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
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. 1
Issued: March 31, 2020

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 1, 2020, 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 2011301, 2011302, 2011303, 2011304, 2011305). Table 1a shows the expected specimen values and clinical assessments for Galactoceramidase (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 Assessmet Code*	Expected Value GAA	Pompe Assessment Code*	Expected Value IDUA	MPS-1 Assessme Code*
2011301	9.08	1	5.62	1	7.34	1
2011302	3.17	1	0.20	2	3.68	1
2011303	4.80	1	5.08	1	14.72	1
2011304	7.61	1	21.12	1	0.12	2
2011305	4.56	1	9.05	1	7.56	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*
2011301	27.16	1	30.93	1
2011302	2.46	2	13.23	1
2011303	22.97	1	50.30	1
2011304	67.54	1	4.06	2
2011305	40.32	1	25.76	1

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

Distribution of PT Specimens

On January 14, 2020, a PT panel of five unknown DBS specimens was distributed to 26 domestic laboratories.

Participant Results

Quantitative Data

We processed data from 21 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, seven 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, ten used an FIA-MS/MS non-kit multiplexed enzyme reaction assay, seven reported using digital microfluidics, one reported NeoLSD MS/MS, and one used a fluorometric method. For IDUA, two laboratories reported using LC-MS/MS, ten reported using FIA-MS/MS non-kit multiplexed enzyme reaction, seven reported using DMF, one reported NeoLSD MS/MS, and one used a fluorometric method. Cutoff information by method is provided in Table 2. Tables 3a-c show summary screening results sorted by method.

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

Cutoff	FIA MS/MS GALC	FIA MS/MS GAA	DMF GAA	FIA MS/MS IDUA	DMF IDUA
N	6	9	6	9	6
Mean (µmol/hr/L)	0.75	2.00	9.07	1.10	5.14
Median	0.64	2.10	9.10	1.11	5.00
Range	0.51 – 1.17	1.00 – 2.24	7.20 – 10.50	0.52 – 1.64	4.00 – 6.00

Table 3a. Screening Results for GALC

Specimen	FIA-MS/MS N	FIA-MS/MS Mean (µmol/hr/L)	FIA-MS/MS SD
2011301	7	7.26	3.01
2011302	7	2.50	0.96
2011303	7	3.37	1.42
2011304	7	6.17	2.36
2011305	7	3.66	1.49

Table 3b. 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
2011301	10	5.96	2.65	7	19.94	3.80
2011302	10	0.71	1.14	7	2.01	0.42
2011303	10	5.38	2.30	7	17.76	2.83
2011304	10	20.23	7.54	7	55.61	15.75
2011305	10	8.70	3.28	7	31.78	5.00

Table 3c. 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
2011301	10	6.20	2.41	7	26.94	3.23
2011302	10	3.04	1.16	7	9.52	1.37
2011303	10	11.88	4.34	7	43.43	4.97
2011304	10	0.20	0.18	7	3.65	0.42
2011305	10	6.22	2.25	7	26.62	2.13

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 4a-c.

Table 4a. Frequency Distribution of Reported Clinical Assessments - GALC

Specimen	No follow-up required (Screen Negative)	Follow-up required (Screen Positive)
2011301	10	0
2011302	10	0
2011303	10	0
2011304	10	0
2011305	10	0

Table 4b. Frequency Distribution of Reported Clinical Assessments - GAA

Specimen	No follow-up required (Screen Negative)	Follow-up required (Screen Positive)
2011301	21	0
2011302	1	20
2011303	21	0
2011304	21	0
2011305	21	0

Table 4c. Frequency Distribution of Reported Clinical Assessments - IDUA

Specimen	No follow-up required (Screen Negative)	Follow-up required (Screen Positive)	Borderline
2011301	21	0	0
2011302	21	0	0
2011303	21	0	0
2011304	0	19	2
2011305	21	0	0

Evaluations

Overall participants reported one Pompe (GAA) misclassification.

Future Shipments

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

Acknowledgements

We would like to thank Barbara Waters-Pick (Duke University Medical Center) for the supply of umbilical cord units.

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.

INQUIRIES TO:
Irene Williams, Editor
Centers for Disease Control and Prevention (CDC), Newborn Screening Quality Assurance Program
Mailstop F-19, 4770 Buford Highway, N.E., Atlanta, GA 30341-3724
E-mail: NSQAPDMT@cdc.gov