amp; Not performed</td>
<td></td>
</tr>
<tr>
<td>&lt;55 &amp; Normal</td>
<td></td>
</tr>
</tbody>
</table>
| **Birth Weight < 2500 grams:** | If the newborn was premature or sick, a repeat screen at 14 days of age is recommended. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.
| **17 OHP ng/ml** | **Steroid Profile** |
| <50 & Not performed | |
| ≥50 & Normal | |
| **Birth Weight ≥2500 grams:** | Borderline Congenital Adrenal Hyperplasia (CAH) Protocol:
- Monitor Basic Metabolic Panel (BMP) daily until final screen results are reported (if BMP is abnormal, promptly consult with a pediatric endocrinologist),
- Repeat filter paper within 24 – 48 hours. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”,
- Monitor for signs and symptoms (S&S) of adrenal insufficiency (change in feeding patterns, poor weight gain, vomiting, diaphoresis, tachypnea, pale mucous membranes, hypoglycemia, and dehydration), and
- Consult with a Pediatric Endocrinologist (within 24 hours) for any of the following: Abnormal BMP, Ambiguous genitalia, signs and symptoms of adrenal insufficiency, or abnormal repeat filter paper.
| **17 OHP ng/ml** | **Steroid Profile** |
| ≥55 to 80 & Pending | |
| 30 to 54 & Abnormal | |
| **Birth Weight < 2500 grams:** | Presumptive for Congenital Adrenal Hyperplasia (CAH) Protocol:
- Contact family within 8 hours,
- Clinically evaluate infant within 24 hours,
- Lab work must include serum 17-OHP by DLO laboratories and Stat Basic Metabolic Panel (BMP),
- Repeat filter paper (not required),
- Assess infant for ambiguous genitalia and signs and symptoms of adrenal insufficiency,
- After assessment and review of BMP results, consult with a pediatric endocrinologist (PE) for medical management recommendations (key information includes gestational age, steroid therapy, BMP values, and clinical assessment findings),
- Refer to the OSDH Emergency Management Guidelines for Newborns with Abnormal CAH Screen Results, and
- Inform family of signs and symptoms of adrenal insufficiency and course of action if symptoms present, utilizing the Parent Information Handout for Congenital Adrenal Hyperplasia.
| **17 OHP ng/ml** | **Steroid Profile** |
| ≥75 & Abnormal | |
| **Birth Weight > 2500 grams:** | Monitoring Protocol Pending Confirmatory Test Results:
1. Immediately notify Pediatric Endocrinologist if infant becomes clinically unstable.
2. Upon receipt of 17-OHP results, contact the PE for management recommendations and final diagnosis.
| **17 OHP ng/ml** | **Steroid Profile** |
| ≥55 & Abnormal | |
| >80 & Pending | |
LABORATORY PROCEDURE:

Normal Filter Paper Result: Birth Weight ≥ 2500 grams: **17 OHP ng/ml** Steroid Profile
- <30 & Not performed
- <55 & Normal

Birth Weight < 2500 grams: **17 OHP ng/ml** Steroid Profile
- <50 & Not performed
- ≥50 & Normal

A two-tier screen is utilized:
1. 17-hydroxyprogesterone (17-OHP) level is tested on each filter paper.
2. If the 17-OHP level is elevated, the filter paper (same specimen) is sent to Mayo Laboratories for a steroid profile. The steroid profile includes testing for 17-OHP, androstenedione, and cortisol with determination of the following ratio: 17-OHP + androstenedione / cortisol. Not all specimens receive steroid profile testing.

NOTE: Steroid (glucocorticoid) therapy may result in a false negative result, please contact program if newborn was on steroid therapy at time of testing.

A filter paper specimen refers to the Newborn Screening Kit ODH #450. Filter paper kits may be ordered from the: Public Health Laboratory Service, OSDH, P.O. Box 24106, Oklahoma City, OK, 73124-0106, call (405) 271-5070, or utilize the OSDH website.

For a Pediatric Endocrinologist:

<table>
<thead>
<tr>
<th>Oklahoma City</th>
<th>Tulsa</th>
</tr>
</thead>
<tbody>
<tr>
<td>David Domek, M.D.</td>
<td>David Jelley, M.D.</td>
</tr>
<tr>
<td>Laura Chalmers, M.D.</td>
<td>(918) 619-4803</td>
</tr>
<tr>
<td>Minu George, M.D.</td>
<td>(405) 271-6764</td>
</tr>
<tr>
<td>Sowmya Krishnan, M.D.</td>
<td>(405) 271-6764</td>
</tr>
<tr>
<td>Jeanie Tryggestad, M.D.</td>
<td>(405) 271-6764</td>
</tr>
<tr>
<td>Monica Marin, M.D.</td>
<td>(405) 271-6764</td>
</tr>
<tr>
<td>Steven Chernausek, M.D.</td>
<td>(405) 271-6764</td>
</tr>
<tr>
<td>David Sparling, M.D.</td>
<td>(405) 271-6764</td>
</tr>
<tr>
<td>Paul Dasari, M.D.</td>
<td>(405) 271-4417</td>
</tr>
</tbody>
</table>

To contact the Newborn Screening Endocrinology Nurse Amanda Patterson, R.N. (405) 271-6764 or Pager: (405) 575-8228

