



Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection Quarterly Report

Volume 4, No. 4

November 2010

INTRODUCTION

This report is the quarterly summary of all data reported within the specified data-reporting period for the Quarter 4, 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 October 4, 2010 a panel of five unknown dried-blood-spot (DBS) specimens was distributed to 29 laboratories in the United States and 30 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 40C1, 40C2, 40C3, 40C4, and 40C5).

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, 9 used Luminex Molecular Diagnos-

tics X-Tag Cystic Fibrosis kit, 5 used Tepnel Diagnostics Elucigene Assays, 3 used an Abbott Laboratories method, 3 used an amplification/gel electrophoresis assay, 3 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, 1 used PCR followed by restriction fragment length polymorphism analysis method, 1 used high resolution melt technology, 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, 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. ❖

One incorrect clinical assessment was reported for Specimen 40C2. No sample failures were reported. Nine 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 January 10, 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 4 – NOVEMBER 2010

LAB XXX

DATA VERIFICATION

Specimen Number	Allele 1	Allele 2	Clinical Assessment
40C1			
40C2			
40C3			
40C4			
40C5			

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
40C1	50	0	0	0
40C2*	0	41	8	0
40C3	50	0	0	0
40C4	50	0	0	0
40C5	11	0	39	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
40C1	0	0
40C2	1	7*
40C3	0	0
40C4	0	0
40C5	0	11

* 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	9
Tepnel Diagnostics Elucigene Assay (CF-29, CF-30, CF-4, or CF-EU)	5
Abbott Laboratories	3
Amplification / gel electrophoresis	3*
Innogenetics Inno-LIPA	3
In-house TaqMan allelic discrimination assay	2
Asuragen Signature CF 2.0	2
Sequencing	2*
PCR/Restriction fragment length polymorphism analysis	1
High Resolution Melt Technology	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
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
40C1	Wild type	Wild type	Wild type	Wild type	1
40C2	F508	R334W	p.Phe508del	p.Arg334Trp	2
40C3	Wild type	Wild type	Wild type	Wild type	1
40C4	Wild type	Wild type	Wild type	Wild type	1
40C5	711+1G>T	Wild Type	c.579+1G>T	Wild type	3

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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