

## MEMORANDUM

**DATE:** December 28, 2005

**TO:** Health Professionals Involved in Neonatal Care

**FROM:** Terry Dwelle, M.D., M.P.H.T.M., State Health Officer  
Barb Schweitzer, Director, Newborn Screening Program

**SUBJECT:** Cystic Fibrosis added to Newborn Screening Panel

As of January 1, 2006, cystic fibrosis will be included in the newborn screening panel of tests. The decision to include cystic fibrosis in the newborn screening panel was as a result of recommendations by the Centers for Disease Control and Prevention (CDC). The North Dakota Newborn Screening Program has an Advisory Committee that had been studying this for the past year. In June 2005, the Newborn Screening Advisory Committee approved and advised the North Dakota State Department of Health to proceed with the necessary administrative rule changes to include cystic fibrosis in the newborn screening panel of tests.

On December 13, 2005, the State Health Council and the Legislative Council's Administrative Rules Committee approved the recommended changes to North Dakota Administrative Code Chapter 33-06-16, Newborn Screening Program.

Since 1992, the Iowa Hygienic Laboratory has been performing newborn screening testing for North Dakota and will continue to serve in this role. **Specimen collection will not change from the current procedure – nothing different needs to be done.** With the addition of cystic fibrosis, the newborn screening fee will increase from \$36.00 to \$42.50.

While newborn screening should identify approximately 99 percent of infants with cystic fibrosis, an occasional child will continue to be diagnosed only when clinical manifestations suggestive of cystic fibrosis develop.

Enclosed is information and educational materials regarding cystic fibrosis. This information may also be downloaded at <http://www.ndmch.com/metabolic-screening/default.asp>.

In addition, Children's Special Health Services, North Dakota Department of Human Services, may be able to assist families to pay for the confirmational diagnosis and treatment of cystic fibrosis (and other conditions included in the newborn screening panel). Please contact Children's Special Health Services for more information at 701.328.2436 or 800.755.2714.

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Please direct any questions relating to newborn screening to Barb Schweitzer, Director, Newborn Screening Program at 701.328.4538 or 800.472.2286 (press 1) or by email to [bschweit@state.nd.us](mailto:bschweit@state.nd.us).

Enclosures

Dear Dr. :

**SAMPLE**

This letter documents the results of the initial newborn screening for Baby Boy\_\_\_\_\_, DOB 01/01/2006, Mom's name\_\_\_\_\_. This infant has had a positive result on the Iowa Neonatal Metabolic Screening Program test for cystic fibrosis. **Please keep in mind that this is a not definitive diagnosis, it is a screening only.**

Date of Collection:

Immunoreactive trypsinogen (IRT): ng/ml (Normal value <65 ng/ml)

CF Mutation Analysis: mutation(s) detected (normal value: no mutations)

According to the screening protocol, those newborns with an IRT  $\geq 170$  ng/ml or with one or two mutant alleles must have sweat chloride testing performed by the Cystic Fibrosis Foundation approved quantitative pilocarpine iontophoresis method. This testing must be obtained at a certified Cystic Fibrosis Center to ensure reliability of results.

Please contact the parents to inform them of the abnormal test results and the need for further testing. You or the parents of your patient should call one of the certified centers to arrange for the sweat test. The certified CF centers in North Dakota are: Heart and Lung Clinic, Bismarck, ND—contact person is Larry Tessmer at 701.530.7500 or MeritCare Medical Center, Fargo, ND—contact person is Carrie Simonson at 701.234.6504.

You will receive results of your patient's sweat test via phone and fax from the CF Coordinator, followed by a letter or a fax confirming the results. If the parents have questions you would like the program to discuss, please feel free to have them contact us.

Sincerely,

Barb Schweitzer, RN Newborn Screening Director 701-328-4538	Becky Bailey, RN Newborn Screening Nurse Consultant 701-328-4526
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## Frequently Asked Questions for Newborn Screening about Cystic Fibrosis (C.F.)

**This is a screening only, this is not a definitive diagnosis.**

### I. What is CF?

- A. A congenital disease that affects the glands in the body that secrete digestive enzymes from the pancreas, mucous glands of the airway, and sweat glands.
  - 1. 30,000 children and adults in the US have CF.
  - 2. In the pancreas, the ducts that secrete enzymes for fat digestion are plugged by thick secretions.
  - 3. In the airways, common bacteria from the environment cause infections. This leads to inflammation and, eventually, permanent lung damage.
  - 4. The abnormally high concentration of salt in the sweat glands provides the most reliable diagnostic test for CF.
- B. Frequency
  - 1. Occurs in 1:3,200 Caucasian births, 1:3,900 for all Americans.
  - 2. 1,000 new cases each year.
  - 3. Without newborn screening, 80% are diagnosed by age 3, but 10% not diagnosed until after age 18.
- C. Symptoms
  - 1. Persistent cough with phlegm.
  - 2. Greasy, bulky stools.
  - 3. Excessive appetite but poor growth.
- D. Treatment: No cure yet, but many measures that provide benefit are more effective the earlier they're started.

