Newborn Screening Advisory Committee
APPROVED Meeting Minutes
July 8, 2022
12:00 p.m.

Hybrid Meeting:

Microsoft Teams Virtual Meeting

Robert Bernstein Building, Room K-100
1100 West 49th Street, Austin, Texas 78756

Agenda Item 1: Welcome, introductions, and logistical announcements

Dr. Michael Speer, Newborn Screening Advisory Committee (NBSAC) Chair, convened the meeting at 12:02 p.m. and welcomed everyone in attendance. He introduced and turned the floor over to Ms. Jacqueline Thompson, Policy & Rules, Advisory Committee Coordination Office (ACCO), Policy & Rules, Texas Health and Human Services Commission (HHSC). Ms. Thompson reviewed logistical announcements, called roll, asked members to introduce themselves, and determined a quorum was present.

Table 1. Newborn Screening Advisory Committee member attendance at the July 8, 2022 meeting.

Member Name	In Attendance
Dr. Kaashif Ahmad	No
Ms. Beryl (Pam) Andrews	Yes
Ms. Khrystal Davis, JD	No
Dr. Titilope Fasipe	Yes
Dr. Melissa Frei-Jones, Vice-Chair	No
Dr. Alice Gong	Yes
Dr. Charleta Guillory, MPH	Yes
Dr. Tiffany McKee-Garrett	Yes
Dr. Barbra Novak, CCC-A	No
Dr. Fernando Scaglia	Yes
Dr. Joseph Schneider	Yes
Dr. Michael Speer, Chair	Yes
Dr. Elizabeth (Kaili) Stehel	No

Yes: Indicates member attended the meeting No: Indicates member did not attend the meeting

Ms. Thompson turned the floor back over to Dr. Speer, who asked Ms. Karen Hess, Unit Director, Texas Department of State Health Services (DSHS) Newborn Screening (NBS) Unit, to introduce herself and staff present. Ms. Hess called on

staff members Dr. Debra Freedenberg, Dr. Rachel Lee, Aimee Millangue, and Laura Arellano to provide brief introductions and turned the floor over to Dr. Speer.

Agenda Item 2: Consideration of April 29, 2022, draft meeting minutes

Dr. Speer reminded members that they received the April 29, 2022, draft meeting minutes in their electronic meeting packets and asked if they had any additions or corrections. Hearing none, he requested a motion to approve the April 29, 2022, meeting minutes.

MOTION: Dr. Joseph Schneider made a motion to approve the April 29, 2022, meeting minutes as presented. Dr. Charleta Guillory seconded the motion. Ms. Thompson conducted a roll call vote and the motion carried with seven in favor, no objections, and no abstentions.

Agenda Item 3: Whole genomic sequencing in newborn screening

Dr. Speer introduced and turned the floor over to Dr. Rachel Lee, technical advisor, DSHS NBS Laboratory, to present agenda items 3, 4, and 5 in sequential order. Dr. Lee referenced the PowerPoint and handout, *Whole Genomic Sequencing in Newborn Screening (NBS).*

Highlights of the presentation included:

- Status of NBS by state in the United States: 2020.
- All 50 states perform molecular testing as a first-tier or second-tier assay.
- Some states perform gene sequencing and variant interpretation, which they do either in house (like Texas) or contract out (like California and Florida).
- Wisconsin, Minnesota, New York, New Jersey, Massachusetts, and Virginia also currently do some sort of sequencing for NBS, mostly as a second tier.
- Utah is working on implementing gene sequencing using next generation sequencing, and they are looking at doing whole-exome sequencing.
- Primary screening for severe combined immunodeficiency (SCID) and spinal muscular atrophy (SMA) uses molecular technology.
- Disorders using molecular testing for second- or third-tier NBS screens include hemoglobinopathies, galactosemia, cystic fibrosis (CF), medium-chain acyl-coenzyme A dehydrogenase deficiency (MCAD) and other fatty acid oxidation disorders, Krabbe, mucopolysaccharidosis type 1 (MPS I) and mucopolysaccharidosis type II (MPS II), guanidinoacetate methyltransferase deficiency (GAMT), adrenoleukodystrophy, SMA (SMN2 copy number), maple syrup urine disease (population-specific), carnitine palmitoyl transferase I (CPT1A), and congenital adrenal hyperplasia (CY21A2) (pilot).
- Texas performs second- and third-tier molecular testing for hemoglobinopathies, galactosemia, CF, MCAD, Very Long Chain Acyl-CoA

