



Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection Quarterly Report

Volume 3, No. 2

June 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 2, 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 April 6, 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 29C1, 29C2, 29C3, 29C4, and 29C5).

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 38 participants. Laboratories were asked to report the genotype. Methods varied widely regarding the panel of mutations detected and the algorithm used for testing. Twelve laboratories used

Third Wave Technologies Invader assay, 6 used Luminex Molecular Diagnostics (Tm Biosciences) Tag-It kit, 5 used Tepnel Diagnostics Elucigene Assays, 4 used an amplification/gel electrophoresis assay, 2 used an in-house TaqMan Allelic Discrimination assay, 2 used Innogenetics Inno-Lipa assay, 2 used an Abbott Laboratories method, 1 used Asuragen's Signature CF 2.0 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 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. One incorrect clinical assessment was reported for Specimen 29C5. One sample failure was reported for Specimen 29C3, and one sample failure was reported for Specimen 29C5. The Newborn Screening Quality Assurance Program will ship next quarter's CF mutation detection PT specimens on July 14, 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 2 – JUNE 2009

LAB XXX

DATA VERIFICATION

Specimen	Allele 1	Allele 2	Clinical Assessments
29C1			
29C2			
29C3			
29C4			
29C5			

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
29C1	38	0	0	0
29C2	0	0	38	0
29C3	3	29	5	1
29C4	38	0	0	0
29C5	0	26	11	1

INCORRECT ASSESSMENTS AND SPECIMENS NOT EVALUATED

Specimen	Incorrect Assessment	Not Evaluated
29C1	0	0
29C2	0	0
29C3	0	8
29C4	0	0
29C5	1	10

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LABORATORY METHODS

Method	Number of Laboratories
Third Wave Technologies Invader Assay	12
Luminex Molecular Diagnostics (Tm Biosciences) Tag-It	6
Tepnel Diagnostics Elucigene Assay (CF 29, CF-30, or CF-HT)	5
Amplification / gel electrophoresis	4*
In-house TaqMan allelic discrimination Assay	2
Abbott Laboratories	2
Innogenetics Inno-LIPA	2
Asuragen Signature CF 2.0	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
Sequencing	1
Home-brew assay	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
29C1	Wild type	Wild type	Wild type	Wild type	1
29C2	F508del	Wild type	p.F508del	Wild type	3
29C3	621+1G→T	N1303K	c.489+1G→T	p.N1303K	2
29C4	Wild type	Wild type	Wild type	Wild type	1
29C5	F508del	2789+5G→A	p.F508del	c. 2789+5G→A	2

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

Alleles were determined/confirmed by the Centers for Disease Control and Prevention 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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