Newborn Screening Quality Assurance Program
Lysosomal Storage Disorders
Proficiency Testing Program (LSDPT)

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 the Quarter 4, 2019, proficiency testing (PT) program for Lysosomal Storage Disorders (LSD) in dried blood spots (DBS) to detect Krabbe disease, Pompe disease and Mucopolysaccharidosis Type I (MPS-1). Reports are distributed to all participants, state laboratory directors, and program colleagues by request. The tables within this report provide certification profiles for the distributed specimens and a summary of submitted analytical and categorical results. An evaluation of your laboratory's data is attached to this summary.

Certification of PT Specimens

This panel of DBS specimens was prepared from human blood, including cord blood from unaffected individuals and leuko-depleted adult blood restored with lymphoblast cells derived from patients with LSD (specimens 419L1, 419L2, 419L3, 419L4, and 419L5). Table 1a shows the expected specimen values and clinical assessments for Galactocerebrosidase (GALC) for Krabbe disease, Acid Alpha-Glucosidase (GAA) for Pompe disease, and Alpha-L-Iduronidase (IDUA) for Mucopolysaccharidosis Type I (MPS-1) in whole blood. The expected values for GALC, GAA, and IDUA were based on NSQAP assayed values by FIA-MS/MS. Table 1b shows the expected specimen values for GAA and IDUA based on NSQAP assayed values by Digital Microfluidics (DMF).

Table 1a. Expected Values – GALC, GAA and IDUA (µmol/hr/L) by FIA-MS/MS

Specimen	Expected Value GALC	Krabbe Assessment Code*	Expected Value GAA	Pompe Assessment Code*	Expected Value IDUA	MPS-1 Assessment Code*
419L1	16.02	1	14.50	1	20.15	1
419L2	6.90	1	6.09	1	7.30	1
419L3	10.15	1	6.08	1	8.27	1
419L4	7.26	1	21.06	1	0.15	2
419L5	0.50	2	10.53	1	19.04	1

Table 1b. Expected Values – GAA and IDUA (µmol/hr/L) by DMF

Specimen	Expected Value GAA	Pompe Assessment Code*	Expected Value IDUA	MPS-1 Assessment Code*
419L1	61.92	1	62.23	1
419L2	27.25	1	28.95	1
419L3	26.18	1	30.66	1
419L4	75.35	1	3.57	2
419L5	27.96	1	48.90	1

*1 = No follow-up required (Screen Negative)
2 = Follow-up required (Screen Positive)
3 = Borderline

Distribution of PT Specimens

On September 24, 2019, a PT panel of five unknown DBS specimens was distributed to 24 domestic laboratories.

Participant Results

Quantitative Data

We processed data from 19 participants. Laboratories were asked to report quantitative results for GALC, GAA, and IDUA in µmol/hr/L. For GALC, two laboratories reported using LC-MS/MS, six used an FIA-MS/MS non-kit multiplexed enzyme reaction assay, and one used a fluorometric method. For GAA, two laboratories reported using LC-MS/MS, nine used an FIA-MS/MS non-kit multiplexed enzyme reaction assay, and seven reported using digital microfluidics. For IDUA, two laboratories reported using LC-MS/MS, nine reported using FIA-MS/MS non-kit multiplexed enzyme reaction, and seven reported using DMF. Cutoff information by method is provided in Table 2. Statistics for screening results for each analyte across all methods is provided in Tables 3a-c. Tables 4a-c show summary screening results sorted by method.

Table 2. Reported Cutoffs by Methods, where N ≥ 3 Participants

Cutoff	FIA MS/MS GALC	ALL GALC	FIA MS/MS GAA	DMF GAA	ALL GAA	FIA MS/MS IDUA	DMF IDUA	ALL IDUA
N	5	8	8	6	17	7	6	16
Mean (µmol/hr/L)	0.60	0.51	1.91	9.19	5.09	0.98	5.11	2.75
Median	0.55	0.50	1.92	9.55	2.10	1.02	5.00	1.91
Range	0.43 - 0.83	0.16 - 0.83	1.00 - 2.27	7.00 - 10.50	0.85 - 10.50	0.42 - 1.61	4.00 - 6.00	0.60 - 6.00

