Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Mutation Detection Quarterly Report

Volume 1 No. 1

March 2007

INTRODUCTION

We initiated a new 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, 2007. 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 February 5, 2007, a panel of ten unknown dried-blood-spot (DBS) specimens was distributed to 13 laboratories in the United States and 16 laboratories in other countries to detect mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene.

PARTICIPANTS' RESULTS

We distributed three types of DBS specimens in this panel. Five specimens were prepared from adult CF patients (specimens 17C1, 17C3, 17C4, 17C9, and 17C10). Two specimens were prepared from an adult donor who screened negative for 31 common CFTR mutations ("wild type" specimens 17C5 and 17C7). Three specimens were prepared by adding Epstein-Barr virus-transformed lymphoblastoid cell lines homozygous or heterozygous for the ΔF508 (p.F508del) mutation in a human whole blood matrix (specimens 17C2, 17C6, and 17C8).

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 "unknown" or "normal" is acceptable. A specimen is considered not evaluated when one 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 22 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. Four laboratories used Tm Biosciences Tag-It kit, 4 used Tepnel Diagnostics Elucigene Assays, 2 used Third Wave Technologies Invader assay, 2 used Innogenetics Inno-Lipa assay, 1 used Abbott Diagnostics Oligonucleotide Ligation assay, 1 used Roche Diagnostics Linear Array, 1 used Assuragen Signature CF 2.0, 1 used a home brew method, 1 used an unspecified in-house assay, 1 used an in-house TaqMan Allelic Discrimination assay, 1 used an in-house hydrolysis probe assay, 1 used an in-house single nucleotide polymorphism assay, 1 used matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF), and 1 used an amplification/gel electrophoresis assay. In addition, three laboratories screened specimens for 1-4 mutations and if a mutation was present, continued testing with an expanded panel. The smallest panel consisted of three mutations. Laboratories were not asked to report the maximum number of mutations that could be detected. Overall, incorrect clinical assessments were reported for specimens 17C2, 17C4, and 17C6. Sample failures were reported by one laboratory for specimen 17C2, one laboratory for specimen 17C5, four laboratories for specimen 17C6, three laboratories for specimen 17C8 and one laboratory for specimen 17C10.❖

The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis Mutation Detection PT specimens on April 2, 2007.❖

ACKNOWLEDGEMENTS

We would like to thank Philip Farrell, M.D., Ph.D. (University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin) and the collection centers for their collaboration and efforts in this project. We would also like to thank the blood donors for participating. Without their contributions, this program would not be possible.❖

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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NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS MUTATION DETECTION PILOT SURVEY

QUARTER 1 – MARCH 2007

SPECIMEN CERTIFICATION

Specimen	Allele 1 (Colloquial name)	Allele 2 (Colloquial name)	Allele 1 (Standard name)	Allele 2 (Standard name)	Expected Clinical Assessment
17C1	G551D	R560T	p.G551D	p.R560T	2
17C2	ΔF508	ΔF508	p.F508del/	p.F508del	2
17C3	ΔF508	ΔF508	p.F508del/	p.F508del	2
17C4	ΔF508	3849+10kbC>T	p.F508del	c.3718-2477C>T	2
17C5	Normal	Normal	Normal	Normal	1
17C6	ΔF508	Normal	p.F508del/	Normal	3
17C7	Normal	Normal	Normal	Normal	1
17C8	ΔF508	ΔF508	p.F508del/	p.F508del	2
17C9	ΔF508	W1282X	p.F508del/	p.W1282X	2
17C10	3120+1G>A	S549N	c.2988+1G>A	p. S549N	2

1 = wild type (normal) 2 = cystic fibrosis positive 3 = cystic fibrosis carrier

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

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SUMMARY OF REPORTED GENOTYPES

Specimen Number	Genotypes	Frequency Distributions
17C1	G551D/R560T	15
	G551D/Unknown	4
	G551D/G551D*	1
	Unknown/Unknown	1
	No mutation detected	1
17C2	ΔF508/ΔF508	20
	ΔF508/unknown*	1
	Failed to amplify	1
17C3	ΔF508/ΔF508	22
17C4	ΔF508/3849+10kbC>T	16
	ΔF508/unknown	6
17C5	Wild type/Wild type	10
	Unknown/Unknown	6
	Normal/Normal	3
	Negative/Negative	1
	No detection	1
	No mutation	1

Specimen Number	Genotypes	Frequency Distributions
17C6	ΔF508/Wild type	9
	ΔF508/Unknown	5
	ΔF508/Normal	3
	ΔF508/ΔF508*	1
	Failed to amplify	3
	Unsuitable for testing	1
17C7	Wild type/Wild type	10
	Unknown/Unknown	6
	Normal/Normal	3
	Negative/Negative	1
	No detection	1
	No mutation	1
17C8	ΔF508/ΔF508	20
	Failed to amplify	1
	Unsuitable for testing	1
17C9	ΔF508/W1282X	15
	ΔF508/Unknown	5
	ΔF508/Normal	1
	ΔF508/G542X*	1
17C10	3120+1G>A/S549N	7
	3120+1G>A/Unknown	2
	3120+1G>A/Wild type	3
	Unknown/Unknown	4
	Normal/Normal	2
	Wild type/Wild type	1
	No mutation	1
	Failed to amplify	2

* Incorrect genotype.

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FREQUENCY OF REPORTED CLINICAL ASSESSMENTS

Specimen	Wild type (Normal)	Cystic Fibrosis Positive	Cystic Fibrosis Carrier	Sample Failure
17C1	2	16	4	0
17C2	0	20	1	1
17C3	0	22	0	0
17C4	0	16	6	0
17C5	22	0	0	0
17C6*	0	1	16	4
17C7	22	0	0	0
17C8	0	19	0	3
17C9	0	16	6	0
17C10	8	7	5	2

*One laboratory did not provide an assessment for this specimen.

LABORATORY METHODS

Method	Number of Laboratories
Tepnel Diagnostics Elucigene Assay (CF 29, CF-30, or CF-HT)	5
Tm Biosciences Tag-It	4
Third Wave Technologies Invader Assay	2
Innogenetics Inno-Lipa	2
Abbott Diagnostics Oligonucleotide Ligation assay	1
Roche Diagnostics Linear Array	1
Assuragen Signature CF 2.0	1
Home brew Assay	1
Unspecified in-house assay	1
In-house TaqMan Allelic Discrimination Assay	1
In-house single nucleotide polymorphism assay	1
Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry	1
Amplification / gel electrophoresis	1

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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