



Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection Quarterly Report

Volume 4, No.1

February 2010

INTRODUCTION

We initiated a proficiency testing (PT) program for cystic fibrosis (CF) mutation detection. This report is the quarterly summary of all data reported within the specified data-reporting period for Quarter 1, 2010. 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 distributions summary for expected interpretations. We distribute this PT report to all participants, state laboratory directors, and program colleagues by request.

On January 11, 2010 a panel of five unknown dried-blood-spot (DBS) specimens was distributed to 25 laboratories in the United States and 24 laboratories in other countries to detect mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

PARTICIPANT RESULTS

We distributed one type of DBS specimens in this panel. Five specimens were prepared from adult CF patients (specimens 10C1, 10C2, 10C3, 10C4, and 10C5).

Evaluations are based on the clinical assessment of each specimen. Expected genotypes may differ by participant because of the panel of mutations tested. In these cases, an answer of "no mutation detected" is acceptable. A specimen is considered not evaluated when one or both of the expected mutations is not detected by the laboratory's method or if the specimen cannot be assayed (sample failure).

We processed data from 44 participants. Laboratories were asked to report the genotype. Methods varied widely with regard to the panel of mutations detected and the algorithm used for testing. Fourteen used Third Wave Technologies Invader assay, 9 used Luminex Molecular Diagnostics (Tm

Biosciences) Tag-It kit, 4 laboratories used Telpel Diagnostics Elucigene Assays, 2 used an amplification/gel electrophoresis assay, 2 used an in-house TaqMan Allelic Discrimination assay, 3 used Asuragen's Signature CF 2.0 assay, 2 used an Abbott Laboratories method, 1 used Innogenetics Inno-Lipa assay, 1 used an in-house PCR followed by restriction fragment length polymorphism analysis method, 1 used an in-house multi-plex PCR-heteroduplex and restriction enzyme method, 1 used a home-brew method, 1 used an in-house single nucleotide polymorphism assay, 1 used sequencing, 1 used allele-specific oligonucleotide PCR, 1 used in-house PCR with high resolution melt analysis, 1 used a PCR/heteroduplex analysis, 1 used an in-house allele-specific hybridization method, 1 used Matrix Assisted Laser Desorption /Ionization- Time Of Flight (MALDI-TOF) mass spectrometry, and 1 did not report the method used. Some laboratories used more than one method for their screening. One laboratory screened specimens for 4 mutations and if a mutation was present, continued testing with an expanded panel. The smallest panel consisted of 3 mutations. Laboratories were not asked to report the maximum number of mutations that could be detected. One incorrect clinical assessment was reported for Specimen 10C4. No sample failures were reported. ❖

The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis Mutation Detection PT specimens on April 5, 2010. ❖

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).

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

Phone : 770-488-7828
FAX: 770-488-4255
E-mail: MEarley@cdc.gov

Editor : Marie Earley
Production: Connie Singleton



NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS MUTATION DETECTION SURVEY

QUARTER 1 – FEBRUARY 2010

LAB XXX

DATA VERIFICATION

Specimen Number	Allele 1	Allele 2	Clinical Assessment
10C1			
10C2			
10C3			
10C4			
10C5			

Reviewer's Comments

EVALUATION:

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

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FREQUENCY OF REPORTED CLINICAL ASSESSMENTS

Specimen	Screen Negative (Normal)	Likely Cystic Fibrosis Positive	Likely Cystic Fibrosis Carrier	Sample Failure
10C1	44	0	0	0
10C2	0	0	44	0
10C3	44	0	0	0
10C4	0	25	19	0
10C5	44	0	0	0

INCORRECT ASSESSMENTS AND SPECIMENS NOT EVALUATED

Specimen	Incorrect Assessment	Not Evaluated
10C1	0	0
10C2	0	0
10C3	0	0
10C4	1	18
10C5	0	0

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LABORATORY METHODS

Method	Number of Laboratories
Hologic (Third Wave Technologies) Invader Assay	14
Luminex Molecular Diagnostics (Tm Biosciences) Tag-It	9
Tepnel Diagnostics Elucigene Assay (CF-29, CF-30, or CF-4, CF-EU1)	4
Asuragen Signature CF 2.0	3
Abbott Laboratories	2
Amplification / gel electrophoresis	2*
In-house TaqMan allelic discrimination Assay	2
Sequencing	1*
Innogenetics Inno-LIPA	1
In-house PCR/Restriction fragment length polymorphism analysis	1
Allele-specific oligonucleotide PCR	1
In-house PCR with high resolution melt analysis	1*
Amplification/heteroduplex/restriction analysis	1
In-house single nucleotide polymorphism assay	1
Home-brew assay	1
In-house allele-specific hybridization	1
Matrix Assisted Laser Desorption /Ionization- Time Of Flight (MALDI-TOF) mass spectrometry	1
PCR with Real Time Probe and Heteroduplex Analysis (F508del only)	1*
Not reported	1

*Assays used in addition to another method listed.

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QUARTER 1 – FEBRUARY 2010

SPECIMEN CERTIFICATION

Specimen	Allele 1 (Colloquial name)	Allele 2 (Colloquial name)	Allele 1 (Standard name)	Allele 2 (Standard name)	Expected Clinical Assessment
10C1	Wild type	Wild type	Wild type	Wild type	1
10C2	F508del	Wild type	p.F508del	Wild type	3
10C3	Wild type	Wild type	Wild type	Wild type	1
10C4	2184delA	394delTT	c.2052delA	c.262_263delTT	2
10C5	Wild type	Wild type	Wild type	Wild type	1

1 = screen negative (normal) 2 = likely cystic fibrosis positive 3 = likely cystic fibrosis carrier

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

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

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Newborn Screening and Molecular Biology Branch

Carla Cuthbert, Ph.D.

Chief Emeritus

Newborn Screening and Molecular Biology Branch

W. Harry Hannon, Ph.D.



Contributors: Barbara W. Adam
Carol Bell
Dana Chafin
Paul Dantonio
Victor R. De Jesus, Ph.D.
Marie C. Earley, Ph.D.
Elizabeth M. Hall
L. Omar Henderson, Ph.D.
Sharon Kerr
Francis Lee, Ph.D.
Lixia Li, Ph.D.
Timothy Lim, Ph.D.
Zuzheng (Roy) Luo
Joanne Mei, Ph.D.
Nancy Meredith
Hien Nguyen
Shannon O'Brien
David Simms
Sherri Stevens
Robert Vogt, Ph.D.
Golriz Yazdanpanah
Hui Zhou, Ph.D.

Production: Sarah Brown
Felicia Manning
Teresa Moore
Connie Singleton



ASSOCIATION OF PUBLIC HEALTH LABORATORIES
SILVER SPRING, MD 20910

President

Susan U. Neill, Ph.D., M.B.A.

Chairman, Newborn Screening and Genetics in Public Health Committee

Cheryl Hermerath, M.B.A., DLM(ASCP), RM(NRCM)

Chairman, Newborn Screening Quality Assurance Quality Control Subcommittee

Gary Hoffman, B.S.

INQUIRIES TO:

Carol Bell, 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: CBell@cdc.gov