Newborn Screening Advisory Committee

Thursday, June 29, 2023
2:00 pm - 5:00 pm

MONTANA DPHHS
Healthy People. Healthy Communities.
Department of Public Health & Human Services

Role Call / Introductions

1. Name
2. Organization
3. Role
4. Physical Description (e.g. age, skin color, gender, hairstyle and hair color, clothes description, any distinctive accessories)*

*Please include a physical description of yourself for meeting participants who may be visually impaired. Share only those attributes you feel comfortable sharing. Thank you!

Agenda

Meeting Goals:

- Discuss and vote on x-linked adrenoleukodystrophy (x-ALD)

Time	Agenda Item
2:00p - 2:10p	**Welcome & Roll Call** ● Voting & Non-Voting Members
2:10p - 2:20p	**Unfinished Business** ● Private Meeting Request
2:20p - 2:40p	**Newborn Screening Advisory Committee Next Steps** ● Prepare document outlining Advisory Committee's decision and rationale ● Send document to DPHHS Director for review ● Schedule next meeting ● Additional business - subcommittees & in-person meetings

Time	Agenda Item
2:40p - 3:40p	**x-ALD Nomination Packet & Screening Review** Determination of selection criteria met **Information Shared from Wisconsin**
3:40p - 4:20p	**x-ALD Discussion** Questions / concerns about adding x-ALD at this time
4:20p - 4:40p	**Vote on x-ALD** Voting members Explanation of voting options Vote to recommend the addition of x-ALD to the Montana Newborn Screening panel Vote count
4:40p - 4:50p	**Public Comment Period**
4:50p - 5:00p	**Meeting Close**

Public Comment Period (10 minutes)

- Moderator will announce comment period
- Use “raise hand” feature”
- Moderator will call your name
- Unmute yourself
- 2 minute max per comment
- Please email additional comments up to 1 hour after meeting ends to: HHSNewbornAdvisoryCommittee@mt.gov

Ground Rules

- Mute
- Video
- Clarifying questions
- Avoid interrupting
- Avoid acronyms
- Use specific examples
- Focus on the collective interests and goals
- Additional meetings or communications may be scheduled
- Next steps assigned to ensure accountability
- Facilitators may call on attendees for input
- Safe space

Ground rules adapted from Strategy Management Consulting *"Ground Rules for Effective Meetings and Strategic Planning Offsites"*

Voting

- Only voting members who have submitted their COI statement can vote on x-ALD
- Quorum = simple majority

Voting Members with COI

- Dr. Abe Elias
- Dr. Allison Young
- Amanda Osborne
- Jennifer Banna
- Marion Rudek
- Miranda Prevel
- Sarah Sullivan
- Shelly Eagen

Non-Voting Members

- Amber Bell
- Crystal Fortune
- Jeanne Lee
- Jacqueline Isaly
- Deborah Gibson
- Margaret Cook-Shimanek

Unfinished Business

Internal Committee Updates

- Annual Conflict of Interest statements received
- x-ALD Conflict of Interest statements received -1
- Private meeting request

Additional Committee Business

- In Person meeting request - take vote
- Subcommittee request - take vote
- Voting in Absentia - take vote via Google Form
    - This decision will not apply to today's vote

Next Advisory Committee Meeting

- In Person?
- Date range
  - Last two weeks of September
  - Third & Fourth week of October

Next Steps

- Follow Up from this Meeting
  - Meeting materials will be shared
  - Public website will be updated
  - Decision memo packet will be drafted & sent to DPHHS Director
  - Director will make a decision & decision will be posted to website

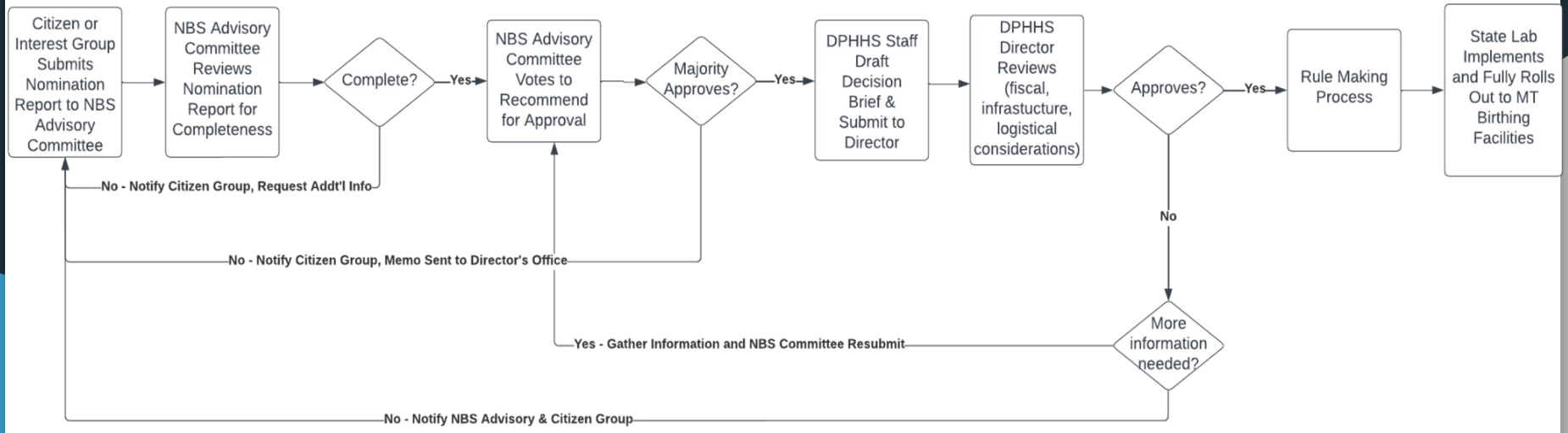
- Next Meeting
  - Doodle Poll will be sent out to determine dates
  - Will include: annual review of bylaws, possibly CMV, possibly Krabbe

Nomination Process Procedures

Activity	Timeline	Next Steps
1. Nomination packet is sent to NBS Program joint email: HHSNewbornAdvisoryCommittee@mt.gov	48 hours	Notify the sender that the packet was received.
2. CSHS & Lab (and potentially Chair and Vice Chair) decide if the nomination packet is complete. Additional information may be requested.	2 weeks	Notify the sender that the packet was complete / incomplete.
3. Send completed nomination packet to full Advisory Committee for review.	1 month prior to meeting where it will be reviewed*	Put the nominated condition on the next available meeting agenda.
4. Designated person (or Chair) leads the Advisory Committee through the nomination packet during the meeting. Additional information will be presented from SME, Lab, and Family Story as appropriate.	X number of meetings*	Vote on the nominated condition in a Committee meeting once the process is complete.
5. Hold vote for nominated condition at Committee Meeting	1 week	Send report to DPHHS Director for review

*Depends on the number of conditions that are already in the queue to be reviewed.

Nomination Flow Chart



x-ALD Nomination Packet Review

Selection Criteria

Selection Criteria	True	Unsure	No
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.	X		
2. A test with appropriate sensitivity and specificity is available.	X		
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).	X		
4. Effective treatment is available and access to follow-up care and counseling is generally available.	X	Some concerns w/ availability (transplant not avail. In MT)	
5. There are demonstrated benefits of early detection, timely intervention, and efficacious treatment.	X		
6. The benefits to babies and to society outweigh the risks and burdens of screening and treatment	X		

Selection Criteria (Continued)			
Selection Criteria	True	Unsure	No
7. There are minimal financial impacts on the family.	X		
8. There is a public health benefit to conducting the test.	X		
9. There exist responsible parties who will follow up with families and implement necessary interventions.	X		
10. The condition's case definition and spectrum are well described.	X - but remember it is a spectrum		
11. FOR LAB USE ONLY - The public health laboratory can support the testing resources and expertise necessary to provide accurate and timely results.	X		

X-ALD Cost Analysis - In-House Start up Costs

MTPHL Up-front	Estimate
Additional clinical laboratory scientist (CLS) salary and benefits	~$100,000*
Training and travel expense for two CLSs	$10,000
Tandem mass spectrometry (MS/MS) instrument	$285,000
Validation cost ~1,300 samples per month for six months at $5.00*/sample	$39,000 (six-month time frame)
Total	**$434,000***
***Estimated cost, subject to annual increase**	

X-ALD Cost Analysis - In-house continuous costs

MTPHL annual	Estimate	Ongoing	Estimate
Additional clinical laboratory scientist (CLS) salary and benefits	~$100,000*	Screening fee increase (screens are currently $140.00)	Approximately **$15.00/sample**
MS/MS service agreement (charge per year)	$28,000	**Total screen fee** (i.e. patient cost for testing)	$2,418,000 (based on 15,600 screens/year at $155.00/screen)*
$6.40/test/1,300 samples per month (15,600/year)	$99,840		
Consumable laboratory items	~$2,000*		
Total	**$229,840**		

***Estimated cost, subject to annual increase**

X-ALD Cost Analysis - Referral to WSLH

Ongoing	Estimate
Screening fee increase (screens are currently $140.00)	Approximately **$15.00/sample.** **New panel fee will be $155.00**
Sample referral to reference lab (if not tested at MTPHL) MTPHL pays WSLH for screening a portion of the MT panel	Currently $36.72 for WSLHL screen=$572,676 for 15,600 screens per year New charge: $41.72* (with addition of X-ALD) for 15,600 screens per year=**$650,832**
Total screen fee **(i.e. patient cost for testing)**	**$2,418,000** (based on 15,600 screens/year at $155.00/screen)*
***Estimated cost, subject to annual increase**	

Information Shared from Wisconsin
Dr. Mei Baker

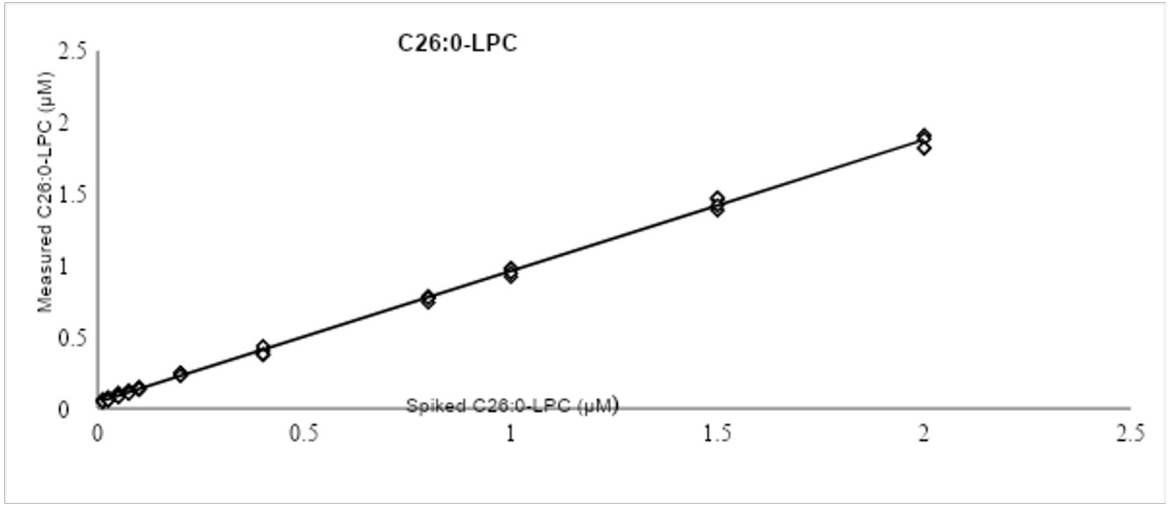
X-ALD NBS Assay: Development and Validation

Mei Baker, MD, FACMG
Wynne Mateffy Professor, Department of Pediatrics
Director, Newborn Screening Laboratory at WSLH
University of Wisconsin School of Medicine and Public Health

Assay Principles

- *ABCD1* pathogenic variants result in ALDP deficiency, which leads VLCFA accumulation.
- Screening markers: C26:0-lysophosphatidylcholine (C26:0-LPC)
- FIA-MS/MS and negative ion mode MRM analysis

Assay Linearity Study



Slope: 0.916

Coefficient of determination (R^2): 0.999

Assay Accuracy

C26-LPC

CDC Sample 1 (0.2 µM)		CDC Sample 2 (0.4 µM)		CDC Sample 3 (1.0 µM)		CDC Sample 4 (2.0 µM)	
Expected (µM)	Obtained (µM)	Expected (µM)	Obtained (µM)	Expected (µM)	Obtained (µM)	Expected (µM)	Obtained (µM)
0.15-0.25	0.19-0.30	0.30-0.50	0.38-0.51	0.75-1.25	0.84-1.03	1.50-2.50	1.84-2.14

Assay Intra-run Precision

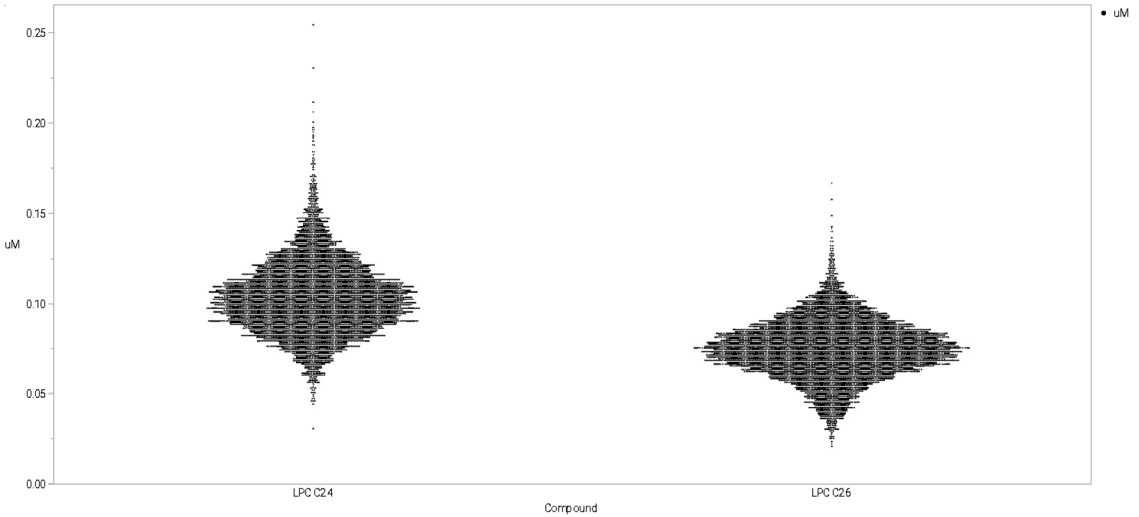
Sample	C26-LPC CV (%)
CDC Sample 1 (0.2µM)	4, 4, 3, 13, 7
CDC Sample 2 (0.4µM)	9, 4, 9, 9, 7
CDC Sample 3 (1.0µM)	7, 1, 7, 1, 5
CDC Sample 4 (2.0µM)	2, 3, 2, 1, 2

Assay Inter-run Precision

Sample	C26-LPC CV (%)
CDC Sample 1 (0.2µM)	10
CDC Sample 2 (0.4µM)	7
CDC Sample 3 (1.0µM)	6
CDC Sample 4 (2.0µM)	4

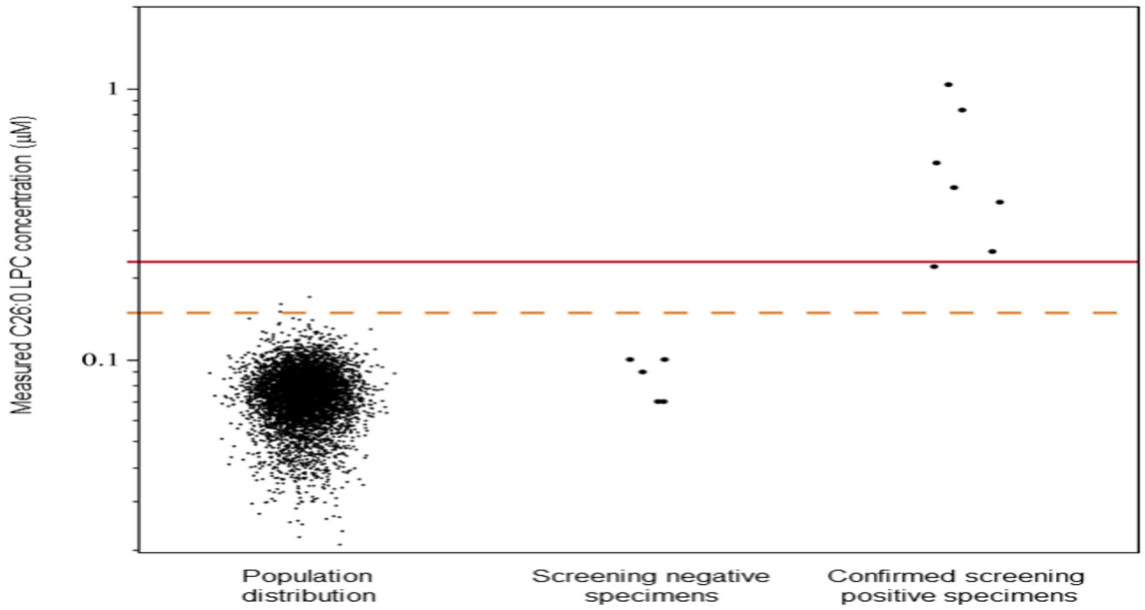
Population Data

N=5,881



C26:0 LPC Borderline Positive Cutoff	C26:0 LPC Presumptive Positive Cutoff
0.15 – 0.23 µmol/L (mean plus 4 SDs)	> 0.23 µmol/L (mean plus 8 SDs)

Clinical Validity Study



Sample ID	WI C26 LPC value (uM)	Expected Result
Sample	0.11	Normal
Sample	0.42	Positive-XALD
Sample	0.10	Normal
Sample	1.04	Positive-XALD
Sample	0.09	Normal
Sample	0.13	Normal
Sample	0.71	Positive-XALD
Sample	0.08	Normal
Sample	0.10	Normal
Sample	0.10	Normal
Sample	0.69	Positive-XALD
Sample	0.10	Normal
Sample	0.09	Normal
Sample	0.09	Normal
Sample	0.10	Normal
Sample	0.11	Normal
Sample	1.39	Positive-XALD
Sample	0.10	Normal
Sample	0.09	Normal
Sample	0.09	Normal
Sample	1.64	Positive-ZW

Sample ID	WI C26 LPC value (uM)	Expected Result
Sample	0.08	NEG
Sample	1.09	POS
Sample	0.34	BORD
Sample	0.09	NEG
Sample	1.09	POS
Sample	0.09	NEG
Sample	0.23	BORD
Sample	0.35	POS
Sample	0.24	BORD
Sample	0.55	POS
Sample	0.35	BORD
Sample	0.82	POS

International Journal of
Neonatal Screening

MDPI

Article

Newborn Screen for X-Linked Adrenoleukodystrophy Using Flow Injection Tandem Mass Spectrometry in Negative Ion Mode

Tarek A. Teber [1,†], Brian J. Conti [1,†], Christopher A. Haynes [2], Amy Hietala [3] and Mei W. Baker [1,4,5,*]

Abstract: X-linked adrenoleukodystrophy (X-ALD) is a genetic disorder caused by pathogenic variants in the ATP-binding cassette subfamily D member 1 gene (*ABCD1*) that encodes the adrenoleukodystrophy protein (ALDP). Defects in ALDP result in elevated cerotic acid, and lead to C26:0-lysophosphatidylcholine (C26:0-LPC) accumulation, which is the primary biomarker used in newborn screening (NBS) for X-ALD. C26:0-LPC levels were measured in dried blood spot (DBS) NBS specimens using a flow injection analysis (FIA) coupled with electrospray ionization (ESI) tandem mass spectrometry (MS/MS) performed in negative ion mode. The method was validated by assessing and confirming linearity, accuracy, and precision. We have also established C26:0-LPC cutoff values that identify newborns at risk for X-ALD. The mean concentration of C26:0-LPC in 5881 de-identified residual routine NBS specimens was 0.07 ± 0.02 μM (mean + 1 standard deviation (SD)). All tested true X-ALD positive and negative samples were correctly identified based on C26:0-LPC cutoff concentrations for borderline between 0.15 μM and 0.22 μM (mean + 4 SD) and presumptive screening positive at ≥0.23 μM (mean + 8 SD). The presented FIA method shortens analysis run-time to 1.7 min, while maintaining the previously established advantage of utilizing negative mode MS to eliminate isobaric interferences that could lead to screening false positives.

x-ALD Discussion

Vote on x-ALD

Voting Considerations

- Voting members only
- Voting Options:
  - Recommend
  - Do not recommend
  - Do not have enough information to make a decision at this time

“Do not have enough information to make a decision at this time”

What does this mean?

Your final decision depends on specific information that you know is coming. The conversation is expected to continue at the next / upcoming meeting.

Montana NBS Advisory Committee: Voting Members

- Dr. Abe Elias
- Dr. Allison Young
- Amanda Osborne
- Jennifer Banna
- Marion Rudek
- Miranda Prevel
- Sarah Sullivan
- Shelly Eagen

Vote on x-ALD using Google Form link provided in Chat

Public Comment Period (10 minutes)

- Moderator will announce comment period
- Use “raise hand” feature”
- Moderator will call your name
- Unmute yourself
- 2 minute max per comment
- Please email additional comments up to 1 hour after meeting ends to: HHSNewbornAdvisoryCommittee@mt.gov

Follow Up & Thank You

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

HHSNewbornAdvisoryCommittee@mt.gov