Questions regarding follow-up, please contact the Newborn Screening Short-term Follow-up Program at (405) 271-6617 or 1-800-766-2223 or fax to (405) 271-4892. Questions regarding laboratory procedure should be directed to the OSDH Lab at (405) 271-5070 or fax to (405) 271-4850.
Fatty Acid Oxidation Disorder (FAOD) Screening Fact Sheet for Health Care Providers
Newborn Screening Program of the Oklahoma State Department of Health

What are the characteristics of FAOD?
- Autosomal recessive genetic conditions. Most infants are born to parents who are both unknowingly asymptomatic carriers and have NO known history of a fatty acid oxidation disorder in the family.
- The incidence of FAOD’s ranges from 1:10,000 to 1:100,000. MCAD is one of the most common with an incidence of 1:10,000. VLCAD and LCHAD are more rare.
- Symptoms vary by disorder. These disorders can lead to metabolic crisis, especially in infants and children. This crisis can lead to seizures, respiratory failure, cardiac arrest and death. Crisis survivors may experience significant developmental disabilities. Some infants will present during the neonatal period with life threatening symptoms.
- Treatment involves a special diet managed by a metabolic specialist and a metabolic dietician, frequent feedings, and special care during times of illness or stress.

What is the screening methodology for FAOD disorders?
An acylcarnitine profile by Tandem Mass Spectrometry (MS/MS) is performed on each filter paper. Primary and secondary analytes are simultaneously tested on each filter paper. Primary analyte results are used to establish results requiring follow-up. All out-of-range primary analyte results require follow-up. Secondary analyte are used in conjunction with primary analyte results to assign risk. Elevations of the secondary analytes are reported as “not consistent with FAOD” if the primary analyte is in range.

What are the follow-up needs?
The follow-up program will provide detailed guidance on needed actions. The following metabolic specialists have approved all recommendations:
- Klaas Wierenga, M.D. (405) 271-6685
- Michelle Polan, M.D. (405) 271-6685

Metabolic Nurse Specialist – Julie Boyd, RN – phone: (405) 271-8001 ext 42074

What is my role in screening?
If you are listed as the infant’s planned health care provider on the filter paper requisition, you are required by the Newborn Screening Program Regulations to initiate follow-up activities.

<table>
<thead>
<tr>
<th>Primary Marker (µmol/L)</th>
<th>Secondary Analyte (µmol/L)</th>
<th>Potential Disorder</th>
<th>Risk*</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>C0 &gt; 2.00 &amp; ≤ 5.5</td>
<td>NA</td>
<td>CUD</td>
<td>LR</td>
<td>Repeat filter paper. Consult with metabolic specialist as needed.</td>
</tr>
<tr>
<td>C0 ≤ 2.00</td>
<td>NA</td>
<td>CUD</td>
<td>HR</td>
<td>EMERGENCY. Immediate referral to the metabolic specialist is required.</td>
</tr>
<tr>
<td>C4 ≥ 1.27</td>
<td>C4/C2 &lt; 0.66</td>
<td>SCAD &amp; GAIL</td>
<td>LR</td>
<td>Repeat filter paper. Consult with metabolic specialist as needed.</td>
</tr>
<tr>
<td>C4 ≥ 1.27</td>
<td>C4/C2 ≥ 0.66</td>
<td>SCAD &amp; GAIL</td>
<td>HR</td>
<td>Immediate referral to the metabolic specialist is required.</td>
</tr>
<tr>
<td>C4 ≥ 2.00</td>
<td>NA</td>
<td>SCAD &amp; GAIL</td>
<td>HR</td>
<td>Immediate referral to the metabolic specialist is required.</td>
</tr>
<tr>
<td>C8 ≥ 0.40</td>
<td>C8/C10 &lt; 3.0</td>
<td>MCAD &amp; MCAT</td>
<td>LR</td>
<td>Repeat filter paper. Consult with metabolic specialist as needed.</td>
</tr>
<tr>
<td>C8 ≥ 0.40</td>
<td>C8/C10 ≥ 3.0</td>
<td>MCAD &amp; MCAT</td>
<td>HR</td>
<td>Immediate referral to the metabolic specialist is required.</td>
</tr>
<tr>
<td>C14:1 ≥ 0.70</td>
<td>NA</td>
<td>VLCAD</td>
<td>HR</td>
<td>Immediate referral to the metabolic specialist is required.</td>
</tr>
<tr>
<td>C16 ≥ 7.46</td>
<td>C18:1 &lt; 3.0</td>
<td>CACT &amp; CPTII</td>
<td>LR</td>
<td>Repeat filter paper. Consult with metabolic specialist as needed.</td>
</tr>
<tr>
<td>C18:1 ≥ 3.0</td>
<td>C16 &lt; 7.45</td>
<td>CACT &amp; CPTII</td>
<td>LR</td>
<td>Repeat filter paper. Consult with metabolic specialist as needed.</td>
</tr>
<tr>
<td>C18:1 ≥ 3.0</td>
<td>C16 ≥ 7.45</td>
<td>CACT &amp; CPTII</td>
<td>HR</td>
<td>Immediate referral to the metabolic specialist is required.</td>
</tr>
<tr>
<td>C0 ≥ 64</td>
<td>C0/C16+C18≤ 90</td>
<td>CPT1</td>
<td>LR</td>
<td>Repeat filter paper. Consult with metabolic specialist as needed.</td>
</tr>
<tr>
<td>C0 ≥ 64</td>
<td>C0/C16+C18≥ 90</td>
<td>CPT1</td>
<td>HR</td>
<td>Immediate referral to the metabolic specialist is required.</td>
</tr>
<tr>
<td>C16OH ≥ 0.16</td>
<td>C18:1 OH &lt; 0.15</td>
<td>LCHAD/TFP</td>
<td>LR</td>
<td>Repeat filter paper. Consult with metabolic specialist as needed.</td>
</tr>
<tr>
<td>C18:1 OH ≥ 0.15</td>
<td>C16OH &lt; 0.16</td>
<td>LCHAD/TFP</td>
<td>LR</td>
<td>Repeat filter paper. Consult with metabolic specialist as needed.</td>
</tr>
<tr>
<td>C18:1 OH ≥ 0.15</td>
<td>C16OH ≥ 0.16</td>
<td>LCHAD/TFP</td>
<td>HR</td>
<td>Immediate referral to the metabolic specialist is required.</td>
</tr>
</tbody>
</table>

*HR=High Risk
*LR=Low Risk

Cut off values may change. Please contact the OK NBS Program for clarification if needed. More information is available on the OSDH website or call (405) 271-6617.

Newborn Screening Program (405) 271-6917 or 1-800-768-2223
Metabolic Nurse Specialist (405) 271-8885
http://nsp.health.ok.gov

Revised August 3, 2017
General Info- 2.1.1a
FAOD Screening (CUD, SCAD, GAI, MCAT, VLCAD, CACT, CPTII, CPT1A, LCHAD, TFP)
Oklahoma State Department of Health FAOD Protocol

FAOD Screen
Out-of-Range (abnormal)

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW RISK</td>
<td>HIGH RISK</td>
</tr>
</tbody>
</table>

Not consistent with FAOD.
No further action needed.

1. PCP to contact family within 24 hours to assess infant’s clinical status.
2. Consider initiating feeding precautions.
3. Repeat Filter Paper within 48 hours.

In-Range
Out-of-Range

Not consistent with FAOD.
No further follow-up indicated.

From the time the screen is reported to the provider, the Metabolic Nurse Specialist will monitor follow-up by:
1. Confirming the provider contacts family before COB.
2. Facilitating and confirming a clinical evaluation by a provider or metabolic specialist is achieved before COB.
3. Facilitating and confirming infant presents for a diagnostic workup with a metabolic specialist within 24 to 48 hours.
4. Coordinating collection and processing of diagnostic tests and communicating test results to provider and short-term follow-up program (STFU).
5. Communicating with STFU if the above timelines are not met.

Appointment with metabolic specialist for diagnostic testing (testing must be coordinated by the specialist or newborn screening program):
1. Acylcarnitine Profile (plasma)
2. Carnitine (plasma)
3. Urine Organic Acids
4. Other lab and/or DNA may be indicated

Diagnostic Testing
Inconclusive: Monitoring and medical management as advised by metabolic specialist.

Diagnostic Testing Consistent with FAOD: Refer to metabolic specialist for medical management.

Diagnostic Testing Within Normal Limits: Not consistent with FAOD. No further follow-up indicated.

Table 1. In-range FAOD Screen Results:1.

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>Primary Analyte (μmol/L)</th>
<th>Secondary Analyte (μmol/L)</th>
<th>DISORDER</th>
<th>Primary Analyte (μmol/L)</th>
<th>Secondary Analyte (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CUD</td>
<td>C0 = 5.5</td>
<td>NA</td>
<td>VLCAD</td>
<td>C14:1 = 0.70</td>
<td>C14 &lt; 0.71</td>
</tr>
<tr>
<td>SCAD &amp; GAI</td>
<td>C4 &lt; 1.27</td>
<td>C4/C2 ratio &lt; 0.06</td>
<td>C16:4</td>
<td>C16 = 7.46</td>
<td>C8/C10 ratio &lt; 3.0</td>
</tr>
<tr>
<td>GACT &amp; CPTII</td>
<td>C16 = 7.46</td>
<td>C18 = 2.15</td>
<td>MCAD &amp; MCAT</td>
<td>C8 = 0.40</td>
<td>C6 = 0.25</td>
</tr>
<tr>
<td></td>
<td>C18:1 = 3.0</td>
<td>C18:2 = 2.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPT1</td>
<td>C0 = 64.0</td>
<td>C0(C16+C18) &lt; 90</td>
<td>C10</td>
<td>C0 = 0.40</td>
<td>C10:1 = 0.5</td>
</tr>
<tr>
<td></td>
<td>C18:1 OH = 0.15</td>
<td>C18:1 OH = 0.12</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 These values are utilized for newborns less than 60 days old.
2 Elevations of the secondary analytes are reported as “not consistent with FAOD” if primary analyte is in range in-range.

Revised August 25, 2016
General Info- 2.1.2

Newborn Blood Screening - 30
What are the characteristics of Organic Acid Disorders (OAD)?
- Autosomal recessive genetic conditions. Most infants are born to parents who are both unknowingly asymptomatic carriers and have no known history of an Organic Acid disorder in the family.
- The incidence of OAD’s ranges from 1/75,000 – 1/100,000.
- Symptoms vary by disorder. These disorders can lead to metabolic crisis, especially in infants and children. This crisis can lead to seizures, respiratory failure, cardiac arrest and death. Crisis survivors may experience significant developmental disabilities. Some infants may present in the neonatal period without any symptoms.
- Symptoms of a metabolic crisis can be triggered by fever, infection or illness.
- Treatment involves a special diet managed by a metabolic specialist and a metabolic dietitian, frequent feedings, and special care during times of illness or stress.

What is the screening methodology for Organic Acid disorders?
An acylcarnitine profile by Tandem Mass Spectrometry (MS/MS) is performed on each filter paper. Primary and secondary analytes are simultaneously tested on each filter paper. Primary analyte results are used to establish results requiring follow-up. All out-of-range primary analyte results require follow-up. Secondary analyte results are in conjunction with primary analyte results to assign risk. Elevations of the secondary analytes are reported as “not consistent with OA” if the primary analyte is in range.

What are the follow-up needs?
The follow-up program will provide detailed guidance on needed actions. The following metabolic specialists have approved all recommendations:
- Klaas Wierenga, M.D. (405) 271-8685
- Michelle Polan, M.D. (405) 271-8685

Metabolic Nurse Specialist – Julie Boyd, RN phone (405) 271-8001 ext 42074

What is my role in screening?
If you are listed as the infant’s planned health care provider on the filter paper requisition, you are required by the Newborn Screening to initiate follow-up activities.

<table>
<thead>
<tr>
<th>Primary Marker (µmol/L)</th>
<th>Secondary Analyte (µmol/L)</th>
<th>Potential Disorder</th>
<th>Risk</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3 ≥ 7.21</td>
<td>C3/C2 &lt; 0.25</td>
<td>PROP/ITIC/CL-CDC1A+B</td>
<td>LR</td>
<td>Repeat filter paper. Consult metabolic specialist as needed</td>
</tr>
<tr>
<td>C3 ≥ 7.21</td>
<td>C3/C2 ≥ 0.25</td>
<td>PROP/ITIC/CL-CDC1A+B</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>C3DC 0.44-0.59</td>
<td>NONE</td>
<td>MAL</td>
<td>LR</td>
<td>Repeat filter paper. Consult metabolic specialist as needed</td>
</tr>
<tr>
<td>C3DC ≥ 0.60</td>
<td>NONE</td>
<td>MAL</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>C4 1.27 - 1.99</td>
<td>C4/C2 &lt; 0.06</td>
<td>IBG</td>
<td>LR</td>
<td>Repeat filter paper. Consult metabolic specialist as needed</td>
</tr>
<tr>
<td>C4 1.27 - 1.99</td>
<td>C4/C2 ≥ 0.06</td>
<td>IBG</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>C4 ≥ 2.00</td>
<td>IBG</td>
<td>MAL</td>
<td>HR</td>
<td>Repeat filter paper. Consult metabolic specialist as needed</td>
</tr>
<tr>
<td>C5 0.87-2.99</td>
<td>C5/C2 &lt; 0.05</td>
<td>IVA / 2MBG</td>
<td>LR</td>
<td>Repeat filter paper. Consult metabolic specialist as needed</td>
</tr>
<tr>
<td>C5 0.87-2.99</td>
<td>C5/C2 ≥ 0.05</td>
<td>IVA / 2MBG</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>C5 ≥ 0.60</td>
<td>IVA</td>
<td>MAL</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>C5 ≤ 0.10</td>
<td>C5OH+C4DC &lt; 0.80</td>
<td>βKT</td>
<td>LR</td>
<td>Repeat filter paper. Consult metabolic specialist as needed</td>
</tr>
<tr>
<td>C5 ≤ 0.10</td>
<td>C5OH+C4DC ≥ 0.80</td>
<td>βKT</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>C5DC ≥ 0.49</td>
<td>C5DC/C8 &lt; 0.50 &amp; C5DC/C16 &lt; 0.20</td>
<td>GA1</td>
<td>LR</td>
<td>Repeat filter paper. Consult metabolic specialist as needed</td>
</tr>
<tr>
<td>C5DC ≥ 0.49</td>
<td>C5DC/C8 ≥ 0.50</td>
<td>GA1</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>C5DC ≥ 0.49</td>
<td>C5DC/C16 ≥ 0.20</td>
<td>GA1</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
<tr>
<td>C5OH+C4DC &lt; 0.80</td>
<td>C8DC &lt; 0.27</td>
<td>HMGIC/IC/IC/IC/IC/IC</td>
<td>LR</td>
<td>Repeat filter paper. Consult metabolic specialist as needed</td>
</tr>
<tr>
<td>C5OH+C4DC ≥ 0.80</td>
<td>C8DC &lt; 0.27</td>
<td>HMGIC/IC/IC/IC/IC/IC</td>
<td>HR</td>
<td>Immediate referral to metabolic specialist. Confirmatory testing</td>
</tr>
</tbody>
</table>

Cut-off values may change. Please contact the OK NBS Program for clarification if needed. More information available on OSDH website or call (405) 271-6617.

