NBS Advisory Committee Meeting
MINUTES

Thursday, June 29, 2023
2:00 p.m. – 5:00 p.m.

Attendees

Voting Advisory Committee Members Present	
Name	Position
Abdallah "Abe" Elias	Director of Medical Genetics and Clinical Geneticist, Shodair Children's Hospital
Allison Young (Left at 3:00p)	Pediatrician, Western Montana Clinic
Jennifer Banna, Vice Chair	Center Coordinator, Family to Family Parent of child with rare metabolic disorder
Marion Rudek	Nurse Practitioner, Blackfeet Community Hospital
Shelly Eagen, Chair	Nurse Practitioner, Pediatric Pulmonary, Billings Clinic

Voting Advisory Committee Members Absent	
Name	Position
Kotie Dunmire	High School Business and Special Ed Teacher, Butte High School Parent of child with Cystic Fibrosis and PKU
Sarah Sullivan	RN, Parent to two children with homocystinuria
Amanda Osborne	Licensed, Certified Professional Midwife, Helena Birth Studio
Miranda McCabe	EPSDT Program Specialist, DPHHS

Non-Voting Advisory Committee Members	
Name	Position
Amber Bell	Newborn Screening Coordinator, Children's Special Health Services, DPHHS
Crystal Fortune	NBS Follow Up Coordinator, Montana Public Health Laboratory, DPHHS
Debbie Gibson	Lab Services Bureau Chief, Montana Public Health Laboratory, DPHHS
Jeanne Lee	Newborn Screening and Serology Supervisor
Nikki Goosen	Newborn Screening Clinical Laboratory Science Lead
Jacqueline Isaly	Family and Community Health Bureau Chief, DPHHS
Margaret Cook-Shimanek	Acting State Medical Officer, DPHHS
Dani Lindeman	Laboratory System Improvement Manager, DPHHS

Facilitators	
Name	Position
Anna Schmitt	Co-founder, Yarrow
Kirsten Krane	Co-founder, Yarrow

Guests	
Name	Position
Dr. Mei Baker	SME, Wisconsin State Laboratory of Hygiene

Public	
Name	Position
Elisa Seeger	ALD Foundation, Co-Sponsor of Nomination Packet
Miranda McAuliffe	ALD Foundation
Steve Shapero	MT Advocate, Family Member, Sponsor of Nomination Packet
Jami Nooney	FNP Student, Health Policy Meeting

Welcome & Roll Call

(Yarrow Facilitators, Voting & Non Voting Committee Members, Ground Rules)

- Yarrow welcomed the group and did roll call while leading introductions so each person could introduce themselves, providing their roles, organizations, and a description of themselves.
    - Note: physical description is requested during introductions for those that might be seeing impaired.
- Yarrow provided an overview of Agenda, Ground Rules, and Public Comment Period at the end of the meeting.

Unfinished Business Review

- **Internal Committee Updates**
    - All Conflict of Interest annual documents have been received
    - All Conflict of Interest x-ALD documents have been received
        - One voting member has not signed their COI form at the time of the meeting. This person isn't planning to attend the meeting today for the vote, so this is not an issue at this time.
    - Private meetings
        - The Newborn Screening Committee discussions must be open to the public.
        - Committee members should not discuss opinions or thoughts about whether a condition should be approved with other members of the Committee outside of the Committee meetings.
    - In person meetings were suggested to take place approximately annually in Helena.
        - SEagan was supportive
        - AElias was supportive
        - AYoung felt that this would be very difficult for her. Hybrid meeting options are difficult for the people online to hear and fully participate. October is often busy with professional conferences and obligations as well.
        - JBanna stated that this would work well for her
    - Subcommittee around Laboratory-specific issues
        - The MT State Lab staff are interested in creating a "subcommittee" around lab-specific issues
        - Would information discussed, learned, etc. need to stay public as a subcommittee?
            - The group is unsure if this needs to be public, but would probably be impractical for all discussions to be made public
        - It was suggested that maybe this simply would fall under the realm of informal consultation rather than as a formal subcommittee
        - The members present were open to forming a subcommittee for the MT State Lab
    - Next meeting dates were suggested that included: Last two weeks of September or Third & Fourth week of October
        - AElias - Requests - not October
        - AYoung - The MT-AAP has the annual meeting in the first week of October
    - Additional Disorders - Nominations Updates

