Wisconsin Division of Public Health
Metabolic Subcommittee Meeting
Friday, October 18, 2024
10:00 am -1:00 pm
Zoom: https://dhswi.zoomgov.com/j/1605317978?pwd=NXBJcVZ5b3VIeHBDbmxveTlCOFRPUT09
Or call: +1 669 254 5252 or +1 646 828 7666 or +1 551 285 1373 or +1 669 216 1590
Meeting ID: 160 531 7978
Minutes

Meeting Members:					
X	Dr. Mei Baker		Dr. Sam Huang	X	Lisa Obernolte
X	Dr. Donald Basel (Chair)		Dr. Philip James		Stephanie Offord
X	Beth Boyd	X	Jessica Kopesky	X	Matthew Rasberry
X	Therese Breunig	X	Ashley Kuhl	X	Dr. William Rhead
	Anna Cisler		Dr. Jennifer Kwon	X	Dr. Jessica Scott-Schwoerer
X	Nicoletta Drilias	X	Wanda Meeteer		Emily Singh
X	Gretchen Heckel	X	Dr. Roberto Mendez	X	Dr. Bob Steiner
X	Sonja Henry	X	Kaegan Mestel	X	Tammi Timmler
	Caitlin Hessenthaler		Emily Meyer	X	Mary Marcus Walters
X	Tami Horzewski		Susana Morphis	X	Dr. Katie Williams
		X	Dr. Mike Muriello		
Meeting Guests:					
X	Amy White	X	Dr. Julie Thiel	X	Dr. Justin Hopkin
	Jill Beirl		Taylor Duke		Leah Eckstein

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

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	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. Donald Basel **Recorder:** Tami Horzewski			
Info Decision Discuss.	**Time:**	**Topic(s)**	**Follow-up Items** **Decision/action:** **Name:** **Date due:**	**Content-focused minutes**
Decision	10:00-10:10	Welcome, Review and Approve Minutes (Dr. Basel (Chair))		Motion to approve February 2, 2024 minutes: 1st motion: Sonja Henry 2nd motion: Dr. Jess Scott-Schwoerer Motion approved.
Info	10:10-11:00	Acid Sphingomyelinase Deficiency (ASMD)/Niemann-Pick Disease Nomination Background (Jill Beirl/Dr. Justin Hopkin) Review and Vote on Nine Criteria (Dr. Basel/Tami Horzewski/Voting Members)	.	Dr. Justin Hopkin shared a brief background on Acid Sphingomyelinase Deficiency (ASMD)/Niemann-Pick Disease including disease description, diagnosis, screening, treatment, and outcomes. The ten metabolic subcommittee voting members reviewed each of the nine criteria. **Criteria 1** - Mandated testing should be limited to conditions that cause serious health risks in childhood that are unlikely to be detected and prevented in the absence of newborn screening. Vote: 1 (Meets) to 9 (more info needed). Comments: Is there a difference in treatment after symptoms develop?

				With regard to age of onset – is there improved long term visceral outcome if treatment occurs before three months of age? It is difficult to see what the outcomes will be. There's a need for more data. **Criteria 2** - For each condition, there should be information about the incidence, morbidity and mortality, and the natural history of the disorder. Vote: 6 (meets) to 4 (more info needed) Comments: More information needed on natural history and severity. Can measurement of biomarkers help predict severity, need for treatment? **Criteria 3** - Conditions identified by newborn screening should be linked with interventions that have been shown in well-designed studies to be safe and effective in preventing serious health consequences. Vote: 4 (meets) to 6 (more info needed). Comments: We don't know true treatment outcome data for the severe form of ASMD. There is no treatment for the neurologic form, patients will pass away. We're able to treat the long term visceral outcomes. Treatment is available but may not reach everybody. **Criteria 4 -** The interventions should be reasonably available to affected newborns. Vote: 10 (meets) to 0

				Criteria 5 - Appropriate follow-up should be available for newborns who have a false positive newborn screen. Vote: 10 (meets) to 0 **Criteria 6** - The characteristics of mandated tests in the newborn population should be known, including specificity, sensitivity, and predictive value or other convincing. Vote: 1 (meets) 1 (does not meet) 8 (more info needed) Comments: There is a need for a precise case definition – and more information on natural history. There isn't clear information on what positive tests tell us. It's unknown whether true positives are clearly identifying the right infants, those that will benefit from treatment in childhood. **Criteria 7** – N/A **Criteria 8** - Before a test is added to the panel, the details of reporting, follow-up, and management must be completely delineated, including development of standard instructions, identification of consultants, and identification of appropriate referral centers throughout the state/region. Vote: 0 (meets) 1 (does not meet) 9 (more info needed) Comments: No standard operating procedures are currently available. No clear guidance on how to react to a positive test.

				Criteria 9 - Recommendations and decisions should include consideration of the costs of the screening test, confirmatory testing, accompanying treatment, counseling, and the consequences of false positives. The mechanism of funding those costs should be identified. Expertise in economic factors should be available to those responsible for recommendations and decisions. Vote: 1 (meets) 1(does not meet) 8 (more info needed) Comments: Insufficient work is available at this time, could be done in the future. Need more information on counseling and treatment needed. Don't have clarity on the economic variables. Metabolic Subcommittee Motion: ASMD can be a significant infant-onset disorder for which there is therapy that is geared towards the visceral complications associated with the more attenuated phenotype but doesn't impact the neurological outcomes with those patients impacted by the neurovisceral form of ASMD. There's a lack of clarity for easy identification of severe forms (patients with the neurovisceral form of ASMD) and there is insufficient data available at this time in terms of the therapeutic impact on those severe acute neurovisceral forms of ASMD. Questions were raised by the subcommittee regarding the utility of early identification for

				visceral impacts related to the chronic burden of disease for later onset for more attenuated forms. The subcommittee recommendation is that ASMD should not be added to the WI NBS panel at this time because additional information is needed. 1st motion: Dr. Jess Scott-Schwoerer 2nd motion: Dr. Mei Baker Motion approved. The Metabolic Subcommittee recommendation will be forwarded on to the Umbrella Committee for review at the December meeting.
Info	11:00–12:00	Guanidinoacetate Methyltransferase (GAMT) Deficiency Nomination Background (Dr. Scott-Schwoerer/Dr. Mendez) Review and Vote on Nine Criteria (Dr. Basel/Tami Horzewski/Voting Members)		Dr. Scott-Schwoerer shared a nomination for Guanidinoacetate Methyltransferase (GAMT) Deficiency. She provided information on the metabolic pathway, incidence, birth prevalence, access to treatment, goals of treatment, and treatment outcomes. Treated patients do have improvements in developmental and seizure control. She stated that there is a current process in place for follow up and would be managed like other screening disorders. The costs would be about $10/card for testing. There would be costs for special dietary treatment and counseling. Dr. Mendez shared information about lab testing and experiences from four pilot studies of GAMT. Lab assay development has already been started for GAMT through the Propel grant funding. It is not currently FDA approved and requires validation as an LDT. A validation study is in progress.

				The ten voting metabolic subcommittee members reviewed the nine criteria and voted 10 to 0 that the nomination meets all criteria. Metabolic Subcommittee Motion: The metabolic subcommittee recommends the addition of GAMT to the Wisconsin newborn screening panel of conditions. The condition meets all the criteria and the metabolic subcommittee will forward their recommendation to the umbrella committee for consideration of this condition to be screened for in Wisconsin. 1st motion: Dr. Mei Baker 2nd motion: Dr. Michael Muriello Motion approved. The Metabolic Subcommittee recommendation will be forwarded on to the Umbrella Committee for the nomination review at the December meeting.
	12:00-12:10	Break		
Info	12:10-12:20	Department of Health Services (DHS) Update (Tami Horzewski/JDr. Steiner/Julie Thiel)		Tami Horzewski shared the following DHS Update: •Dr. Steiner is back with the NBS Program part-time in the role of DHS NBS Program Medical

				Director. He works primarily on Tuesdays and Thursdays and every other Friday. • The NBS Program is part of the Family Health Section (FHS). The new FHS Manager, Leah Eckstein, recently started and may join some future meetings. •Rulemaking for the NBS blood card fee increase and the addition of two conditions to the NBS panel, X-ALD and MPS 1, is moving through the process. The legislative report was sent to the Governor's Office and addressed the comments received during the public hearing/comment period. Rulemaking review will resume when the legislative session begins around January 2025. •A small workgroup of metabolic, neurology, and stem cell transplant specialists are currently discussing the work that would need to be done in preparation for possible screening for Infantile Krabbe Disease, the development of a care infrastructure in state, and the possibility of initial care out of state. Infantile Krabbe Disease has been recently added to the Recommended Uniform Screening Panel (RUSP). • The Title V, five year needs assessment for setting priorities for maternal and child health work is underway.

				Julie Thiel shared some background. There were focus groups and a state-wide survey. This information will be analyzed in November and in December will look at setting priorities for the next 5 years, 2026-2030.
Info	12:20–12:30	WI State Lab of Hygiene (WSLH) Update (Dr. Baker)		WI State Lab of Hygiene (WSLH) Update • **HRSA-23-065: State Newborn Screening Priorities Program (NBS Propel)** – **Specific Aim 1:** Expand testing capability to improve laboratory readiness for screening Mucopolysaccharidosis types I and II (MPS I and MPS II), and Guanidinoacetate Methyltransferase (GAMT) deficiency.—Guanidinoacetate assay evaluation in progress. – **Specific Aim 2:** Improve NBS specimen transit time via increasing transparency and effective communication.—Ongoing. – **Specific Aim 3:** Establish a system and a process to monitor spinal muscular atrophy screening positive infants and assess treatment efficacy. –REDCap-based 5 year

				SMA follow-up database and associated dashboard • **Alloisoleucine test is sent out to Mayo Labs due to the closure of biochemical genetics lab at WSLH.** • **CAP Self-inspection:** The NBS lab is scheduled for a CAP Self-inspection on October 30, 2024. Other information • **Revised ACHDNC Nomination Process** – Preliminary nomination package – Full nomination package • **MLD Evidence Review**: At the ACHDNC meeting on August 9, metachromatic leukodystrophy (MLD) was voted to move forward to the evidence review stage. • **NIH NBSXWGS** An NIH Pilot Project to Assess the Feasibility of Adding a WGS Component into the US NBS Program – Support a centralized lab for analysis and

				interpretation of genomic sequencing results. – Focus on a limited gene panel of serious / life-threatening rare diseases with early treatment options available. – Achieve equitable access to genomic sequencing in the newborn period – Examine ethical, legal & social implications (ELSI) of population-wide genomic sequencing in the newborn period.
Info	12:30-12:40	X-ALD Screening Progress Report (Dr. Baker)		X-ALD NBS Implementation Demonstration Project The process was reviewed at the last committee meeting and refreshed at this meeting with one major update: the screening borderline cutoff has

				been adjusted from mean plus 4 SD to mean plus 6 SD to reduce unnecessary repeating NBS. Summary: • Total screened newborns: 59,123 (9/20/2023 – 9/19/2024) • Reported screen positive: 6 male and 8 female • Confirmed: 5 male (including 1 ZWS) and 5 female • Other outcomes: 2 false positive (1 male and 1 female) 1 further clinical follow up declined (known heterozygous mother) 1 pending (female) • Screen borderline: 32 screen negative on repeating NBS (3 since 7/3/24 reduced from 5/monthly to 1/monthly); 4 no repeat NBS obtained. • An oral presentation at the upcoming APHL NBS symposium: Effective and Efficient Newborn Screening for X-ALD: One Extraction with Two Injections.

				• Tentative plan to develop a manuscript on the first 18 months experience.
Info	12:40-12:55	2023 Screening Summary (Dr. Mendez)		Dr. Mendez shared the 2023 screening summary, including the number of cases reported for each condition and the number of confirmed cases. In 2023, there were the following number of **confirmed** cases: • 3 confirmed cases of Galactosemia • 6 confirmed cases of late onset Pompe Disease • 6 confirmed cases of PKU • 8 confirmed Organic Acidurias • 2 confirmed Fatty Acid Oxidation Disorders He also shared the number of referrals from Children's Wisconsin (CW) and Waisman for the various disorders. There were a total of 25 referrals from CW and 33 referrals from Waisman. Diet Monitoring numbers were also shared, showing a reduction in the number of specimens and an increase in the number of specimens rejected.
Disc	12:55 – 1:00	Plan Next Meeting/Agenda Items		There was an initial mention of re-nomination of Krabbe Disease with the addition of Infantile Krabbe Disease to the RUSP. The hope is to receive a re-nomination soon as that is needed in order to consider Krabbe Disease for addition to the Newborn Screening panel. Amy White shared her interest in being a resource for a Krabbe nomination. Subcommittee members will continue discussion. Tami Horzewski will send out a doodle poll for

				scheduling the next subcommittee meeting in either February, March, or April 2025.

Next meeting date: TBD
"Parking Lot" Items: