



# Newborn Screening Quality Assurance Program

## PROFICIENCY TESTING

## Cystic Fibrosis Mutation Detection Quarterly Report

Volume 3, No. 3

August 2009

### INTRODUCTION

We initiated a proficiency testing (PT) program for cystic fibrosis (CF) mutation detection. This report is the quarterly summary of all data reported within the specified data-reporting period for Quarter 3, 2009. 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 13, 2009, a panel of five unknown dried-blood-spot (DBS) specimens was distributed to 24 laboratories in the United States and 20 laboratories in other countries to detect mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

### PARTICIPANT RESULTS

We distributed one type of DBS specimens in this panel. Five specimens were prepared from adult CF patients (specimens 39C1, 39C2, 39C3, 39C4, and 39C5).

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 "unknown" or "normal" is acceptable. A specimen is considered not evaluated when one 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 40 participants. Laboratories were asked to report the genotype. Methods varied widely with regard to the panel of mutations detected and the algorithm used for testing. Thirteen used Third

Wave Technologies Invader assay, 8 used Luminex Molecular Diagnostics (Tm Biosciences) Tag-It kit, 5 laboratories used Tepnel Diagnostics Elucigene Assays, 2 used an amplification/gel electrophoresis assay, 2 used an in-house TaqMan Allelic Discrimination assay, 2 used Asuragen's Signature CF 2.0 assay, 2 used an Abbott Laboratories method, 1 used Innogenetics Inno-Lipa assay, 1 used restriction fragment length polymorphism analysis, 1 used an in-house PCR/heteroduplex/restriction enzyme method, 1 used a home-brew method, 1 used an in-house single nucleotide polymorphism assay, 1 used sequencing, 1 used allele specific oligonucleotide PCR, 1 used in-house PCR with high resolution melt analysis, and 1 used a PCR/heteroduplex analysis. 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. The smallest panel consisted of 3 mutations. Laboratories were not asked to report the maximum number of mutations that could be detected. One incorrect clinical assessment was reported for Specimen 39C2. Three sample failures were reported for Specimen 39C1, 1 sample failure was reported Specimen 39C4, and 1 was reported for Specimen 39C5. The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis Mutation Detection PT specimens on October 5, 2009.

### 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 2009

LAB XXX

DATA VERIFICATION

<b>Specimen Number</b>	<b>Allele 1</b>	<b>Allele 2</b>	<b>Clinical Assessment</b>
39C1			
39C2			
39C3			
39C4			
39C5			

Reviewer's Comments
EVALUATION:

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FREQUENCY OF REPORTED CLINICAL ASSESSMENTS

Specimen	Screen Negative (Normal)	Likely Cystic Fibrosis Positive	Likely Cystic Fibrosis Carrier	Sample Failure
39C1	0	35	2	3
39C2	1	0	39	0
39C3	1	8	31	0
39C4	39	0	0	1
39C5	39	0	0	1

INCORRECT ASSESSMENTS AND SPECIMENS NOT EVALUATED

Specimen	Incorrect Assessment	Not Evaluated
39C1	0	2
39C2	1	0
39C3	0	32
39C4	0	0
39C5	0	0

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LABORATORY METHODS

Method	Number of Laboratories
Third Wave Technologies Invader Assay	13
Luminex Molecular Diagnostics (Tm Biosciences) Tag-It	8
Tepnel Diagnostics Elucigene Assay (CF-29, CF-30, or CF-4, CF-EU1)	5*
Amplification / gel electrophoresis	2*
In-house TaqMan allelic discrimination Assay	2
Asuragen Signature CF 2.0	2
Abbott Laboratories	2
Innogenetics Inno-LIPA	1
Restriction fragment length polymorphism analysis	1
Allele-specific oligonucleotide PCR	1
In-house PCR with high resolution melt analysis	1
Amplification/heteroduplex/restriction analysis	1
In-house single nucleotide polymorphism assay	1
Home-brew assay	1
Unspecified	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
39C1	F508del	I507del	p.F508del	p.I507del	2
39C2	F508del	Wild type	p.F508del	Wild type	3
39C3	CFTRdele 2,3	G542X	CFTRdele 2,3	p.G542X	2
39C4	Wild type	Wild type	Wild type	Wild type	1
39C5	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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