Nebraska Newborn Screening Program

March 2012 Notice of Cystic Fibrosis Screening Algorithm Change

(Effective with samples received at the laboratory on April 2, 2012)

The Clinical and Laboratory Standards Institute recently published guidelines for screening for Cystic fibrosis. The extensive guidelines report among other data sources, findings of a 10 year retroactive review of Wisconsin CF screening data.

Impact of Age at Specimen Collection on Screening Results:

One of the findings was that in the first 24 hours of life Immunoreactive trypsinogen (IRT) levels show a slight decrease, then remain fairly stable until about 2 weeks of age and then gradually decrease. In reviewing those guidelines the Newborn Screening Advisory Committee recommended evaluating our data. Based on the analysis of IRT levels produced at Nebraska's screening laboratory, PerkinElmer Genetics Laboratory, it appears that on average at 12 days of age levels decrease.

Nebraska's Response:

Therefore, to reduce the risk of missing an affected patient, the IRT cut-off for specimens collected at or greater than 12 days of age, will be lowered from 90 to 80 ng/mL. Specimens collected at less than 12 days will continue to have 90 ng/mL as the IRT cut-off. All specimens with IRT's above the cut-off for the first time* will continue to reflex to look for the ΔF508 mutation most commonly associated with clinical disease.

(* Note, we identify "for the first time" because occasionally although rarely, a repeat specimen will be the first time the IRT showed an elevation.)

When <u>no ΔF508</u> is found, a repeat dried blood spot specimen should be collected. If the repeat specimen continues to have an elevated IRT it will reflex to the Luminex x-TAG 39 + 4 CFTR mutation panel.

When a specimen is found to have <u>one copy of the ΔF508</u> the test will reflex to the Luminex x-TAG 39 + 4 CFTR mutation panel. If no other or one other mutation is found these patients are recommended to be referred to an Accredited CF Center for sweat testing and evaluation. At a minimum these patients are carriers, but the evaluation is essential because over 1800 mutations associated with CF have been identified. Therefore these babies are at risk of having another mutation associated with clinical disease. There is no screening test that is able to identify all mutations.

When the initial specimen is found to have <u>two copies of the ΔF508</u> these babies should also be referred to an Accredited CF Center for sweat testing and evaluation.

A Final Note on "Expedited Diagnosis"

The CLSI guidelines also report on studies to evaluate the upper limit of age before clinical manifestations are sufficiently established as to worsen prognosis. They found patients diagnosed after 2 months of age have worse disease and greater treatment costs than infants diagnosed and receiving care before that time. After 2 months of age babies may experience irreversible abnormalities related to the malnutrition or lung disease. Therefore, as with all screened conditions, rapid, appropriate follow-up actions are essential to successfully identifying and treating newborns to achieve the best outcomes.