



Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection Quarterly Report

Volume 5, No. 4

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INTRODUCTION

This report is the quarterly summary of all data reported within the specified data-reporting period for the Quarter 4, 2011, 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 3, 2011, 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, carriers or unaffected individuals (specimens 41C1, 41C2, 41C3, 41C4, and 41C5).

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 58 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. The specific methods and the number of laboratories that use them are shown in the Laboratory Methods Table. Some laboratories screen specimens for a limited number of mutations and if a mutation was present, continue testing with an expanded panel. Laboratories were not asked to report the maximum number of mutations that could be detected.

Six incorrect clinical assessments were reported among specimens 41C2, 41C3, and 41C5; three would not have any effect on screening results, two were assessed as false positives and one was assessed as false negative. Sample failure was reported for specimens 41C1 and 41C5. One laboratory 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 9, 2012.

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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LAB XXX

Specimen Number	Allele 1	Allele 2	Clinical Assessment
41C1			
41C2			
41C3			
41C4			
41C5			

Reviewer's Comments

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FREQUENCY OF REPORTED CLINICAL ASSESSMENTS

Specimen	Screen Negative (Normal)	Likely Cystic Fibrosis Positive	Likely Cystic Fibrosis Carrier	Sample Failure	Clinical Assessment Not Reported
41C1	11	1	44	1	1
41C2	1	45	10	0	2
41C3	11	43	3	0	1
41C4	0	51	5	0	2
41C5	53	1	1	2	1

INCORRECT ASSESSMENTS AND SPECIMENS NOT EVALUATED

Specimen	Incorrect Assessment	Not Evaluated*
41C1	0	14
41C2	1	11
41C3	3	12
41C4	0	7
41C5	2	4

*Includes sample failures, no reported clinical assessments, and when one or both mutations are not part of the laboratory's mutation panel.

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LABORATORY METHODS

Method	Number of Laboratories
Hologic (Third Wave Technologies) Invader Assay	19
Luminex Molecular Diagnostics X-Tag Cystic Fibrosis kit	10
Gen-Probe Elucigene Assay (CF-29, CF-30, CF-4, or CF-EU)	7*
Innogenetics Inno-LIPA	5*
Abbott Laboratories	5
Real-time allelic discrimination assay (i.e. TaqMan assay)	3*
PCR/Restriction fragment length polymorphism analysis	3*
Amplification / gel electrophoresis	2*
High Resolution Melt Technology	2
Sequencing	2*
In-house SNP assay	1
Allele-specific oligonucleotide PCR	1
Matrix Assisted Laser Desorption /Ionization- Time Of Flight (MALDI-TOF) mass spectrometry	1
Autogenomics INFINITI® CFTR-15 Assay	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
41C1	1717-1G ->A	1154insTC	c.1585-1G->A	c.1022_1023insTC	2, 3*
41C2	621+1G ->T	F508del	c.489+1G>T	p.Phe508del	2
41C3	W1282X	W1282X	p.Trp1282X	p.Trp1282X	2
41C4	R553X	F508del	p.Arg553X	p.Phe508del	2
41C5	Wild Type	Wild Type	Wild Type	Wild Type	1

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

*Allele 2 would only be detected by sequencing or other similar technique, therefore either presumptive carrier or presumptive CF positive are considered correct.

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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