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
Volume 9, No. 3
Issued: August 28, 2019

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 3, 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
319A1	8.9	1	11.5	21.5	41.5	51.5	1.5	0.8	1
319A2	53.5	2	51.5	26.5	101.5	11.5	1.5	0.8	1
319A3	8.5	1	11.5	21.5	41.5	51.5	1.5	0.8	1
319A4	10.1	1	11.5	21.5	41.5	51.5	11.5	0.8	1
319A5	11.1	1	11.5	21.5	41.5	51.5	1.5	0.8	1

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

Distribution of PT Specimens

On June 25, 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 29 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
319A1	20	9.4	3.1
319A2	20	50.7	8.5
319A3	20	8.7	2.4
319A4	20	10.0	3.1
319A5	20	9.8	3.8

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
319A1	25	12.7	6.1	25	21.5	5.1	25	44.8	10.4
319A2	28	57.0	10.3	28	25.6	6.3	28	115.0	22.4
319A3	24	10.6	1.8	24	21.5	5.0	24	43.9	8.5
319A4	24	13.8	10.2	24	21.8	6.2	24	42.2	7.6
319A5	24	11.8	3.0	24	23.0	6.0	24	45.2	8.9

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
319A1	19	56.6	16.2	18	1.1	1.8
319A2	21	15.1	11.3	19	0.9	1.3
319A3	19	56.3	15.0	17	1.25	2.6
319A4	19	64.1	16.9	19	10.6	2.5
319A5	19	57.1	13.5	17	0.9	1.6

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
319A1	27	1	1
319A2	24	4	1
319A3	25	2	2
319A4*	16	11	2
319A5	25	2	2

*Specimen 319A4 was not evaluated due to lack of 80% consensus of reporting laboratories.

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

Specimen	All Laboratories	Domestic	International
MEAN	1.7	1.1	2.0
MODE	1.0	1.0	2.5
MIN	0.1	0.9	0.1
MAX	9.0	1.4	9.0

Evaluations

Of the evaluated specimens, participants reported nine misclassifications based on the LC-MS/MS final Clinical Assessment.

Future Shipments

The Newborn Screening Quality Assurance Program will ship next quarter's PT specimens for CAHPT on September 24, 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, AS

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