NBS Advisory Committee Meeting
MINUTES

Wednesday, May 21, 2025
12:00 p.m. – 3:00 p.m.

Attendees

Voting Advisory Committee Members Present (Name - Position)

- **Jennifer Banna**, Committee Vice Chair - Center Coordinator, Family to Family; Parent of child with rare metabolic disorder; Representative of an advocacy association regarding newborns with medical conditions or rare disorders
- **Steve Shapero** - Family member of persons affected by a rare genetic disorder
- **Shawnalea Chief Goes Out** - Representative of the Medicaid insurance industry, Perinatal Health Program Officer at the Health Resources Division, DPHHS
- **E Lynne Wood** - Pediatric Neurologist, Billings Clinic
- **Abdallah "Abe" Elias** - Director of Medical Genetics and Clinical Geneticist, Shodair Children's Hospital

Voting Advisory Committee Members Absent (Name - Position)

- **Kotie Dunmire** - High School Business and Special Education Teacher, Butte High School and Parent of child with Cystic Fibrosis and PKU
- **Marion Rudek** - Nurse Practitioner, Blackfeet Community Hospital, Representative of a tribal health care system
- **Shelly Eagen**, Committee Chair - Nurse Practitioner, Pediatric Pulmonary, Billings Clinic
- **Amanda Osborne** - Licensed, Certified Professional Midwife, Helena Birth Studio

Non-Voting Advisory Committee Members (Name - Position)

- **Dani Lindeman** - Laboratory System Improvement Manager, DPHHS
- **Debbie Gibson** - Lab Services Bureau Chief, Montana Public Health Laboratory, DPHHS
- **Jeanne Lee** - Newborn Screening and Serology Supervisor, DPHHS
- **Douglas Harrington** - State Medical Officer, DPHHS
- **Chelsea Pugh** - Nurse Consultant, Newborn Screening, DPHHS
- **Miranda Reddig** [absent] - Program Specialist, Newborn Screening, DPHHS
- **Amber Bell** [absent] - Newborn Screening Coordinator, Children's Special Health Services, DPHHS
- **Jacqueline Isaly** [absent] - Family and Community Health Bureau Chief, DPHHS
- **Nikki Goosen** [absent] - Newborn Screening Clinical Laboratory Science Lead, DPHHS

Facilitators (Name - Position)

- **Stephanie Burkholder** - Public Health Specialist, Yarrow
- **Mikaela Miller** - Public Health Specialist, Yarrow

Guests (Name - Position)

- **Gerald Raymond, MD** - SME - Clinical Geneticist and Neurologist, Johns Hopkins Medicine
- **Justin Hopkin, MD** - Family Presenter - Chief, Division of Hospital Medicine Strong Memorial Hospital School of Medicine and Dentistry

Public (Name - Position)

- **None**

Welcome & Roll Call

- Vice Chair, Jenn Banna, 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.

Updates

- Gaucher Disease
    - At our November 2024 meeting to vote on adding Gaucher Disease to the NBS panel, the advisory committee voted NOT to include it on the panel. The recommendation was then forwarded onto the Director of MT DPHHS and he concurred with the committee's recommendation on 12/20/2024. Thus, moving forward, Gaucher Disease will officially not be included on the Montana screening panel.
    - There are stipulations in the nomination packets that allow for re-submission in the future if needed.

Acid Sphingomyelinase Deficiency (ASMD) Nomination Packet Review

Please note that this is a broad overview drawn from the nomination packet, but further details will be provided by the Subject Matter Expert (SME) and family presenter later in the meeting.