Dehydrogenase Deficiency (VLCAD), SMA (SMN2 copy number), and X-linked adrenoleukodystrophy (X-ALD).

- Molecular NBS second- or third-tier sequencing tests are done for hemoglobinopathies, Krabbe, Pompe, X-ALD, MPS 1, VLCAD, and CF and in development for SCID.
- Currently, the Texas NBS Laboratory does Sanger sequencing for VLCAD, X-ALD and selected samples in hemoglobinopathies.
- As conditions are added to Texas NBS, more genes will be added to the sequencing panel, including those for Pompe, MPS 1, MPS 2, GAMT, and those associated with SCID.
- Since Sanger sequencing means sequencing one gene at a time, it has become less efficient, very time consuming and labor intensive; therefore, the Texas NBS Laboratory is looking into implementation of whole genomic sequencing.
- The laboratory has started doing some pilots run by using volunteer samples, doing some sequencing in house, and developing their own informatics pipeline to analyze the whole genomic sequencing data and interpret pathogenicity of the variants identified.
- While the laboratory has procured some reagents and instruments, they hope to get the instruments they need to handle human genomic sequencing by early 2023, then implement whole genomic sequencing when they implement lysosomal storage disorders in May 2024.

Members discussed:

- Whole genomic sequencing will be used for second tier testing instead of diagnosing new disorders or adding new conditions.
- With whole genomic sequencing, the Laboratory will only look at the data that is associated with genes related to the very-specified NBS panel.
- The approval process the laboratory must go through for using NBS data in samples for pilot studies before becoming participating in them.
- What the laboratory is allowed to report if disorders come up through whole genomic sequencing that are not on the Texas NBS list and the ethical considerations and possible issues.
- How DSHS and the NBS program regards the possibility of incidental findings in genes that could relate to actionable disorders and diseases and how they will conduct themselves if findings occur.
- The need for the laboratory to have a Research Steering Committee (RSC) and Institutional Review Board (IRB) approval to open up and look at genes not related to conditions on the Texas NBS panel.

- Whether whole-exome sequencing could be targeted to only what is on the Texas NBS panel and how the laboratory handles variants of unknown significance.
- The laboratory part of whole genomic sequencing will not be targeted, but the bioinformatics part is – the laboratory will be able to target specific genes during data analysis.
- Physicians will receive reports of variations of unknown significance.
- Whether data analysis could still pick up variants of clinical significance for unexpected diseases that are actionable.
- Addressing the perception providers and families may have if the laboratory uses whole genomic sequencing, which is that sequencing of the whole genome has been done, and whether reports will reflect that. This may lead to issues where reports may not include anything abnormal, but it only reflects targeted NBS results instead of the whole genome.
- Clarifying that whole genomic testing is the technology the Laboratory will be using, but their reports will probably state they are using next generation sequencing technology only to identify variants of associated with certain NBS conditions.
- How to educate providers in terms of what testing and analysis can be done and what their expectations can be.
- Members are excited about the new technology being implemented in Texas, but further discussion is needed about what could and should be actionable as it relates whole genomic sequencing technology and testing, especially from a global public health standpoint and clinically.

Agenda Item 4: Congenital Hypothyroidism pilot project

Dr. Speer turned the floor over to Dr. Lee to provide a congenital hypothyroidism pilot project update. She referenced the PowerPoint and handout, *Congenital Hypothyroidism Pilot Project*.

