



# Newborn Screening Quality Assurance Program

## PROFICIENCY TESTING

## Cystic Fibrosis Mutation Detection Quarterly Report

Volume 4, No.3

August 2010

### INTRODUCTION

This report is the quarterly summary of all data reported within the specified data-reporting period for the Quarter 3, 2010 program for cystic fibrosis (CF) mutation detection. The attached tables provide the certification profiles for the distributed specimens, the verification of your reported data, the summary of reported genotypes, and the frequency distributions summary for expected interpretations. We distribute this PT report to all participants, state laboratory directors, and program colleagues by request.

On July 12, 2010, a panel of five unknown dried-blood-spot (DBS) specimens was distributed to 27 laboratories in the United States and 27 laboratories in other countries to detect mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

### PARTICIPANT RESULTS

This panel consisted of five DBS specimens prepared from adult CF patients (specimens 30C1, 30C2, 30C3, 30C4, and 30C5).

Evaluations are based on the clinical assessment of each specimen. Expected genotypes may differ by participant because of the panel of mutations tested. In these cases, an answer of "no mutation detected" is acceptable. A specimen is considered not evaluated when one or both of the expected mutations is not detected by the laboratory's method or if the specimen cannot be assayed (sample failure).

We processed data from 50 participants. Laboratories were asked to report method used and the genotype for each specimen. Methods varied widely with regard to the panel of mutations detected and the algorithm used for testing. Seventeen laboratories used Hologic (formerly Third Wave Technologies) Inplex CF assay, 8 used Luminex Molecular Diagnostics X-Tag Cystic Fibrosis kit, 4 used Tepnel Diagnostics Elucigene Assays, 4 used an Abbott Laboratories

method, 3 used an in-house TaqMan Allelic Discrimination assay, 2 used Asuragen's Signature CF 2.0 assay, 2 used an amplification/gel electrophoresis assay, 2 used Innogenetics Inno-Lipa assay, 2 used sequencing, 2 used PCR followed by restriction fragment length polymorphism analysis method, 1 used high resolution melt technology, 1 used allele-specific oligonucleotide PCR, 1 used amplification refractory mutation system PCR (ARMS PCR), 1 used Matrix Assisted Laser Desorption /Ionization-, Time Of Flight (MALDI-TOF) mass spectrometry, 1 used an in-house multiplex PCR-heteroduplex and restriction enzyme method, and 1 did not report the method used. Some laboratories used more than one method for their screening. One laboratory screened specimens for four mutations and if a mutation was present, continued testing with an expanded panel. Laboratories were not asked to report the maximum number of mutations that could be detected. ❖

Three incorrect clinical assessments were reported for Specimen 30C1, two for Specimen 30C2, and one for Specimen 30C5. One laboratory reported a sample failure for specimen 30C4 and one laboratory reported a sample failure for specimen 30C5. Four laboratories did not report data this quarter. ❖

The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis Mutation Detection PT specimens on October 4, 2010. ❖

### ACKNOWLEDGMENTS

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**CDC/APHL**

This program is cosponsored by the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL).

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NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS MUTATION DETECTION SURVEY

QUARTER 3 – AUGUST 2010

LAB XXX

DATA VERIFICATION

<b>Specimen Number</b>	<b>Allele 1</b>	<b>Allele 2</b>	<b>Clinical Assessment</b>
30C1			
30C2			
30C3			
30C4			
30C5			

Reviewer's Comment

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FREQUENCY OF REPORTED CLINICAL ASSESSMENTS

Specimen	Screen Negative (Normal)	Likely Cystic Fibrosis Positive	Likely Cystic Fibrosis Carrier	Sample Failure
30C1	10	37	3	0
30C2*	2	42	5	0
30C3	50	0	0	0
30C4	1	48	0	1
30C5	48	1	0	1

\*One laboratory could not specify between a likely carrier and a likely positive due to the method used and was not included in this table.

INCORRECT ASSESSMENTS AND SPECIMENS NOT EVALUATED

Specimen	Incorrect Assessment	Not Evaluated
30C1	3	10
30C2	2	6*
30C3	0	0
30C4	0	2
30C5	1	1

\* Number includes the specimen not counted in above table.  
Clinical assessment of the specimen was not provided by the participant.

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LABORATORY METHODS

Method	Number of Laboratories
Hologic (Third Wave Technologies) Invader Assay	17
Luminex Molecular Diagnostics X-Tag Cystic Fibrosis kit	8
Tepnel Diagnostics Elucigene Assay (CF-29, CF-30, CF-4, or CF-EU)	4
Abbott Laboratories	4
In-house TaqMan allelic discrimination Assay	3
Asuragen Signature CF 2.0	2
Amplification / gel electrophoresis	2*
Innogenetics Inno-LIPA	2
Sequencing	2*
PCR/Restriction fragment length polymorphism analysis	2
High Resolution Melt Technology	1
Allele-specific oligonucleotide PCR	1
ARMS PCR	1
Matrix Assisted Laser Desorption /Ionization- Time Of Flight (MALDI-TOF) mass spectrometry	1
Amplification/heteroduplex/restriction analysis	1
Not reported	1

\*Assays used in addition to another method listed.

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SPECIMEN CERTIFICATION

Specimen	Allele 1 (Colloquial name)	Allele 2 (Colloquial name)	Allele 1 (Standard name)	Allele 2 (Standard name)	Expected Clinical Assessment
30C1	W1282X	W1282X	p.Trp1282X	p.Trp1282X	2
30C2	G551D	F508del	p.Gly551Asp	p.Phe508del	2
30C3	Wild type	Wild type	Wild type	Wild type	1
30C4	F508del	F508del	p.Phe508del	p.Phe508del	2
30C5	Wild type	Wild type	Wild type	Wild type	1

1 = screen negative (normal) 2 = likely cystic fibrosis positive 3 = likely cystic fibrosis carrier

Alleles were determined/confirmed by CDC and/or were included with the samples from the provider.

This **NEWBORN SCREENING QUALITY ASSURANCE PROGRAM** report is an internal publication distributed to program participants and selected program colleagues. The laboratory quality assurance program is a project cosponsored by the **Centers for Disease Control and Prevention (CDC)** and the **Association of Public Health Laboratories**.

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