- Two main types - A and B: The signs and symptoms between the two types are highly variable.
    - Type A:

        - Age of onset: early infancy
        - Signs/symptoms: Enlarged liver and/or spleen, accumulation of fluid in the abdomen, jaundice, feeding difficulties, constipation, nausea, vomiting, significant gastrointestinal reflux, failure to thrive, irritability, loss of reflexes, and progressive loss of muscle tone (hypotonia), and respiratory issues.
    - Type B:
        - Age of onset: infancy to adulthood
        - Signs/symptoms: Similar to Type A but not as severe. Enlarged liver and/or spleen, increased infections, prolonged bleeding, abdominal pain, liver disease, respiratory issues, neurological issues, delayed growth/puberty, and bone thinning.
- How is this disorder currently identified?
    - Symptomatic presentation followed by a blood test
- Why should it be screened at birth?
    - Early detection and management can help mitigate some of these serious health risks and improve quality of life
- How is this disorder treated?
    - Is there a treatment available?
        - Yes - FDA approved enzyme replacement therapy (ERT)
    - Is the treatment in the experimental phase?
        - No
- Proposed screening test method
    - Dried blood spot
- Status of the condition in the United States:
    - States currently screening for the condition: 2 (Illinois & New Jersey)
    - Condition has been reviewed by RUSP: Yes
    - Registries or databases currently established for the condition: 2

Selection Criteria:

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
2. A test with appropriate sensitivity and specificity is available. - True
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
4. Effective treatment is available and access to follow-up care and counseling is generally available. - True
5. There are demonstrated benefits of early detection, timely intervention, and efficacious treatment. - True
6. The benefits to babies and to society outweigh the risks and burdens of screening and treatment. - True
7. There are minimal financial impacts on the family. - True
8. There is a public health benefit to conducting the test. - True

9. There exist responsible parties who will follow up with families and implement necessary interventions. - True
10. The condition's case definition and spectrum are well described. - True

ASMD Packet Discussion

Comments/questions on the selection criteria:

- Jenn asked for clarification on the RUSP documentation for ASMD: It has been reviewed but the review letter is from 2008 - was ERT available? It was reviewed but was ultimately determined not to add ASMD to the RUSP. Dr. Hopkin mentioned it was not worthy of a RUSP nomination at that time but that an ERT treatment WAS approved two years ago.

- Jenn asked about A/B differentiation. Dr. Hopkin emphasized that it is the same gene and the same disease but it is a spectrum disorder.

- Dr. Elias: clarification that the treatment (ERT) available is related to the visceral aspect and not the neurological aspect.
    - More on how it affects liver, spleen, and lungs but not how it affects the nervous system

- Steven Shapero: two states are currently testing but how long have they been testing?
    - NJ has been testing for 5 years, and Illinois has been testing for over a decade

ASMD Presentation and Background Information

- **SME Presentation**
    - **Gerald Raymond, MD**: Dr. Raymond is a professor of Genetic Medicine and Neurology at Johns Hopkins in Baltimore where he serves as the director of the lysosomal storage disease program. He graduated from the University of Connecticut School of Medicine and did specialty training in pediatrics, child neurology, and genetics. He has been involved in the clinical care and research in neurogenetic disorders. He has been involved in newborn screening especially that of X-linked adrenoleukodystrophy consulting with New York's program and other states and advocated for its inclusion on the RUSP. He presently serves as the chair of the Maryland State Advisory Council on Hereditary and Congenital disorders.
    - Niemann-Pick is an older term, and over the years there have been multiple forms described
    - 4-6 types - Type A, Type A/B, Type B, C1, C2, and D
        - Types A, Type A/B, and Type B will be the focus today
        - Types A, A/B, and B are secondary to Acid Sphingomyelinase Deficiency due to deficiency in the sphingomyelin phosphodiesterase-1 gene
    - Occurs due to variants in SMPD1
    - Provides instructions for acid sphingomyelinase