Highlights of the presentation included:

- Laboratory previously only used Thyroxine (T4) as the primary analyte when screening for congenital hypothyroidism (CH), but decided to do a pilot study to screen for T4 and thyroid-stimulating hormone (TSH) levels for 10 months to gather data and determine an optimal CH algorithm for the state of Texas.
- Planned project timeline:
  - September 2020 – received funding and switched instruments to enable screening for T4 and TSH at same time for all specimens.
  - December 2020 – September 2021 – ran tests for 10 months.

    - After September 2021 – Reviewed and analyzed data and determined algorithm.
    - June 2022 – implement algorithm.
- Best algorithm for finding all the primary and some of the secondary hypothyroidism
    - First screen – TSH only (collected less than 7 days)
    - Second screen – TSH and T4 at same time (collected on or after 7 days of age)
    - Retest phase – T4 and TSH at same time
    - Algorithm was option 4 of 4, which identified all the cases relative to option 3 (screen all specimens for TSH and T4), would reduce the false positive rate, and cost less for reagents, consumables, and staffing.
- Due to the laboratory's competing priorities, such as updating their laboratory information management system, implementation of the algorithm is pushed to February 2023.
- Implementation will require laboratory process modification in that they will need to identify which specimens need the second screen before testing.
- The laboratory plans to share data at the Newborn Screening Symposium in October and hopefully publish the data.

Dr. Debra Freedenberg, M.D., Ph.D., Medical Director, DSHS Newborn Screening Unit, added that after discussing clinical implications with endocrinologists, the algorithm was the best choice. So, the algorithm was selected based on both clinical outcomes and laboratory procedures.

Members discussed:

- This was nicely done and will help screening immensely without losing specificity.

Agenda Item 5: DSHS Newborn Screening Laboratory building shutdown and plans

Dr. Speer requested Dr. Lee move to agenda item 5. Dr. Lee referenced the PowerPoint and handout, *Texas Department of State Health Services Newborn Screening Laboratory Shutdown and Plans*.

Highlights of the presentation included:

- Laboratory building built in early 2000 and has had no major renovations.
- Need to replace air handling system, exhaust system, emergency generator, and main power supply, which will require the laboratory to shut down.
- Only certain instruments currently on emergency generator, so most of the instruments will go down when the power goes out suddenly.

- Narrowed down shutdown schedule options to two proposals, both of which have phases of shutdowns, preparation and construction and are not finalized.
- The laboratory has contracts and agreements with four back-up laboratories (Perkin Elmer Genomics, Oregon NBS Lab, Washington NBS Lab, and Florida NBS Lab) to handle the large volume of Texas specimens.
- Proposals are being evaluated by leadership and the contractor for feasibility.
- Option 2 looks the most promising with preparation to begin in mid-October, and they will probably stop receiving samples on the Saturday, October 22, 2022 or Monday, October 24, 2022 and forward to the back-up laboratory leading up to the first phase of a six-day shutdown.
- During shutdown, the specimens will be forwarded to, and results will be available from, the back-up laboratory, which DSHS will attach and provide to the submitters in the regular format – online module, fax outs and mail outs – but not on the HL7 interface.
- Throughout November will be phases of shutdown and construction and resuming testing until December.
- The laboratory is currently in the process of communicating with all the back-up laboratories to determine which ones have the capacity, and the turnaround time for results, panels of disorders they are currently screening, testing processes, and reporting process to see which would work best.
- The laboratory will also do some pilot runs of samples and make sure everything goes well.
- Utilizing backup laboratories will involve a lot of planning, coordination, and provider education and communication.

Members discussed:

- What physicians will if they do not receive their regular HL7 results.
- If reports will be formatted to the Texas laboratory, or if they will be in the Oregon or Washington form, depending on where the sample went.
- Texas cannot change reference laboratory results.
- The follow-up staff will continue to receive out-of-range results, but there may be differences in what the back-up labs are screening for and their follow-up algorithms and cut-offs.
- The downside of keeping testing in Texas and delaying testing during a four-day period when the lab is shut down and the back-up plan for unforeseen emergencies, like what happened during the winter storm.
- How the other labs could handle the volume of specimens from Texas, and if the labs are in two-screen states.

- Logistics of how samples are forwarded and if the blood spot samples will be sent back to the Texas lab.
- Encouraging the DSHS Laboratory to pick states who could receive and send HL7 feeds, which will lessen the educational effort and probability somebody will be missed and speed up transmission.

Agenda Item 6: Future condition implementation updates

Dr. Speer introduced Dr. Freedenberg to co-present future condition implementation updates with Dr. Lee. Dr. Lee and Dr. Freedenberg referenced the PowerPoint and handout, *Future Condition Implementation Updates*.

Highlights of the presentation included:

- DSHS is working on implementing lysosomal storage disorders.
- Two lysosomal disorders are currently on the Recommended Uniform Screening Panel (RUSP), Pompe and mucopolysaccharidosis type I (MPS 1), which they are planning to implement in May 2024 if they could receive funding by November 2022 for implementation activities such as doing next generation sequencing.
- The laboratory is also applying for Centers for Disease Control and Prevention grant funding for implementation activities they can start earlier.
- The laboratory was informed that they will receive most of the funding they requested, and they are optimistic that it is enough to start lysosomal storage disorder implementation soon.
- DSHS is waiting for final United States Health and Human Services Secretary determination on mucopolysaccharidosis type II (MPS 2) and guanidinoacetate methyltransferase deficiency (GAMT) being added to the RUSP.
- If approved, adding GAMT to the Texas panel may be a little easier than MPS 2 because it could be added to the current tandem mass spectrometry metabolic methodology, which would require a validation study and can be added when they replace instruments.
- If approved, MPS 2 would be added with Pompe and MPS 1.
- The federal Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) is considering three other conditions nominated for the RUSP: Krabbe Disease, congenital cytomegalovirus (CMV), and duchenne muscular dystrophy.
- ACHDNC is conducting an evidence review of Krabbe Disease, which is being reconsidered due to new treatment availability and technology improvements for second-tier testing.

- When conditions are submitted to ACHDNC, they go through administrative review, condition prioritization workgroup, then full review (of which they have capability to do two a year).
- Concerns with CMV include testing with saliva versus dried blood spots, which would be a whole new system.
- Duchenne muscular dystrophy is in the start of the review process.
- There has been a lot of talk about the pace at which conditions are being added to NBS, both in the ACHDNC review process and the NBS labs capability to keep up with everything suggested, so that is why new technologies are being considered as well.
- As more conditions are proposed for NBS, considerations include figuring out ways for the workforce to deal with it, preparing and educating providers, developing follow up and long term follow up processes with technical advisors and specialists, and identifying challenges.
- The NBS Laboratory has a timeline of projects planned through 2024, which shows they have a number of competing priorities that are taking longer to complete.

Members discussed:

- Concerns with the timeline showing facility HL7 systems going live before the laboratory is back up from shutdowns.

Agenda Item: Break

Dr. Speer announced a 10-minute break.

Agenda Item 7: Screened conditions status updates

Dr. Speer reconvened the meeting at 1:38 p.m. and requested Ms. Thompson conduct a roll call. Ms. Thompson called roll and announced that six members were present.

Dr. Speer turned the floor over to Dr. Freedenberg. Dr. Freedenberg referenced the PowerPoint and Handout, *Screened Condition Status Updates.*

Highlights of the presentation included:

- For the 55 blood spot based RUSP conditions in 2021, there was a total of 922 babies, but that number may change with late diagnosis and changes, and more detail is available for X-ALD and SMA, which were the last two conditions added to the RUSP.
- Year to year, the numbers are consistent with overall numbers dropping in 2021.

- They saw some variation for conditions, where some have increased from what they have detected as well.
- For X-ALD through June 2022, they have identified 38 males who are hemizygous affected, 21 female heterozygotes, 1 case of Klinefelter, 1 case of contiguous gene deletion, and 10 cases and 1 carrier of Zellweger.
- They identified seven cases of other peroxisomal disorders, which includes one peroxisomal biogenesis, two have a bifunctional protein, one PEX6, one TREX1, one Aicardi-Goutières, and one NAXE leukoencephalopathy (but on further exploration and discussion, they believe there is another PEX gene pathogenic variant).
- Texas continues to identify more individuals, and they would argue against other states who are considering screening only males and not females given the data and implications for families.
- When they have identified female heterozygotes, many are symptomatic, but at a later onset age and without a childhood cerebral presentation, as this is an X-linked condition.
- For SMA, Texas is up to 26 cases confirmed with clinical and molecular diagnosis through June 2022: 1 with 1 copy SMN2, 11 with 2 copies of SMN2, 10 with 3 copies of SMN2, and 4 with 4 copies of SMN2.
- Overall distribution of the number of copies of SMN2 is what they expected and fits in with what has been previously reported and in the literature.

Members discussed:

- Genetic variants for the NAXE leukoencephalopathy case.
- If all the SMA cases have received therapy and what forms are available.

Agenda Item 8: Sickle Cell Subcommittee reporting

Dr. Speer introduced Dr. Titilope Fasipe, Subcommittee Co-chair. Dr. Fasipe referenced the handout, *Sickle Cell Subcommittee Meeting Minutes.*

Highlights of the presentation included:

- Last meeting held June 16.
- Subcommittee members reviewed a draft survey they would like to distribute statewide to pediatric hemoglobinopathy consultants list to compile a list of adult providers, which the subcommittee sees as an important link for transition and long-term follow up.
- Have a goal to look for ways to link with adult specialty systems.
- Annual review and update of Action (ACT) and Fact sheets are being finalized by DSHS staff, and the subcommittee should be able to share them with the NBSAC soon.

- Subcommittee chose January for annual ACT and Fact sheet review.
- Subcommittee also wants to continue to explore how to optimize the hemoglobinopathy disorder long-term follow form.
- Announced the next Hemoglobinopathy Consultants meeting is on July 29, and they will let providers know about ACT and Fact sheets and clinic personnel list updates.

Hearing no questions, Dr. Speer moved to the next agenda item.

Ms. Thompson called roll to reflect that Ms. Andrews, Dr. Frei-Jones, Dr. Stehel, and Dr. Guillory had rejoined the meeting, and announced the presence of a quorum.

Agenda Item 9: Rare Diseases Subcommittee reporting

Dr. Speer announced that the Rare Diseases Subcommittee did not meet, therefore there is nothing to report.

Agenda Item 10: Health Information Technology (HIT) Subcommittee retirement

Dr. Speer introduced Dr. Joseph Schneider, Subcommittee Chair.

Highlights of the presentation included:

- Restating the original purpose of the subcommittee.
- Recommending the subcommittee pause or retire, since the subcommittee goal of a link between vital statistics and the newborn screening program to understand that they are getting all the children screened is becoming a reality.

Members discussed:

- Whether members needed to vote to suspend subcommittee activity.
- Thanked Dr. Schneider for all the good work.

MOTION: Dr. Schneider made a motion to disband the subcommittee. Dr. Gong seconded the motion. Ms. Thompson conducted a roll call vote and the motion carried unanimously.

Agenda Item 11: Consideration of amended Bylaws

Dr. Speer reminded members that their packets include a clean copy and a red line copy of the amended Bylaws. Dr. Speer requested DSHS staff point out any important changes before proceeding with discussion and a vote. Dr. Speer called

on Ms. Aimee Millangue, Advisory Committee Coordinator and Ombudsman, DSHS Newborn Screening Unit, to review the changes.

Highlights of the presentation included:

- The Texas Administrative Code codifying the House Bill replaced the House Bill information.
- Wording and formatting changes for how information is described for the committee submitting recommendations.
- Definitions were added such as "Conflict of Interest," "High Level of Integrity," and "Personal or private interest."
- Members being appointed must be appointed by the DSHS commissioner.
- Added a part to all members serving a term of three years, to state "except when appointed to complete the remaining unexpired term of an outgoing member."
- A member may serve a maximum of three terms was changed to two terms, per HHSC policy.
- Included that applicants who submitted applications but were not selected may be reconsidered for membership.
- Changed that members may participate, vote, and attend in person or by video conference call instead of telephone call.
- Added, in compliance with the ACCO template, that the DSHS committee liaison will ensure an item for bylaws discussion is included on the agenda to be posted on the Secretary of State's Open Meetings website and proposed changes to the bylaws must be distributed before the meeting for their consideration.
- Changed, in compliance with the ACCO template, that a member must confirm that he or she will require interpreters, attendants or other support persons, if any, to comply with the confidentiality requirement.
- Added information identifying when members are and are not allowed to claim or appear to represent HHSC, DSHS, or the committee, in compliance with the ACCO template.
- Added information about the DSHS commissioner removing a member.
- Information was stricken related to the commissioner removing members for certain violations related to conflict of interest.
- Additional minor word changes and non-substantive edits were made in compliance with the ACCO template and accessibility standards.
- The revisions page lists all the changes, which also includes removing requirements for who can preside over meetings and travel and clarifying member expectations.

Members discussed:

- Not being able to find the statement in the Bylaws requiring the chair or vice-chair to conduct the meetings and adding that if the chair or vice chair is not available to preside over meetings, a member or member designated by the chair can.
- Impact of reducing the terms to two terms.
- If a grandfather clause can be added regarding the maximum number of terms members may serve so that existing members would not all become ineligible to reapply all at once.
- Needing to have changes reviewed and approved by Legal and ACCO.
- Tabling a vote until members can get clarification on their questions, which NBS staff will send to ACCO and Legal.
- How to stagger membership and terms so there is still continuity on the committee.

MOTION: Dr. Schneider made a motion to table a vote on the Bylaws.
Ms. Thompson conducted a roll call vote, and the motion carried unanimously.

Agenda Item 12: Public comment

No public comment was received for this meeting.

Agenda Item 13: Future agenda items, next meeting date, and adjournment

Dr. Speer turned the floor over to Ms. Millangue to provide a list topics and action items for a future meeting.

Agenda and action items included:

- Bylaws
- Newborn Screening Preservation Account
- Whole genomic sequencing
- Distribution of Medicaid funding received from newborn screening kits
- Standing items:
  - Screened conditions
  - Updates
  - Future conditions
  - Implementation updates
  - Reports from the Sickle Cell and Rare Diseases subcommittees
- Action item follow up list:
  - Continuity of operations

    - Updated funding request for meeting timeliness goals and estimated cost of a seven-day working lab to include follow up care costs of babies not screened
- Newborn Screening Laboratory shutdown and plans
- Congenital Hypothyroidism Pilot Project

Members discussed:

- Next meeting date
- The laboratory shut down in three to four months will influence the content of what they can have and may even impact the meeting.

Dr. Speer requested that members send any additional items to him, the vice-chair, or Ms. Millangue for consideration on the next agenda and stated the next meeting is tentatively scheduled for October 24, 2022.

Dr. Speer adjourned the meeting at 2:30 p.m.

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Below is the link to the archived video of the July 8, 2022, Newborn Screening Advisory Committee (NBSAC) that will be available for viewing approximately two years from date meeting was posted on website and based on the DSHS records retention schedule.

https://texashhsc.new.swagit.com/videos/176815