*HR-High Risk
*LR-Low Risk

Newborn Blood Screening - 31
**Newborn Blood Screening**

**OA Screening** (PROP/MUT/MAL/IBG/IVA/2MBG/8KT/GA1/3MCC/HMG/2MGA/MCD)

**OAB Screen**

- Not consistent with OA. No further action needed.
- YES
  - LOW RISK
    - From time of report, the contacted provider will:
      1. Contact family by CCW within one hour of notification.
      2. Immediate consultation with Metabolic Specialist.
      3. Arrange for a clinical evaluation immediately utilizing the OSDH Emergency Management Protocol (assessment can be done by provider or metabolic specialist).
      4. PROP / MUT immediate admission
      5. MAL / IBG / IVA / GA1 / 8KT / HMG etc evaluation must occur on day of notification.
      6. Refer for a diagnostic work-up by Metabolic Specialist within 24 to 48 hours. Metabolic nurse specialist will assist with appointment.

- HIGH RISK
  - In-Range
  - Out-of-Range

**Diagnostic Testing**

- Inconclusive: Monitoring and medical management as advised by metabolic specialist.
- Consistent with OA: Refer to metabolic specialist for medical management.

**Table 1. In-range OAB Screen Results**

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>Primary Analyte (µmol/L)</th>
<th>Secondary Analyte (µmol/L)</th>
<th>DISORDER</th>
<th>Primary Analyte (µmol/L)</th>
<th>Secondary Analyte (µmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROP / MUT</td>
<td>C₃ &lt; 7.21</td>
<td>C₃/C₂ &lt; 0.25</td>
<td>GA1</td>
<td>C₅₀/C₈ &lt; 0.46</td>
<td>C₅₁/C₈ &lt; 0.40 &amp; C₅₀/C₆ &lt; 0.20</td>
</tr>
<tr>
<td>MAL</td>
<td>C₃D &lt; 0.44</td>
<td>NONE</td>
<td>8KT</td>
<td>C₅₁ &lt; 0.10</td>
<td>C₅₁+C₄DC &lt; 0.80</td>
</tr>
<tr>
<td>IBG</td>
<td>C₄ &lt; 1.27</td>
<td>C₄/C₂ &lt; 0.96</td>
<td>HMG</td>
<td>C₅₀+C₇DC &lt; 0.80</td>
<td>C₆₇C &lt; 0.27 for HMG &amp; 3MGA only</td>
</tr>
<tr>
<td>IVA / 2MBG</td>
<td>C₅ &lt; 0.87</td>
<td>C₅/C₂ &lt; 0.05</td>
<td>3MGA</td>
<td>3MCC</td>
<td>MCD</td>
</tr>
</tbody>
</table>

*These values are utilized for newborns less than 60 days old.

*Deviations of the secondary analytes are reported as 'Not consistent with PAOD' if primary analyte is in range.
Fatty Acid Disorders FOLLOW-UP

FILTER PAPER RESULTS | INDICATED PROCEDURES
--- | ---
**Fatty Acid Screen - Normal Result** | If specimen was collected before the infant was 24 hours of age, a specimen should be collected and submitted to the Oklahoma State Department of Health (OSDH) Laboratory for testing when the infant is 3 to 5 days of age. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.

**Fatty Acid Screen – Low Risk Result** | Repeat Filter Paper specimen should be collected and sent to the OSDH laboratory within 48 hours. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.

**Fatty Acid Screen – High Risk Result** | Immediate referral to a metabolic specialist is indicated.

**Two Abnormal Fatty Acid Screen Results on Filter Paper** | Immediate referral to a metabolic specialist is indicated.

LABORATORY PROCEDURE
1. Fatty Acid analytes are tested on each filter paper.

<table>
<thead>
<tr>
<th>Primary Analyte (µmol/L)</th>
<th>Secondary Analyte (µmol/L)</th>
<th>Potential Disorder</th>
<th>Risk</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>C0 ≥ 2.00 &amp; ≤ 5.5</td>
<td>NA</td>
<td>CUD</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C0 ≤ 2.00</td>
<td>NA</td>
<td>CUD</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C4 ≥ 1.27</td>
<td>C4/C2 &lt; 0.06</td>
<td>SCAD &amp; GA II</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C4 ≥ 1.27</td>
<td>C4/C2 ≥ 0.06</td>
<td>SCAD &amp; GA II</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C4 ≥ 2.00</td>
<td>NA</td>
<td>SCAD &amp; GA II</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C8 ≥ 0.04</td>
<td>C8/C10 &lt; 3.0</td>
<td>MCAD &amp; MCAT</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C8 ≥ 0.04</td>
<td>C8/C10 ≥ 3.0</td>
<td>MCAD &amp; MCAT</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C14:1 ≥ 0.70</td>
<td>NA</td>
<td>VLCAD</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C16 ≥ 7.46</td>
<td>C18:1 &lt; 3.0</td>
<td>CACT &amp; CPT II</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C18:1 ≥ 3.0</td>
<td>C16 &lt; 7.46</td>
<td>CACT &amp; CPT II</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C18:1 ≥ 3.0</td>
<td>C16 ≥ 7.46</td>
<td>CACT &amp; CPT II</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C0 ≥ 64.00</td>
<td>C0/(C16+C18) &lt; 90</td>
<td>CPT I</td>
<td>Low Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C0 ≥ 64.00</td>
<td>C0/(C16+C18) ≥ 90</td>
<td>CPT I</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C16OH ≥ 0.16</td>
<td>C18:1 OH &lt; 0.15</td>
<td>LCHAD/TFP</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C18:1 OH ≥ 0.15</td>
<td>C16OH &lt; 0.16</td>
<td>LCHAD/TFP</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C18:1 OH ≥ 0.15</td>
<td>C16OH ≥ 0.16</td>
<td>LCHAD/TFP</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
</tbody>
</table>

A filter paper specimen refers to the Newborn Screening Kit ODH #450. Filter paper kits may be ordered from the: Public Health Laboratory Service, OSDH, P.O. Box 24106, Oklahoma City, OK, 73124-0106, call (405) 271-5070, or utilize the OSDH website.