        - A nomination form for general CMV screening was received by the Department. This was reviewed and found to be incomplete. The nominator was told that the packet was incomplete and asked to make the necessary updates before resubmitting.
    - Nomination Packet Clarifications
        - AElias wondered if the nomination packet forms were available in the most usable format? He had spoken with someone who had had some trouble downloading and filling out the form.
            - The link on the DPHHS website should allow a person to download a PDF of the packet and they can fill out and return. If there are issues with the format, it would be helpful to get that feedback so that we can fix and simplify this process.
    - Selection Criteria Considerations
        - Dr. Elias - Need to develop questions for the group that help define the review of the selection criteria in more detail.
            - Ex. define the risks and burdens
            - SMA is similar - CHA is similar
                - SMA - don't develop Sx right away
                - CHA don't have Tx in MT
                - So these might not fit although they are already screed for
        - **Suggest that the Nomination Packet be updated to include space for the person filling out the packet to list the risks, burdens, and management of the risks**
        - Consider looking at the decision from the RUSP and the supporting papers, how they assessed the risks and challenges associated with each condition. The RUSP may not always be sufficient in answering all of our state-specific questions, but could provide a good framework for knowing what to deliberate specifically. For example, it is helpful to committee members to know things like that the xALD was added to the RUSP in 2015.
            - **The Internal Planning Team should automatically provide/make these documents available prior to the Advisory Coalition meeting where the condition will be discussed**
            - Link to find this information provided by Vice Chair Jenn Banna **https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp/previous-nominations**
        - Consider asking the SME to address these Selection Criteria questions so that we can get all of the information prior to reviewing the Selection Criteria formally as a Committee. Will be important to ensure that we continue to solicit information from unbiased professionals.
    - Vote process
        - **Voting in Absentia** - We discussed whether it would be appropriate to allow voting members to vote through email or other survey method. Committee members were asked to vote on the following:

          "Final wording will be approved by the Advisory Committee if it is deemed appropriate to amend the bylaws for absentee voting. With that in mind, please select your decision about adding an absentee voting amendment to the bylaws:"

- *Yes, amend bylaws*
- *No, do not amend bylaws*
- *Only allow voting by email if amend for absentee voting*
- *Only allow voting by proxy if amend for absentee voting*
- *I do not have enough information to make a decision at this time*

    - Jenn Banna
    - Shelly Eagen
    - Allison Young
    - Abdallah Elias
    - Marion E. Rudek

All 5 of committee members present voted: "Yes, amend bylaws"
This passed with a quorum.

- **Expanding Voting Members** - AYoung suggested that we might want to have a larger number of Committee voting members so that we are more likely to have a quorum.
    - Dr. Carol Cadi from Community Medical Center in Missoula is an Immunologist who is interested in participating in this committee

x-ALD Nomination Packet Review and Discussion

- **Nomination Packet Review** (for completeness, correctness, and selection criteria)

The following Selection Criteria were reviewed and discussed:

1. It can be identified at a period of time (24 to 48 hours after birth) at which it would not ordinarily be clinically detected. (True)

- No discussion

2. A test with appropriate sensitivity and specificity is available. (True)

- See today's SME Discussion
- The lab in WI can use one marker (C26) with high specificity and sensitivity to screen for this condition. The positive predictive value is high (approxametly 80%) which compares well to other tests that we are already doing.

3. There is a significant risk of illness, disability, or death if babies are not treated promptly (within the recommended time frame for the condition). (True)

- Adrenal insufficiency in males can be identified quickly and help families and providers to carefully monitor and treat as necessary

4. Effective treatment is available and access to follow-up care and counseling is generally available. (True)

- Some treatment is available in Montana to follow adrenal insufficiency and monitor symptoms.
- Bone marrow transplants are generally available out of state with referrals to Denver or Salt Lake
    - Not available at all in Montana

- This is an x-linked disorder to identify female carriers and other individuals at risk, so there is cascade testing. This should be noted in the recommendations.

5. There are demonstrated benefits of early detection, timely intervention, and efficacious treatment. (True)

- Treatment of adrenal insufficiency early and throughout life can be efficacious. The condition has a non-specific presentation and unless you actually check the cortisol, it would be easily missed. Yes there is adequate treatment for adrenal insufficiency, but being able to detect early enough is a concern if it is not part of normal newborn screening.

