Citrulline (Urea Cycle Disorder) Screening Fact Sheet for Health Care Providers
Newborn Screening Program of the Oklahoma State Department of Health

What is the differential Diagnosis?
Citrullinemia type I, Argininosuccinic Aciduria; Citrullinemia Type II (citrin deficiency)

What are the characteristics of urea cycle disorders?
- Autosomal recessive genetic conditions.
- Most infants are born to parents who are both unknowingly asymptomatic carriers and have NO known history of a urea cycle disorder in their family.
- Disorders of citrulline metabolism are included in a larger group of disorders, known as urea cycle disorders.
- The incidence of all urea cycle disorders is estimated to be about 1/8,000 live births. In citrullinemia and in argininosucuccinc academia (ASA), the accumulation of ammonia and other toxic metabolites occurs during the first few days of life.
- Newborns with these disorders often appear normal initially but rapidly develop cerebral edema and the related signs of lethargy, anorexia, hyperventilation or hypoventilation, hypothermia, seizures, neurologic posturing, and coma.
- Urea cycle disorders **are life threatening**. Immediate intervention is warranted to prevent hyperammonemia and death.
- Lifelong treatment includes a special diet, and special care during times of illness or stress.

What is the screening methodology for citrulline?
1. An amino acid profile by Tandem Mass Spectrometry (MS/MS) is performed on each filter paper.
2. Citrulline is the primary analyte.
3. If citrulline is elevate the citrulline/arginine ratio will also be evaluated.

What is an in-range (normal) screen result for citrulline?
Citrulline less than 55 μmol/L is NOT consistent with a disorder of citrulline metabolism.
See Table 1.

What is an out-of-range (abnormal) screen for citrulline?
Citrulline > 55 μmol/L is out of range.

What screen results will require diagnostic testing?
All out-of-range Citrulline screens will require immediate action. The follow-up program will provide detailed guidance on required actions and an *Emergency Management Protocol* will be provided.

TABLE 1.
In-range Citrulline Newborn Screening Results

Primary Analyte	In-Range (μmol/L)	
Citrulline	<	55

Secondary Analytes[1]	In-Range
Citrulline/Arginine ratio	< 6.5

[1] Elevations of the secondary analytes are reported as "not consistent with an amino acid disorder" 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:

Integris Pediatric Specialty Clinic, Inborn Error of Metabolism (IEM) Clinic
Geneticist pager: (405) 630-3794

OU Children's Physicians – Genetics Clinic
Page Operator: (405) 271-3636

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.