For a Metabolic Specialist:
Klaas Wierenga, M.D. (405) 271-8685
Michelle Polan, M.D. (405) 271-8685

Questions regarding follow-up, please contact the Newborn Screening Short-term Follow-up Program at (405) 271-6617 or 1-800-766-2223 or fax to (405) 271-4892. Questions regarding laboratory procedure should be directed to the OSDH Lab at (405) 271-5070 or fax to (405) 271-4850.
Organic Acid Disorders FOLLOW-UP

<table>
<thead>
<tr>
<th>FILTER PAPER RESULTS</th>
<th>INDICATED PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organic Acid Screen - Normal Result</td>
<td>If specimen was collected before the infant was 24 hours of age, a specimen should be collected and submitted to the Oklahoma State Department of Health (OSDH) Laboratory for testing when the infant is 3 to 5 days of age. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td>Organic Acid Screen – Low Risk Result</td>
<td>Repeat Filter Paper specimen should be collected and sent to the OSDH laboratory within 48 hours. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td>Organic Acid Screen – High Risk Result</td>
<td>Immediate referral to a metabolic specialist is indicated.</td>
</tr>
<tr>
<td>Two Abnormal Organic Acid Screen Results on Filter Paper</td>
<td>Immediate referral to a metabolic specialist is indicated.</td>
</tr>
</tbody>
</table>

LABORATORY PROCEDURE
1. Organic Acid analytes are tested on each filter paper.

Summary of out-of-range Organic Acid Analytes and Follow-up Recommendations

<table>
<thead>
<tr>
<th>Primary Analyte (µmol/L)</th>
<th>Secondary Analyte (µmol/L)</th>
<th>Potential Disorder</th>
<th>Risk</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3 ≥ 7.21</td>
<td>C3/C2 &lt; 0.25</td>
<td>PROP/MUT/CBL-C,D/CBL-A,B</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C3 ≥ 7.21</td>
<td>C3/C2 ≥ 0.25</td>
<td>PROP/MUT/CBL-C,D/CBL-A,B</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C3DC 0.44 - 0.59</td>
<td>NA</td>
<td>MAL</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C3DC ≥ 0.60</td>
<td>NA</td>
<td>MAL</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C4 1.27 - 1.99</td>
<td>C4/C2 &lt; 0.06</td>
<td>IBG</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C4 1.27 - 1.99</td>
<td>C4/C2 ≥ 0.06</td>
<td>IBG</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C4 ≥ 2.00</td>
<td>NA</td>
<td>IBG</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C5 0.87 - 2.99</td>
<td>C5/C2 &lt; 0.05</td>
<td>IVA/2MBG</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C5 0.87 - 2.99</td>
<td>C5/C2 ≥ 0.05</td>
<td>IVA/2MBG</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C5 ≥ 3.00</td>
<td>NA</td>
<td>IVA/2MBG</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C5:1 ≥ 0.10</td>
<td>C5OH+C4DC &lt; 0.80</td>
<td>βKT</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C5:1 ≥ 0.10</td>
<td>C5OH+C4DC ≥ 0.80</td>
<td>βKT</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C5DC ≥ 0.46</td>
<td>C5DC/C8 &lt; 4.60 &amp; C5DC/C16 &lt; 2.0</td>
<td>GA1</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C5DC ≥ 0.46</td>
<td>C5DC/C8 ≥ 4.60</td>
<td>GA1</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C5DC ≥ 0.46</td>
<td>C5DC/C16 ≥ 0.20</td>
<td>GA1</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C5OH+C4DC ≥ 0.80</td>
<td>C6DC &lt; 0.27</td>
<td>HMG/3MCC/3MGA/MCD/2M3HBA</td>
<td>Low Risk</td>
<td>Repeat filter paper</td>
</tr>
<tr>
<td>C5OH+C4DC ≥ 0.80</td>
<td>C6DC ≥ 0.27</td>
<td>HMG/3MCC/3MGA/MCD/2M3HBA</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
<tr>
<td>C5OH+C4DC ≥ 2.0</td>
<td>NA</td>
<td>HMG/3MCC/3MGA/MCD/2M3HBA</td>
<td>High Risk</td>
<td>Immediate referral</td>
</tr>
</tbody>
</table>