Table 3a. Screening Results for GALC — All methods

Specimen	N	Mean (µmol/hr/L)	SD
419L1	10	10.00	4.3
419L2	10	4.97	2.0
419L3	10	6.67	2.7
419L4	10	5.69	2.0
419L5	10	0.39	0.2

Table 3b. Screening Results for GAA – All methods

Specimen	N	Mean (µmol/hr/L)	SD
419L1	19	27.92	20.4
419L2	19	13.74	11.0
419L3	19	12.11	8.9
419L4	19	35.60	21.4
419L5	19	16.65	10.0

Table 3c. Screening Results for IDUA – All methods

Specimen	N	Mean (µmol/hr/L)	SD
419L1	19	30.70	19.9
419L2	19	14.35	9.9
419L3	19	15.05	10.8
419L4	19	1.77	2.3
419L5	19	29.56	16.3

Table 4a. Screening Results for GALC – by Method, where N ≥ 3 Participants

Specimen	FIA-MS/MS N	FIA-MS/MS Mean (µmol/hr/L)	FIA-MS/MS SD
419L1	6	12.73	1.9
419L2	6	6.29	0.7
419L3	6	8.45	1.1
419L4	6	6.93	1.3
419L5	6	0.47	0.2

Table 4b. Screening Results for GAA – by Method, where N ≥ 3 Participants

Specimen	FIA-MS/MS N	FIA-MS/MS Mean (µmol/hr/L)	FIA-MS/MS SD	DMF (SEEKER) N	DMF (SEEKER) Mean (µmol/hr/L)	DMF (SEEKER) SD
419L1	9	14.64	4.36	7	52.81	7.81
419L2	9	6.63	1.6	7	27.03	5.4
419L3	9	6.29	1.7	7	23.11	2.7
419L4	9	22.36	4.8	7	61.22	10.5
419L5	9	11.3	3.4	7	27.54	7.5

*99% outlier removed

Table 4c. Screening Results for IDUA– by Method, where N ≥ 3 Participants

Specimen	FIA-MS/MS N	FIA-MS/MS Mean (µmol/hr/L)	FIA-MS/MS SD	DMF (SEEKER) N	DMF (SEEKER) Mean (µmol/hr/L)	DMF (SEEKER) SD
419L1	9	16.90	3.0	7	54.74	10.1
419L2	9	7.36	1.38	7	26.81	1.9
419L3	9	7.39	1.02	7	28.74	2.0
419L4	9	0.36	0.5	7	4.28	1.8
419L5	9	20.11	3.5	7	48.41	14.4

Clinical Assessments

Laboratories were asked to report qualitative results as “No follow-up required (Screen Negative)” or “Follow-up required (Screen Positive)”. A “Borderline” assessment category is included to more accurately assess those labs that identify milder disease forms, carriers, or pseudo deficiencies. The frequency distribution of participants’ clinical assessments is shown in Tables 5a-c.

Table 5a. Frequency Distribution of Reported Clinical Assessments - GALC

Specimen	No follow-up required (Screen Negative)	Follow-up required (Screen Positive)
419L1	10	0
419L2	10	0
419L3	10	0
419L4	10	0
419L5	0	10

Table 5b. Frequency Distribution of Reported Clinical Assessments - GAA

Specimen	No follow-up required (Screen Negative)	Follow-up required (Screen Positive)
419L1	19	0
419L2	19	0
419L3	19	0
419L4	19	0
419L5	19	0

Table 5c. Frequency Distribution of Reported Clinical Assessments - IDUA

Specimen	No follow-up required (Screen Negative)	Follow-up required (Screen Positive)	Borderline
419L1	19	0	0
419L2	19	0	0
419L3	19	0	0
419L4	1	17	1
419L5	19	0	0

Evaluations

Overall participants, one misclassification was reported for IDUA (MPS-1).

Future Shipments

The Newborn Screening Quality Assurance Program will ship next quarter's LSDPT specimens on January 14, 2020.

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The content of this report may also be located on our website at: https://www.cdc.gov/labstandards/nsqap_reports.html

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