

Memo

To: Birthing Centers and Hospitals, Physician Offices

From: Scott J. Zimmerman, DrPH, MPH, HCLD (ABB), Director
NC State Laboratory of Public Health



CC: Ann Grush, Acting Newborn Screening Manager

Date: June 10, 2016 (replaces version dated 06/03/2016)

Re: Cystic fibrosis DNA testing reinstated

The North Carolina State Laboratory of Public Health (NCSLPH) has been working to reinstate cystic fibrosis DNA testing as a second tier test to identify babies with the highest risk for cystic fibrosis. To accomplish this, we have established an agreement with the Wisconsin State Laboratory of Hygiene (WSLH) to conduct cystic fibrosis transmembrane receptor (CFTR) mutational analysis using the MiSeqDx Cystic Fibrosis 139-Variant Assay on specimens with elevated immunoreactive trypsinogen (IRT) values.

As a reminder, our longstanding algorithm for cystic fibrosis screening starts with the evaluation of IRT, a biomarker for cystic fibrosis. This will remain unchanged. Starting today, specimens with IRT values ranking greater than the 96th percentile will be reported as having an elevated IRT and an interpretation will be included to assist health care providers in determining the urgency for sweat chloride testing. In addition, a portion of the specimen will be sent to the WSLH to conduct CFTR mutational analysis. The expected turn-around-time for this testing is 7 - 14 days.





Examples of the new reporting structure for CF specimen ranking greater than the 96%tile are provided below:

Specimens having IRT values ≥ 100 ng/ml, will be reported in the following way:

CYSTIC FIBROSIS ELEVATED IRT ≥ 100 ng/ml

Neo IRT Results _____ ng/ml

Attention: Due to the Hologic CF DNA test recall, the CF DNA test has not been performed by the NC State Laboratory of Public Health as of 4/1/16. Beginning 06/03/16 specimens with IRT values ≥ 100 ng/ml will be sent to the Wisconsin State Laboratory of Hygiene (WSLH) for **Cystic Fibrosis CFTR mutation (DNA)** screening.

Interpretation: An IRT value of ≥ 100 ng/ml may indicate a higher risk for CF. A quantitative sweat chloride test at one of the accredited CF centers is recommended to rule out CF in this infant. Additionally, Cystic Fibrosis CFTR mutation screening results from the WSLH will follow in a supplemental report. These results will be helpful in determining the need for sweat chloride tests for infants weighing less than 2000g.

It is recommended that specimens having IRT values ranking greater than the 96%tile but less than 100 ng/ml use the results obtained from CFTR mutational analysis to aid in determining the need for a sweat chloride test. Please look for this information on a supplemental report from the NCSLPH 7 - 14 days after the reporting of an elevated IRT value. Specimens in this category will be reported in the following manner:

CYSTIC FIBROSIS ELEVATED IRT $>96\%$ tile

Neo IRT Results _____ ng/ml

Attention: Due to the Hologic CF DNA test recall, the CF DNA test has not been performed by the NC State Laboratory of Public Health as of 4/1/16. Beginning 06/13/16 specimens with IRT values $>96\%$ tile will be sent to the Wisconsin State Laboratory of Hygiene (WSLH) for **Cystic Fibrosis CFTR mutation (DNA)** screening.

Interpretation: An IRT value $>96\%$ tile may indicate a higher risk for CF. Cystic Fibrosis CFTR mutation screening results from the WSLH will follow in a supplemental report. These results will aid in determining the need for a sweat chloride test in this infant. If symptoms or a family history of CF is present a sweat chloride test at one of the CF centers is recommended.

Results obtained from CFTR mutational analysis will be provided in a Supplemental Report from the NCSLPH that will be available 7 - 14 days after the reporting of an





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Director, Division of Public Health

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Laboratory Director

Results obtained from CFTR mutational analysis will be provided in a Supplemental Report from the NCSLPH that will be available 7 - 14 days after the reporting of an elevated IRT value. Specimens with mutations in the CFTR gene will be reported in the following manner:

Abnormal Specimen Report. Cystic Fibrosis: CFTR Mutations Detected. Please see the attached report from the Wisconsin State Laboratory of Hygiene.

Specimens in which no CFTR gene mutations were detected will be reported in the following manner:

Cystic Fibrosis: CFTR Mutations Not Detected. Please see the attached report from the Wisconsin State Laboratory of Hygiene. Although there is a minimal risk for Cystic Fibrosis in the absence of the 139 mutations tested, the elevated IRT value previously reported for this patient may be indicative of CF in the presence of a mutation not screened. Perinatal stresses can also cause high IRT levels. If this patient is exhibiting clinical signs associated with CF such as persistent diarrhea, poor weight gain, chronic cough or respiratory problems or if there is a family history of CF contact one of the specialists at an accredited CF center.

We appreciate your patience and cooperation as we continue our work to restore CFTR mutational analysis locally to allow for timely and accurate detection of babies at the highest risk for CF in a fiscally responsible way.

If you have any questions, please contact Ann Grush 919-807-8881.

