



Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection Quarterly Report

Volume 3, No. 1

March 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 1, 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 January 12, 2009, a panel of five unknown dried-blood-spot (DBS) specimens was distributed to 23 laboratories in the United States and 18 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 19C1, 19C2, 19C3, 19C4, and 19C5).

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 41 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. Twelve used Third Wave Technologies Invader assay, 7 used Luminex Molecular Diagnostics (Tm Biosciences) Tag-It kit, 5 laboratories used Tepnel

Diagnostics Elucigene Assays, 3 used an in-house TaqMan Allelic Discrimination assay, 3 used an amplification/gel electrophoresis assay, 3 used Innogenetics Inno-Lipa assay, 2 used Asuragen's Signature CF 2.0 assay, 2 used an Abbott Laboratories method, 2 used restriction fragment length polymorphism analysis, 1 used an in-house PCR/heteroduplex/restriction enzyme method, 1 used matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF), 1 used a home-brew method, 1 used an in-house single nucleotide polymorphism assay, 1 used direct sequencing for 5 exons in the CFTR gene, 1 used allele specific oligonucleotide PCR, 1 used in-house PCR with High Resolution Melt analysis, 1 did not specify a method. 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. The smallest panel consisted of three mutations. Laboratories were not asked to report the maximum number of mutations that could be detected. An incorrect clinical assessment was reported for Specimen 19C5. Two sample failure was reported for Specimen 19C5. The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis Mutation Detection PT specimens on April 6, 2009. ❖

ACKNOWLEDGEMENT

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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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LAB XXX

DATA VERIFICATION

Specimen	Allele 1	Allele 2	Clinical Assessments
19C1	Normal	Normal	
19C2	dF508	W1282X	
19C3	dF508	dF508	
19C4	dF508	R560T	
19C5	G551D	G551D	

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

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
19C1	41	0	0	0
19C2	0	32	8	0
19C3	0	41	0	0
19C4	0	31	10	0
19C5	3	34	3	1

INCORRECT ASSESSMENTS AND SPECIMENS NOT EVALUATED

Specimen	Incorrect Assessment	Not Evaluated
19C1	0	0
19C2	0	9
19C3	0	0
19C4	0	10
19C5	2	5

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LABORATORY METHODS

Method	Number of Laboratories
Third Wave Technologies Invader Assay	12
Luminex Molecular Diagnostics (Tm Biosciences) Tag-It	7
Tepnel Diagnostics Elucigene Assay (CF 29, CF-30, or CF-HT)	5
In-house TaqMan Allelic Discrimination Assay (1 of 3 laboratories*)	3*
Amplification / gel electrophoresis	3*
Innogenetics Inno-Lipa (1 of 3 laboratories*)	3*
Asuragen Signature CF 2.0	2
Abbott Laboratories	2
Restriction Fragment Length Polymorphism Analysis	2*
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
Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry	1
Direct sequencing of 5 exons	1
Home-brew assay	1
Method not specified	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
19C1	Wild type	Wild type	Wild type	Wild type	1
19C2	F508del	W1282X	p.F508del	p.W1282X	2
19C3	F508del	F508del	p.F508del	p.F508del	2
19C4	R560T	F508del	p.R560T	p.F508del	2
19C5	G551D	G551D	p.G551D	G551D	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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