
Newborn Screening Quality Assurance Program

Second-tier Congenital Adrenal Hyperplasia (CAH) Proficiency Testing Program (PT)

In co-sponsorship with Association of Public Health Laboratories (APHL)
Provided by the Newborn Screening and Molecular Biology Branch
Centers for Disease Control and Prevention
4770 Buford Highway NE, MS/F19
Atlanta, GA 30341-3724
Email: NSQAPDMT@cdc.gov

Quarterly Report
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Report Authorization

This report has been reviewed and authorized by Dr. Joanne Mei, Laboratory Chief, Newborn Screening Quality Assurance Program.

Confidentiality Statement

NSQAP participant information and evaluations are strictly confidential and shared only with individual participants, unless written authorization for release is received.

Introduction

This report summarizes data collected within the specified reporting period for the Quarter 1, 2019 Second-tier Congenital Adrenal Hyperplasia (CAH) Proficiency Testing (PT) Program event. Reports are distributed to all participants, state laboratory directors, and program colleagues by request. The tables within this report provide certification information for the PT specimen panel, statistical analysis for reported quantitative data, and the frequency distribution summaries for expected interpretations. An evaluation of your submitted data is attached to this summary.

Certification of PT Specimens

The dried blood spot (DBS) PT specimens were prepared at 50% hematocrit, with different enrichments of five biomarkers for congenital adrenal hyperplasia (CAH); 17 α -hydroxyprogesterone (17OHP), 4-androstenedione (4AD), cortisol (Cort), 11-deoxycortisol (11D), 21-deoxycortisol (21D). Expected values (sum of endogenous and enrichment values) were determined by EIA (17OHP only) and LC-MS/MS. For determination of the Clinical Assessment (CA) NSQAP applies the formula: clinical ratio = $([17OHP] + [4AD])/[CORT]$. A cutoff of 1.0 is used to assess whether the specimen is Within Normal Limits (1) or Outside Normal Limits (2).

Table 1. Expected Values (ng/mL serum) and Expected Clinical Assessments (CA)

Specimen	EIA 17OHP	EIA CA	LC- MS/MS 17OHP	LC- MS/MS 4AD	LC- MS/MS Cort	LC- MS/MS 11D	LC- MS/MS 21D	LC- MS/MS Clinical Rato	LC- MS/MS CA
119A1	41.2	2	51.5	26.5	101.5	11.5	1.5	0.8	1
119A2	79.2	2	91.5	37.5	21.5	6.5	41.5	6.0	2
119A3	81.3	2	91.5	37.5	21.5	6.5	41.5	6.0	2
119A4	82.4	2	81.5	26.5	121.5	21.5	1.5	0.9	1
119A5	8.4	1	11.5	21.5	41.5	51.5	11.5	0.8	1

1 = Within Normal Limits
 2 = Outside Normal Limits
 NE = Not Evaluated

Distribution of PT Specimens

On January 15, 2019, a PT panel of five DBS specimens was distributed eight domestic laboratories and 24 international laboratories.

Participant Results

Quantitative Data

We received results from 28 participants by the data reporting deadline. Laboratories were asked to report concentrations of 17OHP, 4AD, Cort, 11D and 21D analyzed by Second-tier tandem mass spectrometry (LC-MS/MS) and enzyme immunoassay (EIA) (optional). For the statistical summary analysis, we did not include data that were outside the 99% confidence interval.

All data are presented in units of ng/mL serum. Participants whose methods yield data in nM whole blood units were asked to multiply by the following factors for conversion to serum concentration: 0.66 (17OHP), 0.57 (4AD), 0.72 (CORT), and 0.69 (11D and 21D). Data that are not submitted in the requested units (ng/mL serum) are not accepted. Conversion factors are provided on the CAHPT Data Report Form.

Twenty-eight laboratories reported results using LC-MS/MS. Twenty laboratories reported EIA results. The expected analyte concentration values were based on CDC expected values. Overall statistics from EIA (Table 2) and LC-MS/MS (Tables 3a-b) methods were combined so as to not identify an individual laboratory.

Table 2. Overall statistics – 17OHP (ng/mL serum) by EIA

Specimen	N	Mean	SD
119A1	20	54.7	10.5
119A2	20	97.9	20.4
119A3	20	96.6	20.4
119A4	20	89.6	19.7
119A5	20	12.3	5.4

Table 3a. Overall statistics – 17OHP, 4AD, Cort, (ng/mL serum) by LC-MS/MS

Specimen	17OHP N	17OHP Mean	17OHP SD	4AD N	4AD Mean	4AD SD	Cort N	Cort Mean	Cort SD
119A1	28	58.11	16.1	28	26.67	6.2	28	117.59	23.8
119A2	28	100.63	20.0	28	44.81	12.0	28	25.09	7.7
119A3	28	101.87	20.8	28	45.37	11.0	28	25.17	6.7
119A4	28	93.34	22.5	28	28.80	7.7	28	144.94	42.2
119A5	24	13.51	5.9	24	21.03	5.1	24	45.56	13.8

