

Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Second Tier LC-MS/MS CAH
Quarterly Report

Volume 6, No. 1

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INTRODUCTION

This report is the quarterly summary of all data reported within the specified data-reporting period for Quarter 1, 2016. The attached tables provide the certification profiles for the distributed specimens, the verification of your reported data, the statistical analysis of the quantitative data, and the frequency distribution summaries for expected interpretations. We distribute this proficiency testing (PT) report to all participants, and program colleagues by request.

On January 11, 2016 a panel of five unknown dried blood spot (DBS) specimens prepared with different enrichments of five biomarkers for congenital adrenal hyperplasia (CAH) was distributed to six domestic laboratories and fifteen international laboratories. DBS specimens were prepared at 50% hematocrit.

We processed data from 18 participants. Laboratories were asked to report concentrations of 17-hydroxyprogesterone (17-OHP), 4-androstenedione (4AD), cortisol, 11-deoxycortisol and 21-deoxy-cortisol results in ng/mL serum. For the statistical summary analysis, we did not include data that were outside the 99% confidence interval.

Eighteen laboratories reported results using tandem mass spectrometry (LC-MS/MS). Twelve of these labs also reported enzyme immunoassay (EIA) results. The expected analyte concentration values were based on CDC expected values. Overall statistics from EIA (Table 1) and LC-MS/MS (Table 2) methods were combined so as to not identify an individual laboratory.

The frequency distribution of participants' interpretations for screening results is shown in Table 3; your laboratory's interpretations are shown on the Specimen Certification page.

Most programs use a clinical ratio to determine if samples are normal or abnormal. NSQAP uses the formula: $\text{clinical ratio} = ([17\text{-OHP}] + [4\text{-AD}]) / [\text{CORT}]$. Samples with a calculated ratio less than the clinical ratio are considered "normal"; those samples with a calculated ratio greater than the clinical ratio are evaluated as "abnormal." Observations on participant reported LC-MS/MS cutoff values are shown in Table 4.

Expected interpretations (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. For this event, we provided one unenriched sample, 116A5, resulting in artificially high clinical ratios. Because of this artifact, the sample was not evaluated. Overall, participants reported five False-positive and no False-negative results.

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 (17-OHP), 0.57 (4-AD), 0.72 (cortisol), and 0.69 (11- and 21-deoxycortisol). In order to expedite the issuance of this report, data that are not submitted in the requested units (ng/mL serum) will not be accepted. Conversion factors are provided on the Second Tier CAH PT Data Report Form.

NSQAP will ship the next Second Tier Congenital Adrenal Hyperplasia PT specimens on July 11, 2016. If you have any comments or questions about CAH LC-MS/MS quality assurance issues, contact Dr. Joanne V. Mei at 770-488-7945, by fax at 770-488-7459, or by e-mail at jvm0@cdc.gov. ❖

CDC/APHL

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Table 1. Overall Statistics for 17-Hydroxyprogesterone by EIA.

OVERALL STATISTICS - 17-HYDROXYPROGESTERONE (ng/mL Serum)

EIA SCREENING RESULTS

Specimen	N	Mean	SD	%CV
116A1	12	93.59	14.40	15.38
116A2	12	87.28	17.82	20.42
116A3	12	10.32	1.91	18.47
116A4	12	45.83	8.68	18.93
116A5	11	0.49	0.35	71.16

Table 2. Overall Statistics for 17-Hydroxyprogesterone, 4-Androstenedione, Cortisol, 11-Deoxycortisol and 21-Deoxycortisol by LC-MS/MS.

2a. OVERALL STATISTICS - 17-HYDROXYPROGESTERONE (ng/mL Serum)

LC-MS/MS SCREENING RESULTS

Specimen	N	Mean	SD	%CV
116A1	17	91.51	22.32	24.39
116A2	17	93.99	27.97	29.75
116A3	14	11.73	5.54	47.20
116A4	17	47.80	18.39	38.46
116A5	10	0.96	1.02	106.67

2b. OVERALL STATISTICS - 4-ANDROSTENEDIONE (ng/mL Serum)

LC-MS/MS SCREENING RESULTS

Specimen	N	Mean	SD	%CV
116A1	17	42.12	13.85	32.89
116A2	17	42.20	13.90	32.95
116A3	14	20.99	8.17	38.95
116A4	17	24.36	9.51	39.02
116A5	10	1.87	4.01	214.63

**2c. OVERALL STATISTICS - CORTISOL (ng/mL Serum)
LC-MS/MS SCREENING RESULTS**

Specimen	N	Mean	SD	%CV
116A1	17	19.92	6.08	30.53
116A2	17	19.12	3.91	20.44
116A3	14	38.15	10.20	26.74
116A4	17	89.75	19.98	22.26
116A5	10	2.07	2.63	127.04

**2d. OVERALL STATISTICS - 11-DEOXYCORTISOL (ng/mL Serum)
LC-MS/MS SCREENING RESULTS**

Specimen	N	Mean	SD	%CV
116A1	10	14.21	9.23	64.93
116A2	10	16.29	12.39	76.05
116A3	9	5.69	2.74	48.07
116A4	10	4.87	1.92	39.39
116A5	6	1.59	2.41	151.31

**2e. OVERALL STATISTICS - 21-DEOXYCORTISOL (ng/mL Serum)
LC-MS/MS SCREENING RESULTS**

Specimen	N	Mean	SD	%CV
116A1	10	9.55	2.29	24.00
116A2	10	10.52	2.72	25.81
116A3	6	1.36	2.35	173.79
116A4	5	0.40	0.51	125.76
116A5	5	0.47	0.38	82.21

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Table 3. Frequency Distribution of Participant's Final Interpretations
LC-MS/MS METHOD

Specimen	Within Normal Limits (WNL)	Outside Normal Limits (ONL)
116A1	0	18
116A2	0	18
116A3*	13	2
116A4	15	3
116A5**	NE	NE

*Three participants did not report an LC-MS/MS assessment.

**Specimen was Not Evaluated

Table 4. Frequency of LC-MS/MS Clinical Ratio Cutoff Values

	All Laboratories	Domestic	International
MEAN	1.9	1.7	2.0
MODE	2.5	1.0	2.5
MIN	0.2	1.0	0.2
MAX	5.9	2.5	5.9

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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