

Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection Quarterly Report

Volume 7, No. 4

December 2013

INTRODUCTION

This report is the quarterly summary of all data reported within the specified data-reporting period for the Quarter 4, 2013 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 distribution summary for expected interpretations. We distribute this PT report to all participants, state laboratory directors, and program colleagues by request.

On October 23, 2013 a panel of five unknown dried-blood-spot (DBS) specimens was distributed to 33 laboratories in the United States and 33 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 413C1, 413C2, 413C3, 413C4, and 413C5).

The algorithm for evaluating reported data has changed. Evaluations are based on the genotype and clinical assessment of each specimen. Each clinical assessment counts as 10% and each allele counts as 5% of the assessment. Expected genotypes may differ by participant because of the panel of mutations, screening algorithm, or method used. In these cases, an answer of “no mutation detected” is acceptable and participants will receive a 100% Satisfactory assessment.

We processed data from 55 participants. Laboratories were asked to report the method used and the genotype for each specimen. Methods varied widely with regard to the panel of mutations detected, the algorithm used for testing, and DNA extraction methods used. These methods and the number of laboratories that use them are shown in tables included in this report.

The genotype of Specimen 413C3 is R347P/R1066H (p.Arg347Pro/p.Arg1066His). R1066H (p.Arg1066His) is a rare mutation that can only be found through sequencing. This allele was not used to evaluate individual laboratory results; however R347P (p.Arg347Pro) was a gradable allele.

Of the 12 laboratories that use the Luminex CFTR kits, 58% (7 laboratories) commented that the S549R (T>G) mutation could not be called on Specimen 413C4. Of these seven laboratories, three did not report data as they would have asked for a repeat specimen or for DNA sequencing. The remaining four laboratories reported the correct genotype and clinical assessment.

Two laboratories reported an incorrect genotype for Specimens 413C3 and 413C4 and one laboratory reported an incorrect genotype and clinical assessment Specimen 413C3. The Newborn Screening Quality Assurance Program will ship next quarter’s Cystic Fibrosis Mutation Detection PT specimens on January 13, 2013.

Please note that in order to receive an evaluation, you must use the current data report form. This form can be downloaded from our website at http://www.cdc.gov/labstandards/nsqip_resources.html#QCReportForms

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 4 - DECEMBER 2013

PRIMARY METHODS

	Number of Laboratories
CF1 Hologic CF Inplex Molecular Test - ACMG	6
CF2 Hologic CF Inplex Molecular Test 40+4	15
CF4 Luminex Molecular Diagnostics CFTR IVD 39 v2	8
CF5 Luminex Molecular Diagnostics xTAG CF 60 v2	1
CF6 Luminex Molecular Diagnostics xTAG CF 71 v2	2
CF7 Luminex Platform and Laboratory Developed Test	1
CF8 Hologic Gen-Probe Elucigene CF4v2	1
CF10 Hologic Gen-Probe Elucigene CF30	1
CF12 Abbott Molecular CF Genotyping Assay v3	4
CF15 Innogenetics Inno-LiPA Strips 17+19	4
CF16 Sequenom (MALDI-TOF Mass Spectrometry)	1
CF17 ViennaLab Diagnostics GmbH CF StripAssay	1
CF20 Allele-specific Oligonucleotide PCR	2
CF21 High Resolution Melt Technology	2
CF22 Real-time PCR Allelic Discrimination Assay (ie TaqMan)	2
CF27 Amplification and Restriction Fragment Length Polymorphism Analysis (PCR-RFLP)	2
CF28 Amplification and Polyacrylamide Gel Electrophoresis (PCR-PAGE)	1
CF29 Sequencing	1

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SECONDARY METHODS

	Number of Laboratories
CF1 Hologic CF Inplex Molecular Test - ACMG	2
CF2 Hologic CF Inplex Molecular Test 40+4	4
CF4 Luminex Molecular Diagnostics CFTR IVD 39 v2	5
CF12 Abbott Molecular CF Genotyping Assay v3	3
CF16 Sequenom (MALDI-TOF Mass Spectrometry)	1
CF22 Real-time PCR Allelic Discrimination Assay (ie TaqMan)	1
CF25 PCR/Heteroduplex Analysis/Gel Electrophoresis	1
CF26 Capillary Electrophoresis	1
CF28 Amplification and Polyacrylamide Gel Electrophoresis (PCR-PAGE)	1
CF29 Sequencing	7

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EXTRACTION METHODS

	Number of Laboratories
X1 Qiagen QIAamp spin columns (manual or robotic)	4
X2 Qiagen magnetic bead kit (EZ1 or BioSprint 96)	2
X3 Qiagen Generation DNA Purification & DNA Elution Solutions	23
X4 Sigma Aldrich Extract-N-Amp	1
X5 in-house alkaline lysis prep	4
X6 in-house MeOH boiling prep	4
X7 in-house lysis boiling prep	4
X19 Other	11

OVERALL FREQUENCY OF CLINICAL ASSESSMENTS

SPECIMEN ID	SCREEN NEGATIVE (Normal)	SCREEN POSITIVE (1 or 2 mutations detected)	NOT ASSESSED	NO DATA SUBMITTED	LATE*	INCORRECT CLINICAL ASSESSMENTS**
413C1	0	55	0	9	2	0
413C2	0	54	1	9	2	0
413C3	9	46	0	9	2	1
413C4	3	47	5	9	2	0
413C5	0	54	1	9	2	0

*Late results are maintained by NSQAP, but not included in evaluation statistics

**Methods vary widely based upon panel of mutations detected, the algorithm used for testing and DNA extraction methods.

OVERALL FREQUENCY OF REPORTED GENOTYPES

		F508del (p.Phe508del)	N1303K (p.Asn1303Lys)	R347P (p.Arg347Pro)	R1066H (p.R1066His)	G551D (p.Gly551Asp)	NO MUTATIONS DETECTED*	NO GENOTYPE REPORTED (Cell left blank)	INCORRECT GENOTYPE (by allele)	INCORRECT CLINICAL ASSESSMENTS**
413C1	Allele 1	55						0	0	0
	Allele 2		49				6	0	0	
413C2	Allele 1	54						1	0	0
	Allele 2	54						1	0	
413C3	Allele 1			45			10	0	2	1
	Allele 2				4		51	0	0	
413C4	Allele 1					47	3	5	0	0
	Allele 2					46	4	5	1	
413C5	Allele 1	54						1	0	0
	Allele 2	54						1	0	

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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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