Wisconsin Department of Health Services
Wisconsin Division of Public Health
Umbrella Committee Meeting
Newborn Screening Program
Minutes
Friday, December 1, 2017
10:00 AM – 2:00 PM

Meeting Invitees:

X	Dr. Mei Baker	X	Dr. Gary Kirk	X	Dr. Michael Rock
X	Dr. Jeff Britton		Alison LaPean-Kirschner		Camille Rodriguez
X	Erin Cronn	X	Heather Kramer	X	Dr. Paul Scott
X	Dr. Patricia Donohoue	X	Mary Marcus	X	Kelsey Stevenson
X	Dr. Norman Fost	X	Dr. Michelle Miller		Angela Thies
X	Dr. Patrice Held	X	Karen McKeown	X	Angie Thompson
X	Dr. John Hokanson		Dr. Pilar Ossorio	X	Marijke Van Roojen
X	Tami Horzewski	X	Dr. Greg Rice	X	Ann Zenk
Meeting Guests					
X	Dr. Meredith Schultz	X	Dr. Matthew Harmelink	X	Dr. Michael Uhing
X	Dr. Mary Schroth	X	Dr. Frederick Edelman	X	Audrey Tluczek
X	Anita Laxova	X	Danyelle Sun	X	Sam Dawe
X	Emily Schumacher	X	Amy Boyer	X	Kate Segal

Agenda:

Friday, December 1, 2017 10:00 AM – 2:00 PM		
Topic:	Lead:	Content-focused minutes:
Welcome, Introductions, and Review of Minutes	Dr. Gary Kirk	Motion to approve May 5, 2017 minutes First motion: Dr. Jeff Britton Second motion: Dr. Mike Rock

Topic:	Lead:	Content-focused minutes:
Newborn Screening (NBS) Program Updates: •Department of Health Services (DHS) Updates	Dr. Gary Kirk	DHS updates: Dr. Kirk provided an update on the following: • The Birth Defects Registry has recently changed to an opt-out system of reporting. We believe that change will make the Registry more robust over time. The recent Registry change also allows the Birth Defects Council, by unanimous consent, to add conditions to the Registry. The current list of conditions will be sent to each Subcommittee member. Members can suggest any new conditions. If there is consensus that certain conditions should be added at the individual Subcommittee level, those suggestions can be forwarded to Tami. Tami, in turn, will share the suggested conditions with Liz Oftedahl, the epidemiologist serving the Birth Defects Council, and Liz will get them to the Council. There will be other opportunities to add conditions to the Birth Defects Registry as well. • There is a new Executive Order that took effect beginning September 1, 2017. All state agencies are to post all open meeting notices (agendas) and meeting minutes on the public meeting notices website https://publicmeetings.wi.gov/. There is a timeframe of 30 days for draft minutes to be sent for posting and then once approved; final minutes will need to be sent for posting as well. Due to this time requirement, everyone involved in the drafting of meeting minutes will need to expedite the process following each meeting.

Topic:	Lead:	Content-focused minutes:
•WI State Lab of Hygiene (WSLH) Updates	Dr. Mei Baker	WSLH updates: Dr. Baker provided an update on the following: •Dr. James Schauer took the position of Director of the WSLH on 6-1-2017, and he has been actively engaged with NBS •NBS lab is in year 2 for a New Disorders Implementation Award from APHL as one of three Peer Network Resource Centers. The funding is used to develop both next generation sequencing and Sanger sequencing assays for Pompe, MPS I and X-ALD. The funding budget has been increased this year to support reagents need for developing a droplet digital PCR (ddPCR) assay to better assess the SMN2 copy numbers. The lab is going to purchase a ddPCR system using funding from Biogen. •NBS lab is in year 3 for NBS timeliness improvement award with the current emphasis on HLA7 messaging. •Routine NBS testing –Multiple instrument upgrades –Starting this May, the lab has implemented a new operational policy of "no more than one day gap for time critical conditions". The lab regularly operates from Monday to Saturday. In the situation of Monday holidays, the operation schedules will be adjusted to be sure that the lab operation has no more than a one day gap. –CAP inspection in November went well for both the WSLH as a whole, and NBS lab specifically. We have addressed some documental compliance concerns. •NBS report disclaimer: The NBS cutoffs are established based on the values from newborns (mostly 24-48 hours after birth). Those cutoffs may not appropriate for older children, such as international adoption at one years old age. This concern was initially brought up by the metabolic subcommittee. Based on the discussion with this committee, the laboratory has developed the NBS disclaimer below. 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. There are no suggested edits from the committee members, but it was suggested that this disclaimer be removed from reports in the situation of repeating NBS requested by the lab. The suggestion was accepted by the lab. •SCID/SMA screening assay development: With a finding support from Biogen, the lab has developed a multiplex assay that can be used to simultaneously screen for SCID and SMA. This assay will not detect SMA carriers. The assay's performance appears satisfactory based on the data generated from 25,000 de-identified residual NBS specimens.