- Enzyme found in lysosomes, which is involved in converting sphingomyelin to ceramide
- It is an autosomal recessive disorder occurring in about 1 in 250,000 and about 1 in 40,000 in the Ashkenazi Jewish population
- Lysosomes are the recycling centers in the cells and are involved in nutrient regulation and digesting a variety of compounds, including sphingomyelins
    - Enzymatic step is sphingomyelinase and when that doesn't work you get an accumulation of sphingomyelin, which leads to ballooning of cells
    - Accumulation and severity are on a continuum
- Type A:
    - Infants develop hepatosplenomegaly around three months of age, leads to failure to thrive, by 12 months of age there is a progressive loss in mental and motor abilities and interstitial lung disease that ultimately leads to respiratory failure. On eye exam, cherry red spots can be found - the retina are dying on the macule and it's the last of the retina that is being preserved
    - This is a progressive disorder without treatment that often leads to death in early childhood
- Type B:
    - Sometimes occurs in infancy but usually in mid childhood
    - Similar findings but not as severe
    - Hepatosplenomegaly, recurrent lung infections, thrombocytopenia, short stature/slowed mineralization of bones, ⅓ have cherry red spot
    - There is adult survival so there are those in adulthood with this condition
- It is a continuum
    - Type A: severe early-onset form (neurovisceral form)
    - Type B: later onset, chronic visceral form (typically no brain involvement)
    - Chronic neurovisceral ASMD (NPD-A/B) - not as severe as the infantile form but may present with ataxia, other motor manifestations
- There is therapy:
    - Enzyme replacement therapy (ERT): Olipudase alfa (Xenpozyme) was approved in Aug 2022. However, this treatment does not impact the neurocognitive issues. These enzymes are large molecules and cannot cross the blood brain barrier (BBB) and therefore all ERTs do not impact the nervous system.
    - Hematopoietic Stem Cell Therapy
        - Corrects the metabolic defect
        - Improves blood counts
        - Reduces liver and spleen volumes
        - Does not stabilize neurologic disease
        - Does have a significant morbidity/mortality - it is an aggressive therapy but even in the best of conditions it has a mortality of about 5%
    - Wasserstein, et al. (2022) randomized controlled trial publication:
        - This study looked at the use of olipudase alfa ERT for treating chronic ASMD in adults

                - Results: for those randomized to the ERT group, there were reductions in spleen volume, increases in platelet counts, reduction in liver size and improvements in interstitial lung disease
                - This indicates that ERT is highly effective therapy for the visceral manifestations.
    - Newborn screening for ASMD:
        - Possible though Tandem Mass Spectrometry
        - Measurement of activity in dried blood spots
        - Second tier is possible for LysoSM quantification or SMPD1 gene analysis
        - It is not on the RUSP
        - Presently only being screened in Illinois and NJ, piloted in NY through Screen Plus
            - Screen Plus is an opt-in screening for a handful of disorders
        - Illinois group published a paper in 2024 describing a pilot testing between 2014-2015 on 93,000+ infants and they had 1 infant identified. Expanded to statewide testing, and statewide they had 9 infants screen positive out of 1,137,108 tested.
        - NO borderline results.
            - 8 out of 10 are Type B
            - Disease incidence about 1 in 126,345 (0.79 in 100,000 births)
    - What difference does it make if we identify early versus when they are symptomatic later on?
        - Sinha, et al. (2025): study of two siblings
            - Older sibling identified around age 5, started ERT at 7 years of age when it became available
            - Other sibling started ERT at 3 years of age
            - Younger sibling - no deceleration in growth and older sibling had interstitial lung disease and organomegaly
            - Unclear if older sibling suffered irreparable harm
            - With treatment they both came to about the same place with spleen/liver sizes and the older one had catch-up growth
            - He is not 100% clear that identifying the visceral forms overall resulted in irreparable harm
    - In summary, ASMD is a lysosomal storage disease that presents as a continuum from severe early-onset, infantile neurovisceral (type A) through a later-onset, chronic visceral form (type B)
    - Approved therapy Olipudase alfa (Xenpozyme) for visceral manifestations – Not the central nervous system forms
    - Bone marrow transplant if presymptomatic detection of type A?
    - Detectable through newborn screening using available technology
    - Experience suggests accurate with low levels of false positives

- Limited prospective experience suggests early detection and treatment offers moderate benefits in terms of preventing growth issues, lung disease, and hepatosplenomegaly