6. The benefits to babies and to society outweigh the risks and burdens of screening and treatment. (True)

- We can't know who will have the severe form of xALD. For those who do have it, the treatment is very clear and it is treatment with cortisol (steroids) which is cheap and has no significant side effects and works lifelong.
- If you don't treat it, it causes severe illness and death
- Stem cell transplant and newer treatments are helpful too, but don't know a lot about it yet
- It is important to note the benefits of screening for female carriers who are affected and may or may not need treatment
    - Brings up questions about carrier screening in minors
    - Some instances it is clear there is benefit, but often it is complicated
- MT is an opt out state for metabolic newborn screening. Hospitals will do the screening unless parents refuse.

7. There are minimal financial impacts on the family. (True)

- Estimate that initial screening will cost approximately $5 per child. Confirmatory, one time test is more expensive - between $200-500.
- Important to consider the practical aspects of the laboratory testing.
    - The initial test is specific enough that it doesn't need to be repeated.
    - NBS will make confirmatory test recommendations to primary care provider of patient
    - Confirmatory test of long-chain fatty acids will be covered by a different lab, but all testing will be covered financially by insurance.
- MRI testing and regular lab tests may also be required to follow the condition, should be covered by insurance
    - Bone marrow transplants are likely to be more expensive with out of state travel, but much of this is also covered by insurance or unnecessary for many families.
- The screening testing itself is not expensive to families, all things considered.
    - Diagnostic testing would not require out-of-state travel
- According to Dr. Baker, Preventive Genetics might be able to provide the confirmatory test for free, but this is usually for studies of the testing and likely only available for free for a short period of time
- Some of the other tests that we are screening for are similar to this - requiring confirmatory testing in the same price point ballpark and are covered by insurance.

8. There is a public health benefit to conducting the test. (True)

- No discussion

9. There exist responsible parties who will follow up with families and implement necessary interventions. (True)

- This would be similar to metabolic conditions already on the panel

10. The condition's case definition and spectrum are well described. (True)

- At the same time, it is important to note that it is a spectrum - with males who are affected with symptoms occurring later in life. Females are less affected, but do have symptoms later in life and generally less severe.

11. FOR LAB USE ONLY - The public health laboratory can support the testing resources and expertise necessary to provide accurate and timely results. (True)

- This test will require 3 spots. One punch and 2 for the repeats.
    - At the very least, we'd need 1 spot for this test and that leaves very little room for additional spots.
- The lab will likely need to redesign the cards to allow for the additional spots
- Timeframe: Typically, results from WI are received in 2-3 days. Some types of tests are only conducted on certain days of the week.
    - Dr. Baker indicated that it would likely take an extra day to run this test compared to others that are sent to their lab
    - Keep in mind - this is NOT a condition with rapid, severe onset. x-ALD onset can be contrasted with those conditions that can develop and present immediately (ex. 6-8 hours). x-ALD is not like that and additional day(s) for the testing will not cause harm.
- Families could return for the follow up confirmatory similarly to how families present for other metabolic screening tests.
- Could **not** do this screening "in house" in MT, but with WI completing this test, it would be possible to screen accurately and in a timely manner.

- **Presentation from SME**
    - See Mei Baker's slides and recordings
        - Can use one marker (C26) with high specificity and sensitivity to screen between negative (normal) and positive
        - Better than previous tests, this is significant
        - Positive predictive value - how likely a positive screen is a true positive - is very high for this assay (80%)
    - Discussion
        - Dr. Elias asked if reflex / follow-up test with very long chain fatty acid via blood test would be required and if that is considered in costs
            - It is required for confirmation, not included in initial test costs
        - Prevention Genetics provides free genetic testing to follow up testing for x-ALD NBS
            - Can also be helpful for reproductive and potential family counseling
        - Positive predictive value is at least 80% according to Dr. Mei Baker
        - Good sensitivity and specificity for this assay

        - Have studied other assays for x-ALD, but they are not as specific or sensitive - not worthwhile
            - Don't want to miss any cases
            - Better to have false positives because can confirm with secondary testing
        - CFortune asked about the turnaround time for initial and confirmatory tests
            - Wisconsin will only analyze initial screenings, but not confirmation testing
            - Initial screening turnaround time should be just like others in the panel - though it may have an additional 3 days because WI is still piloting some aspects. Can go live with this assay in mid-August 2024. x-ALD is not a priority at this time to turn around.
            - Confirmatory testing is the long-chain fatty acid test and would be done through Kreiger or Mayo labs - this would be part of the NBS follow up procedures - necessary to consider in this decision.
        - NBS Follow-Up
            - In WI, when screening occurs the first line is genetics, then arrange a confirmatory test. In WI, haven't fully decided on preventive genetics - she would like to do that, but other confirmatory testing would be necessary.
                - Need to consider that when they have positive results in the initial screening, they will be confirmed by geneticists who would then connect with family physicians. At this point, the care team would determine what kind of tests they need to order, where to send the tests, and then schedule a time to see the patient
        - What is the discrimination range for females?
            - Male is slightly higher but not different enough to require different cutoff
            - If C26 is elevated in females, then they need to be evaluated
    - Dr. Baker asked- if we do vote to include this, how long would it take to start testing in MT for x-ALD?
        - Depends on the lab and NBS follow-up procedures and legislative process
        - (See additional timeline discussion below)
    - Timeline would also depend on if more room on cards is needed
        - Yes- more room on the cards would be needed. In MT we already have a hard time getting all that is needed from spots that we are currently getting
        - Need at least an additional three spots for this test. Currently, there is space on the cards for 5 spots and 3 of those are being used for current testing.
            - This will be an internal challenge for the lab
        - If these three spots are added - can other conditions be tested with these 3 spots?
            - Possibly for Pompe and something else - Dr. Baker is looking into it
                - May be able to do enzyme assay tests on these spots

<u>Discussion Period</u>

- Yarrow opened the floor for questions and discussion

- Timeline Considerations:
    - First, a Decision Memo will need to be drafted and sent to the Director (concur or disagree) (2 months)
    - Then, proceed through the Rulemaking Process (3-6 months)
        - If this is in Rule (rather than MCA), then we do not need to be in legislative session to make this change.
        - Draft this new rule to add x-ALD, allow for public comment, work around blackout periods around legislative sessions
    - Lab would need close to 6-12 months after the rule is finalized before officially moving forward, depending on whether the test is completed in- or out- of house.
        - Would increase fees
        - If in house: equipment would need to be purchased, installed, staff would need to be trained (approx 12 months) – **We are not suggesting in-house testing for xALD.**
        - If out of house: update contracts with labs that we are working with (6 months)
            - If we are pretty positive that we are moving forward, then we could start amending the contract with WI so that the test could be ordered. If the final rule wasn't approved for some reason, then we just wouldn't order it.
- Redesign of the blood spot cards
    - Can be done without permission of the legislature or rulemaking process
    - Could look at other states' cards and the information collected on them when thinking about redesign.
    - We do not want spots too close the edge of the card or too close to each other
    - Would likely need to redesign for 8 total spots (if including x-ALD)
    - Cards are printed/ordered by the state and the state lab labels with facility information and then distributs to facilities based on their needs.
    - There is some discussion about doing some refresher training on obtaining the blood spots with hospitals

Newborn Screening Advisory Committee Vote on x-ALD

- **Quorum was not achieved. No vote was conducted.**

Newborn Screening Advisory Committee Public Comment Period, & Wrap Up

Public Comment Period

- Miranda McAuliffe - At the next meeting, will there be additional discussion? Or, will there just be a vote on x-ALD?
    - We will just vote. Committee members will be expected to have viewed this meeting recording if they were not present

    - "Has this been nominated to the RUSP?" Could be a question that is added to our Selection Criteria
    - A lot of the questions that we were laboring over, these considerations are addressed in the RUSP.
- During today's vote, we agreed that we would like to amend the bylaws to allow for Absentee Voting. We will need to update the bylaws before voting absentee.

Thanks and Next Steps

- Follow up email will be sent soon and will include:
    - Meeting minutes
    - Recording
    - Transcription
    - Presentation slides
    - Feedback survey

- Please email if you have questions, comments, or need anything

This meeting was concluded by Anna Schmitt at 4:30 pm on June 29, 2023, via Zoom.