



Wisconsin Division of Public Health  
Newborn Screening Advisory Metabolic Subcommittee Meeting  
**Friday, October 13, 2017**  
**WI State Lab of Hygiene – Ag Drive**  
**10am – 2pm**  
Minutes

Meeting Attendees:					
x	Dr. Mei Baker	x	Dr. Gary Kirk	x	Dr. Greg Rice
	Linda Beischel	x	Jessica Kopesky	x	Dana Schippman
x	Beth Beyer		Jessica Krause	x	Dr. Jessica Scott-Schwoerer
x	Therese Breunig	x	Ashley Kuhl	x	Dr. Robert Steiner
	Erin Cronn		Gina Lewis		Vicky Tiberi
x	Nicoletta Drillias		Haley Lynn	x	Tammi Timmler
x	Dr. Patrice Held	x	Emily Moe		Erica Walters
x	Sonja Henry		Lisa Oernalte	x	Amy White
x	Tami Horzewski	x	Stephanie Offord		Dr. Samuel Yang
x	Kate Johnson	x	Matt Rasberry		Linda Yim-Drouin
		x	Dr. William Rhead		



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**Purpose of Meeting:**

The Metabolic Subcommittee serves in an advisory capacity to the Umbrella Committee and NBS Program regarding the specific screening-related condition(s) in the following areas:

**Expert Knowledge in Condition-Specific Clinical Care and Research**

- Advises on condition-specific clinical care including ongoing changes in treatment options for affected individuals, emerging newborn screening technology, and condition-specific research.

**Quality Assurance**

- Reviews de-identified screening and confirmatory testing data to monitor screening test performance, such as screening positive predictive value, screening false positive rate and false negative rate.
- Recommends changes in NBS practice to the Umbrella Committee and NBS Program.

**Education for Families and Providers**

- Reviews and provides feedback on information and education materials for general public, families, and providers to assure accuracy of health information related to the specific condition(s).

**Addition/Deletion of Conditions**

- Recommends and/or reviews nominations for addition and deletion of conditions related to the subcommittee

Facilitator/Chair: \_\_\_\_\_ Dr. Greg Rice \_\_\_\_\_ Recorder: \_\_\_\_\_ Tami Horzewski \_\_\_\_\_

Info Decision Discuss.	Time:	Topic(s)	Follow-up Items	Content-focused minutes
			Decision/action: Name: Date due:	
Info	10:00 – 2:00 (Lunch 12:00)	Welcome and Introductions (Dr. Rice (Chair)) Review and Approve Minutes		Motion to approve the Minutes 1st motion Dr. Mei Baker 2nd motion Dr. Scott-Schwoerer Motion to approve minutes from Jan 27, 2017. Accepted.



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Info		Department of Health Services (DHS) Updates (Kirk)		<p>The Birth Defects registry is now opt out. Suggested to look at NBS conditions that are on the Birth Defects Registry.</p> <p>Welcome Dr. Gary Kirk, new Chief Medical Officer, Bureau of Community Health Promotion, Department of Health Services.</p>
Info/Disc		Krabbe Literature Review (Rice/All)		<p>Dr. Rice welcomed the Cushman family and friends. The subcommittee discussed a review of current Krabbe literature. A recent article was less convincing, showing a 10% increase in mortality associated with the treatment. The subcommittee will continue to be vigilant of new Krabbe literature and will do a re-evaluation when the condition is again reviewed at the national level.</p>
		Update SACNBS recommendation on CPT IA (Rice)		<p>The Secretary's Advisory Committee on Newborn Screening met on October 12, 2017. The committee recommended the addition of CPT IA to the WI Newborn Screening Panel of Conditions. A written report with the committee's recommendation will be sent to the Secretary of the Department of Health Services for a final decision.</p> <p>The timeline for the Secretary's decision is unknown at this time.</p>



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Info		Pompe Screening Update & clinical follow-up of the new Pompe babies identified since the pilot started (Dr. Baker/Dr. Rhead)	Determine which standard tool to use for psychosocial assessment at the clinics.	<p>Mei reviewed the current screening process:</p> <ol style="list-style-type: none"><li>1. All the specimens undergo a 6-plex enzyme activity measurement assay. If the situation of GAA activity is less than 15% of the daily median, the lab will review the other 5 enzymes' activities (ASM- Niemann–Pick disease, GLA- Fabry disease, IDUA- MPS I, ABG- Gaucher disease, and GALC- Krabbe disease). With one or more additional enzyme activity lower than 15% of the daily median, the specimen will be deemed as unsatisfactory.</li><li>2. All specimens undergo CLIR assessment.</li><li>3. Specimens with GAA 10-15% of daily median are reported as possible abnormal</li><li>4. Specimens will undergo GAA gene sequencing assay and are sent to Mayo for the second tier testing (PD2T) when GAA is lower than 10% daily median, and/ or there are indications of likely Pompe by CLIR.</li><li>5. The lab will communicate the GAA enzyme and PD2T results to the PCP and a metabolic physician.</li><li>6. GAA gene sequencing results are usually available within one week</li></ol> <p>Mei also provided the following Pompe screening summary for the screening period between 7/14/17 to 10/7/17.</p>
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					Number
				Total Screened Infants	16,500
				Screening Abnormal	4
				Screen Possible Abnormal	1
				Screening Inconclusive	1
				Screening Opt-out	0
				Mean of Assay 10% of Daily Median (N = 57)	1.55
				SD of Assay 10% of Daily Median (N = 57)	0.06
				<p>The group discussed the following items:</p> <p><b>Multiple Enzymes in the Assay</b> The multiplexing assay was chosen to assess the specimen quality, and thereby reduce the false positive results. There was a long and active discussion regarding ethical concerns on collecting other 5 enzyme activity data which may indicate diseases that are not screened for. The group agreed that Mei would seek consultation from Dr. Norman Frost, and bring back his recommendations.</p> <p><b>Results Communication Timing</b> Depending on the time at which the lab receives the PD2T results, the lab has called the PCPs and metabolic physicians beyond regular lab operation hours. The group has agreed that the lab only accesses the PD2T results, and calls out the results during the lab regular operation hours (8:00am-4:00pm on Monday-Saturday).</p> <p><b>Cutoff Discussion</b> There is a desire to adjust the screening cutoff, and so further reduce the identification of LOPD. The group agreed to come back with this item later when we have more experience to draw on.</p>	



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				<p><b>Follow-up Data Elements</b> In order to meet the funding agency (NIH) data collection and reporting requirements and the NewSTEPs data entry requirement, we will develop a short-term follow-up data element table. As the PI, Mei will work with the Pompe NBS pilot team to establish a set of common short-term follow-up data elements.</p> <p><b>GAA Gene Sequencing Report</b> Based on the feedback from the metabolic physicians, the lab will include variant category when report GAA variants. Here is an example.</p> <table><tr><td></td><td><b>Pompe Center Classification</b></td><td><b>ClinVar</b></td></tr><tr><td></td><td>Potentially Mild</td><td>Pathogenic</td></tr><tr><td></td><td>Very severe</td><td>Likely Pathogenic</td></tr></table>		<b>Pompe Center Classification</b>	<b>ClinVar</b>		Potentially Mild	Pathogenic		Very severe	Likely Pathogenic
	<b>Pompe Center Classification</b>	<b>ClinVar</b>											
	Potentially Mild	Pathogenic											
	Very severe	Likely Pathogenic											
Info		Disclaimer language – variation in age/timing of screening (Dr. Baker/Dr. Held)		<p>Disclaimer Language – Variation in Age/timing of Screening (Mei Baker)</p> <p>As a result of discussion on how to handle “NBS” requests for children beyond the newborn period, the lab has developed a disclaimer to be included in the report. The group reviewed and approved the disclaimer language as below.</p> <p>The screening tests performed on this specimen were intended for newborns. Reference ranges provided within this report were established within the newborn population. A screening test result should not be used for diagnosis. If the newborn is showing clinical signs or symptoms of a disease on the screening panel, the standard diagnostic assessment is recommended.</p>									
		Working Lunch											



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Discuss		Review of Testing/Cutoffs for SCHADD/Malonic Acidemia (Dr. Held)		<p>Dr. Held reported to the committee two failed PT challenges for the analyte C4OH/C3DC. Both failed challenges were due to cutoff being set too high (8 standard deviations from mean). The laboratory asked the committee to consider lowering cutoff to be able to achieve a passing score on the PT specimens.</p> <p>However, the committee felt that more information was needed and decided to remain the current cutoff (3.03uM). Motion to leave the current cutoff as is. First motion – Greg Rice. Second motion – Bob Steiner.</p> <p>The laboratory will consult with CDC, review data from the one confirmed Wisconsin case (malonic acidemia), and consult with other states and possibly obtain DBS punches from other confirmed cases to evaluate.</p>
Discuss		Review of Testing/Cutoffs for Carnitine Uptake Deficiency (Dr. Held)		<p>Dr Held reported a large number of false positives for CUD. In two years, 170 had an initial abnormal CUD profile. 142 of the 170 had a normal repeat specimen. 28 of the 170 had an abnormal repeat specimen, consistent with CUD and were referred for confirmatory testing. Confirmatory testing revealed 1 CUD case, 6 cases of maternal CUD, 20 false positives, and 1 still pending.</p> <p>The committee agreed to review the testing algorithm to reduce the number of false positives. The laboratory will consider the impact of prematurity and whether there is an increased false positive rate amongst babies in the NICU. Additionally, the laboratory will review whether any of the false positive cases were actually maternal CUD.</p>
Discuss		Review of Testing/Cutoffs for 3-MCC/3-MGA/MCD (Dr. Held)		<p>Dr. Held reported an increased number of referrals for elevated C5OH over the past three years, with majority being false positives. Of the 12 confirmed cases from 2015-2017, all but one were from MCW. The committee discussed how cases were determined to true cases or false positives. MCW agreed to review their data on confirmed cases. Dr. Held will review region 4 database for more comparison information regarding cutoffs.</p>



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Discuss		Clinical Formula Pledge and Proof of Residency (Rasberry)		Matt Rasberry, UW-Waisman Center, shared a Clinical Formula Pledge form for review by the committee. The committee agreed that the use of the form is beneficial. Matt will make slight changes to the draft form.
		Plan Next Meeting/Agenda Items		Tami will send out a doodle poll for the scheduling of the next metabolic subcommittee meeting. No agenda items for the next meeting mentioned at the time of the meeting.

“Parking Lot” Items: