NBS Advisory Committee Meeting
MINUTES

Monday, April 29, 2024
1:00 p.m. – 5:00 p.m.

Attendees

Voting Advisory Committee Members Present	Position
Shelly Eagen, Chair	Nurse Practitioner, Pediatric Pulmonary, Billings Clinic
Jennifer Banna, Vice Chair	Center Coordinator, Family to Family, Parent of child with rare metabolic disorder
Kotie Dunmire	High School Business and Special Ed Teacher, Butte High School Parent of child with Cystic Fibrosis and PKU
Abdallah "Abe" Elias	Director of Medical Genetics and Clinical Geneticist, Shodair Children's Hospital
Amanda Osborne	Licensed, Certified Professional Midwife, Helena Birth Studio
Sarah Sullivan	RN, Parent to two children with homocystinuria
Marion Rudek	Nurse Practitioner, Blackfeet Community Hospital

Voting Advisory Committee Members Absent	Position
Allison Young	Pediatrician, Western Montana Clinic
Miranda McCabe	EPSDT Program Specialist, DPHHS

Non-Voting Advisory Committee Members	Position
Amber Bell	Newborn Screening Coordinator, Children's Special Health Services, DPHHS
Miranda Reddig	Program Specialist, Newborn Screening, DPHHS
Debbie Gibson	Lab Services Bureau Chief, Montana Public Health Laboratory, DPHHS
Jeanne Lee	Newborn Screening and Serology Supervisor, DPHHS
Jacqueline Isaly	Family and Community Health Bureau Chief, DPHHS
Margaret Cook-Shimanek (Absent)	Acting State Medical Officer, DPHHS
Dani Lindeman	Laboratory System Improvement Manager, DPHHS
Nikki Goosen (Absent)	Newborn Screening Clinical Laboratory Science Lead, DPHHS
Chelsea Pugh (Absent)	Nurse Consultant, Newborn Screening, DPHHS

Facilitators	Position
Anna Schmitt	Co-founder, Yarrow
Mikaela Miller	Public Health Specialist, Yarrow

Guests	Position
Sabina Cook	Genetic Counselor, Utah Department of Health
Dr. David Viskochil	Professor, Pediatric Genetics Department, University of Utah
Erin Hoch	Pompe Mother and Advocate

Public	Position
Ingrid [Unknown]	Unknown
Joe Cross	Pompe Advocate
Jaclyn Haven	Chief Administrative Officer of Medical Genetics
Madalyn Turner	Genetic Counseling Assistant, GeneDx
Ryan Colburn	Researcher, Odimm Inc.
Jedidiah [Unknown]	Unknown
Paloma Juarez	Pompe Advocate
Amanda Joost	Marshall's Mountain, Pompe Advocate
Krista [Unknown]	Unknown
Sandy [Unknown]	Unknown
Jessica Harding	Unknown
Sandy DeMars	Pompe Grandparent and Advocate
Leslie [Unknown]	Unknown
Dorothy Perez	Unknown

Alison Breitbarth	Pompe Advocate
Beth [Unknown]	Unknown

Welcome & Roll Call

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

Pompe Nomination Packet Review

- Symptoms and age of onset:
    - Pompe is detectable as early as birth
    - Symptoms include cardiomyopathy, respiratory distress, muscle weakness, feeding difficulties
- How is this disorder currently identified?:
    - The disorder is initially identified through symptomatic presentation followed by a blood test.
- Why should it be screened at birth?:
    - If undiagnosed, Infantile Pompe Disease can lead to death within the first year of life. Treatment can significantly reduce disease progression and prolong life.
- How is this disorder treated?:
    - Is there a treatment available?
        - Yes – there are currently 3 FDA approved Enzyme Replacement Therapy treatments.
    - Is the treatment in the experimental phase?
        - No
- Proposed screening test method:
    - First tier: GAA enzyme activity in blood sample
    - Confirmatory tier: Variant detection from blood sample
- Status of condition in the United States:
    - States currently screening for the condition: 45
    - Registries or databases currently established for the condition: 2

Pompe Packet Discussion

- Voting committee members expressed no concerns over the nomination packet.
- One member elaborated on the testing methods and noted that there is a third method that focuses on enzyme activity.

Pompe Presentation and Background Information

- **Lab Presentation**
    - Jeanne Lee, Newborn Screening and Serology Supervisor (DPHHS), joined us today to provide the Montana State Laboratory Presentation component.
        - Presentation slides are attached.
    - There is minimal financial impact to families receiving the test and great public health benefits to conducting the test.
    - Pompe Cost
        - Wisconsin (Jan 2024) cost is $11 per specimen.
        - Montana Public Health Laboratory
            - Purchase Instrument:
                - 10 year amortization
                    - Instrument $380,000.00 / 132,000 babies (10 years) = $2.88
                    - Service contract $50,000/ 13,200 (1 year) = $3.79
                    - Kits $6,930 x 15/year = $103,950 / 13,200 = $7.88
                        - Total = $14.55/screen if we amortize the instrument over 10 years
                - 5 year amortization
                    - Instrument $380,000.00 / 66,000 babies (5 years) = $5.76
                    - Service contract $50,000/ 13,200 (1 year) = $3.79
                    - Kits $6,930 x 15/year = $103,950 / 13,200 = $7.88
                        - Total = $17.43/screen if we amortize the instrument over 5 years
            - Reagent Rental
                - 1 QSight and everything needed to operate: Approximate cost per kit = $14,535
                    - $14,535/kit x 15 kits = $218,085/ 13,200 = $16.51/screen
                - 2 QSight's would be ~$23,521 per kit
                    - $23,521 x 15 kits = $26.73/screen
- **Family Presentation**
    - Erin Hoch, Pompe advocate and mother joined us today to provide the Family Presentation component.
        - Presentation slides are attached.

- Introduction: Erin is from Kalispell and is a mother to a medically complex 9 year old boy who has infantile onset Pompe disease. She acts as an advocate to make it better for other families who are coming into a new diagnosis and need their needs support from another family.
- Erin is the nominator for Pompe and works with Jenn Banna (voting committee member) as the Association of Maternal & Child Health Programs (AMCHP) Representative for State of Montana via the University of Montana Rural Institute for Inclusive Communities.
- Experience: To begin, she had an otherwise healthy pregnancy until her son was born.
    - Her son initially had blood sugar issues and failed 2 hearing tests (a symptom of Pompe). He had weight issues during his first 6 months and frequent "gurgling" sounds in his chest. He had other various issues that were all dismissed as minor issues by his doctors.
    - At 6 months he came down with a serious cold and ended up in the doctors. On this visit they found an enlarged heart and tongue. He was eventually sent to Seattle Children's Hospital where they did genetic testing that found he was positive for Infantile Pompe disease.
    - Since the diagnosis, Jaxen has been in and out of hospitals for various serious conditions and treatments. His care is currently managed by around 32 providers, including pulmonology, cardiology, gastrointestinal, neurological, genetic, audiological, primary care, physical and occupational therapy, and others, and he must be homeschooled due to scheduling and the risk of illness.
    - Erin also shared the stories of other people and families impacted by Pompe disease. (see slides or recording for additional details)
        - Lathen Jr
            - Late-onset Pompe Disease
            - Diagnosed during newborn screening tests in Washington in 2023
        - Marshall
            - Late-onset Pompe Disease
            - Diagnosed during newborn screening in Ohio in 2019
        - Joe
            - Late-onset Pompe Disease
            - Lives in Montana
            - Diagnosed clinically as an adult in 2018
        - Grant
            - Infantile-onset Pompe Disease
            - Diagnosed during newborn screening in Indiana in 2021
        - Vaun and Koen (brothers)
            - Both were diagnosed during newborn screening but Vaun's treatment began at 23 days old and Koen's began at 3 days old

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        - This led to greatly different health outcomes so it is important to consider how days matter
    - Closing: It does cost money to add these things to the panel. But it costs lives. Or endless state funds to help provide for those who are missed and diagnosed late like Jaxen. Life and quality of life are equally as important. A quote from Paloma, Pompe mother, caregiver, and advocates, "Being born in one state or another should not be the reason that one child has access to better outcomes."
    - Erin thanks the audience for listening to her story.