- **Family Presentation**
  - **Justin Hopkin, MD**: Dr. Justin Hopkin is a rare disease parent, physician, and advocate. As chief of the Hospital Medicine Division at the University of Rochester, he provides strategic and operational leadership with responsibility across the division's missions. He is vice chair of the board for Uplifting Athletes, Chief Scientific Officer for the International Niemann Pick Disease Registry, and an emeritus board member for the National Niemann Pick Disease Foundation (NNPDF), the patient support organization for patients and families with Niemann Pick Disease. As an advocate, he works to support and empower patient communities. He is particularly interested in promoting collaboration between patients, industry and regulators with a focus on drug development, clinical trial design, patient-owned registries and newborn screening.
  - Wyoming native, WWAMI graduate. Used to reside in Lander, WY.
  - Garrett is his son, and he was diagnosed with ASMD a bit after 12 months of age - were told likely Type A and consider engaging with palliative care at that point with a life expectancy of approximately 3 years
    - Several family members are carriers
    - His wife was the one who noticed he was not on the same trajectory of growth as his siblings, poor feeding, poor sleep, delayed growth - blamed on ear infections and reflux initially but then his clinician noticed enlarged spleen and they had an evaluation at Colorado Children's
  - ASMD is a spectrum disorder:
    - Lysosomes and cells exist throughout the body so it impacts many parts of the body
    - Those on physical exam stand out: hepatosplenomegaly can be remarkable
    - Lung disease is marked
    - Neurologic: some patient population with significant disease throughout the body, including the brain, with shortened life span
  - He feels his son falls in the middle of the spectrum - closer to Type A/B or chronic neurovisceral presentation
  - There are very few patients who fit neatly into 2-3 of these categories. He led a group that considered changing the name from type A or type B, as far as the ICD codes are concerned, to make it more acid sphingomyelinase deficiency. Clinicians would be able to differentiate it from the 5 other types, because it's very confusing. But the other reason is that this is a spectrum disorder, and we wanted treatments to be available to all patients because it was really hard, clinically for even the most astute clinicians to identify which patients had which forms early on in life.
  - Cassiman (2016) article: age of onset of symptoms is very, very low in many patients who die from this disorder regardless of when they die in the first 10, 20, or 30 years of life but even those without significant neurologic symptoms, many die before age of 10

and many before the age of 30. Symptom onset is almost always in the first few years of life.

- Reiterated symptoms: in addition to neurologic symptoms, almost all who die have significant visceral disease (lungs, GI tract)
- With Garrett, sleep was a challenge because nutrition was a challenge.
    - Hepatosplenomegaly led to increased vomiting, moving around was a challenge (ataxia or related to enlarged organs in abdomen
    - Liquid diet (Pediasure) helped during first several years of life
- Fell at home and had fractures, needed a spica cast
    - Cast covered his abdomen but made it difficult to breathe
    - CPAP was helpful with breathing due to the enlarged organs in abdomen
- Miranda (2000) article
    - This study is over 20 years in the making
    - Study showed symptom improvement in visceral (not neurological) forms of the disease
- Trial enrollment
    - Graded into different age groups
    - Only trial site at Mount Sinai
        - Flew out multiple times to NYC
        - On the flight back home looked worse, less than 24 hours later he was admitted to Colorado Children's ICU with influenza
        - *C. diff* infection, bone marrow failure
        - Found out during this hospital stay that he was enrolled in the clinical trial
        - Significant difficulty breathing d/t the interstitial lung disease
    - 2 weeks later started his first infusion
        - Had to be present in NYC every 2 weeks for what they thought would be a year
        - Kept house in Lander, kept medical practice, temporarily moved to Rochester - thinking this would be a short experience
    - 6 months into the trial his abdomen size had decreased markedly
    - 1 year clinical trial turned into 6 years before they would get approval, so a total of 8 years in Rochester to maintain access to his life-saving ERT
- Garrett is living his best life. The enzyme therapy is among the best as far as treatments for lysosomal disorders.
    - He is among the two sickest in the clinical trial but his neurological symptoms have been stable for the last 8 years receiving ERT even though it's not supposed to cross the blood brain barrier
- Discussed current advocacy priorities: global access to the therapy (everyone in the U.S. who wants it can get it - it is well covered), expanding newborn screening, patient registry
- GelbChem being used in NJ and Illinois

