



Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection Quarterly Report

Volume 5, No. 2

May 2011

INTRODUCTION

This report is the quarterly summary of all data reported within the specified data-reporting period for the Quarter 2, 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 April 4, 2011, a panel of five unknown dried-blood-spot (DBS) specimens was distributed to 29 laboratories in the United States and 29 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 21C1, 21C2, 21C3, 21C4, and 21C5).

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 53 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. Nineteen laboratories used

Hologic (formerly Third Wave Technologies) Inplex CF assay, 9 used Luminex Molecular Diagnostics X-Tag Cystic Fibrosis kit, 4 used an Abbott Laboratories method, 4 used Gen-Probe Elucigen Assays, 2 used PCR followed by restriction fragment length polymorphism analysis method, 3 used an amplification/gel electrophoresis assay, 3 used Innogenetics Inno-Lipa assay, 3 used an in-house real time PCR Allelic Discrimination assay, 1 used Asuragen’s Signature CF 2.0 assay, 2 used sequencing, 1 used high resolution melt technology, 1 used an in-house single nucleotide polymorphism assay, 2 used allele-specific oligonucleotide (or ARMS) PCR, 1 used Matrix Assisted Laser Desorption/Ionization-Time Of Flight (MALDI-TOF) mass spectrometry, and 2 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.

Four incorrect clinical assessments were reported for specimens 21C1, 21C2, and 21C3; one of which would lead to a false-positive result. The others were false-negative results. One sample failure was reported for specimen 21C1. Five 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 July 11, 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

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LAB XXX

DATA VERIFICATION

Specimen Number	Allele 1	Allele 2	Clinical Assessment

Reviewer's Comments

EVALUATION:

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

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FREQUENCY OF REPORTED CLINICAL ASSESSMENTS

Specimen	Screen Negative (Normal)	Likely Cystic Fibrosis Positive	Likely Cystic Fibrosis Carrier	Sample Failure
21C1*	0	38	13	1
21C2	12	1	40	0
21C3	52	0	1	0
21C4	53	0	0	0
21C5*	0	52	0	0

*One laboratory could not distinguish between a likely carrier and a likely positive due to the method used and these results were not included in this table.

INCORRECT ASSESSMENTS AND SPECIMENS NOT EVALUATED

Specimen	Incorrect Assessment	Not Evaluated
21C1*	1	13
21C2	2	10
21C3	1	0
21C4	0	0
21C5*	0	1

* This table includes the data not included in the Frequency of Reported Clinical Assessments table above.

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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	9
Abbott Laboratories	4
Gen-Probe Elucigene Assay (CF-29, CF-30, CF-4, or CF-EU)	4
PCR/Restriction fragment length polymorphism analysis	2*
Amplification / gel electrophoresis	3*
Innogenetics Inno-LIPA	3
Real-time allelic discrimination assay	3
Asuragen Signature CF 2.0	1
Sequencing	2*
High Resolution Melt Technology	1
In-house SNP assay	1
Allele-specific oligonucleotide PCR	2
Matrix Assisted Laser Desorption /Ionization- Time Of Flight (MALDI-TOF) mass spectrometry	1
Not reported	2

*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
21C1	A455E	F508del	p.Ala455Glu	p.Phe508del	2
21C2	1717-1G→A	1154insTC*	c.1585-1G→A	c.1022_1023insT C*	2 or 3)*
21C3	Wild type	Wild type	Wild type	Wild type	1
21C4	Wild type	Wild type	Wild type	Wild type	1
21C5	F508del	F508del	p.Phe508del	p.Phe508del	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.

*1154insTC (c.1022_1023insTC) is typically only found by laboratories that sequence the *CFTR* gene. Therefore, clinical assessment codes 2 and 3 were accepted.

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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