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- **SME Presentation**
    - Sabina Cook with the Utah Department of Health and Dr. David Viskochil with the University of Utah joined us today as Pompe Subject Matter Experts and provided a presentation on the disease.
        - Presentation slides are attached. See slides for additional details.
    - Pompe Disease or Glycogen Storage Disease Type 2 causes the accumulation of lysosomal glycogen which leads to progressive damage to skeletal and cardiac muscle.
    - There is a broad spectrum of illnesses from infantile to adult-onset and all require treatment.
    - Pompe is autosomal recessive with 1:17,000 newborns being affected
        - Infantile 1:150,000
        - Late-onset 1:19,000
        - Late onset to infantile = 8:1
    - Clinical Presentation
        - Infantile: poor muscle tone, delays or respiratory symptoms due to heart failure. Patients appear able to understand their environment but cannot move or react to it. Macroglossia, hepatomegaly (due to heart failure, not glycogen storage), protuberant abdomen, death in 1-2 years.
        - Juvenile: skeletal muscle (not heart) involvement. Slowly progressive. Causes respiratory failure and death by 20 years of age.
        - Adult: Slowly progressive proximal myopathy. Most patients require respiratory support (BiPAP) at night.
    - Diagnosis
        - Symptoms include cardiomegaly with cardiac hypertrophy, muscle weakness, progressive respiratory insufficiency, low GAA enzyme activity in white blood cells
        - Urine tests for Hex4
        - DNA tests for GAA
        - In vitro tests for low GAA activity (but does not confirm disease)
        - Genotyping
        - Cross reactive immunologic material status (CRIM)
    - Treatment
        - Enzyme replacement therapy (ERT)

        - Experimental gene therapy
    - Summary
        - Lysosomal storage disorder resulting in glycogen accumulation impairing the function of the heart and skeletal muscle.
        - Newborn screening identifies infantile onset (require immediate therapy) and adult onset (require close follow up) Pompe Disease to allow early treatment
        - Initiate treatment by 2 weeks of age in infantile onset
        - Clinical evaluation for screen positive
        - Identified with WBC GAA enzyme activity, urine Hex4, DNA testing
        - Cardiology evaluation (ECG followed by ECHO, chest X-ray, CK)
    - Utah
        - Utah is a 2-screen state with the first screening done in 24-48 hours of life and the second screening done in 7-16 days of life
        - As of April 2024, they identified 44 conditions
        - RUSP recommended screening for Pompe disease in 2015
        - Utah began testing for Pompe and MPS I in July of 2023

Pompe Discussion

- Dr. Elias comments on lab options, and needing to have the capacity to test for Lysosomal Storage Disorders (LSDs).
    - Jeanne confirmed: Cost would go down as add more test for LSDs.
    - Shelley - how can the state decide on purchase for in house versus sending for testing to Wisconsin.
        - This needs to be considered internally now that more of these conditions are being nominated.
        - May have to bring this to legislation.
        - MT would likely use WI first while figuring this out if this should be added.
            - Need to consider turn around time with sending out.
- Dr. Elias commented - a review of how long it takes for a decision for a state to bring on a new condition to implementation was done recently - it often takes a long time.
    - Necessitates considering multiplexing (testing multiple conditions), sending out labs, etc.
    - MT would need to think more broadly about how new conditions are added.
        - Would multiplexing for xALD, Pompe, etc. decrease costs over time?
- Jenn - how many tests can we do on the blood samples we do get?
    - Jeanne - this year we will start looking at the blood spot cards, some states do collect more spots on their cards, some collect 8 - MT will consider this as we add conditions, it is starting to get tight.
        - 2 spots for MT testing
        - Send 3 to WI