Table 3b. Overall statistics –11D, 12D (ng/mL serum) by LC-MS/MS

Specimen	11D N	11D Mean	11D SD	21D N	21D Mean	21D SD
119A1	19	13.54	3.1	17	0.87	1.2
119A2	19	7.46	4.1	20	45.52	7.4
119A3	19	7.17	2.5	20	45.90	6.6
119A4	19	25.37	6.3	17	0.58	0.6
119A5	17	63.95	17.8	17	11.02	2.2

Qualitative Clinical Assessments

Qualitative assessments may differ by participant because of specific assessment practices. The frequency distribution of participants’ Clinical Assessments for screening results is shown in Table 4.

Most programs use a clinical ratio to determine if samples are normal or abnormal. Specimens with a calculated ratio less than the cutoff are considered “within normal limits”; those specimens with a calculated ratio greater than the cutoff are evaluated as “outside normal limits”. LC-MS/MS cutoff values are summarized in Table 5.

Table 4. Frequency Distribution of Participants’ Clinical Assessments (LC-MS/MS)

Specimen	Within Normal Limits (WNL)	Outside Normal Limits (ONL)	Not Reported
119A1	25	3	0
119A2	0	28	0
119A3	0	28	0
119A4	24	4	0
119A5*	21	6	1

*Specimen 119A5 was not evaluated due to lack of 80% consensus among reporting laboratories.

Table 5. LC-MS/MS Clinical Ratio Cutoff Values

Specimen	All Laboratories	Domestic	International
MEAN	1.68	1.05	1.96
MODE	1.00	1.00	1.00
MIN	0.10	0.90	0.10
MAX	9.00	1.40	9.00

Evaluations

Of the evaluated specimens, participants reported seven False-positive results and no False-negative results based on the LC-MS/MS final Clinical Assessment.

Specimen 119A5 was considered “not-evaluated” due to lack of 80% consensus among reporting laboratories.

Future Shipments

The Newborn Screening Quality Assurance Program will ship next quarter’s PT specimens for CAHPT on June 25, 2019.

Direct Inquiries

If you have any comments or questions about CAHPT MS/MS analysis, contact Dr. Joanne V. Mei at 770-488-7945 or by email at <mailto:jvm0@cdc.gov>

For data reporting questions, contact Irene Williams at nsqapdmt@cdc.gov

The content of this report may also be located on our website at:

https://www.cdc.gov/labstandards/nsqap_reports.html

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

Robert R. Redfield, M.D.

Director

National Center for Environmental Health

Patrick Breysse, 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

Carter Asef, BS

Nicole Baird, Ph.D

John Bernstein, MS

Quan Bui, MS

Suzanne Cordovado, Ph.D

Paul Dantonio, MS

Katherine Duneman, MS

Sharon Flores, MS

Christopher Greene, Ph.D

Elizabeth Hall, BS

Laura Hancock, MS

Christopher Haynes, Ph.D

Jessica Hendricks, MS

Miyono Hendrix, MS

Laura C. Hildreth, BS

Deborah Koontz, Ph.D

Francis Lee, Ph.D

LiXia Li, Ph.D

Tim Lim, Ph.D

Daniel Mandel, Ph.D

Joanne Mei, Ph.D

Kristina Mercer, Ph.D

Stanimila Nikolova, Ph.D

Gyliann Pena, BS

Kostas Petritis, Ph.D

C. Austin Pickens, Ph.D

Blanche Temate, Ph.D

E. Shannon Torres, Ph.D

Robert Vogt, Ph.D

Irene Williams, MS

Sophia Winchester, BS

Golriz Yazdanpanah, MS

Sherri Zobel, BS

Production

Vinay Anumula, MS

Kizzy Stewart

Joy Pressley

ASSOCIATION OF PUBLIC HEALTH LABORATORIES SILVER SPRING, MD 20910

President

Joanne Bartkus, PhD

Chairman, Newborn Screening and Genetics in Public Health Committee

Michele Caggana, Sc.D., FACMG

Chairman, Newborn Screening Quality Assurance Quality Control Subcommittee

Patricia R. Hunt, B.A. and Joseph Orsini, Ph.D.

Chairman, Newborn Screening Molecular Subcommittee

Rachel Lee, Ph.D.

INQUIRIES TO:

Irene Williams, Editor

Centers for Disease Control and Prevention (CDC), Newborn Screening Quality Assurance Program

Mailstop F-24, 4770 Buford Highway, N.E., Atlanta, GA 30341-3724

E-mail: NSQAPDMT@cdc.gov