        - Test developed and extensively studied
        - High sensitivity and specificity
        - Most states blinding the results for Niemann-Pick
    - Clinical guidelines are important
        - Helped to pull international guidelines together (diagnosis, considerations for treatment, etc.)
    - Therapy was approved (after approx 20 years) to treat **symptoms** of the disease
        - Included patients in the trial but also those who were on managed access programs - 3 with significant neurologic disease (and all three are still alive after age 5)
        - Amelioration of symptoms (lung, GI) was a marked improvement for those patients, helped them be able to be off oxygen and to tolerate tube feeds
        - FDA approved for age 0 (birth) for those visceral symptoms and want to continue capturing those data. Currently recruiting more patients in the clinical trial
    - Wylder Nation Foundation - nonprofit organization
    - Picnic Health online registry
    - Ongoing research:
        - Targeting the endocannabinoid system
        - Type C platform therapy: not to treat NPC but to treat inflammation, theoretically should work well in ASMD patients
        - Regeneron looking to use gene therapy (CRISPR) to cause the liver to produce the protein that will cross the BBB and deliver enzyme into the brain
    - Think we have a predictive biomarker (lyso-sphingomyelin level)
    - Rare Revolution Magazine article featuring Garrett's two older siblings and how the diagnosis and move has impacted the family

- **Lab Presentation**
    - Jeanne Lee, Newborn Screening and Serology Supervisor (DPHHS), joined us today to provide the Montana State Laboratory Presentation component. Background on testing in Montana:
        - All of Montana's Newborn Screening samples come to the Montana Public Health Laboratory by our courier from 16 facilities or overnight shipping through carrier services like UPS or FedEx
        - The newborn bloodspot samples are received Monday through Saturday. Testing begins here in the laboratory for 7 of the 31 bloodspot conditions on the Montana panel. That means 24 core conditions are tested at the Wisconsin State Lab of Hygiene, where we ship samples daily, excluding Sundays.
        - Through the 1990s and early 2000s, there was an explosion of NBS conditions to screen for, and the MTPHL was not able to bring on testing because of funding. MTPHL is not funded through the state legislature, but rather is a fee-for-service laboratory, meaning we cover our costs through testing fees. So, in 2007, when the Montana legislature mandated additional tests to be added to the panel, the

MTPHL contracted with Wisconsin to do this testing for fees that would cost less than we could bring the testing on ourselves. When bringing on new tests, there are many things to consider, like instrumentation, expertise in methods, whether there is an FDA-approved test, and what the cost will be.

- We currently have Pompe disease in the rule-making process to add to Montana's newborn screening panel, and we have decided that Wisconsin will perform this test for us. This is because we are not in a position to purchase instrumentation, nor do we have the laboratory space to bring on new instruments with the remodel that is happening now. However, this is something we can consider in the future.
- Later this year or early 2026, with Pompe disease added to the panel, Wisconsin will begin testing. ASMD is a test that can be multiplexed with Pompe disease. Multiplexing means that ASMD can be tested alongside Pompe disease using the same bloodspot punch.
- Reached out to Wisconsin, and even though they don't currently run this test on their panel, they could validate it and perform it for us. Didn't get a straight answer on the cost of adding ASMD alongside Pompe. Even though it shouldn't be much of an addition to the price, I estimate it might cost up to $15/test. Since the Newborn screening panel in Montana is currently $150.50 without Pompe. Adding Pompe disease and ASMD would mean the new cost could make the panel as much as $180.50. I want to note here that newborn screening is covered by insurance and Medicaid. Families that don't have insurance or Medicaid would be paying this amount out of pocket.
- Presentation slides are attached. See slides for additional details.
    - ASMD can be multi-plexed with Pompe disease.
    - Both tests can be assayed from the same sample
    - Wisconsin indicated that they could perform ASMD testing, and it will cost up to $15 per test.

- Dr. Hopkin has also reached out to Wisconsin and they told him it would cost very little to add ASMD.
- Jenn reiterated that the NBS committee has been active for less than two years and we are awaiting nominations to consider these conditions that were not on the RUSP such as MPS. Dependent on getting a nomination and those are on a first-come first looked-at basis. So it is a limitation.

ASMD Discussion

- Dr. Elias: regarding the research paper regarding starting treatment at an earlier age vs later age. Today we would be able to diagnose Niemann-Pick fairly quickly with how our diagnostic workflows go. So if treatment started a few years earlier or right after birth versus a few years later, do we know anything more about the outcome?