    - This is something that needs to be considered when adding conditions.
- Dr. Elias - thanked presenters - asked about questions asked during follow up calls with positive first test.
    - A lot of calls were to babies in NICU, were asked if they had a significant cardiac finding, had a geneticist review if they had existing tests or would call a doctor and get an assessment.
    - Clear signs in infants:
        - Macroglossia may appear within the first week of life for a child with Pompe.
        - Hypotonia
        - Second screen has been really helpful before doing full clinical assessment because it can be very burdensome to do full assessment, especially for false positives.
    - MT is a one screen state, but will do repeats if needed.
    - Balance between high false positives and second testing, and need to start treatment as early as possible, clinical information could be really helpful.
        - Could do second tier testing earlier than 1 week old?
            - Utah hasn't had an infantile Pompe positive yet, so still working on the process.
            - Was difficult for rural areas to do infant electrocardiogram (EKG).
            - So this felt like the balance at this time.
    - Utah has 40,000 - 45,000 births per year, with a Pompe rate of 1:150,000. This will take some time, but they are ready.
- Dr. Elias - Erin presented her story well. Permanent muscle damage, especially of the heart, is difficult, are there ongoing cardiac problems for Jaxen or has the ERT stabilized this?
    - Jaxen's heart is fully reversed, apart from a small edge that is thicker. It has been stable, but they do an EKG and ECHO annually to monitor, otherwise the heart is functioning well.
    - It took about a full year of treatments to get him to this stage.
    - They started a double dose of treatment for Jaxen in the past year, due to fatigue and muscle weakness issues.
- Thank you to the presenters. End of presentation discussion.

Public Comment Period

- Paloma Juarez
    - Mother and Pompe Advocate
    - In her experience, the biggest impact with the Kansas state legislature was financial
        - How can they do this fiscally responsibly?
        - The committee should consider the fact that if Erin didn't have the option to educate and treat Jaxen, how much state-paid assistance would have been required.

        - Kansas legislature saw that although it costs more upfront to test, it will cost less overall for addressing the untreated condition over time - this was the fiscally responsible decision.
- Ryan Colburn
    - Odimm Incorporated (does Pompe research)
    - Wanted to offer corrections, 3 approved treatments, one pending has been approved.
    - 30 companies working in the space to make more and cheaper treatments available.
    - Testing techniques - multiplexing is a great strategy to test more conditions and bring down costs.
    - Good to price out Tandem Mass Spectrometry, this seems to be the most favored approach.
        - The more screening tests that are performed, the lower the cost per test.
    - Workflow timing is important - days of delay are detrimental.
    - Late or adult onset is a misnomer - no such thing as late onset, just slower or later progression, the issue is there from the start - there is literature showing this.
    - Places without NBS diagnose on average less than 3% of the people who have Pompe, whereas states with newborn screening diagnose those up into the 90th percentile.
    - There are deadly consequences from not diagnosing, with meaningful quality of life impacts as well.
    - False negatives are more harmful than false positives.
    - Two screen workflows are valuable.
    - Diagnosis and start of treatment is possible and vital in days not months as shown by other states and countries.
    - It is important to consider all forms of Pompe Disease.
- Amanda Joost
    - Mother to Marshall
    - There has been a lot of research in central nervous system involvement, it isn't just cardiac and skeletal muscle affected.
    - Deficiencies in metabolic processes do happen early on, even with late onset.
    - There is a new publication that has highlighted diagnostic costs.
- Erin
    - Reiterates that days matter.
    - She also thanks everyone who joined the meeting today.
- Sandy DeMars (email comment submission)
    - My husband and I are the grandparents of Jaxen Flores, Erin Hoch's Child. We just wanted to add our thoughts about newborn Pompe screening.
    - If Jax would have had this screening done as a newborn, he would have not been so advanced in his disease before he began having treatments. His quality of life & the life of his family would have been better at that time and most likely be better now.
    - The life of the parents and family of Jax was made even more traumatic than it already was, by not having a diagnosis for so long. The doctors would have known what was going on and this would have put some of them in a better position to be open to

listening to the mother and be able to treat Jax. As it was, they missed some important signs that Erin had to struggle to get recognized as even something wrong. There would have been no fight on the family's side to try and convince anyone that something was wrong. The doctors would have known right away.
    - There are so many positives for everyone involved that we hope that newborn screening for this disease will begin soon in MT and in every state.
- Additional comments via email were accepted up to 4:00pm MT on April 29th.

Unfinished Business Review

- **Internal Committee Updates**
    - Process Memo to Director
        - We did not hear back on this memo but we did not have a specific ask, however, we can be sure that he did see the memo.
        - Since that time, Krabbe has been added to the RUSP, so we will likely review it again in the future.
    - Updated Condition Nomination Forms
        - Instructions - updated to reflect the new AccessGov online nomination form.
        - Example nomination packet is on the website as well.
        - Nomination Form - converted to AccessGov online nomination form.
            - Dr. Elias: Can this form be saved as you go?
                - Yes, there is an option to Save and Exit.
    - The committee reviewed the Summary of Nominated Conditions and Current Status table and it is now available on the website.
    - The committee reviewed the Member Attendance Requirements in the Bylaws as follows:
        - *Regular attendance is expected of all Committee members. Members may not send a substitute to attend a meeting in their place. If a member fails to attend two (2) consecutive meetings without proper notice, an inquiry shall be made of that member concerning their continued participation. The results of the inquiry, together with recommendation of the Committee, shall be forwarded to the Director of DPHHS for a decision on the member's status.*
        - An online MT NBS Committee application form has been created
            - If members have any referrals, please have any member you refer email us or fill out an application
- **Review RUSP vs. MT Conditions**
    - Review primary vs secondary conditions
    - Do we want this document to be public facing?
        - We prefer to keep this document internal since it may not always be current.
        - We will email voting members this spreadsheet.
        - There is an updated handout - but they are grouped into types which is why it looks like less. Amber will send PDF copy to go out with the meeting minutes, they also have many printed versions.

New Business

- **Membership Considerations**
    - Member Attendance Requirements are stated in the Bylaws as follows:
        - *Regular attendance is expected of all Committee members.*
        - *Members may not send a substitute to attend a meeting in their place.*
        - *If a member fails to attend two (2) consecutive meetings without proper notice, an inquiry shall be made of that member concerning their continued participation. The results of the inquiry, together with recommendation of the Committee, shall be forwarded to the Director of DPHHS for a decision on the member's status.*
    - Mandated Members Term Limits
        - *Member terms are established under section 50-19-205, MCA. They are described as follows:*
            - *The initial appointment of voting members is based upon staggered terms of one, two, and three years so that the terms of no more than four members expire in any given year.*
            - *The term for all subsequent appointments is for a term of three years and each member may be re-appointed for one succeeding term.*
        - *Member terms were reviewed for two considerations*
            - *One: how to stagger current members to meet the bylaws - a survey was shared with voting members to state if they would be willing to end their current term one year short to assist with this process, and/or if they are interested in a second term*
            - *Two: those members for whom an adequate replacement is not available may serve additional terms until an adequate replacement is found.*
    - Rules for New Appointments
        - A process for enrolling new members was discussed and added to the Bylaws as follows:
            - *In order to maintain the aforementioned member positions, on the established three year staggered terms, new members shall be appointed as follows:*
                - *Interested members will submit a completed standard application to the non-voting NBS Advisory Committee members*
                - *The non-voting NBS Advisory committee members will review all applications and determine fit for position*
                - *Recommendations for new membership will be submitted to the Director for review and approval*
        - A survey was shared with voting members to accept or reject the bylaws changes

- Additional changes were requested per Co-Chair Jenn Banna to specify how to inform the committee if a member is unable to attend a meeting underlined as follows:
    - If a member fails to attend two (2) consecutive meetings without proper notice of at least 24 hours in advance to the Advisory Committee facilitator, an inquiry shall be made of that member concerning their continued participation.
- All 6 members present agreed to accept the updated bylaws

Thanks and Next Steps

- Follow up email will be sent soon and will include:
    - Meeting minutes
    - Recording
    - Transcription
    - Presentation slides
    - Bylaws survey & membership survey for those voting members not in attendance
    - Drafted updated bylaws
    - Feedback survey
- A doodle poll will be sent out to schedule the next meeting.
    - The next meeting will occur in the fall
        - Should we have another meeting sooner?
            - Dr. Elias: Yes, these things take a lot of time but he believes it would be beneficial to have an additional meeting.
            - Ideally the new member transition would occur after the members who were present at this meeting were able to vote on Pompe in the fall or sooner.
            - Add consideration and follow-up form for members to vote on considering a summer meeting.
- Please email if you have questions, comments, or need anything.

This meeting was concluded by Anna Schmitt at 03:35 pm on April 29, 2024.

Commented [3]: work with Anna on creating this and potentially discuss with the internal team to see if we want to just do a short meeting with the Pompe vote while it is fresh