

# Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection  
Quarterly Report

Volume 9, No. 2

May 2015

## INTRODUCTION

This report is the quarterly summary of all data reported within the specified data-reporting period for the Quarter 2, 2015 program for cystic fibrosis (CF) mutation detection. The attached tables provide the certification profiles for the distributed specimens, the summary of frequencies of clinical assessments reported, the summary of frequencies of reported genotypes, 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 April 6, 2015, a panel of five unknown dried blood spot (DBS) specimens was distributed to 32 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 (215C1, 215C2, 215C3, 215C4, and 215C5) prepared from adult CF patients, carriers, or unaffected individuals.

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. If one or both alleles in a specimen are not part of a laboratory's testing panel or would not be identified based on their screening algorithm, the specimen is considered not

evaluated. Each participant is only graded on samples for which they can evaluate the alleles fully.

We received and processed data from 62 participants. Laboratories were asked to report the method(s) used in their testing and the alleles found for each specimen. One laboratory reported clinical assessments only and did not report any alleles.

For specimen 215C1, one laboratory reported an incorrect clinical assessment, and two laboratories reported an incorrect allele. Ten methods are able to detect the S549N (c.1646G>A) allele included in specimen 215C1, resulting in the specimen being evaluated for the 45 participants that use these methods.

For specimen 215C2, 15 methods can detect the W1282X (c.3846G>A) allele included in specimen 215C2, resulting in the specimen being evaluated for the 53 participants that use these methods.

For specimen 215C3, all participant methods detect the F508del (c.1521\_1523delCTT) allele. One laboratory did not report a clinical assessment due to sample failure and one laboratory reported an incorrect allele.

For specimen 215C4, one laboratory reported an incorrect clinical assessment. Twelve methods can detect the 1898+1G>A (c.1766+1G>A) allele included in specimen 215C4, resulting in the specimen being evaluated for the 47 participants that use these methods.

For specimen 215C5, 13 methods can detect the 3659delC (c.3528delC) allele, resulting in the specimen being evaluated for the 51 participants that use these methods.

CDC/APHL

This program is cosponsored by the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL).

Direct inquiries to:  
Centers for Disease Control and Prevention (CDC)  
4770 Buford Highway, NE, MS/F43  
Atlanta, GA 30341-3724

Phone: 770-488-4048  
FAX: 770-488-4255  
E-mail: SCordovado@cdc.gov

Editor: Susanne Cordovado  
Irene Williams  
Joanne Mei



The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis Mutation Detection PT specimens on July 13, 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](http://www.cdc.gov/labstandards/nsqap_resources.html#QCReportForms)

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NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS MUTATION DETECTION SURVEY

QUARTER 2 –2015

TABLE 1. SPECIMEN CERTIFICATION

Specimen	Allele 1	Allele 2	Expected Clinical Assessment
215C1	S549N (c.1646G>A)	No mutations detected	2
215C2	F508del (c.1521_1523delCTT)	W1282X (c.3846G>A)	2
215C3	F508del (c.1521_1523delCTT)	F508del (c.1521_1523delCTT)	2
215C4	1898+1G>A (c.1766+1G>A)	No mutations detected	2
215C5	F508del (c.1521_1523delCTT)	3659delC (c.3528delC)	2

1 = Screen Negative (Normal)

2 = Screen Positive - 1 or 2 Mutations Detected

Alleles were determined or confirmed by CDC

TABLE 2. OVERALL FREQUENCY OF CLINICAL ASSESSMENTS

SPECIMEN ID	SCREEN				NO DATA SUBMITTED	INCORRECT CLINICAL ASSESSMENTS**
	SCREEN NEGATIVE	POSITIVE 1 OR 2 MUTATIONS DETECTED	NO CLINICAL ASSESSMENT REPORTED	INCORRECT MUTATIONS DETECTED		
C1	18	44	0	3	1	
C2	0	62	0	3	0	
C3	0	61	1	3	0	
C4	15	47	0	3	1	
C5	0	62	0	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.

TABLE 3. OVERALL FREQUENCY OF REPORTED GENOTYPES

SPECIMEN ID	S549N (c.1646G>A)	F508del (c.1521_1523delCTT)	W1282X (c.3846G>A)	1898+1G>A (c.1766+1G>A)	3659delC (c.3528delC)	S492F (c.1475C>T)	NO MUTATIONS DETECTED*	NO GENOTYPE REPORTED (Cell left blank)	INCORRECT GENOTYPE (by allele)	INCORRECT CLINICAL ASSESSMENTS**
C1	43					1	17	1	1	1
	1						60	1	1	1
C2		61					8	1		0
			53					1		
C3		60					1	2		0
		59						2	1	
C4				47			14	1		1
							61	1		
C5		61			51		10	1		0
								1		

\*\*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.

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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	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
CF7 Luminex Platform and Laboratory Developed Test	1
CF8 Hologic Gen-Probe Elucigene CF4v2	1
CF10 Hologic Gen-Probe Elucigene CF30	2
CF11 Hologic Gen-Probe Elucigene CFEUv1	2
CF12 Abbott Molecular CF Genotyping Assay v3	5
CF15 Innogenetics Inno-LiPA Strips 17+19	1
CF16 Sequenom (MALDI-TOF Mass Spectrometry)	3
CF20 Allele-specific Oligonucleotide PCR	2
CF21 High Resolution Melt Technology	3
CF22 Real-time PCR Allelic Discrimination Assay (ie TaqMan)	1
CF27 Amplification and Restriction Fragment Length Polymorphism Analysis (PCR-RFLP)	2
CF29 Sequencing	3
CF19 Other	4
No response	4

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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	5
CF12 Abbott Molecular CF Genotyping Assay v3	3
CF14 Innogenetics Inno-LiPA Strip 19	1
CF15 Innogenetics Inno-LiPA Strips 17+19	2
CF16 Sequenom (MALDI-TOF Mass Spectrometry)	2
CF17 ViennaLab Diagnostics GmbH CF StripAssay	1
CF25 PCR/Heteroduplex Analysis/Gel Electrophoresis	1
CF26 Capillary Electrophoresis	1
CF27 Amplification and Restriction Fragment Length Polymorphism Analysis (PCR-RFLP)	1
CF29 Sequencing	6
CF19 Other	4
No response	31

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TABLE 6. EXTRACTION METHODS

	Number of Laboratories
X1 Qiagen QIAamp spin columns (manual or robotic)	7
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	6
X6 in-house MeOH boiling prep	5
X7 in-house lysis boiling prep	2
X19 Other	14
No response	7

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**.

**CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)**  
**ATLANTA, GA 30341**

**Director**

Thomas R. Frieden, M.D., M.P.H.

**Director**

**National Center for Environmental Health**

Patrick Breyse, Ph.D.

**Director**

**Division of Laboratory Sciences**

James L. Pirkle, M.D., Ph.D.

**Chief**

**Newborn Screening and Molecular Biology Branch**

Carla Cuthbert, Ph.D.



**Contributors:**

Barbara W. Adam	Patrick Pickens
Suzanne Cordovado, Ph.D.	Kelsey Sheard
Paul Dantonio	Jennifer Taylor, Ph.D.
Victor R. De Jesus, Ph.D.	Robert Vogt, Ph.D.
Zachary Detwiler	Irene Williams
Marie C. Earley, Ph.D.	Golriz Yazdanpanah
Sharon Flores	Hui Zhou, Ph.D.
David Foreman	Sherri Zobel
Stephanie Foster	
Travis Gilliland	
Christopher Greene, Ph.D.	
Elizabeth M. Hall	
Laura Hancock	
Christopher Haynes, Ph.D.	
Miyono Hendrix	
Sarah Klass	
Deborah Koontz, Ph.D.	
Francis Lee, Ph.D.	
Lixia Li, Ph.D.	
Timothy Lim, Ph.D.	
Daniel Mandel, Ph.D.	
Joanne Mei, Ph.D.	
Stanimila Nikolova, Ph.D.	

**Production:**

Sarah Brown  
Iris Landers  
Felicia Manning  
LoNeka Shockley

**ASSOCIATION OF PUBLIC HEALTH LABORATORIES**  
**SILVER SPRING, MD 20910**



**President**

Dan Rice, DrPH, MS.

**Chairman, Newborn Screening and Genetics in Public Health Committee**

Susan M. Tanksley, Ph.D.

**Chairman, Newborn Screening Quality Assurance Quality Control Subcommittee**

Patrick Hopkins, B.S.

**INQUIRIES TO:**

*Suzanne K. Cordovado, Editor • Centers for Disease Control and Prevention (CDC)*  
*Newborn Screening Quality Assurance Program • Mailstop F-43*  
*4770 Buford Highway, N.E. • Atlanta, GA 30341-3724*  
*Phone (770) 488-4582 • FAX (770) 488-4255 • E-mail: SCordovado@cdc.gov*