Status of Newborn Screening for Lysosomal Storage Disorders in Wisconsin

Technical Workshop on Methods to Detect Pompe Disease and other Lysosomal Storage Disorders (LSDs) by Newborn Bloodspot Screening

Atlanta, Georgia

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Relevant Facts

- NIH funded Pompe NBS pilot study
- NBS for six LSD bill was introduced
  - Krabbe, Fabry, Pompe, Niemann–Pick, Gaucher, and MPS I
- Possibility of implementing routine NBS for Pompe
  - Secretary's letter regarding Pompe recommendation to the RUSP
  - The Newborn Screening Saves Lives Reauthorization Act

Pompe DMF Assay Validation

Analytic Accuracy: Manufacturer QC Samples

- All 120 QCL data points were within 3 SD of the manufacturer provided range.
- One in total 120 QCH data points exceeded upper 3 SD of the manufacturer provided range by 2%
- One in total 96 QCM data points was below lower 3 SD of the manufacturer provided range by 4%

Pompe DMF Assay Validation

Analytic Precision

	Manufacturer QC Samples				CDC QC Samples		
	QCL	QCM	QCH		QCL	QCM	QCH
CV 1 - 5%	6	14	6		9	15	20
CV 5.1 - 10%	14	10	15		10	8	3
CV 10.1- 15 %	4	0	3		3	1	1
CV 15.1 - 20%	0	0	0		2*	0	0
Total	24	24	24		24	24	24

* 15. 02% and 16.22%

Pompe DMF Assay Validation

Analytic Reproducibility

	Manufacturer QC Samples				CDC QC Samples		
	QCL	QCM	QCH		QCL	QCM	QCH
CV 1 - 5%	2	0	1		1	1	1
CV 5.1 - 10%	3	4	5		2	4	1
CV 10.1- 15 %	1	2	0		2	2	4
CV 15.1 - 20%	0	0	0		1*	0	0
Total	6	6	6		6	6	6