Topic:	Lead:	Content-focused minutes:
Subcommittee Updates Secretary's Advisory Committee on Newborn Screening (SACNBS) Update - Carnitine Palmitoyltransferase IA (CPT IA) Nomination	All Chairs Dr. Norm Fost	Secretary's Advisory Committee on Newborn Screening (SACNBS) (Dr. Fost): The Committee met on Oct 12 by teleconference and voted unanimously to recommend adding Carnitine Palmitoyltransferase 1A (CPT 1A) deficiency to the required screening panel. Some nomination form criteria were considered to need more information, particularly relating to test characteristics (sensitivity, specificity, predictive value), but these data are unavoidably unavailable because of the rarity of the condition and the lack of data on newborn screening for this condition. Dr Fost noted that this should not be cited as a generalization for the claim that some of the criteria are not necessary or important. Each disorder needs to be evaluated on its own merits. In the case of CPT1A deficiency, the risks of treatment appear to be very low. The psychosocial risks also appear to be low, as a false positive test is unlikely and there is little/no risk of carrier detection. Endocrine (Dr. Donohoue): No report. Meeting rescheduled. Immunodeficiency (Dr. Baker): No report. Meeting in April, 2018. CF (Dr. Baker for Rock): No report. Meeting scheduled for April 13, 2018. Metabolic (Dr. Rice): The following items were discussed at the metabolic subcommittee meeting in October: • The subcommittee reviewed new literature in regard to Krabbe Disease. The literature provided more evidence not to screen. Testing is not ready and until the condition is included on the on RUSP at the federal level and after thorough review will the subcommittee consider adding the condition to the WI screening panel. Treatment shows 27% mortality and there is difficulty in determining who needs transplant. As of now the subcommittee recommended not going forward. • Cut off levels were reviewed and needed re-tweaking. • A Pompe pilot update was shared. • Disclaimer language was discussed and approved. • The signing of a pledge form was discussed for those who live in WI and are on special dietary treatment. The pledge states specific agreements including not wasting product. The pledge will be sent forward to the umbrella committee to be discussed. • Dr. Rice shared the discovery that Mayo Health System in WI does expanded newborn screening, screening for conditions that we have not included or approved for addition to the WI panel. Some examples are screening for: Pompe, Hurlers, and XALD and some of these babies may have to be seen in follow up clinic. These patients may not always be followed up on due to insurance. Further discussion to occur.

Topic:	Lead:	Content-focused minutes:
		Education (LaPean-Kirschner/Cronn): Erin shared the following updates from the last education subcommittee meeting on October 20th: • A discussion of language for the subcommittee charge occurred. Final language will be reviewed by the subcommittee. • Revisions to the back page of the three screen brochure were discussed. Language will be changed to better support parent's understanding of the material and purpose of the brochure. Revisions will be finalized at the next meeting. • Marijke, Out of Hospital (OOH) Coordinator, provided an update on a prenatal education pilot, outreach to Amish birth attendants, NBS training session for all 3 screens for licensed midwives, updates to the WI SHINE website, and resources. • Erin shared that she will plan to meet with each subcommittee to discuss any potential QI projects. The education subcommittee will be involved in ongoing QI projects. • Other agenda items were tabled until the next meeting as time ran out. Hearing (Vacant): No report. Hemoglobinopathy (Dr. Scott): Dr. Scott shared the following hemoglobinopathy subcommittee update: • The Bartz letter was reviewed and potential changes were discussed. • There were two transcribe report errors – both were babies with SC disease and were in the NICU. There continues to be an urgent need for an electronic data system in order to access results/records. Critical Congenital Heart Disease (CCHD) (Dr. Hokanson) Dr. Hokanson shared the following updates: The CCHD screening algorithm was incorporated into an online "POX Screening Decision Tool" that is available on the SHINE website and can be downloaded onto a smart phone for use even when internet access isn't available. This may be converted to a proper smart phone application if the users would find that helpful. https://wisconsinshine.org/screening/ The CCHD subcommittee is in the process of surveying WI hospitals to determine what resources are on-site in terms of neonatal assessment and neonatal echocardiography. This is to help decision making regarding the referral of babies who have failed their CCHD screening but might also be of use when considering evaluation of suspected Pompe disease. Lis Oftedahl will be retiring in the spring and the hope to complete a summary of the first three years of CCHD screening in Wisconsin based on her data collection.