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Abbreviations for Amino Acid Disorders include:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARG</td>
<td>Argininemia</td>
</tr>
<tr>
<td>ASA</td>
<td>Argininosuccinic aciduria</td>
</tr>
<tr>
<td>CIT</td>
<td>Citrullinemia type I</td>
</tr>
<tr>
<td>CIT II</td>
<td>Citrullinemia type II</td>
</tr>
<tr>
<td>HCY</td>
<td>Homocystinuria</td>
</tr>
<tr>
<td>MET</td>
<td>Hypermethioninemia</td>
</tr>
<tr>
<td>MSUD</td>
<td>Maple Syrup Urine Disease</td>
</tr>
<tr>
<td>PKU</td>
<td>Phenylketonuria</td>
</tr>
<tr>
<td>H-PHE</td>
<td>Benign hyperphenylalaninemia</td>
</tr>
<tr>
<td>BIOPT (BS)</td>
<td>Bioppterin defect in cofactor biosynthesis (BIOPT [BS])*</td>
</tr>
<tr>
<td>BIOP (REG)</td>
<td>Bioppterin defect in cofactor regeneration (BIOPT [REG])*</td>
</tr>
<tr>
<td>TYR I</td>
<td>Tyrosinemia Type I</td>
</tr>
<tr>
<td>TYR II</td>
<td>Tyrosinemia Type II</td>
</tr>
<tr>
<td>TYR III</td>
<td>Tyrosinemia Type III</td>
</tr>
</tbody>
</table>

Abbreviations for Fatty Acid Oxidation Disorders include:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CUD</td>
<td>Carnitine uptake defect</td>
</tr>
<tr>
<td>SCUD</td>
<td>Short-chain acyl-CoA thiolase deficiency</td>
</tr>
<tr>
<td>GAIi</td>
<td>Glutaric academia Type II</td>
</tr>
<tr>
<td>MCAT</td>
<td>Medium-chain ketoacyl-CoA dehydrogenase deficiency</td>
</tr>
<tr>
<td>MCAD</td>
<td>Medium-chain acyl-CoA dehydrogenase deficiency</td>
</tr>
<tr>
<td>VLCAD</td>
<td>Very long-chain acyl-CoA dehydrogenase deficiency</td>
</tr>
<tr>
<td>CACT</td>
<td>Carnitine acylcarnitine translocase deficiency</td>
</tr>
<tr>
<td>CPT IA</td>
<td>Carnitine palmitoyltransferase I deficiency</td>
</tr>
<tr>
<td>CPT II</td>
<td>Carnitine palmitoyltransferase II deficiency</td>
</tr>
<tr>
<td>LCHAD</td>
<td>Long-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency</td>
</tr>
<tr>
<td>TFP</td>
<td>Trifunctional protein deficiency</td>
</tr>
</tbody>
</table>

Abbreviations for Organic Acid Disorders include:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROP</td>
<td>Propionic acidemia</td>
</tr>
<tr>
<td>MUT</td>
<td>Methylmalonic academia</td>
</tr>
<tr>
<td>MAL</td>
<td>Malonic academia</td>
</tr>
<tr>
<td>IBG</td>
<td>Isobutyrylglycinuria (Isobutyryl-CoA dehydrogenase deficiency)</td>
</tr>
<tr>
<td>IVA</td>
<td>Isovaleric academia</td>
</tr>
<tr>
<td>2MBG</td>
<td>2-Methylbutyrylglycinuria</td>
</tr>
<tr>
<td>3-MCC</td>
<td>3-Methylcrotonyl-CoA carboxylase deficiency</td>
</tr>
<tr>
<td>3MGA</td>
<td>3-Methylglutaconic aciduria</td>
</tr>
<tr>
<td>HMG</td>
<td>3-Hydroxy-3-methylglutaric acidemia</td>
</tr>
<tr>
<td>MCD</td>
<td>Holocarboxylase synthetase deficiency (multiple carboxylase deficiency)</td>
</tr>
<tr>
<td>2M3HBA</td>
<td>2-Methyl-3-hydroxybutyric aciduria</td>
</tr>
<tr>
<td>βKT</td>
<td>Beta ketothiolase deficiency</td>
</tr>
<tr>
<td>GA I</td>
<td>Glutaric academia type I</td>
</tr>
</tbody>
</table>

Updated August 10, 2009
Biotinidase Deficiency FOLLOW-UP

<table>
<thead>
<tr>
<th>FILTER PAPER RESULTS</th>
<th>INDICATED PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotinidase Enzyme Present</td>
<td>If specimen was collected before the infant was 24 hours of age, a specimen should be collected and submitted to the Oklahoma State Department of Health (OSDH) Laboratory for testing when the infant is 3 to 5 days of age. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td>≥ 57 U</td>
<td></td>
</tr>
<tr>
<td>Biotinidase Enzyme Decreased</td>
<td>Repeat Filter Paper specimen should be collected and sent to the OSDH laboratory within 48 hours. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td>≥ 20 – 56.9 U</td>
<td></td>
</tr>
<tr>
<td>Biotinidase Enzyme Low</td>
<td>Immediate referral to a metabolic specialist is indicated.</td>
</tr>
<tr>
<td>&lt; 20 U</td>
<td></td>
</tr>
<tr>
<td>Two Abnormal Biotinidase Results on Filter Paper</td>
<td>Immediate referral to a metabolic specialist is indicated.</td>
</tr>
</tbody>
</table>

LABORATORY PROCEDURE

1. Biotinidase enzyme activity is tested on each filter paper.

 Normal Filter Paper Result: Biotinidase Enzyme Activity Present

A filter paper specimen refers to the Newborn Screening Kit ODH #450. Filter paper kits may be ordered from the: Public Health Laboratory Service, OSDH, P.O. Box 24106, Oklahoma City, OK, 73124-0106, call (405) 271-5070, or utilize the OSDH website.

