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

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 3, 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 319L1, 319L2, 319L3, 319L4, and 319L5). 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 in whole blood. The expected values 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*
319L1	0.47	2	10.73	1	20.82	1
319L2	2.94	1	0.38	2	3.50	1
319L3	5.04	1	5.18	1	15.12	1
319L4	4.72	1	8.89	1	7.92	1
319L5	16.80	1	5.94	1	6.64	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*
319L1	40.73	1	53.66	1
319L2	2.99	2	11.35	1
319L3	24.09	1	63.09	1
319L4	38.77	1	37.41	1
319L5	22.49	1	23.18	1

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

Distribution of PT Specimens

On June 25, 2019, a PT panel of five unknown DBS specimens was distributed to 21 domestic laboratories.

Participant Results

Quantitative Data

We processed data from twenty 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, eight used an FIA-MS/MS non-kit multiplexed enzyme reaction, and one used a fluorometric method. For GAA, two laboratories reported using LC-MS/MS, eleven used an FIA-MS/MS non-kit multiplexed enzyme reaction, five reported using digital microfluidics, and one used a fluorometric method. For IDUA, two laboratories reported using LC-MS/MS, eleven reported using FIA-MS/MS non-kit multiplexed enzyme reaction, five reported using digital microfluidics, and one used a fluorometric method. 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 result 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	6	9	9	4	16	11	4	16
Mean (µmol/hr/L)	0.78	0.63	2.04	8.41	3.83	1.14	5.17	2.39
Median	0.63	0.50	2.10	8.82	2.29	1.00	5.30	1.52
Range	0.44 -1.50	0.16 – 1.50	1.00-3.00	5.50-10.50	0.78 –10.50	0.31 -2.60	4.89 -6.00	0.31 – 6.00

Table 3a. Screening Results for GALC — All methods

Specimen	N	Mean (µmol/hr/L)	SD
319L1	11	0.32	0.12
319L2	11	2.22	0.80
319L3	11	3.06	1.37
319L4	11	3.38	1.37
319L5	11	11.71	5.19

Table 3b. Screening Results for GAA – All methods

Specimen	N	Mean (µmol/hr/L)	SD
319L1	20	16.02	8.12
319L2	19	2.06	5.52
319L3	20	9.92	6.77
319L4	20	16.90	11.48
319L5	20	10.97	7.90

Table 3c. Screening Results for IDUA – All methods

Specimen	N	Mean (µmol/hr/L)	SD
319L1	20	27.36	14.77
319L2	20	7.60	10.03
319L3	20	23.03	14.26
319L4	20	14.67	11.29
319L5	20	11.21	7.83

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

Specimen	FIA-MS/MS N	FIA-MS/MS Mean (µmol/hr/L)	FIA-MS/MS SD
319L1	8	0.37	0.10
319L2	8	2.60	0.47
319L3	8	3.65	0.82
319L4	8	4.05	0.71
319L5	8	14.17	2.56

Table 4b. Screening Results for GAA – by Method, where N $\geq$ 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
319L1	8	12.32	3.12	5	25.59	5.28
319L2	8	0.34	0.21	4*	2.27	0.17
319L3	8	6.04	1.16	5	18.56	3.11
319L4	8	10.37	2.20	5	31.37	6.92
319L5	8	6.64	1.34	5	22.17	4.95

*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
319L1	8	18.02	3.78	5	46.41	7.16
319L2	8	3.28	0.51	5	17.79	16.72
319L3	8	13.70	2.22	5	40.38	6.62
319L4	8	7.39	1.16	5	29.73	6.93
319L5	8	6.01	1.08	5	21.24	3.08

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)
319L1	0	11
319L2	11	0
319L3	11	0
319L4	11	0
319L5	11	0

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

Specimen	No follow-up required (Screen Negative)	Follow-up required (Screen Positive)
319L1	20	0
319L2	1	19
319L3	20	0
319L4	20	0
319L5	20	0

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

Specimen	No follow-up required (Screen Negative)	Follow-up required (Screen Positive)	Borderline
319L1	20	0	0
319L2	19	0	1
319L3	20	0	0
319L4	20	0	0
319L5	20	0	0

Evaluations

Overall participants, one misclassification was reported for GAA (Pompe).

Future Shipments

The Newborn Screening Quality Assurance Program will ship next quarter's LSDPT specimens on September 24, 2019.

Acknowledgements

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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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