Newborn Screening Quality Assurance Program X-linked Adrenoleukodystrophy in Dried Blood Spots Proficiency Testing Program (XALDPT)

In co-sponsorship with Association of Public Health Laboratories (APHL)
Provided by the Newborn Screening and Molecular Biology Branch
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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 period for Quarter 1, 2020, for the detection of X-ALD by analysis of the biomarkers 24:0-Lysophosphatidylcholine (24LPC) and 26:0-Lysophosphatidylcholine (26LPC) in dried blood spots (DBS). It is distributed to all participants, state laboratory directors, and program colleagues by request. The tables within this report provide certification profiles for the distributed specimens, statistical analysis of participant quantitative data, and frequency of clinical assessments. An evaluation of your laboratory's data is attached to this summary.

Certification of PT Specimens

DBS specimens were prepared from Type A+ human whole blood, which was adjusted to a hematocrit of 50 ± 1% and enriched with the biomarkers 24LPC and 26LPC. Expected values for each were determined by LC-MS/MS in units of µmol/L blood. Clinical assessments were based on the NSQAP cut-off of 0.47 µmol/L blood for 24LPC and 0.39 µmol/L blood for 26LPC. Table 1 shows the NSQAP expected values and clinical assessments for each specimen.

Table 1. Expected Values – 24LPC and 26LPC (µmol/L blood)

Specimen	Expected 24LPC	24LPC Assessment Code*	Expected 26LPC	26LPC Assessment Code*
2010201	0.20	1	0.05	1
2010202	1.10	2	0.95	2
2010203	0.20	1	0.05	1
2010204	0.20	1	0.05	1
2010205	0.20	1	0.05	1

*1 = Within Normal Limits
2 = Outside Normal Limits

Distribution of PT Specimens

On January 14, 2020 a PT panel of five unknown DBS specimens was distributed to 19 domestic laboratories and 11 foreign laboratories.

Participant Results

Quantitative Data

We processed data from 23 participants, with one participant submitting two method assessments. Laboratories were asked to report concentrations of 24LPC and 26LPC results in µmol/L blood. Data not submitted in the requested units were not accepted. The conversion factor from µg/mL to µmol/L blood is provided on the XALDPT Data Report Form.

Overall statistics from MS/MS methods were combined so as to not identify an individual laboratory. We also did not include data that were outside the 99% confidence interval. The statistical summary analysis for all methods is provided in Tables 2a-b.

Beginning this quarter, partcipants had the option of reporting 24LPC and 26LPC results for both first-tier and second-tier assessment schemes. For 24LPC, fifteen participants submitted quantitative results, and two of those did not report a clinical assessment. Twenty-three participants reported quantitative results and clinical assessments for 26LPC. A variety of method combinations were reported across all participants, which are shown in Table 3. Tables 4a-c show the cutoff statistics for 24LPC and 26LPC by method. One participant reported cutoffs for 24LPC and 26LPC using multi-variate analysis by a post-analytic tool and 2nd tier testing when indicated. The frequency distribution of clinical assessments is shown in Tables 5a-b.

Table 2a. Screening Results for 24LPC– All MS/MS Methods

Specimen	N 1st Tier	Mean 1st Tier (µmol/L)	SD 1st Tier	N 2nd Tier	Mean 2nd Tier (µmol/L)	SD 2nd Tier
2010201	15	0.22	0.13	6	0.13	0.06
2010202	15	0.85	0.32	7	0.79	0.31
2010203	15	0.22	0.13	6	0.15	0.07
2010204	15	0.30	0.33	6	0.14	0.08
2010205	15	0.23	0.17	6	0.13	0.07

Table 2b. Screening Results for 26LPC – All MS/MS Methods

Specimen	N 1st Tier	Mean 1st Tier (µmol/L)	SD 1st Tier	N 2nd Tier	Mean 2nd Tier (µmol/L)	SD 2nd Tier
2010201	22	0.22	0.16	7	0.08	0.07
2010202	22	1.09	0.38	14	0.92	0.20
2010203	22	0.21	0.16	7	0.08	0.06
2010204	22	0.29	0.32	7	0.08	0.08
2010205	22	0.22	0.15	7	0.09	0.08

Table 3. Method Algorithms for Reported by ≥2 Participating Laboratories

1st Tier Method	2nd Tier Method	Number of Labs
FIA-MS/MS non-derivitized non-kit	LC-MS/MS positive ion mode	3
LC-MS/MS positive ion mode	LC-MS/MS positive ion mode	2
LC-MS/MS negative ion mode	NA	4
Non-derivatized MS/MS Neobase™2 PerkinElmer	LC-MS/MS positive ion mode	3
Non-derivatized MS/MS Neobase™2 PerkinElmer	LC-MS/MS negative ion mode	3
Non-derivatized MS/MS Neobase™2 PerkinElmer	NA	3
FIA-MS/MS derivatized non-kit	LC-MS/MS positive ion mode	2

Table 4a. Analyte Cutoffs Statistics by Method - 24LPC (µmol/L)*

Method	N	Mean	SD	Median	Range
FIA-MS/MS non-derivitized non-kit	2	0.50	0.14	0.50	0.40 – 0.60
LC-MS/MS positive ion mode	4	0.40	0.14	0.40	0.25 – 0.55
Non-derivatized MS/MS Neobase™2 PerkinElmer	6	0.91	0.45	0.88	0.25 – 1.65

Table 4b. Analyte Cutoffs Statistics by Method - 26LPC (µmol/L)*

Method	N	Mean	SD	Median	Range
FIA-MS/MS non-derivitized non-kit	3	0.39	0.19	0.36	0.22 – 0.60
LC-MS/MS positive ion mode	6	0.24	0.08	0.22	0.15 – 0.39
LC-MS/MS negative ion mode	3	0.22	0.15	0.16	0.12 – 0.39
Non-derivatized MS/MS Neobase™2 PerkinElmer	8	0.34	0.17	0.40	0.10 – 0.58

Clinical Assessments

Laboratories were asked to report qualitative results as “Within Normal Limits” or “Outside Normal Limits”. Qualitative assessments may differ because of specific assessment practices. The frequency distribution of participants’ clinical assessments is shown in Tables 5a-b.

Table 5a. Frequency Distribution of Clinical Assessments for 24LPC

Specimen	Within Normal Limits (WNL)	Outside Normal Limits (ONL)
2010201	13	0
2010202	2	11
2010203	13	0
2010204	12	1
2010205	13	0

Table 4b. Frequency Distribution of Reported Clinical Assessments for 26LPC

Specimen	Within Normal Limits (WNL)	Outside Normal Limits (ONL)
2010201	23	0
2010202	1	22
2010203	23	0
2010204	22	1
2010205	23	0

Evaluations

Overall, three misclassifications were reported for 24LPC. Two misclassifications were reported for 26LPC.

Future Shipments

The Newborn Screening Quality Assurance Program will ship next quarter's PT specimens on June 23, 2020.

Direct Inquiries

If you have any comments or questions about XALDPT MS/MS analysis, contact Dr. Christopher A. Haynes at 770-488-7019 or by e-mail at cph7@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.

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