Topic:	Lead:	Content-focused minutes:
NBS Program Quality Improvement Updates	Dr. Patrice Held/ Dr. Gary Kirk	Dr. Held In 2017, greater than 97% of specimens were collected between 24-48 hours. Greater than 99% of specimens were received within three days after collected, largely due to implementation of "no greater than one day lapse in testing" rule. The percentage of unsatisfactory specimens increased slightly from 1.4% in 2016 to 1.9% in 2017 and the percentage of specimens missing key information remained constant at 3.5%. Both unsatisfactory specimens and specimens missing key information will be the target of outreach efforts for 2018. The implementation of an electronic orders and results system with Columbia St. Mary's (Milwaukee and Ozaukee) drastically reduced the percentage of specimens missing key information for these facilities. Dr. Kirk There are potential QI projects emerging. In follow up to the QI project planning effort and subsequent review by the umbrella committee back in 2014, consumer education was voted second on the list of priority focus areas. DHS in collaboration with the education subcommittee will be reaching out to the subcommittees for the development of some potential consumer education projects.

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<tr><th>Topic:</th><th>Lead:</th><th>Content-focused minutes:</th></tr>
<tr><td>Pompe Pilot Update</td><td>Dr. Baker</td><td>Dr. Baker provided the following Pompe screening summary for the screening period between 7/14/17 to 11/25/17.
<table>
<tr><th></th><th>Number</th><th>Confirmatory Results</th></tr>
<tr><td>Total Screened Infants</td><td>23,895</td><td></td></tr>
<tr><td>Screening Abnormal</td><td>6</td><td>All asymptomatic LOPD, one c.-32-13T>G homozygote and five c.-32-13T>G compound Heterozygote</td></tr>
<tr><td>Screen Possible Abnormal</td><td>1</td><td>Repeat Pompe screening normal</td></tr>
<tr><td>Screening Inconclusive</td><td>2</td><td>Repeat Pompe screening normal</td></tr>
<tr><td>Screening Opt-out</td><td>3</td><td></td></tr>
<tr><td>Mean of Assay 10% of Daily Median (N = 57)</td><td>1.58</td><td></td></tr>
<tr><td>SD of Assay 10% of Daily Median (N = 57)</td><td>0.08</td><td></td></tr>
<tr><td>First CDC PT</td><td>4</td><td>100% correct</td></tr>
</table>
The assay kits used for Pompe screening contain other five enzymes besides GAA for Pompe. The multiple enzyme assay was chosen to assess the specimen quality, and thereby reduce false positive results. There was a long and active discussion regarding ethical concerns on collecting other 5 enzyme activity data that may indicate diseases that are not screened for. The group concluded that the current practice is fine, and approved the following statement:
The current Pompe screening assay is in a 6-plex format. Besides