### II. What does abnormal CF Newborn Screen mean?

- A. The initial test on the blood spot collected from the infant as part of newborn screening for various congenital and metabolic disorders is trypsinogen, a pancreatic enzyme that is elevated in infants with cystic fibrosis.
- B. A genetic panel of DNA for the 25 most common gene abnormalities associated with cystic fibrosis is performed on those with the highest levels of trypsinogen.
- C. A test of the chloride content in sweat is performed as a diagnostic test for cystic fibrosis in those who are screened positive in this two-step procedure.
- D. Only about one in six infants with the positive screen will have cystic fibrosis – the others will generally be carriers like at least one of their parents.

### III. What causes CF?

- A. CF is an inherited genetic recessive disorder. This means the defective gene must be passed from both parents to children at conception for the child to have CF.



- B. One person in every 29 people who are Caucasian is a carrier of a defective CF gene. One in 46 Hispanic Americans, one in 65 African Americans, and one in 90 Asian Americans carries an altered gene.
- C. Both parents must carry altered CF genes and pass them to a particular child in order for that child to have CF. Since genes are paired, parents who don't have CF but are carriers have a normal functioning gene paired with the defective gene. Each parent provides one of the pairs of genes at conception. When both parents don't have CF but are carriers of a defective gene, each pregnancy has a 25 percent chance of producing a child with CF by receiving the defective gene from both parents. There is a 50 percent chance that the child will be a carrier just like the one of their parents when a defective gene is received from one parent and a normal gene from the other. There is a 25 percent chance that the child will not receive an altered gene from either parent and will neither have CF nor be a carrier when the normal gene of the pair is passed at conception from each parent. Those children who are only carriers will have no disease or clinical problem from the carrier status.

IV. What is a Sweat Test?

- A. CF affects the sweat glands causing the sweat to be very salty. We can measure this salt to determine whether a baby has CF. This is the best test for CF but requires that the appropriate method for sweat collection and measurement be done by experienced personnel. The Cystic Fibrosis Foundation certifies CF centers who are required to meet specific standards for sweat testing.
- B. A special device will be used to stimulate a small part of the baby's arm or leg to sweat. The skin may feel warm and tingly while the device is on and may appear reddened. The skin is not burned. Some babies may cry during this part of the test, but it is not painful. The sweat is collected on gauze, filter paper discs, or a small plastic coil. After 30 minutes the collected sweat is sent to the lab, where the sweat salt content (chloride) is measured. The results should generally be available later that day if the test is done in the morning.
- C. What do the results mean?
  1. Negative: A normal amount of salt was present in the sweat. It is very rare for a person to have CF if the sweat test result is negative.
  2. Positive: A high amount of salt was present. The baby likely has CF. The baby should have a second sweat test and a checkup with a CF specialist at the CF Center.
  3. Borderline: The saltiness of the sweat is higher than normal but not high enough to diagnose CF. The baby should have another sweat test, and possibly a checkup and a blood test to examine more specifically for CF genetic abnormalities.
  4. QNS: This means Quality Not Sufficient. There was not enough sweat on the gauze or disc. The baby will need another sweat test.

V. What does it mean to be a carrier?

- A. A positive genetic carrier test for CF means a person has a single defective copy of the CF gene with the other gene of the pair having normal function. The child will only have CF if a defective CF gene is inherited from both parents.



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- B. A negative carrier test for CF means a person does not have a copy of one of the 25 defective genes, which were tested. With more than 1,000 different mutations of the CF gene identified, there are some very rare ones not screened for on the panel of 25. If the test is negative, there is still a very small chance of carrying a rare mutation. This chance is dependent on race and ethnic group, as well as the type of carrier test done.

Available Resources:

1. [www.ccf.org](http://www.ccf.org) - C.F. Foundation
2. [www.slh.wisc.edu/newborn/](http://www.slh.wisc.edu/newborn/) - Wisconsin CF program
3. <http://uhl.uiowa.edu> - Iowa website
4. [www.nsgc.org](http://www.nsgc.org) - National Society of Genetic Counselors
5. [www.aap.org](http://www.aap.org) - American Academy of Pediatrics
6. Certified C.F. Centers:
  - a. Bismarck: Heart & Lung Clinic—contact person is Larry Tessmer @ 701-530-7000
  - b. Fargo: Meritcare Medical Center---contact person is Carrie Simonson @ 701-234-6504.



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## North Dakota Newborn Screening Cystic Fibrosis (C.F.) Reporting

**Please note this is not a definite diagnosis, it is only a screening.**

**Reporting of Screening Results:** Normal screening results will be reported out as has previously been done. Those infants requiring follow-up will be reported to the primary care physician. The Iowa laboratory will call and fax those abnormal only test results (IRT and CFTR mutation analysis) and the patient information collected with the routine NBS specimen to the North Dakota Health Department Newborn Screening Program.

**Reporting Ranges:**

IRT  $\geq$  170ng/mL

One mutant allele (and top 5% of daily IRT results)

Two mutant alleles (and top 5% of daily IRT results)

Screening for cystic fibrosis using the two-tiered IRT / DNA approach cannot always distinguish babies who are CF carriers from babies who are affected. Sweat chloride testing by the CFF-approved quantitative pilocarpine iontophoresis method is recommended for all babies with either one or two identified mutations.

Sweat testing will also be recommended for babies with no detectable mutations but with an extremely elevated IRT  $\geq$  170ng/mL.

Based on this information the laboratory anticipates reporting three categories of infants to the consultant for CF follow-up. These include:

1. **Possible Cystic Fibrosis:** IRT:  $\geq$  170ng/mL  
No CFTR mutations detected

Laboratory interpretation: *An elevated trypsinogen result may be indicative of Cystic Fibrosis due to mutant alleles other than the 25 mutations included in the screening panel.*

2. **Possible Cystic Fibrosis:** One CFTR mutation detected

Laboratory interpretation: *The presence of one CFTR mutant allele is indicative of a Cystic Fibrosis carrier, although this does not rule out CF disease due to the possibility of a second mutant allele other than the 25 mutations included in the screening panel.*

3. **Definite Cystic Fibrosis:** Two CFTR mutations detected

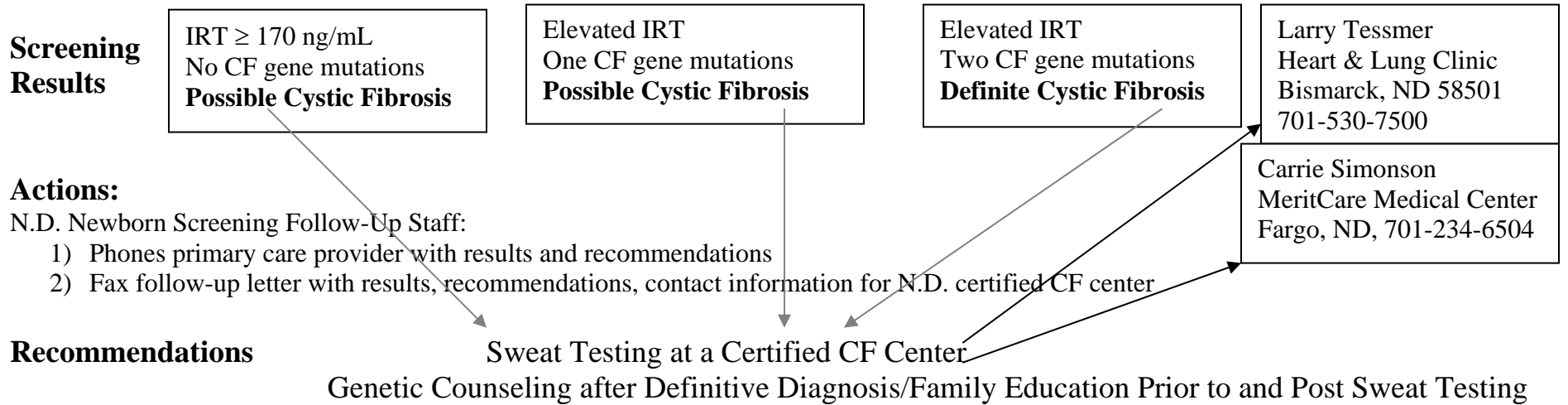
Laboratory interpretation: *The presence of two CFTR mutant alleles is consistent with Cystic Fibrosis.*

**Detection Rate:** It is estimated that screening with the two-tiered approach for 25 CF mutations will detect 99% of babies with CF.

**Screening Practice Considerations:** Primary care providers should continue to consider Cystic Fibrosis as a potential diagnosis in patients with negative newborn screening results and persistent diarrhea, poor weight gain, and chronic cough or respiratory problems. Newborns with meconium ileus may demonstrate normal IRT levels. If a newborn presents with meconium ileus, contact should be made with a CF specialist.

**Questions, please contact the North Dakota Newborn Screening Program @ 701.328.4538**

**Follow-up Algorithm**  
**For Cystic Fibrosis (C.F.)**



**Actions:**  
CF clinic coordinator provides education about sweat testing

**Confirmatory**  
**Testing Results**

The C.F. Center will notify the primary care provider and the NDNBS program