    - Dr. Raymond: It's the only paper I could find in the time I had. I agree, if present with hepatosplenomegaly we would get to an exome or genome and get the diagnosis. However, if we diagnose Type A right in the newborn period if they would be better candidates for bone marrow transplant?
    - For example, with MPS-1 at the severe end of the spectrum, they don't do particularly well with enzyme replacement therapy and still have neural disease, but we know that bone marrow transplant in that population might make a difference
        - So if we were to do a bone marrow transplant early on might have relatively reasonable developmental outcomes
        - On the fence about how much of a difference it will make for the later forms and Type A's might benefit from this the most.
- Steven: Do we know if other states are considering adopting ASMD into their newborn screening? Any other states waiting?
    - Dr. Hopkin: most of this is advocacy based, including the RUSP
    - Dr. Raymond: Reminder that the national committee has been disbanded, RUSP is still there and in regulation, but getting things added to it is in limbo at the moment
        - This disorder would be high, but a lot of things in the queue at the state level too that they're juggling
        - RUSP changed their application process 1.5 years ago and so they began a new ASMD application, however due to the recent changes it was stalled
        - NC is pending a pilot, Missouri may be moving forward with screening however this cannot be confirmed
        - Indiana and Pennsylvania are also hearing
        - Massachusetts is also pending
    - Steven: Have they approached California?
        - This will be a legislative approach, also in Texas
- Shawnalea: Do you know if there is follow-up care and counseling available and located in Montana?
    - Dr. Hopkin: No there are not. National Nieman-Pick Disease Foundation has identified comprehensive care centers - these have experience treating patients with ASMD
    - NY is part of Screen Plus, which is a pilot program with certain hospitals in the 9 of the highest birth rate hospitals in New York - program for screening for additional disorders - Gaucher, Niemann-Pick, others
        - They have a family services manager to help families, patients, and clinicians connect
    - Would love to start one in Montana
- Dr. Raymond: What is the birth rate in Montana?
    - Dr Elias: Approximately 12,000 births per year
        - Dr. Raymond cited Illinois with 9 positives over 1 million so about 1 in 125,000 over a few years
    - Dr. Raymond, so based on that you'll have one ASMD case every 10 years

- Dr. Elias: On the one hand you have clearly effective treatment for some aspects, and the testing is not a problem. My struggle is what we know about starting treatment that is triggered by newborn screening vs treatment started after a clinical diagnosis - not completely clear what the data tells us.
    - Dr. Hopkin: The patient reported outcomes paper speaks to morbidity of patients in the early years and their quality of life. There were times with the delayed diagnosis where we were living without a treatment, and there is a lot of morbidity reported in that paper. For those with significant neurological disease, what we know from other lysosomal storage disorders is that as soon as there are neurons damaged and that damage can be irreversible. So identifying patients early on is important to start treatment and prevent neurological damage and they will want to enroll them in clinical trials as best they can.
- Dr. Wood: Where are these clinical trials happening?
    - Dr. Hopkin: Clinical trials: These are all preclinical programs that we haven't started clinical trials. This is data that's being presented in different places. But none of these are to a patient-centered clinical trial. There are patients that have access to these therapies that are off label so, for instance, right now, I'm trying to get my son access because he has ataxia, cognitive delays, and things like that to the therapy that's approved for Niemann pick type C, which was just recently approved for Niemann pick type C, so we need to learn more and gather more data about all of these in this space. And so trying to make the diagnosis early so we can identify those and enroll patients is the point I was making. And you could make that for a lot of disorders.
        - Need to convince the companies to invest and move forward in the climate we're in but hopefully coming up in the near future.
- Break: 10 minutes
- Dr. Hopkin: As far as newborn screening in the U.S., we have the RUSP application 15-16 years ago before there was therapy available. After the approval of this therapy, in 2022, we started working on another RUSP application. RUSP has actually changed their application process about a year and a half ago, I think it was, and we had started to work through that application with them with 4 just original screening questions. So we were working with them when they were still taking nominations. I think we got some encouragement from them. But now, as you all know, that process is sort of uncertain at this point in time. So we're taking an approach of going state by state, and progressive states like Montana, that have an application, and we presented to Georgia 2 years and a half ago. I think they're very excited about it. They moved it into Pilot. So Dr. Cox is leading things down there. We hear that Missouri is actually moving forward with ASMD screening, though I cannot confirm this. So I think from what I'm told they're going to start screening for it as well. They had contemplated it many years ago, and are going to pick it back up. Wisconsin, like I said, I've been on 2 or 3 of their meetings. We're continuing that discussion, and I'm hopeful that they'll be one of the States that adds, and then Indiana and Pennsylvania also have applications that they are looking at, but they don't have a formal hearing process like Montana does. Then from a legislative perspective we've been close in Massachusetts. They're close to considering it, and they screen for 4 or 5 other states around