For a Metabolic Specialist:
Klaas Wierenga, M.D. (405) 271-8685
Michelle Polan, M.D. (405) 271-8685

Questions regarding follow-up, please contact the Newborn Screening Short-term Follow-up Program at (405) 271-6617 or 1-800-766-2223 or fax to (405) 271-4892. Questions regarding laboratory procedure should be directed to the OSDH Lab at (405) 271-5070 or fax to (405) 271-4850.
Severe Combined Immunodeficiency (SCID) FOLLOW-UP

<table>
<thead>
<tr>
<th>FILTER PAPER RESULTS</th>
<th>INDICATED PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCID Screen – Normal Result</td>
<td>If specimen was collected before the infant was 24 hours of age, a specimen should be collected and submitted to the Oklahoma State Department of Health (OSDH) Laboratory for testing when the infant is 3 to 5 days of age. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td>SCID Screen – Decreased Result</td>
<td>If the infant is ≥ 37 weeks gestation: Repeat Filter Paper specimen should be collected and sent to the OSDH laboratory within 48 hours. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”. If the infant is &lt; 37 weeks gestation: Repeat Filter Paper specimen should be collected and sent to the OSDH laboratory when the infant reaches an adjusted gestation age of ≥ 37 weeks. Indicate specimen is a repeat on the filter paper requisition. Mark “ALL TEST”.</td>
</tr>
<tr>
<td>SCID Screen – Low Result</td>
<td>Immediate referral to a pediatric immunologist is indicated.</td>
</tr>
<tr>
<td>Two Abnormal SCID Results on Filter Paper (only if the infant is ≥ 37 weeks gestation for both specimens)</td>
<td>Immediate referral to a pediatric immunologist is indicated.</td>
</tr>
</tbody>
</table>

LABORATORY PROCEDURE

1. T-cell receptor excision circles or TREC is tested on each filter paper.

   Normal Filter Paper Result: > 23 TREC copies for Gestational Age < 37 weeks
   Or
   > 28.5 TREC copies for Gestational Age >= 37 weeks

A filter paper specimen refers to the Newborn Screening Kit ODH #450. Filter paper kits may be ordered from the: Public Health Laboratory Service, OSDH, P.O. Box 24106, Oklahoma City, OK, 73124-0106, call (405) 271-5070, or utilize the OSDH website.

For a Pediatric Immunologist:
Tim Trojan, M.D. (844) 422-4362
James Love, M.D., PhD (918) 307-1613

Questions regarding follow-up, please contact the Newborn Screening Short-term Follow-up Program at (405) 271-6617 or 1-800-766-2223 or fax to (405) 271-4892. Questions regarding laboratory procedure should be directed to the OSDH Lab at (405) 271-5070 or fax to (405) 271-4850.
REFUSAL FORM

Oklahoma State Department of Health
Refusal of the Newborn Screening Blood Test
Religious Tenets and Practices Refusal

Infant’s Name: __________________________ Medical Record Number: __________________________

Date of Birth: __/__/____

Attending Physician or Provider, print name: ____________________________________________

Place of Birth:
___ Hospital, print name __________________________

___ Birthing Facility, print name __________________________

___ Home Birth

Type of Screen Refused: ______ Newborn Blood Test ______ Pulse Oximetry Screen

I have received and read the parent educational brochure printed by the Oklahoma Department of Health on the
Newborn Screening blood test and pulse oximetry screening. I understand that these disorders are easily detected
by testing a small blood sample from my baby’s heel or by measuring the amount of oxygen in my baby’s blood.

I have been informed that all newborns are required by law (under 63 O.S. 2002, Sections 1-533 and
1-534) to have a newborn screening test collected and pulse oximetry screen performed.

I have been informed and I understand that this screening is done to detect these disorders because symptoms
sometimes do not appear for several weeks or months, and irreversible damage can occur before symptoms
become apparent to a family or a physician.

I have been informed and I understand that, if untreated, these conditions may cause permanent damage to my
child, including mental retardation, growth failure, and even death. This permanent health damage can be
prevented through early detection and treatment.

I have discussed the newborn screening test and pulse oximetry screening with my physician or health care
provider and I understand the risks to my child if the screening test is not completed.

I understand that the law allows a parent or guardian to refuse newborn screening and pulse oximetry screening
based on the grounds that such examination conflicts with a person’s religious tenets and practices. I elect to
refuse newborn screening on that such testing of my infant conflicts with my religious tenets and practices. My
decision was made freely and I accept the legal responsibility for the consequences of this decision.

Print Parent/legal Guardian’s Name __________________________ Signature of Parent/legal Guardian
________________________ Date ___/___/____

Print Witness Name _________________ Signature of Witness __________________________ Date ___/___/____

Original to infant’s record, provide a copy to parent, and forward copy by fax or mail to: Oklahoma State
Department of Health, Newborn Screening Program Coordinator, 1000 NE Tenth Street, Oklahoma City, OK
73117-1299, (405) 271-6617 or 1-800-766-2223; Fax (405) 271-4892.