



Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection Quarterly Report

Volume 4, No.2

May 2010

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 2, 2010. 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 April 5, 2010 a panel of five unknown dried-blood-spot (DBS) specimens was distributed to 25 laboratories in the United States and 25 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 20C1, 20C2, 20C3, 20C4, and 20C5).

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 47 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. Fourteen laboratories used Hologic (formerly Third Wave Technologies) Inplex CF assay, 9 used Luminex Molecular Diagnostics X-Tag Cystic Fibrosis kit, 4 used Tepnel Diagnostics Elucigene Assays, 3 used Asuragen's

Signature CF 2.0 assay, 3 used an Abbott Laboratories method, 2 used an amplification/gel electrophoresis assay, 2 used an in-house TaqMan Allelic Discrimination assay, 2 used sequencing, 2 used PCR followed by restriction fragment length polymorphism analysis method, 2 used Innogenetics Inno-Lipa assay, 1 used an in-house multi-plex PCR-heteroduplex and restriction enzyme method, 1 used a home-brew method, 1 used an in-house single nucleotide polymorphism assay, 1 used amplification refractory mutation system PCR (ARMS PCR), 1 used allele-specific oligonucleotide PCR, 1 used in-house PCR with high resolution melt analysis, 1 used PCR, 1 used PCR with real time probes and heteroduplex analysis, 1 used Matrix Assisted Laser Desorption /Ionization-Time Of Flight (MALDI-TOF) mass spectrometry, 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. 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 20C5. One laboratory reported sample failures for specimens 20C1 and 20C2 because of extraction failure. ❖

The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis Mutation Detection PT specimens on July 12, 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 2 – MAY 2010

LAB XXX

DATA VERIFICATION

Specimen Number	Allele 1	Allele 2	Clinical Assessment
20C1			
20C2			
20C3			
20C4			
20C5			

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
20C1	46	0	0	1
20C2	46	0	0	1
20C3	0	47	0	0
20C4	0	42	5	0
20C5	2	9	36	0

INCORRECT ASSESSMENTS AND SPECIMENS NOT EVALUATED

Specimen	Incorrect Assessment	Not Evaluated
20C1	0	0
20C2	0	0
20C3	0	0
20C4	0	5
20C5	1	36

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LABORATORY METHODS

Method	Number of Laboratories
Hologic (Third Wave Technologies) Invader Assay	14
Luminex Molecular Diagnostics X-Tag Cystic Fibrosis kit	9
Tepnel Diagnostics Elucigene Assay (CF-29, CF-30, CF-4, or CF-EU)	4*
Asuragen Signature CF 2.0	3
Abbott Laboratories	3
Amplification / gel electrophoresis	2*
In-house TaqMan allelic discrimination Assay	2
Sequencing	2*
PCR/Restriction fragment length polymorphism analysis	2*
Innogenetics Inno-LIPA	2*
Allele-specific oligonucleotide PCR	1
ARMS 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
Matrix Assisted Laser Desorption /Ionization- Time Of Flight (MALDI-TOF) mass spectrometry	1
PCR with Real Time Probe and Heteroduplex Analysis (F508del only)	1*
PCR (CFTR dele2, 3 deletion only)	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
20C1	Wild type	Wild type	Wild type	Wild type	1
20C2	Wild type	Wild type	Wild type	Wild type	1
20C3	F508del	F508del	p.F508del	p.Phe508del	2
20C4	F508del	R553X	p.F508del	p.Arg553X	2
20C5	G542X	CFTR dele2, 3	p.Gly542X	c.(?_54)_(273_?) del	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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