

Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection
Quarterly Report

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INTRODUCTION

This report is the quarterly summary of all data reported within the specified reporting period for the Quarter 4, 2014 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 proficiency testing (PT) report to all participants, state laboratory directors, and program colleagues by request.

On October 6, 2014 a panel of five unknown dried blood spot (DBS) specimens was distributed to 33 laboratories in the United States and 31 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 414C1, 414C2, 414C3, 414C4, and 414C5).

Evaluations are based on the genotype and clinical assessment for 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 63 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.

One laboratory reported only clinical assessments for all specimens. Two laboratories reported an incorrect genotype for specimen 414C1. One laboratory reported an incorrect genotype for specimen 414C2. One laboratory reported and incorrect genotype for specimen 414C3 and one laboratory reported an incorrect clinical assessment for specimen 414C3. The 2055del9A mutation in specimen 414C4 is included in five assays and five participants reported this mutation. For the other participants, this specimen was not evaluated. Two laboratories reported an incorrect genotype for specimen 414C5. The Newborn Screening Quality Assurance Program will ship next quarter’s Cystic Fibrosis Mutation Detection PT specimens on January 12, 2015.

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/nsqap_resources.html#QCReportForms

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CDC/APHL

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CYSTIC FIBROSIS MUTATION DETECTION SURVEY

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SPECIMEN CERTIFICATION

Specimen	Allele 1	Allele 2	Expected Clinical Assessment
414C1	F508del (p.Phe508del)	F508del (p.Phe508del)	2
414C2	F508del (p.Phe508del)	A455E (p.Ala455Glu)	2
414C3	2789+5G->A (c.2657+5G->A)	No mutations detected	2
414C4	2055del9>A (c.1923_1931del9insA)	No mutations detected	2
414C5	F508del (p.Phe508del)	F508del (p.Phe508del)	2

1 = screen negative (normal)
2 = 1 or 2 mutations detected

Alleles were determined/confirmed by CDC and/or were included with the samples from the provider.

OVERALL FREQUENCY OF CLINICAL ASSESSMENTS

SPECIMEN ID*	SCREEN NEGATIVE	SCREEN POSITIVE 1 OR 2 MUTATIONS DETECTED	NO CLINICAL ASSESSMENT REPORTED	NO DATA SUBMITTED	INCORRECT CLINICAL ASSESSMENTS**
414C1	0	63	0	1	0
414C2	0	63	0	1	0
414C3	12	51	0	1	1
414C4	58	5	0	1	0
414C5	0	61	1	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. These factors are considered in evaluation determination.

OVERALL FREQUENCY OF REPORTED GENOTYPES

		F508del	A455E	2789+5G>A	2055del9>A	NO MUTATIONS DETECTED*	NO GENOTYPE REPORTED (Cell left blank)	INCORRECT GENOTYPE†	INCORRECT CLINICAL ASSESSMENTS*
414C1	Allele 1	62				0	1	2	0
	Allele 2	61				1	1		
414C2	Allele 1	62				0	1	0	0
	Allele 2		52			10	1		
414C3	Allele 1			51		11	1	1	1
	Allele 2					61	2		
414C4	Allele 1				5	56	2	0	0
	Allele 2					61	2		
414C5	Allele 1	60				0	3	2	0
	Allele 2	60				1	2		

*Methods vary widely with regard to the panel of mutations detected, the algorithm used for testing, and DNA extraction methods. These factors are considered in evaluation determination.

†Incorrect genotypes include reporting the wrong allele, reporting no mutation detected when the method should identify it, or not reporting an allele (except when due to sample failure).

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PRIMARY METHODS

	Number of Laboratories
CF1 Hologic CF Inplex Molecular Test - ACMG	3
CF2 Hologic CF Inplex Molecular Test 40+4	19
CF3 Luminex Molecular Diagnostics xTAG CF - ACMG only	1
CF4 Luminex Molecular Diagnostics CFTR IVD 39 v2	7
CF5 Luminex Molecular Diagnostics xTAG CF 60 v2	1
CF6 Luminex Molecular Diagnostics xTAG CF 71 v2	1
CF7 Luminex Platform and Laboratory Developed Test	1
CF8 Hologic Gen-Probe Elucigene CF4v2	1
CF10 Hologic Gen-Probe Elucigene CF30	3
CF11 Hologic Gen-Probe Elucigene CFEUv1	2
CF12 Abbott Molecular CF Genotyping Assay v3	5
CF15 Innogenetics Inno-LiPA Strips 17+19	3
CF16 Sequenom (MALDI-TOF Mass Spectrometry)	3
CF17 ViennaLab Diagnostics GmbH CF StripAssay	1
CF20 Allele-specific Oligonucleotide PCR	2
CF21 High Resolution Melt Technology	3
CF23 In-house Amplification Refractory Mutation System	1
CF27 Amplification and Restriction Fragment Length Polymorphism Analysis (PCR-RFLP)	2
CF28 Amplification and Polyacrylamide Gel Electrophoresis (PCR-PAGE)	1
CF29 Sequencing	1
CF19 Other	2

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SECONDARY METHODS

	Number of Laboratories
CF2 Hologic CF Inplex Molecular Test 40+4	6
CF4 Luminex Molecular Diagnostics CFTR IVD 39 v2	5
CF12 Abbott Molecular CF Genotyping Assay v3	3
CF13 Innogenetics Inno-LiPA Strip 17	1
CF14 Innogenetics Inno-LiPA Strip 19	2
CF16 Sequenom (MALDI-TOF Mass Spectrometry)	2
CF26 Capillary Electrophoresis	1
CF27 Amplification and Restriction Fragment Length Polymorphism Analysis (PCR-RFLP)	1
CF28 Amplification and Polyacrylamide Gel Electrophoresis (PCR-PAGE)	1
CF29 Sequencing	6
CF19	5

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EXTRACTION METHODS

	Number of Laboratories
X1 Qiagen QIAamp spin columns (manual or robotic)	6
X2 Qiagen magnetic bead kit (EZ1 or BioSprint 96)	1
X3 Qiagen Generation DNA Purification & DNA Elution Solutions	20
X4 Sigma Aldrich Extract-N-Amp	1
X5 in-house alkaline lysis prep	6
X6 in-house MeOH boiling prep	5
X7 in-house lysis boiling prep	2
X19 Other	15

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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