



# Newborn Screening Quality Assurance Program

## PROFICIENCY TESTING

## Cystic Fibrosis Mutation Detection Quarterly Report

Volume 5, No.1

March 2011

### INTRODUCTION

This report is the quarterly summary of all data reported within the specified data-reporting period for the Quarter 1, 2011 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 January 17, 2011 a panel of five unknown dried-blood-spot (DBS) specimens was distributed to 30 laboratories in the United States and 29 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 11C1, 11C2, 11C3, 11C4, and 11C5).

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 54 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. Nineteen laboratories used

Hologic (formerly Third Wave Technologies) Inplex CF assay, 8 used Luminex Molecular Diagnostics X-Tag Cystic Fibrosis kit, 5 used an Abbott Laboratories method, 4 used Tepnel Diagnostics Elucigene Assays, 3 used PCR followed by restriction fragment length polymorphism analysis method, 2 used an amplification/gel electrophoresis assay, 2 used Innogenetics Inno-Lipa assay, 2 used an in-house TaqMan Allelic Discrimination assay, 2 used Asuragen's Signature CF 2.0 assay, 2 used sequencing, 2 used high resolution melt technology, 1 used an in-house single nucleotide polymorphism assay, 1 used allele-specific oligonucleotide PCR, 1 used an in-house hydrolysis probe assay, 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, 1 used amplification and heteroduplex analysis, and 1 did not report the method used. Some laboratories used more than one method for their screening. One laboratory screened specimens for 4 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. ❖

No incorrect clinical assessments were reported and no sample failures were reported. Five 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 April 4, 2011. ❖

### 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 1 – MARCH 2011

LAB XXX

DATA VERIFICATION

<b>Specimen Number</b>	<b>Allele 1</b>	<b>Allele 2</b>	<b>Clinical Assessment</b>
11C1			
11C2			
11C3			
11C4			
11C5			

Reviewer's Comments

EVALUATION: No data reported.

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FREQUENCY OF REPORTED CLINICAL ASSESSMENTS

Specimen	Screen Negative (Normal)	Likely Cystic Fibrosis Positive	Likely Cystic Fibrosis Carrier	Sample Failure
11C1	6	44	4	0
11C2	54	0	0	0
11C3*	0	45	8	0
11C4	54	0	0	0
11C5*	0	53	0	0

\*One laboratory could not distinguish 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
11C1	0	10
11C2	0	0
11C3	0	9
11C4	0	0
11C5	0	1

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LABORATORY METHODS

Method	Number of Laboratories
Hologic (Third Wave Technologies) Invader Assay	19
Luminex Molecular Diagnostics X-Tag Cystic Fibrosis kit	8
Abbott Laboratories	5
Tepnel Diagnostics Elucigene Assay (CF-29, CF-30, CF-4, or CF-EU)	4*
PCR/Restriction fragment length polymorphism analysis	3*
Amplification / gel electrophoresis	2*
Innogenetics Inno-LIPA	2
In-house TaqMan allelic discrimination assay	2
Asuragen Signature CF 2.0	2
Sequencing	2*
High Resolution Melt Technology	2*
In-house SNP assay	1
Allele-specific oligonucleotide PCR	1
In-house hydrolysis probe assay	1
Matrix Assisted Laser Desorption /Ionization- Time Of Flight (MALDI-TOF) mass spectrometry	1
Amplification/heteroduplex/restriction analysis	1
Amplification/heteroduplex 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
11C1	N1303K	621+1G→T	p.Asn1303Lys	c.489+1G→T	2
11C2	Wild type	Wild type	Wild type	Wild type	1
11C3	G85E	F508del	p.Gly85Glu	p.Phe508del	2
11C4	Wild type	Wild type	Wild type	Wild type	1
11C5	F508del	F508del	p.Phe508del	p.Phe508del	2

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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