

Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection
Quarterly Report

Volume 10, No. 1

February 2016

INTRODUCTION

This report is the quarterly summary of all data reported within the specified data-reporting period for the Quarter 1, 2016 program for cystic fibrosis (CF) mutation detection for the Newborn Screening Quality Assurance Program. The attached tables provide the certification profiles for the distributed specimens, the overall summary of clinical assessments reported, the overall summary of reported alleles, the primary and secondary methods used by participants, the DNA extraction methods used by participants and the verification of your reported data. Methods varied widely with regard to the panel of mutations detected, the algorithm used for testing, and DNA extraction methods used. We distribute this PT report to all participants, state laboratory directors, and program colleagues by request.

On January 11, 2016, a panel of five unknown dried blood spot (DBS) specimens was distributed to 32 laboratories in the United States and 36 laboratories in other countries to detect mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Note that the evaluation scheme for this quarter has changed. All specimens are evaluated for all participants based on their specific method, panel of mutations and algorithm. Thus, the clinical assessments may vary between laboratories while still being correct.

PARTICIPANT RESULTS

This panel consisted of five DBS specimens (116C1, 116C2, 116C3, 116C4, and 116C5) prepared from adult CF patients, carriers, or unaffected individuals.

Evaluations are based on the genotype and clinical assessment of each specimen. Each clinical assessment is worth

10% and each identified allele is worth 5% of the assessment. Since participants are graded according to their screening method(s) and algorithm, the clinical assessments may vary from laboratory to laboratory.

We received and processed data from 63 participants. Laboratories were asked to report the method(s) used in their testing and how the methods are used and the alleles found for each specimen. Five laboratories did not report data for this quarter.

For specimen 116C1, 24 participants reported a clinical assessment of screen negative and 39 participants reported a clinical assessment of screen positive. All assessments were correct based on participant's mutation panel and/or algorithm.

For specimen 116C2, all participants reported the correct clinical assessment of screen negative.

For specimen 116C3, 60 participants reported a clinical assessment of screen negative and 3 participants reported a clinical assessment of screen positive. All assessments were correct based on participant's mutation panel and/or algorithm.

For specimen 116C4, all participants reported the correct clinical assessment of screen positive and all reported alleles were correct.

For specimen 116C5, all participants reported the correct clinical assessment of screen positive. One laboratory did not to identify the 621+1G>T (c.489+1G>T) that was part of their reported panel.

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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The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis Mutation Detection PT specimens on April 4, 2016.

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

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NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS MUTATION DETECTION SURVEY

QUARTER 1 –2016

TABLE 1. SPECIMEN CERTIFICATION

Specimen	Allele 1	Allele 2	Expected Clinical Assessment
116C1	Y1092X (c.3276C>A)	No mutations detected	2
116C2	No mutations detected	No mutations detected	1
116C3	663delT (c.531delT)	No mutations detected	2
116C4	F508del (c.1521_1523delCTT)	F508del (c.1521_1523delCTT)	2
116C5	F508del (c.1521_1523delCTT)	621+1G>T (c.489+1G>T)	2

1 = Screen Negative (Normal)

2 = Screen Positive - 1 or 2 Mutations Detected

Alleles were determined or confirmed by CDC

TABLE 2. OVERALL REPORTED CLINICAL ASSESSMENTS

SPECIMEN ID	SCREEN NEGATIVE	SCREEN POSITIVE 1 OR 2 MUTATIONS DETECTED	NO CLINICAL ASSESSMENT REPORTED	NO DATA SUBMITTED	INCORRECT CLINICAL ASSESSMENTS
C1	24	39	0	5	0
C2	63	0	0	5	0
C3	60	3	0	5	0
C4	0	63	0	5	0
C5	0	63	0	5	0

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

Screening method(s) and algorithms used by participants differ, thus the clinical assessments may vary from laboratory to laboratory.

TABLE 3. OVERALL REPORTED ALLELES

		Y1092X (c.3276C>A)	663delT (c.531delT)	F508del (c.1521_1523delCTT)	621+1G>T (c.489+1G>T)	NO MUTATIONS DETECTED	NO MUTATIONS REPORTED	INCORRECT ALLELES
C1	Allele 1	38				25		
	Allele 2	1				62		
C2	Allele 1					63		
	Allele 2					63		
C3	Allele 1		3			60		
	Allele 2					63		
C4	Allele 1			63				
	Allele 2			63				
C5	Allele 1			32	29	2		
	Allele 2			31	22	10		1

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CYSTIC FIBROSIS MUTATION DETECTION SURVEY

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TABLE 4. PRIMARY METHODS

	Number of Laboratories
CF1 Hologic CF Inplex Molecular Test - ACMG	3
CF2 Hologic CF Inplex Molecular Test 40+4	20
CF4 Luminex Molecular Diagnostics CFTR IVD 39 v2	7
CF5 Luminex Molecular Diagnostics xTAG CF 60 v2	1
CF7 Luminex Platform and Laboratory Developed Test	1
CF8 Elucigene Diagnostics CF4v2	1
CF10 Elucigene Diagnostics CF30	3
CF11 Elucigene Diagnostics CFEUv2	1
CF12 Abbott Molecular CF Genotyping Assay v3	2
CF15 Inno-LiPA Strips 17+19	3
CF17 Sequenom assays other than HerediT CF (MALDI-TOF Mass Spectrometry)	1
CF18 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
CF23 In-house Amplification Refractory Mutation System	1
CF24 In-house single nucleotide primer extension assay (SNuPe)	1
CF27 Amplification and Restriction Fragment Length Polymorphism Analysis (PCR-RFLP)	2
CF29 Next Gen Sequencing - Illumina MiSeqDx 139 Variant Assay	1
CF30 Next Gen Sequencing - Multiplicom Molecular Diagnostics CFTR MASTR v2	2
CF32 All other gene sequencing protocols including Sanger and Next Gen	5
CF99 Other	1
No response	5

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TABLE 5. SECONDARY METHODS

	Number of Laboratories
CF1 Hologic CF Inplex Molecular Test - ACMG	1
CF2 Hologic CF Inplex Molecular Test 40+4	6
CF4 Luminex Molecular Diagnostics CFTR IVD 39 v2	4
CF11 Elucigene Diagnostics CFEUv2	1
CF12 Abbott Molecular CF Genotyping Assay v3	1
CF14 Inno-LiPA Strip 19	1
CF15 Inno-LiPA Strips 17+19	2
CF17 Sequenom assays other than HerediT CF (MALDI-TOF Mass Spectrometry)	1
CF23 In-house Amplification Refractory Mutation System	1
CF25 PCR/Heteroduplex Analysis/Gel Electrophoresis	2
CF26 Capillary Electrophoresis	1
CF27 Amplification and Restriction Fragment Length Polymorphism Analysis (PCR-RFLP)	1
CF31 Next Gen Sequencing - Ion AmpliSeq CFTR Community Panel	1
CF32 All other gene sequencing protocols including Sanger and Next Gen	5
CF99 Other	3
No response	37

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CYSTIC FIBROSIS MUTATION DETECTION SURVEY

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TABLE 6. EXTRACTION METHODS

	Number of Laboratories
X1 Qiagen QIAamp spin columns (manual or robotic)	5
X2 Qiagen magnetic bead kit (EZ1 or BioSprint 96)	2
X3 Qiagen Generation DNA Purification & DNA Elution Solutions	22
X4 Sigma Aldrich Extract-N-Amp	3
X5 in-house alkaline lysis prep	7
X6 in-house boiling prep	6
X7 in-house lysis boiling prep	1
X19 Other	11
No response	11

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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