Newborn Screening Quality Assurance Program

PROFICIENCY TESTING — Cystic Fibrosis Quarterly Report

Volume 7 No. 1 — February 2008

INTRODUCTION

The Cystic Fibrosis (CF) proficiency testing (PT) report is the quarterly summary of all data reported within the specified data-reporting period for Quarter 1, 2008. The attached tables provide the certification profiles (Immunoreactive Trypsinogen and DNA) for the distributed specimens, the verification of your reported data, the statistical analysis of the quantitative data, and the frequency distributions summary for presumptive clinical (qualitative) assessments. We distribute this PT report to all participants, state laboratory directors, and program colleagues by request.

On January 14, 2008, a panel of five unknown dried-blood-spot (DBS) specimens enriched with predetermined concentrations of IRT was distributed to 40 laboratories in the United States and 74 laboratories in other countries.

PARTICIPANTS' RESULTS

We processed data from 96 participants. Laboratories were asked to report IRT results in ng/mL blood. For the statistical summary analysis, we did not include data that were outside the 99% confidence interval. There were 19 outliers for this survey. Results of our evaluation suggest that the endogenous level of IRT was less than 15 ng/mL blood.

Twenty-one laboratories reported using Delfia to measure IRT, 64 used AutoDelfia, 2 used MP Biomedicals, 5 used BioRad Quantase, 2 used Bioclone, and the remaining 2 reported using "other." The expected IRT values are based on CDC assayed values. IRT is stable in the dried blood matrix. Table 1 illustrates comparability of the recovery of IRT from each specimen by method.

Presumptive clinical classifications (qualitative assessments) may differ by participant because of specific assessment practices. When the reported clinical assessment differs from our expected clinical assessment, the grading algorithm is used to evaluate test performance. An explanation of the grading algorithm can be found on the NSQAP data-reporting Web site or in the annual summary report. Two reported clinical assessments, which were otherwise incorrect, were judged correct by this procedure. Overall, IRT participants reported one false-positive clinical assessment and three false-negative clinical assessments. Specimen 1885 was determined to be non-gradable and was not evaluated for IRT or DNA. Domestic and foreign laboratories reported various cutoffs for IRT. The median and mode cutoffs for domestic participants were 86.4 ng/mL blood and 62 ng/mL blood, respectively. The median and mode cutoffs for foreign participants were 67.2 ng/mL blood and 70 ng/mL blood, respectively.

We distributed a DBS prepared from blood of a ΔF508 carrier (specimen 1881) and a DBS prepared from blood of a ΔF508 homozygous CF patient (specimen 1883). These specimens were enriched with IRT to create proficiency testing materials that expressed both phenotype (elevated IRT) and genotype (ΔF508) for CF. Specimen 1885 was prepared using a human whole blood matrix and Epstein-Barr virus transformed lymphoblast cells that are homozygous for ΔF508.

Participants were asked to confirm specimens that screened IRT positive. Thirty-three laboratories reported DNA confirmatory results. Nine laboratories reported using Third Wave Technologies Inplex assay, 4 used Tm Biosciences Tag-It Cystic Fibrosis kit, 4 used Tepnel Diagnostics Elucigene assay, 3 used Innogenetics Inno-LiPA method, 3 used an in-house assay, 2 used PCR amplification of DNA, 1 used the Roche Linear Array, 1 used the Assuragen Signature CF assay, 1 used the Celera Diagnostics assay, 1 used an in-house TaqMan Allelic Discrimination assay, 1 used a fluorescent ARMS CF assay, 1 used a matrix assisted laser desorption/ionization time of flight mass spectrometry assay, 1 used a hydrolysis probe assay, and 1 did not specify the method used. One laboratory reported an incorrect clinical assessment for specimen 1883. Twenty-nine laboratories could not report data for specimen 1885 because of sample failure. As noted above, specimen 1885 was created in the laboratory. Although every effort is made to have constructed-specimens reflect a true newborn specimen as closely as possible, sample failures have been seen before with this type of specimen. We are continuing to evaluate our methods for preparing specimens to avoid amplification failures by participants. In the interim, we are relying more on actual-patient samples for this program.❖

The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis PT specimens on July 14, 2008.❖

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 : 770-488-4023
FAX: 770-488-4255
E-mail: CBell@cdc.gov

Editor: Carol Bell
Production: Connie Singleton
Sarah Brown

CDC — Centers for Disease Control and Prevention

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS PROFICIENCY TESTING

QUARTER I – FEBRUARY 2008

SPECIMEN CERTIFICATION

IRT

CDC ASSAYED LEVELS

Analyte	Specimen 1881	Specimen 1882	Specimen 1883	Specimen 1884	Specimen 1885
Immunoreactive Trypsinogen CDC Mean Assayed Value (ng/mL blood)	101.2 ±11.7	45.3 ± 4.4	116.6 ± 11.8	12.4 ± 0.8	105.1 ± 8.6

EXPECTED PRESUMPTIVE CLINICAL ASSESSMENTS

Disorder	Specimen 1881	Specimen 1882	Specimen 1883	Specimen 1884	Specimen 1885
Cystic Fibrosis	2	1	2	1	NE

1 = within normal limits 2 = outside normal limits NE = Not Evaluated assessment

DNA

CDC IDENTIFIED GENOTYPES

Analyte	Specimen 1881	Specimen 1882	Specimen 1883	Specimen 1884	Specimen 1885
DNA	ΔF508/ Wild Type	Wild Type/ Wild Type	ΔF508/ ΔF508	Wild Type/ Wild Type	ΔF508/ ΔF508

EXPECTED DNA CONFIRMED CLINICAL ASSESSMENTS

Analyte	Specimen 1881	Specimen 1882	Specimen 1883	Specimen 1884	Specimen 1885
Cystic Fibrosis	3	1	2	1	NE

1 = wild type (normal) 2 = cystic fibrosis positive 3 = cystic fibrosis carrier 4 = not tested

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CYSTIC FIBROSIS - IRT

QUARTER I - FEBRUARY 2008

OVERALL STATISTICS - IRT

Specimen	N*	Outliers	Mean	UL (95%)	LL (95%)
1881	92	4	115.5	153.6	77.3
1882	92	4	46.8	60.1	33.5
1883	92	4	167.3	217.9	116.8
1884	92	4	12.8	16.6	8.9
1885	92	3	95.6	119.7	71.6

* Outliers are not included in N. UL = upper limit LL = lower limit

FREQUENCY DISTRIBUTION OF PARTICIPANTS' CLINICAL ASSESSMENTS

Specimen	Within Normal Limits	Outside Normal Limits
1881	5	91
1882	95	1
1883	0	96
1884	96	0
1885	10	86

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CYSTIC FIBROSIS - IRT

QUARTER I - FEBRUARY 2008

IMMUNOREACTIVE TRYPSINOGEN BY METHOD

Table 1. Recovery of IRT (ng/mL blood) by method

Specimen No.	Specimen 1881	Specimen 1882	Specimen 1883	Specimen 1884	Specimen 1885
Expected Value	101.2	45.3	116.6	12.4	105.1
Method (N)					
Delfia (21)	99.1 ± 11.3	42.4 ± 7.2	144.7 ± 17.7	12.6 ± 1.9	91.5 ± 9.7
AutoDelfia (64)	121.0 ± 18.1	48.8 ± 5.3	174.4 ± 24.0	13.2 ± 2.9	97.1 ± 11.2
Bio-Rad Quantase (5)	122.4 ± 20.2	40.5 ± 3.5	184.4 ± 23.4	10.0 ± 0.3	94.9 ± 19.4
Other* (6)	106.4 ± 26.8	43.9 ± 13.1	158.2 ± 22.4	13.2 ± 3.8	95.1 ± 25.0

N = Number of observations Outliers not included in mean calculation.

*Methods with fewer than 3 users have been grouped into the "Other" category to avoid identifying individual laboratories.

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CYSTIC FIBROSIS - DNA

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SUMMARY OF PARTICIPANTS' GENOTYPES

Specimen	Genotype	N
1881	ΔF508/ ΔF508/Unknown ΔF508/Wild Type Not Tested	3 1 28 1
1882	Wild Type/Wild Type Not Tested	3 30
1883	ΔF508/ΔF508	33
1884	Wild Type/Wild Type Not Tested	1 32
1885	Wild Type/Wild Type Unknown/Unknown Sample Failed Not Tested	1 1 29 2

FREQUENCY DISTRIBUTION OF PARTICIPANTS' CLINICAL ASSESSMENTS

Specimen	Wild Type (Normal)	Cystic Fibrosis Positive	Cystic Fibrosis Carrier	Not Tested
1881	0	0	32	1
1882	3	0	0	30
1883	1	32	0	0
1884	1	0	0	32
1885	2	0	0	2

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
Julie Louise Gerberding, M.D., M.P.H.
Director
National Center for Environmental Health
Howard Frumkin, M.D., Dr.P.H., M.P.H.
Director
Division of Laboratory Sciences
Eric J. Sampson, Ph.D.
Chief
Newborn Screening and Molecular Biology Branch
W. Harry Hannon, Ph.D.

Contributors:
Barbara W. Adam
Carol Bell
Paul Dantonio
Victor De Jesus, Ph.D.
Rena Driscoll-Dunn
Marie C. Earley, Ph.D.
F. Hugh Gardner
L. Omar Henderson, Ph.D.
Meredith Kennedy
Sharon Kerr
Lixia Li, Ph.D.
Timothy Lim, Ph.D.
Elizabeth McCown
Joanne Mei, Ph.D.
Nancy Meredith
Shannon O'Brien
Sherri Stevens
Anand Swamy, Ph.D.
Robert Vogt, Ph.D.

Production:
Sarah Brown
Felicia Manning
Connie Singleton

ASSOCIATION OF PUBLIC HEALTH LABORATORIES
WASHINGTON, DC 20036-3320

President
Frances-Pouch-Downes, Dr.P.H.
Chairman, Newborn Screening and Genetics in Public Health Committee
Cheryl Hermerath, M.B.A., DLM(ASCP), RM(NRM)
Chairman, Newborn Screening Quality Assurance Subcommittee
John Sherwin, Ph.D.

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