GAA activity for Pompe, the assay also includes ASM for Niemann–Pick disease, GLA for Fabry disease, IDUA for MPS I, ABG for Gaucher disease, and GALC for Krabbe disease. If GAA activity is less than the cutoff value, the lab will review the other five enzyme activities. With one or more additional enzyme activity lower than 15% of the daily median, the specimen will be deemed unsatisfactory. The multiplexing assay was chosen for the purpose of specimen quality assessment, and to thereby reduce the false positive results. Therefore, except for the targeted GAA, the other five enzyme activities are not reportable regardless of their values.</td></tr>
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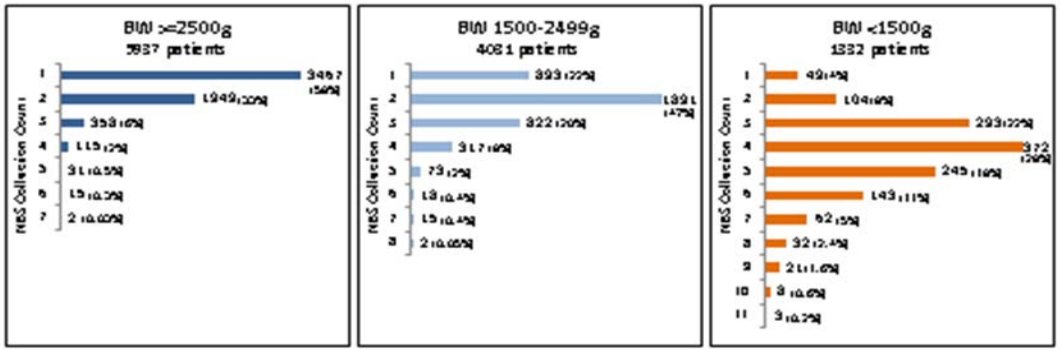
Topic:	Lead:	Content-focused minutes:
Spinal Muscular Atrophy (SMA) Nomination Discussion and Review (Working Lunch)	Dr. Meredith Schultz/Dr. Mary Schroth	Dr. Meredith Schultz is a Neurologist at the University of Wisconsin School of Medicine and Public Health and Co Director of the Pediatric Neuromuscular Clinic and the Neurogenetics Clinic. Dr. Schultz shared some background on Spinal Muscular Atrophy (SMA), the condition nominated to the WI NBS panel and answered questions from committee members. Dr. Kirk guided the committee through the review of each of the nine criteria pertaining to the SMA nomination submission. Criteria 1, 2, 3, 4, 6, and 8, were voted on unanimously as "meets" the criterion. See below regarding criterion 5, 7, and 9. Criterion 5 – "Appropriate follow-up should be available for newborns who have a false positive newborn screen" This criterion was voted as "meets" by five of the twelve committee members. The other seven members voted that more information is needed. Comment noted - available follow up will depend on findings/type. Criterion 7 – "If a new sample collection is needed to add a disorder, reliability and timeliness of sample collection must be demonstrated." This criterion was not applicable. Criterion 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." All twelve members voted that more information is needed. There were several concerns noted. Screening for SMA could have a financial impact on the two university hospital institutions, there could be different long term costs, there could be an impact on the WI Medicaid Program, and there could be more expensive formula/special dietary treatment. The question raised was who pays the difference? Even with the vote for the need for more information on the two criterion mentioned, the committee voted 12-0 in favor of the recommendation for the addition of SMA to the WI NBS panel of conditions. The committee will share their recommendation with the Secretary's Advisory Committee on Newborn Screening (SACNBS) for their deliberations. The committee felt that the SACNBS may need some more information in regard to the financial impact as mentioned above.

Topic:	Lead:	Content-focused minutes:
Repeat NBS in NICU	Dr. Mei Baker/Dr. Michael Uhing	Late June this year, Dr. Uhing, a Medical Director of the NICU at Children's in Milwaukee, contacted Dr. Baker to express his challenges and concerns regarding excessive NBS repeats in NICU resulted from the current policy and procedure. The discussion has led to a systematic review the data from the current practice. Drs. Uhing, Baker and Dawe presented findings that are summarized in the slide below. **Data Summary on Repeated NBS in NICU** 24 months (6/1/15 – 5/31/17) 11,300 NICU patients **Count of NBS Collections for NICU Patients by Birthweight Category *** **standard categorization*  The following slide summaries the relation between repeated NBS and CH detection.

Topic:	Lead:	Content-focused minutes:

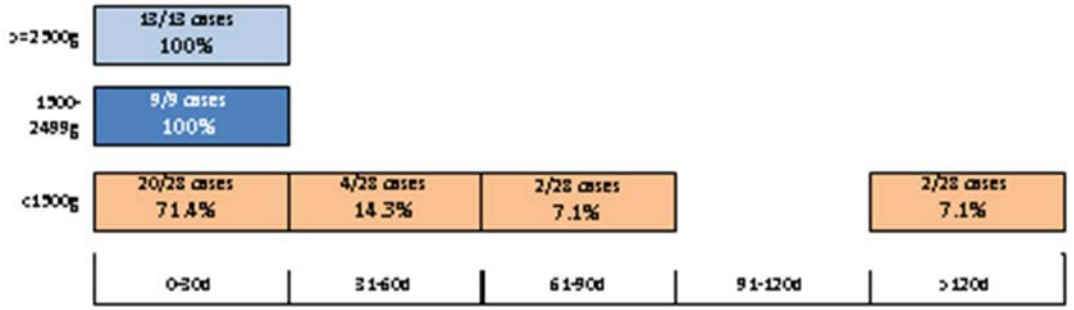
Repeated NBS and Congenital Hypothyroidism