New England, which would be a big catchment, I guess, as far as patients are concerned. So that's where we're at as far as expanding newborn screening. In addition to those places in New York State that we talked about.

- Steven: What about in California?
    - Dr. Hopkin: They don't have a process by which we can do this from an application perspective. We would like to do that, but I think it's going to be legislative approach at this point. In Texas, we are also looking at a legislative approach, too.
    - And when I say we, there's like 2 or 3 of us working on this, it is a small we, but we're moving it forward.
- Reviewed selection criteria, visually displayed
- Jenn: late onset: does this particular test catch the entire spectrum?
    - Dr. Hopkin: So to clarify this, we're just looking at the 3 diseases that Dr. Raymond said were A, A/B, and B, so the C is a different disease. It's a different newborn screen test they're doing in that New York specific to the ASMD group, which is those 3. And I think the Illinois data suggests that yes, we do capture those with a less severe phenotype, because it appears that of the 10 or so that have tested positive in Illinois, almost all of them don't have significant neurologic diseases they're following. And so they are picking up all of the phenotypes, including those that are less severely affected.
- What about those less severely affected?
    - Dr. Hopkin: The clinical guideline that we created is meant to be expert opinion and anyone with symptoms of the disease should be considered for treatment. If you're asymptomatic then the therapy is likely not going to be significantly beneficial. We are looking at developing guidance for infants specifically diagnosed in newborn screening. At birth, they are all going to be relatively symptomatic and trying to ID the right time to treat (informed decision making) … Currently not a lot of guidance on when to start ERT.
    - The thought is earlier treatment will result in better outcomes. We just don't have enough data to determine whether starting early is beneficial but right now we're focusing on symptoms
- Jeanne: Assays: I know the Revvity assay is FDA approved but is GelbChem FDA-approved?
    - Dr. Hopkin: YES. Both tests screen for the same 6 disorders, they're just two different companies. Some states tend to gravitate towards that one over the other. But there are two out there.
- Steven: Are there people who are carriers that do not show any symptoms?
    - Dr. Hopkin: Yes - ASMD is autosomal recessive disease, so in order to have the disease you need to inherit an abnormal gene from both parents. I am a carrier and my wife is a carrier but we don't have the disease. Bone marrow transplant was discussed by Dr. Raymond and what we would do is replace the child's bone marrow with someone else's but not from someone who is a carrier. Often best candidates for bone marrow transplants are siblings. Both of his other kids were tested (they each carry one of the two genes each) and those aren't good candidates for bone marrow transplant.
    - 1 in 200 in the U.S. population is the carrier rate
    - If two carriers have children, they have a 1 in 4 chance of having a child with the disease

- Dr. Elias: Cost of newborn screening. Based on our birth rate, it is a fair estimate that you would have to screen for 10 years to see one child with ASMD. Based on $15 per test, per year would be $180,000 for testing and over 10 years $1.8 million. Can we get a more precise estimate from Wisconsin? It is a significant cost.
    - Right now this one test would be a little less than 10% of the overall cost of newborn screening
    - Jeanne: I did not receive a straight answer from Mei Baker on the cost - the answer was "let's talk when it gets added to your panel." With the recent rise in costs and tariffs, we can expect to see an increased cost; however, the cost will likely vary lower due to the ability to multiplex with Pompe.
        - Dr. Hopkin: In my discussions with Wisconsin and with Georgia, both labs they both use the assay with Revvity and both labs said there are no additional costs because they're blinding their results because if you run Pompe or you run MPS, one on either of those or Krabbe, now that it's been approved that you actually have to blind the results. And so I'm not sure where the extra cost that you're having, in addition to Pompe would come from. But there's definitely cost considerations if you have either true, positive, or false positive to the system. And so that's I think that's worth considering how many of these tests are going to require follow up. Who's going to do that? Follow up in the public health system, and those sorts of things should definitely be considered. But from a lab perspective, I'm not sure why. Why, on a per test, if you're testing for one, why, there would be extra test. But I'm not a lab person.
            - Jeanne: I agree. We will have to find out from Mei Baker
        - Dr. Elias: I do think that there you have to run QC and control samples, Jeanne mentioned staffing…so those are the kinds of costs that are more significant than the consumables. If a lab director tells me it wouldn't cost to add anything, that's more of a conceptual instead of a practical answer.
        - Jenn: due to the current economics, our cost things change between meetings and between votes and that's not something we've had to consider before
        - Jeanne: Illinois and New Jersey. Laboratory practice will be establishing a cutoff for your population. Do you have a feel based on package insert if they have to change their cutoffs for their assays?
            - Dr. Hopkin: I think it's 15% of their average daily mean but not sure
        - Jeanne: Did Illinois have a lab developed test?
            - Dr. Hopkin: I believe they used the product that was present. When they started with the pilot, I can't remember if they used their own or the commercially available one
        - Lynne: With the discussions earlier about the potential cost for the number of patients we will be benefitting in a ten-year period, did Wisconsin give you a sense of when they might consider adding it to theirs? Particularly if we're thinking our costs will go down if they add it.

        - Dr. Hopkin: presented to Wisconsin two weeks ago and they requested more time to digest the new information prior to voting. He needs to resubmit his full packet again that has more current and complete info from when it was originally submitted. They are currently in the process of re-reviewing this information. They may be able to evaluate this decision within the next 6 months.
            - If approved, Wisconsin owns the equipment, has the reagent, can run the test…will likely begin testing fairly quickly if it is approved in their state, likely in less than 1 year.
            - Jeanne: when we added X-ALD to the Montana panel, it took approximately 9 months to begin testing.
- Lynne: trying to find the sweet spot regarding approval, Wisconsin able to run the tests in a cost-effective manner and then have clinical trials up and running where we could send kids who test positive
- Steven: Will there be support available in Montana fairly quickly?
    - Dr. Elias: Yes, we have a metabolic NBS follow-up program in which the patient would be referred and receive genetic evaluation.
    - If there is a need later on, they can be referred to a center. The ERT infusions are started at low doses then ramped up, with infusions occurring approximately every 2 weeks. Would need to organize the infusion here in Montana, which we do for other disorders.
- Dr. Elias: We know that there is ERT therapy. Early therapy is beneficial, I think, and Niemann-Pick, even though it's such a rare disorder, it is very distinct. Is it fair to say, though, that we were still in terms of numbers, and you know we can't even talk about larger numbers, because even in the US. The number of patients that are diagnosed every year is limited. So to enroll them into studies that all takes some time, of course. How much do we know about treatment that was initiated shortly after birth, for example, versus later at 2 years or 3 years of age. We have limited data, but that data is being produced as we speak, is that a fair statement?
        - Yes, we do not see significant long term effects after therapy has begun. Is early diagnosis as vital for the more severe phenotypes? We are still learning the answer to this.
        - Even adult patients got significantly better after beginning ERT.
- Dr. Elias:
    - Among the states that are currently considering adding the condition, how many are doing a pilot?
        - This depends on the state's committee so this answer is unknown at this time.
    - Jenn: How would a pilot apply in Montana?
        - We would likely not do a pilot in Montana.

- Thank you to the presenters. End of presentation discussion.

Public Comment Period

- Additional comments via email were accepted up to 03:45 pm MT on May 21st.
    - No additional comments were sent.

Thanks and Next Steps

- Follow up email will be sent soon and will include:
    - Meeting minutes
    - Recording
    - Presentation slides
- A doodle poll will be sent out to Committee members to schedule the next meeting.
    - The next meeting will occur in the fall.
- Please email if you have questions, comments, or need anything.

This meeting was concluded by Mikaela Miller at 02:45 pm on May 21, 2025.