

Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

**Cystic Fibrosis Mutation Detection
Quarterly Report**

Volume 8, No. 3

August 2014

INTRODUCTION

This report is the quarterly summary of all data reported within the specified reporting period for the Quarter 3, 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 July 14, 2014 a panel of five unknown dried blood spot (DBS) specimens was distributed to 33 laboratories in the United States and 32 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 314C1, 314C2, 314C3, 314C4, and 314C5).

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 61 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.

Two laboratories reported an incorrect genotype for specimen 314C1. One laboratory reported an incorrect clinical assessment for specimen 314C1. The A559T mutation in specimen 314C5 is included in seven assays and 15 participants reported this mutation. For the other participants, this specimen was not evaluated. The E60X mutation in specimen 314C1 is included in nine assays and 30 participants reported this mutation. The specimen was not evaluated for the other participants. The Newborn Screening Quality Assurance Program will ship next quarter’s Cystic Fibrosis Mutation Detection PT specimens on October 6, 2014.

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

ACKNOWLEDGMENTS

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CDC/APHL

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SPECIMEN CERTIFICATION

Specimen	Allele 1	Allele 2	Expected Clinical Assessment
314C1	E60X (p.Glu60X)	No mutations detected	2
314C2	No mutations detected	No mutations detected	1
314C3	F508del (p.Phe508del)	3905insT (c.3773_3774insT)	2
314C4	F508del (p.Phe508del)	F508del (p.Phe508del)	2
314C5	A559T (p.Ala559Thr)	No mutations detected	2

1 = screen negative (normal)

2 = 1 or 2 mutations detected

Alleles were determined or confirmed by CDC.

OVERALL FREQUENCY OF CLINICAL ASSESSMENTS

SPECIMEN ID	SCREEN NEGATIVE	SCREEN POSITIVE		NO CLINICAL ASSESSMENT REPORTED	NO DATA SUBMITTED	INCORRECT CLINICAL ASSESSMENTS**
		1 OR 2 MUTATIONS DETECTED				
314C1	29	31	1	3	1	
314C2	60	0	1	3	0	
314C3	0	60	1	3	0	
314C4	0	60	1	3	0	
314C5	45	15	1	3	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

SPECIMEN ID	Allele	E60X	F508del	3905insT	A559T	NO MUTATIONS DETECTED*	NO GENOTYPE REPORTED (Cell left blank)	INCORRECT GENOTYPE (by allele)†	INCORRECT CLINICAL ASSESSMENTS**
314C1	Allele 2	0	0	0	0	60	1	0	
314C2	Allele 1	0	0	0	0	60	1	0	0
314C2	Allele 2	0	0	0	0	59	2	0	
314C3	Allele 1	0	60	0	0	0	1	0	0
314C3	Allele 2	0	0	47	0	13	1	0	
314C4	Allele 1	0	60	0	0	0	1	0	0
314C4	Allele 2	0	60	0	0	0	1	0	
314C5	Allele 1	0	0	0	15	45	1	0	0
314C5	Allele 2	0	0	0	0	59	2	0	

*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.

**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.

†Incorrect genotypes include reporting the wrong allele or reporting no mutation detected when the method should identify it.

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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	1
CF12 Abbott Molecular CF Genotyping Assay v3	3
CF15 Innogenetics Inno-LiPA Strips 17+19	4
CF16 Sequenom (MALDI-TOF Mass Spectrometry)	4
CF17 ViennaLab Diagnostics GmbH CF StripAssay	2
CF20 Allele-specific Oligonucleotide PCR	1
CF21 High Resolution Melt Technology	3
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	3

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SECONDARY METHODS

	Number of Laboratories
CF1 Hologic CF Inplex Molecular Test - ACMG	1
CF2 Hologic CF Inplex Molecular Test 40+4	8
CF4 Luminex Molecular Diagnostics CFTR IVD 39 v2	5
CF10 Hologic Gen-Probe Elucigene CF30	1
CF12 Abbott Molecular CF Genotyping Assay v3	2
CF14 Innogenetics Inno-LiPA Strip 19	1
CF15 Innogenetics Inno-LiPA Strips 17+19	1
CF16 Sequenom (MALDI-TOF Mass Spectrometry)	3
CF25 PCR/Heteroduplex Analysis/Gel Electrophoresis	1
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	3
CF19 Other	2

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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	22
X4 Sigma Aldrich Extract-N-Amp	1
X5 in-house alkaline lysis prep	7
X6 in-house MeOH boiling prep	4
X7 in-house lysis boiling prep	3
X19 Other	13

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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