* 15.75%

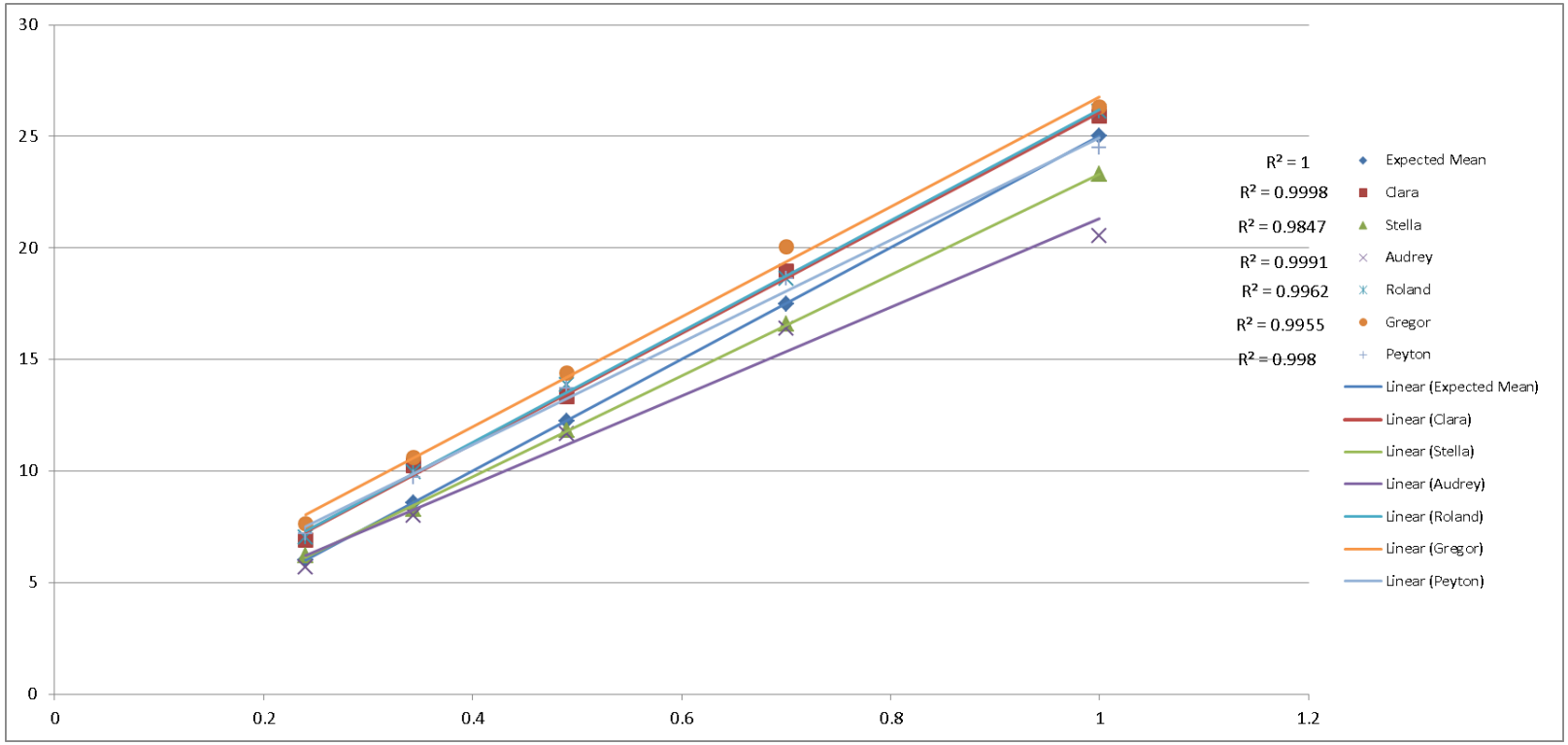
Pompe DMF Assay Validation

Instrument Comparison

	Manufacturer QC Samples				CDC QC Samples		
	QCL	QCM	QCH		QCL	QCM	QCH
Stella	3.64	14.18	25.05		2.43	15.92	25.97
Audrey	3.36	13.44	24.34		2.98	16.99	29.28
Roland	3.52	14.42	25.87		3.02	17.89	30.06
Gregor	3.80	15.03	26.73		2.99	17.85	29.68
Peyton	3.48	14.36	26.06		2.93	16.06	26.54
Clara	3.39	13.04	24.47		2.45	15.99	27.25
Mean	**3.53**	**14.08**	**25.42**		**2.80**	**16.78**	**28.13**
SD	**0.17**	**0.72**	**0.95**		**0.28**	**0.87**	**1.60**
CV (%)	**4.71**	**5.11**	**3.74**		**10.10**	**5.16**	**5.68**

Pompe DMF Assay Validation

Analytic Linearity



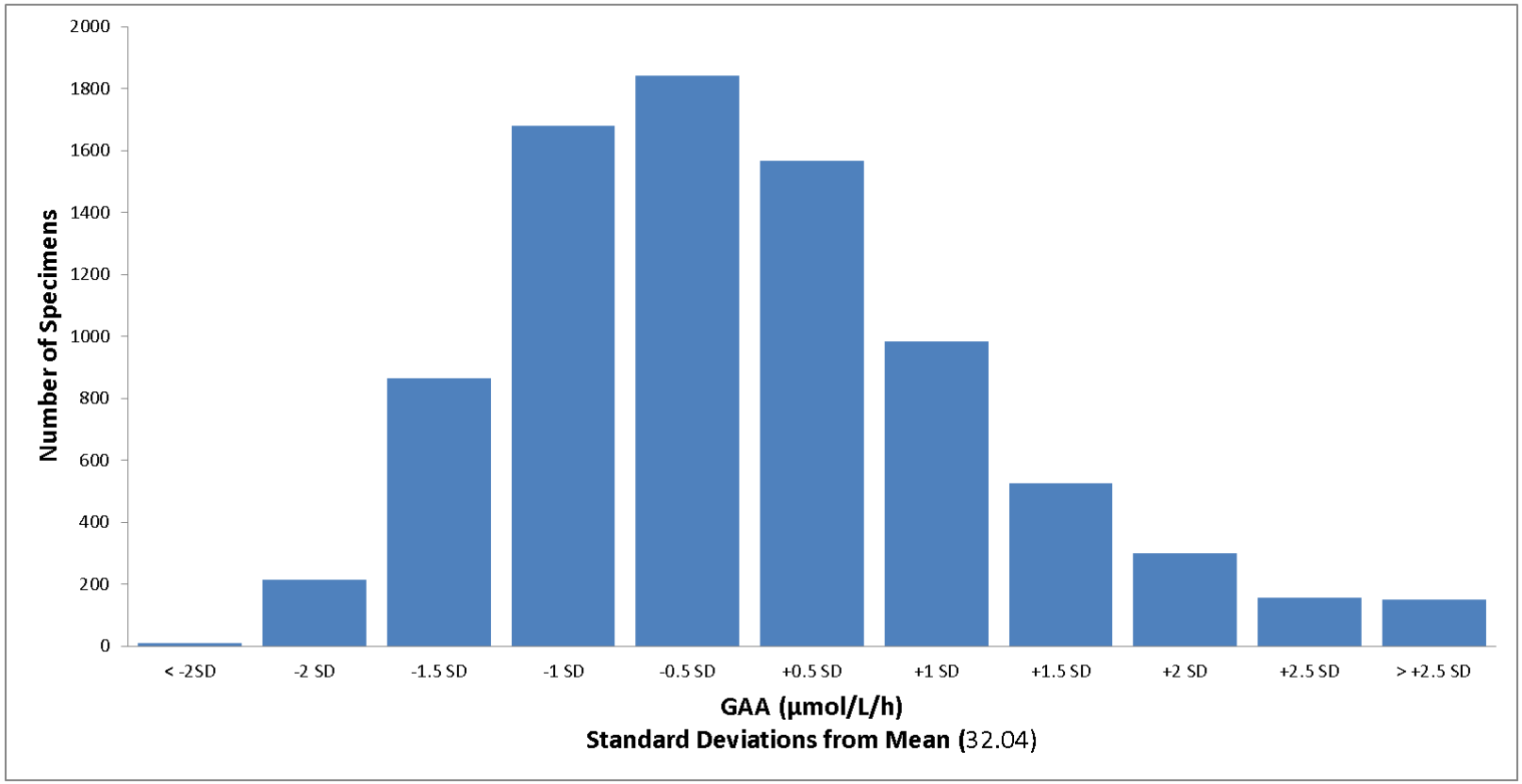
Pompe DMF Assay Validation

Normal Range Study

- Total 8,315 de-identified residual NBS specimens.
- Eight samples were deemed assay failure
- The sample mean is 32.04, and the sample median is 30.6
- 12 sample with GAA less than 7.1 (0.4 – 6.9)

Pompe DMF Assay Validation

Normal Range Study



Pompe DMF Assay Validation

Clinical Validity

ID	WI GAA	MO GAA	MO GAA at Date of Reported	Confirmatory Result	Initial Assessment
MO 31	26.69	23.23	NA	Normal	likely in-range
MO 37	31.40	28.94	NA	Normal	likely in-range
MO 28	11.63	10.09	NA	Normal	likely in-range
MO 10	15.28	16.88	NA	Normal	likely in-range
MO 26	21.32	18.86	NA	Normal	likely in-range
MO 32	24.36	20.24	NA	Normal	likely in-range
MO 21	21.53	22.22	NA	Normal	likely in-range
MO 24	24.95	24.24	NA	Normal	likely in-range
MO 14	28.44	25.06	NA	Normal	likely in-range
MO 34	31.10	28.75	NA	Normal	likely in-range
MO 18	35.75	31.11	NA	Normal	likely in-range
MO 19	38.57	36.59	NA	Normal	likely in-range
MO 15	45.52	46.5	NA	Normal	likely in-range

Pompe DMF Assay Validation

Clinical Validity

ID	WI GAA	MO GAA	MO GAA at Date of Reported	Confirmatory Result	Initial Assessment
MO 23	3.48	3.66	5.13	Pompe, classical infantile	re-testing in duplicates, likely out-of-range
MO 8	5.43	5.64	4.43	Pompe, classical infantile	re-testing in duplicates, likely out-of-range
MO 11	6.54	5.28	5.55	Pompe, nonclassical infantile	re-testing in duplicates, likely out-of-range

Pompe DMF Assay Validation

Clinical Validity

ID	WI GAA	MO GAA	MO GAA at Date of Reported	Confirmatory Result	Initial Assessment
MO 25	5.96	4.88	5.2	Pompe, late onset	re-testing in duplicates, likely out-of-range
MO 12	6.81	5.16	6.44	Pompe, late onset	re-testing in duplicates, likely out-of-range
MO 6	6.38	5.63	5.22	Pompe, late onset	re-testing in duplicates, likely out-of-range
MO 17	5.58	5.75	5.81	Pompe, late onset	re-testing in duplicates, likely out-of-range
MO 35	7.05	6.01	6.81	Pompe, late onset	re-testing in duplicates, uncertain
MO 9	7.49	6.11	6.49	Pompe, late onset	re-testing in duplicates, uncertain
MO 27	7.10	6.2	5.86	Pompe, late onset	re-testing in duplicates, uncertain

Pompe DMF Assay Validation

Clinical Validity

ID	WI GAA	MO GAA	MO GAA at Date of Reported	Confirmatory Result	Initial Assessment
MO 3	5.56	4.78	3.83	Pompe, w/ unknown significance genotype	re-testing in duplicates, likely out-of-range
MO 13	7.77	7.6	6.56	Pompe, w/ unknown significance genotype	likely in-range
MO 20	6.10	5.08	6.1	Pompe, unknown onset	re-testing in duplicates, likely out-of-range

Pompe DMF Assay Validation

Clinical Validity

ID	WI GAA	MO GAA	MO GAA at Date of Reported	Confirmatory Result	Initial Assessment
MO 22	5.03	3.97	5.53	Pseudodeficiency	re-testing in duplicates, likely out-of-range
MO 38	6.73	4.15	3.8	Pseudodeficiency	re-testing in duplicates, uncertain
MO 29	6.42	3.99	4.5	Pseudodeficiency	re-testing in duplicates, likely out-of-range
MO 30	6.80	6	6.33	Pseudodeficiency	re-testing in duplicates, likely out-of-range

Pompe DMF Assay Validation

Clinical Validity

ID	WI GAA	MO GAA	MO GAA at Date of Reported	Confirmatory Result	Initial Assessment
MO 33	5.10	4.63	4.19	Pompe carrier	re-testing in duplicates, likely out-of-range
MO 16	8.90	8.37	6.71	Pompe carrier	likely in-range

Acknowledgements

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