24 months (6/1/15 – 5/31/17)

11,300 NICU patients

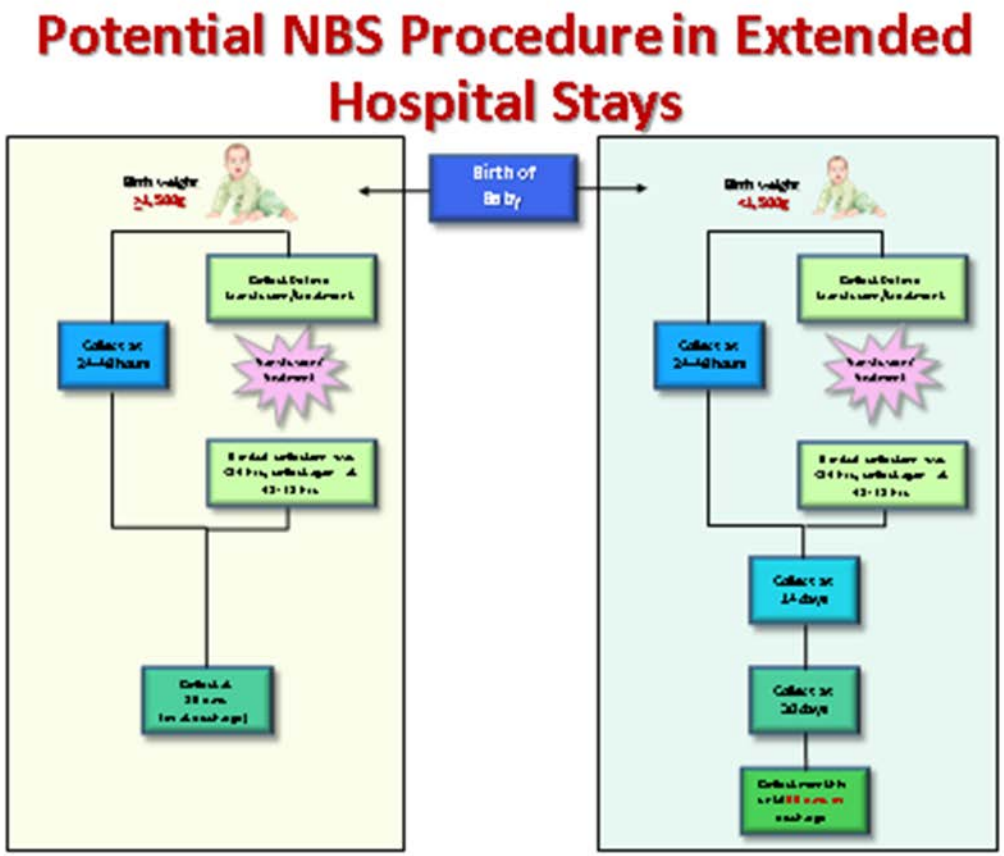
50 confirmed CH cases

Age at Collection of NBS with First Abnormal TSH for Confirmed CH Cases (by Birthweight Category)



The following next steps were proposed by Dr. Baker, Uhing and Dawe, and accepted by the committee.

- Further investigate the two CH cases identified at 6 months old
- Present the data at the next endocrine subcommittee meeting
- Present the data at the metabolic subcommittee meeting
- Present the data at the CF subcommittee meeting
- Assess the need for further data analysis based on the discussion at this umbrella committee meeting and feedback from all relevant subcommittees
- Discuss the need for policy and procedure modifications at the next umbrella committee meeting
- A potential modified procedure was also presented (slide below), and a follow up discussion will be scheduled for the next umbrella committee meeting.

Topic:	Lead:	Content-focused minutes:
		
Plan Next Meeting/Agenda Items	All	Next meeting (May 4, 2018) agenda items: • Dr. Baker to share 2017 screening summary

Next meeting date: Friday, May 4, 2018

"Parking Lot" Items: