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THE ADVISORY COMMITTEE ON
HERITABLE DISORDERS IN NEWBORNS AND CHILDREN

Advisory Committee Meeting - Day 1
November 3, 2022
9:30 A.M. to 3:00 P.M.

HRSA Headquarters
5600 Fishers Lane
Rockville, Maryland 20857

In-person and via Webinar
Attended via Zoom Webinar

C O M M I T T E E M E M B E R S

Kyle Brothers, MD, PhD

Endowed Chair of Pediatric Clinical and
Translational Research

Associate Professor of Pediatrics

University of Louisville School of Medicine

Ned Calonge, MD, MPH (Chairperson)

Associate Professor of Family Medicine

University of Colorado School of Medicine

Jannine D. Cody, PhD

Professor, Department of Pediatrics

Director, Chromosome 18 Clinical Research Center

Founder and President

The Chromosome 18 Registry & Research Society

Jane M. DeLuca, PhD, RN

Associate Professor

Clemson University School of Nursing

Metabolic Nurse Practitioner

The Greenwood Genetic Center

C O M M I T T E E M E M B E R S

(continued)

Ashutosh Lal, MD

Professor of Clinical Pediatrics

University of California San Francisco (UCSF) School
of Medicine

UCSF Benioff Children's Hospital

Jennifer M. Kwon, MD, MPH, FAAN

Director, Pediatric Neuromuscular Program

American Family Children's Hospital

Professor of Child Neurology

University of Wisconsin School of Medicine

Shawn E. McCandless, MD

Professor, Department of Pediatrics

Head, Section of Genetics and Metabolism

University of Colorado

Anschutz Medical Campus

Children's Hospital Colorado

C O M M I T T E E M E M B E R S

(continued)

Chanika Phornphutkul, MD, FACMG

Professor of Pediatrics and Pathology and

Laboratory Medicine and Genetics

Director, Division of Human Genetics

Department of Pediatrics

Brown University

Hasbro Children's Hospital / Rhode Island Hospital

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1 **E X - O F F I C I O M E M B E R S**

2 **Agency for Health care Research & Quality**

3 *Kamila B. Mistry, PhD, MPH*

4 Senior Advisor

5 Child Health and Quality Improvement

6

7 **Centers for Disease Control & Prevention**

8 *Carla Cuthbert, PhD*

9 Chief, Newborn Screening and Molecular Biology Branch

10 Division of Laboratory Sciences

11 National Center for Environmental Health

12

13 **Food & Drug Administration**

14 *Kellie B. Kelm, PhD*

15 Director, Division of Chemistry and Toxicology

16 Devices, Office of In Vitro

17 Diagnostics and Radiological Health

18

19 **Health Resources & Services Administration**

20 *Michael Warren, MD, MPH, FAAP*

21 Associate Administrator

22 Maternal and Child Health Bureau

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E X - O F F I C I O M E M B E R S

(continued)

National Institutes of Health

Diana W. Bianchi, MD

Director, Eunice Kennedy Shriver

National Institute of Child Health and

Human Development

ACTING DESIGNATED FEDERAL OFFICIAL

Soohyun Kim, MPH

Health Resources and Services Administration

Genetic Services Branch

Maternal and Child Health Bureau

1 **ORGANIZATIONAL REPRESENTATIVES** (continued)

2 **Association of Maternal & Child Health Programs**

3 Karin Downs, RN, MPH

4 MCH Director

5 Massachusetts Department of Public Health

6

7 **Association of Public Health Laboratories**

8 Susan M. Tanksley, PhD

9 Manager, Laboratory Operations Unit

10 Texas Department of State Health Services

11

12 **Association of State & Territorial Health Officials**

13 Scott M. Shone, Ph.D., HCLD (ABB)

14 Director

15 North Carolina State Laboratory of Public Health

16

17 **Association of Women's Health, Obstetric and Neonatal**
18 **Nurses**

19 Shakira Henderson, PhD, DNP, MS, MPH, RNCNIC, IBCLC

20 Board Director

21 Vice President, Research Officer

22 University of North Carolina Health

1 **ORGANIZATIONAL REPRESENTATIVES** (continued)

2 **Child Neurology Society**

3 Margie Ream, MD, PhD

4 Associate Professor

5 Director, Leukodystrophy Care Clinic

6 Director, Child Neurology Residency Program

7 Nationwide Children's Hospital, Division of Neurology

8

9 **Department of Defense**

10 Jacob Hogue, MD

11 Lieutenant Colonel, Medical Corps, US Army

12 Chief, Genetics, Madigan Army Medical Center

13

14 **Genetic Alliance**

15 Natasha F. Bonhomme

16 Vice President of Strategic Development

17

18 **March of Dimes**

19 Siobhan Dolan, MD, MPH

20 Professor and Vice-Chair for Research

21 Department of Obstetrics & Gynecology and Women's

22 Health, Albert Einstein College of Medicine

1 **ORGANIZATIONAL REPRESENTATIVES** (continued)

2 **National Society of Genetic Counselors**

3 Cate Walsh Vockley, MS, LCGC

4 Senior Genetic Counselor

5 Division of Medical Genetics

6 UPMC Children's Hospital of Pittsburgh

7

8 **Society for Inherited Metabolic Disorders**

9 Gerard T. Berry, M.D.

10 Harvey Levy Chair in Metabolism

11 Director, Metabolism Program,

12 Division of Genetics and Genomics

13 Boston Children's Hospital

14 Director, Harvard Medical School

15 Biomedical Genetics Training Program

16 Professor of Pediatrics, Harvard Medical School

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Welcome, Roll Call, Opening Remarks, and Committee Business .. 12

Department of Defense Newborn Screening System 38

Implementation of Conditions Recently Added to the Recommended
Uniform Screening Panel..... 99

Lunch Break..... 178

Public Comment..... 179

Krabbe Disease Evidence-Based Review Phase 2 Update 221

P R O C E E D I N G S

**Welcome, Roll Call, Opening Remarks, and
Committee Business**

NED CALONGE: Welcome to the 4th meeting of the Advisory Committee on Heritable Disorders in Newborns and Children in 2022. As we are gathered in-person for the first time since August 2019, I would like to open this meeting by taking a moment to acknowledge the land we gather on today.

We acknowledge that the land and water on which our meeting is taking place was, and is still, inhabited and cared for by the Susquehannock tribe, and Piscataway Peoples, including the Piscataway Conoy Tribe and Choptico Band of the Piscataway Indian Nation. We are grateful for their past and continued stewardship of this land and pay our respects to Maryland's Indigenous community and their elders, both past

1 and present, as well as future generations.

2 We are excited to welcome two new
3 Committee members. Dr. Jannine Cody is currently a
4 Professor of Genetics in the Department of
5 Pediatrics at University of Texas Health San
6 Antonio. In 1985, her daughter Elizabeth was born
7 with a rare chromosome abnormality called 18q-.
8 This was a condition that was easily diagnosed,
9 yet there was virtually no information on medical
10 management or on maximizing the potential of
11 individuals living with 18q-. In 1990, Jannine
12 founded the Chromosome 18 Registry and Research
13 Society as a way to bring affected families
14 together and to learn from each other. In 1997,
15 Jannine earned a Ph.D. in human genetics at
16 University of Texas Health San Antonio. While
17 pursuing her Ph.D., she developed the
18 multidisciplinary Chromosome 18 Clinical Research
19 Center, the goal of which is to make the
20 chromosome 18 conditions the first completely
21 treatable chromosome abnormalities. The center's
22 longitudinal study that includes over 700

1 participants has generated over 60 peer-reviewed
2 publications. Jannine has testified twice before
3 the US Congress and has served on a variety of
4 national committees and organizations related to
5 genetics.

6 Dr. Ash Lal is an attending Physician in
7 Hematology/Oncology at University of California
8 San Francisco Benioff Children's Hospital, and in
9 the and then the Division of Hematology, Blood,
10 and Marrow Transplant Cellular Therapies at the
11 UCSF Medical Center. He's the Director of the
12 UCSF Benioff Children's Hospital Oakland
13 Comprehensive Thalassemia Program and the Iron
14 Disorders Program and is Co-Director of the
15 Hemoglobinopathies Diagnostics Laboratory. Ash
16 serves as a member of the Medical Advisory Board
17 for the Cooley's Anemia Foundation, as well as the
18 Coordinator and Principal Investigator of the
19 Thalassemia Western Consortium.

20 His key areas of interest are
21 thalassemia syndromes, iron overload, iron
22 chelation, clinical gene therapy, nutrition,

1 erythropoiesis modulation, blood transfusion,
2 global hematology, access to care, prenatal
3 screening, newborn screening, and medical records
4 portability.

5 And I wonder as we welcome you, Dr. Lal,
6 if you'd like to make a comment or two.

7 ASHTOUSH LAL: I definitely feel very
8 much honored to be asked to participate in the
9 Committee, and this is my first time. So, I hope
10 to learn and to start making contributions as soon
11 as I can and as much as possible.

12 NED CALONGE: And we're sure you will,
13 and we're so pleased you're joining us. Thank
14 you. So next slide.

15 So, last month, the Maternal and Child
16 Health Bureau welcome Dr. Jeff Brosco as the
17 Director of the Division of Services for Children
18 with Special Health Needs. Dr. Brosco is a
19 historian and physician who teaches and practices
20 general pediatrics and developmental behavioral
21 pediatrics at the University of Miami's Miller
22 School of Medicine. He's directed the MCHB

1 directed leadership education in neurodevelopment
2 disabilities, training program at the Mailman
3 Center for Child Development since 2010 and has
4 served as the Director of Population Health Ethics
5 at the University of Miami's Institute for
6 Bioethics and Health Policy. In the past year, he
7 was named Associate Chair of Population Health for
8 the Department of Pediatrics.

9 His research focuses on history of
10 policy and ethics regarding child health. He has
11 authored fifty peer-reviewed publications and over
12 ninety other publications.

13 For more than two decades, Dr. Brosco
14 has held a series of leadership positions for the
15 Florida Department of Health's Children's Medical
16 Services, which seeks to improve the health of
17 children with special care needs and did this from
18 2017 to 2019. During that time, he was Florida's
19 Deputy Secretary of Health for CMS and he just
20 stepped down after four years as the state's Title
21 V Director for CHHCN.

22 He's also been active in National Health

1 Policy programs, including the Advisory Committee
2 on Heritable Disorders in Newborns and Children
3 and the National Workgroup on Standards for
4 Systems of Care for Children and Youth with
5 Special Health Care Needs.

6 And I wonder if I could ask him to come
7 up and just make a few comments. Thanks, Jeff.

8 JEFF BROSCO: Thank you so much, Ned.
9 It's great to be among friends again. As you
10 heard, I'm completely new to HRSA. It's been like
11 week five or six, but I'm certainly not new to
12 newborn screening and have been part of this group
13 in one way or another for two decades now.

14 So, what does this job mean? My kids
15 keep asking me, what do you actually do, Dad? And
16 I think the way that I think about it is families
17 sometimes have trouble getting what their -- what
18 their children need, and it's basically our job to
19 make sure that families can get everything that
20 their child needs so that they can play, go to
21 school, and grow up to be healthy adults. That's
22 basically it. And the way we're going to get

1 there's the blueprint. There is a series of
2 publications in pediatrics that came out in June.
3 Tomorrow, you'll hear from our colleague, Dennis
4 Kuo, a little bit more about the blueprint and
5 basically, it's the framework for how we get
6 there. How do we get every child to be able to
7 play, go to school, and become healthy adults?
8 How does the Committee fit in?

9 Actually, this Committee is an essential
10 part, it's a critical part of the system of care
11 for children with special health care needs and,
12 in particular, for both equity, equitable
13 distribution, and for fairness.

14 So, the fair part, I think, is one of
15 the really wonderful things about this Committee
16 is that it's an example of how health policy
17 should be done, right? We have community
18 involvement, we have stakeholders who say here are
19 important issues, here are conditions that need to
20 be addressed. We have an evidence review process,
21 it's transparent. We have the public voice, and
22 then we have a decision based on the evidence and

1 the values of our society. There's not a better
2 way to do health policy or a fairer way.

3 There's also an equity component, right?
4 And that is when it's universal, when every child
5 goes through newborn screening, we make sure we're
6 not missing out on kids. And a few of us
7 published something a couple years ago, and one of
8 the examples that I particularly remember is in
9 California, before and after screening for SCID.
10 And I think all of you know, for severe combined
11 immune deficiency, if you do a bone marrow
12 transplant early enough, the child has much better
13 outcomes than if it's clinically determined. And
14 for years, using California as an example, most of
15 the children who got transplanted were white, non-
16 Hispanic. In fact, it was such that we thought
17 population genetics kind of determined who had
18 SCID and who didn't.

19 And in the first two years after
20 universal newborn screening, about eighty percent
21 of the kids who got a bone marrow transplant were
22 Black, Hispanic or Asian. It suggested that this

1 really was about access to care, and that equity
2 could be changed if we have universal approaches
3 to what we do.

4 So, I want to, in particular, thank
5 Jannine and Ash for joining us, for all of you
6 guys for the hard work you do. This has a lot to
7 do to go through, and it's really important. So,
8 thank you.

9 NED CALONGE: We really appreciate the
10 addition of Jeff's leadership as somebody knows
11 the Committee well from his time spent with the
12 Committee and I think both HRSA and the Bureau are
13 so lucky to have him join us.

14 I was remiss, sorry, in not also
15 acknowledging a new organizational representative.
16 Karen Downs is the new organizational
17 representative for the Association of Maternal and
18 Child Health Programs and is joining us virtually
19 today, I believe.

20 She worked for the Massachusetts
21 Department of Public Health since 1999, and then
22 retired in 2022. She was the MCH Director for the

1 Title V Program and Director of the Division of
2 Pregnancy, Infancy, and Early Childhood within the
3 Bureau of Family Health and Nutrition. DPIE
4 promotes physical, social, and emotional well-
5 being and resilience by fostering healthy
6 environments in pregnancy, infancy, and early
7 childhood. Ms. Downs provided oversight for
8 maternal mortality reviews, perinatal home
9 visiting programs, maternal and infant mental
10 health programs, developing early childhood
11 systems of care, and programs focused on
12 addressing inequities and birth outcomes.

13 Prior to her work, at the end, MDPH, Ms.
14 Downs worked in Cambodia, Laos, Thailand, and
15 Nepal, providing emergency relief and
16 reconstruction and working with rural communities
17 to address family health and nutrition and enhance
18 women's economic capacity. Ms. Downs received her
19 BA in anthropology and sociology from Charleston
20 Carleton College, an MS in nursing from Pace
21 University, and an MPH from Boston University with
22 an MCH concentration and certificate in MCH

1 leadership.

2 So, we welcome you, and Ms. Downs, if
3 you'd like to make any comments, and it's
4 certainly okay if you don't. But I do wish to
5 recognize and thank Sabra Anckner for serving as
6 the interim org rep over the last couple of
7 meetings until Ms. Downs was able to join us.

8 So, with that, I'm going to turn things
9 over to Soohyun for the roll call and some
10 announcements.

11 SOOHYUN KIM: Thank you, Ned. I will
12 now do roll call. For Committee members, as I
13 call your name, please also report any new
14 conflict of interest since the last meeting. If
15 you respond no, we will record your attendance as
16 well as no new conflict of interest.

17 Kamala Mistry, from Agency for Health
18 care Research and Quality.

19 KAMALA MISTRY: Here, no conflict.
20 Thanks.

21 SOOHYUN KIM: Thank you. Kyle Brothers.

22 KYLE BROTHERS: No.

1 SOOHYUN KIM: Ned Calonge.

2 NED CALONGE: Here and no conflicts.

3 SOOHYUN KIM: From Centers for Disease
4 Control and Prevention, Carla Cuthbert.

5 CARLA CUTHBERT: I'm here. No conflicts
6 of interest.

7 SOOHYUN KIM: Thank you. Jannine Cody.

8 JANNINE CODY: Here and no conflicts.

9 SOOHYUN KIM: Thank you. Jane DeLuca.

10 JANE DELUCA: Present, no conflicts.

11 SOOHYUN KIM: From the Food and Drug
12 Administration, Kellie Kelm.

13 KELLIE KELM: Present and no conflicts.

14 SOOHYUN KIM: From Health Resources and
15 Services Administration, Michael Warren.

16 MICHAEL WARREN: Here, no conflict.

17 SOOHYUN KIM: Jennifer Kwon.

18 JENNIFER KWON: Here, no conflicts.

19 SOOHYUN KIM: Ash Lal.

20 ASHTOUSH LAL: Here, no conflicts.

21 SOOHYUN KIM: Shawn McCandless.

22 SHAWN MCCANDLESS: Here, no conflict.

1 SOOHYUN KIM: From the National
2 Institute of Health, Melissa Parisi.

3 MELISSA PARISI: Here, no conflicts.

4 SOOHYUN KIM: And Chanika Phornphutkul.

5 CHANIKA PHORNPHTKUL: Here, no
6 conflicts.

7 SOOHYUN KIM: Thank you. I will move on
8 to our organizational representatives. Please let
9 me know if you are present or not.

10 From American Academy of Family
11 Physicians, Robert Ostrander.

12 ROBERT OSTRANDER: Here.

13 SOOHYUN KIM: From the American Academy
14 of Pediatrics, Debra Freedenberg.

15 DEBRA FREEDENBERG: Here.

16 SOOHYUN KIM: From the American College
17 of Medical Genetics, Marc Williams.

18 We will not have a representative from
19 the American College of Obstetricians and
20 Gynecologists at this meeting.

21 From the Association of Maternal and
22 Child Health Programs, Karin Downs.

1 KARIN DOWNS: Here.

2 SOOHYUN KIM: Welcome. From the
3 Association of Public Health Laboratories, Susan
4 Tanksley.

5 SUSAN TANKSLEY: Here.

6 SOOHYUN KIM: From the Association of
7 State and Territorial Health Officials, Scott
8 Shone.

9 SCOTT SHONE: Here.

10 SOOHYUN KIM: Shakira from the
11 Association of Woman's Health, Obstetrics and
12 Neonatal Nurses will be joining us tomorrow.

13 From the Child Neurology Society, Margie
14 Ream.

15 MARGIE REAM: Here.

16 SOOHYUN KIM: From the Department of
17 Defense, Jacob Hogue.

18 JACOB HOGUE: Present.

19 SOOHYUN KIM: From the Genetic Alliance,
20 Natasha Bonhomme.

21 NATASHA BONHOMME: Here.

22 SOOHYUN KIM: From March of Dimes,

1 Siobhan Dolan.

2 SIOBHAN DOLAN: Here.

3 SOOHYUN KIM: From the National Society
4 of Genetic Counselors, Cate Walsh Vockley.

5 And from the Society of Inherited
6 Metabolic Disorders, Gerard Berry.

7 GERARD BERRY: Here.

8 SOOHYUN KIM: Thank you, everyone. I
9 will continue with a few standard members for the
10 Committee. As a Committee, we are advisory to the
11 Secretary of Health and Human Services, not the
12 Congress. For anyone associated with the
13 Committee or due to your membership on the
14 Committee, if you receive any inquiries about
15 ACHDNC, please let Ned and me know prior to
16 responding.

17 I also must remind Committee members
18 that you must recuse yourself from participation
19 in all particular matters likely to affect the
20 financial interests of any organization with which
21 you serve as an officer, director, trustee, or
22 general partner, unless you are also an employee

1 of that organization or unless you have received a
2 waiver from HHS authorizing you to participate.

3 When a vote is scheduled or an activity
4 is proposed, and you have a question about a
5 potential conflict of interest, please notify me
6 immediately.

7 So, according to the Federal Advisory
8 Committee Act, all Committee meetings are open to
9 the public. If the public wish to participate in
10 the discussion, the procedures for doing so are
11 published in the Federal Register Notice. For the
12 November meeting, there will be a public comment
13 period. Public participants may also submit
14 written statements. As a reminder, public
15 participants should be advised that the Committee
16 members are given copies of all written statements
17 submitted by the public and these public comments
18 become part of the official meeting record. Any
19 further participation will be solely at the
20 discretion of the chair and the DFO.

21 So, we have not been in this building
22 for a while. So, as a reminder, visitors only

1 have access to the pavilion which is this space,
2 the cafeteria, and the restrooms, which are right
3 outside this door to the left and the workgroup
4 meeting rooms. All the other areas are
5 restricted, and you require an escort by a HRSA
6 staff member and there are no exceptions.

7 If you need to leave the building and
8 reenter, you will be required to go through
9 security screening again and will require an
10 escort to meet you at security to escort you back
11 here. Fifteen minutes prior to and after the
12 lunch break ends, HRSA escorts will be at the main
13 entrance for those who need to leave and return.
14 If you need to leave and reenter at any other
15 times, please notify a HRSA staff member. They
16 all have escort badges or the registration team
17 outside this room. We also ask that you do not
18 take any pictures or videos in this building.

19 If we do have an emergency, and hope
20 that we do not, and need to exit the building, we
21 will go out the front door where you came in
22 through and turn left, and we're going to gather

1 in the parking lot area. HRSA staff escorts will
2 have a roster and they will make sure that
3 everybody is accounted for. So, please note that
4 you will have to reenter the building and go
5 through security. So, please leave any non-
6 essential items. Here is the map where we are
7 going to be gathering, where the trees are.

8 Let's see, all right. So, for all
9 attendees here, here is the Wi-Fi network
10 information if you need to connect. We will have
11 closed caption displayed on this screen. We're
12 working on that. For Committee members and
13 organizational representatives, if you are able
14 to, we ask that you join the Zoom meeting with
15 your video on, but please make sure that your
16 microphone and speakers are off. Audio will come
17 through the room speakers as they are right now.
18 When you speak, please remember to turn on your
19 microphone and speak into the microphone and
20 please speak clearly and state your full name for
21 ensuring proper recording.

22 For joining us virtually, members of the

1 public, audio will come through your computer's
2 speakers. If you can't access audio through your
3 computer, you may dial into the meeting using the
4 telephone number in the email with the Zoom link.
5 This meeting will not have a chat feature.

6 For Committee members and organizational
7 representatives joining us virtually, audio will
8 come from your computer speakers, and you'll be
9 able to speak using your computer microphone. If
10 you have any issues, you also have the call-in
11 information sent via Email.

12 In order to better facilitate the
13 discussion, Committee members and organization
14 representatives should be using the raise hand
15 feature when you would like to make comments or
16 ask questions. As a reminder, the Chair will call
17 on Committee members first and then organizational
18 representatives. Same here, please speak clearly,
19 and remember to state your name first to ensure
20 proper recording for Committee transcripts and
21 minutes.

22 Finally, to enable closed captioning,

1 please select the closed captioning icon on your
2 Zoom taskbar. From the menu that appears, select
3 show subtitles.

4 And with that, I will turn things back
5 to Ned.

6 NED CALONGE: I hope you can all excuse
7 the formality of the podium today. It helps with
8 the Zoom, and since I'm on camera for those folks
9 who are joining us virtually, it just makes it a
10 little bit easier. So, you'll see a little bit of
11 shuffling back and forth and just bear with us.

12 I'm going to start with Committee
13 business real quickly, starting with a GAMT
14 Deficiency. You'll remember at the May 2022
15 meeting, the Committee voted in favor of
16 recommending adding GAMT Deficiency to the RUSP.
17 Following the meeting, Dr. Powell, chair at the
18 time, sent a letter to Secretary Becerra with the
19 recommendation from the Committee, a copy of which
20 you can find on our website. Please remember that
21 the Secretary makes the final decision on whether
22 or not to accept the Committee's recommendation.

1 And when we receive it, the decision will be
2 posted on our website.

3 I'd also like to inform the Committee
4 that on June 29th, Parent Project Muscular
5 Dystrophy submitted a RUSP nomination package for
6 Duchenne muscular dystrophy. The Nomination and
7 Prioritization Workgroup has begun reviewing the
8 nomination and has been in communication with the
9 nominators and we'll continue to keep you updated
10 on next steps.

11 The Committee had an initial discussion
12 at our February meeting on the capacity to review
13 multiple nominations per year. In August, I
14 mentioned that we intended to form a workgroup
15 comprised of current and former Committee members
16 and other subject matter experts to look at the
17 capacity of the Committee and the NBS system, and
18 to develop criteria and a process for prioritizing
19 the review of nominated conditions. We expect to
20 convene this workgroup and begin work shortly
21 after this meeting, and we'll keep you advised on
22 our progress. Next slide.

1 Thank you to all for reviewing the
2 August 2022 meeting summary. I would ask, are
3 there any corrections to the meeting before we
4 vote to approve? Seeing none, we'll vote to
5 approve. And I'll just read down through the name
6 and Soohyun will record the vote on our voting
7 sheet.

8 I'm going to start with Kamila. And if
9 you're joining by Zoom --

10 KAMILA MISTRY: Yes.

11 NED CALONGE: Thank you. Did you hear
12 her, Soohyun? Okay. Then I have Kyle.

13 KYLE BROTHERS: Approve.

14 NED CALONGE: I vote yes. Carla.

15 CARLA CUTHBERT: Approve.

16 NED CALONGE: Jannine.

17 JANNINE CODY: I'll abstain since I
18 wasn't present for the meeting.

19 NED CALONGE: Thank you. Jane.

20 JANE DELUCA: Approve.

21 NED CALONGE: Kellie.

22 KELLIE KELM: Approve.

1 NED CALONGE: Michael.
2 MICHAEL WARREN: Approve.
3 NED CALONGE: Jennifer.
4 JENNIFER KWON: Approve.
5 NED CALONGE: Ash.
6 ASHTOUSH LAL: I would abstain.
7 NED CALONGE: Thank you. Shawn.
8 SHAWN MCCANDLESS: Approve.
9 NED CALONGE: Melissa.
10 MELISSA PARISI: Approve.
11 NED CALONGE: And Chanika.
12 CHANIKA PHORNPHTKUL: Approve.
13 NED CALONGE: With that, the minutes are
14 approved. I appreciate your attention. Next
15 slide.
16 NED CALONGE: This talks about our
17 topics for this meeting today. We're going to
18 have a presentation by the Department of Defense
19 on the Newborn Screening and Genetic Services
20 System, followed by a roundtable on State
21 Implementation of Conditions Recently Added to the
22 Recommended Uniform Screening Panel. We'll have

1 lunch, and after that, we welcome public comment.
2 And then we'll have a Phase 2 update on the Krabbe
3 Disease Evidence-Based Review. Next slide.

4 For those of you coming back tomorrow,
5 we're going to have a presentation on the
6 Blueprint for Change for Children and Youth with
7 Special Health Care Needs and their Families and
8 the Implications for Newborn Screening. We'll
9 then have workgroup updates from this afternoon's
10 meetings from Follow-up and Treatment, Laboratory
11 Standards and Procedures, and Education and
12 Training. And then we'll have a discussion on the
13 action items to advance newborn screening. Next
14 slide.

15 I want to talk just a moment about the
16 workgroup meetings this afternoon. You remember
17 at the meeting in August, the workgroups convened
18 to discuss successes and challenges in
19 implementing conditions added to the RUSP and
20 potential solutions or resources that could
21 address factors that contribute to the variability
22 of implementation, status of conditions added to

1 the rest of across the country.

2 The charge I have for the workgroups
3 this afternoon, is to start with some of the
4 solutions and ideas that the workgroups identified
5 and identify the top three priority solutions that
6 the Committee can consider in supporting state
7 implementation of conditions added to the RUSP.
8 Also, how to better strengthen the Newborn
9 Screening System. I would like to ask the
10 workgroups to focus on actionable solutions and
11 think about concrete next action steps.

12 Then tomorrow, each workgroup chair will
13 present a summary of their identified solutions
14 and the Committee will have a discussion session
15 to consider what was generated. You can access
16 links to each workgroup meeting at this link on
17 the slide or using the QR code. We will also
18 display this at the end of the meeting later.

19 So, we're going to move into items for
20 today and we're going to start our day with
21 learning more about the Newborn Screening System
22 within the Department of Defense.

1 We know that many military families rely
2 on state newborn screening programs for testing
3 and follow up, while others may use a private
4 laboratory and internal resources. We've invited
5 Dr. Hogue, our organizational representative for
6 the Department of Defense to provide us an update
7 on how newborn screening and genetic services are
8 delivered for military service members and their
9 families.

10 By way of introduction, Dr. Lieutenant
11 Colonel Jacob Hogue is currently the Chief of
12 Genetics at Madigan Army Medical Center, which is
13 located on Joint Base Lewis McChord in Tacoma
14 Washington. Madigan serves as the referral center
15 for complex medical needs for military service
16 members and their dependents throughout the
17 Pacific Northwest. In this role, Dr. Hogue is
18 responsible for the medical care of individuals of
19 all ages with suspected or confirmed genetic
20 conditions throughout the region. Prior to his
21 time at Madigan, Lieutenant Colonel Hogue served
22 as the Chief of Genetics at Brooke Army Medical

1 Center in San Antonio, Texas.

2 In addition to his role as clinician and
3 subject matter expert on genetics in the military,
4 Commander Hogue currently serves as the Chief of
5 the Department of Clinical Investigations and the
6 Chair of the Ethics Board at Madigan. Lieutenant
7 Colonel Hogue graduated summa cum laude -- cum
8 laude from Valparaiso University, then earned his
9 medical degree from the F. Edward Herbert School
10 of Medicine at the Uniformed Services University
11 of Health Sciences. He completed his pediatric
12 residency at Madigan Army Medical Center, and his
13 genetics residency at the University of
14 California, San Francisco. He's board certified
15 in pediatrics and medical genetics, and I feel
16 lucky that we have his representation to the
17 Committee and would like to invite him to the
18 podium.

19 Dr. Hogue.

20 **Department of Defense Newborn Screening System**

21 JACOB HOGUE: Great, thank you. It's
22 always fun to hear myself referred to as the Chief

1 of Genetics. It's just me there, so I always like
2 to -- it's fun to say I'm the chief of myself, I
3 am in charge of myself. I do have two genetic
4 counselors that I'm now in charge of, but mostly,
5 it's just me, so.

6 And I know you were curious who was
7 going to speak on behalf of the Department of
8 Defense today. My uniform kind of gives me away
9 in that respect.

10 They asked me to speak today, I think,
11 primarily related to newborn screening and the
12 context of discussions we've been having at these
13 meetings since I've been a part of these meetings
14 related to variability between states related to
15 adding conditions more recently added to the RUSP.
16 And we certainly bridge across multiple states and
17 regions, and then also related to access to
18 certain services and the availability of services,
19 particularly follow-up services for newborn
20 screening conditions. And so, I'm going to speak
21 both on how we approach newborn screening in the
22 Military Health System, as well as the

1 availability of genetic services, since that's
2 what I most directly am aware of, but I can give
3 other information as well.

4 Okay, I don't have any conflicts of
5 interest. Even though I'm speaking on behalf of
6 the Department of Defense, I do have to tell you
7 that these are my own opinions rather than
8 necessarily the official policy of the Department
9 of Defense, or the Defense Health Agency.

10 In order to understand what I'm talking
11 about today; I think you have to understand a
12 little bit about what our health system is. So,
13 I'm going to give you probably more background
14 than you all want to know about the Military
15 Health System.

16 The Military Health System is the title
17 that we use for all components related to health
18 in the military, sort of the overarching system
19 that's led by the Assistant Secretary of Defense
20 for Health Affairs, responsible not only for
21 health care delivery, but also medical education
22 with the Uniformed Services University of the

1 Health Sciences, my alma mater, is right down the
2 street, public health, private sector
3 partnerships, as well as medical research and
4 development.

5 In total, we serve about 9.6 million
6 beneficiaries, have a budget of about 50.5 billion
7 as of last year, which makes up seven percent of
8 the total DoD budget.

9 The Defense Health Agency is a fairly
10 new organization that you can kind of think of it
11 as the health care delivery arm of the Military
12 Health System. It was just formed in 2013.
13 Congressional mandate to do that. Prior to 2013,
14 military hospitals, also known as military
15 treatment facilities or MTFs, and their personnel
16 were under the control of Individual Services.
17 This Congressional mandate led to the formation of
18 the DHA and gradually have been transitioning to
19 all MTFs going under the control of DHA rather
20 than under the Individual Services. That was
21 actually just completed this last summer.
22 Currently, the director is Lieutenant General

1 Ronald Place. The goals of DHA are to integrate
2 health delivery under both direct care and
3 indirect care, and so, I'll speak to that in a
4 little bit. It manages all the MTFs, coordinates
5 management of the health care markets within
6 regions, and some of the goals are to allow for
7 rapid adoption of best practices, reduce unwanted
8 variation across the Military Health Care System.

9 One of the early pushes of DHA was the
10 creation and deployment of what's called MHS
11 Genesis MHS. MHS Genesis is the new electronic
12 health care system within the military. It
13 doesn't want to tell you about MHS Genesis. Oh,
14 there we go. So, MHS -- we've had an electronic
15 health care record systems going back to 1996
16 within the Military Health System, a number of
17 iterations of that. Prior to MHS Genesis, all of
18 that was kept specifically at different military
19 treatment facilities or regionally. It was not
20 shared across the entire Military Health System.
21 And importantly, it was not integrated with the VA
22 system. So, there was a Congressional mandate

1 with the National Defense Authorization Act of
2 2008 that mandated that the Department of Defense
3 and the VA create a joint use of an electronic
4 health system so that data was better transferred
5 as service members moved out of the military into
6 the VA system.

7 As you will see, with some things
8 related to newborn screening, while the military
9 can rapidly deploy and meet those needs, some
10 things move very slowly in the military, and so
11 that from 2008, the contract for creating that
12 system was awarded in 2015 on a Cerner based
13 platform. 2017, at Madigan Army Medical Center,
14 we were the first system to go live, and it's been
15 a slow process expected to be completed in 2023.
16 The importance of that is that it should have
17 shared access to information to include
18 information about newborn screening test results
19 as our servicemembers and their families move from
20 location to location, which is a very integral
21 component of what happens in the Military Health
22 System.

1 What most people are familiar with when
2 they think of the Military Health System and don't
3 work directly in our system is TRICARE. TRICARE
4 is more generally thought of as a health
5 insurance-like program that pays for care delivery
6 by civilian providers. It does have some
7 components as it relates to the direct care, which
8 is what we provide in military treatment
9 facilities, but a large component of the care that
10 is provided to military beneficiaries is provided
11 by civilian providers and covered by TRICARE.

12 There is always this balance of what we
13 call make and buy decisions within the Military
14 Health Care System of what do we provide directly
15 and what do we contract and send outside of our
16 direct system, and this is a component of that.

17 TRICARE contracts with third-party
18 administrators divided by regions. So currently,
19 the administrators for that are Humana and TRICARE
20 East and HealthNet and TRICARE West. And there's
21 also an overseas component.

22 The initial name TRICARE was -- there

1 were three plans that people could choose from.
2 Those have actually changed over time. So,
3 they've retained the name even though there's more
4 than three plans now.

5 As I alluded to, there's this push and
6 pull back and forth between direct and contract
7 care in the Military Health Care System. So, the
8 direct care system is what we provide at military
9 treatment facilities or clinics. Currently, there
10 are forty-nine inpatient hospitals and medical
11 centers within the Department of Defense, thirty-
12 two of those being within the continental United
13 States and 465 clinics. You can see the numbers
14 that we have for active duty and civilian
15 personnel who work in those military facilities.

16 On the contrast is the amount that is
17 done in the purchased care system, and you can see
18 the large number of network providers and
19 hospitals that are there within that system.

20 I would note that if you look at the
21 most common procedure that is done in the MHS
22 that's billed is childbirth, and so, that kind of

1 reflects the age of our population and the
2 frequency that we care for mothers delivering and
3 newborns as well.

4 This is a map showing where military
5 treatment facilities are in the background. The
6 green represents the numbers of beneficiaries.
7 So, that includes not only active duty, active-
8 duty families, as well as retirees, and their
9 families, and individuals that are in the
10 reserves. When they're activated, they are able
11 to access these services as well. It's small for
12 you to see, but all of the red spots are where
13 there are military clinics and the H's blue -- H's
14 are where there's hospitals.

15 In terms of the direct care system,
16 there are priorities for care at military
17 treatment facilities. The priority is -- the
18 first priority is taking care of active-duty
19 service members. That's the primary mission of
20 the Military Health System is ensuring that we
21 have a ready military force -- a medically ready
22 force. And so, that does -- they do have the

1 first priority for care where that's available.
2 The second priority is for family members of those
3 active-duty individuals, and then you can see that
4 the priority goes down.

5 So, what this means is that if there's a
6 limited amount of space for care at a military
7 treatment facility, as you get further down the
8 priority, those are more likely to be pushed to
9 the network to be cared for by civilian providers
10 utilizing the TRICARE benefit.

11 What do our eligible beneficiaries look
12 like? This was as of 2021 TRICARE evaluation
13 report. In the maroon is the active-duty service
14 members, 2.3 million active-duty service members
15 within the Military Health Care System. The
16 largest piece of this pie is the blue, which is
17 the family members of the active duties. You can
18 see what a large chunk of that is, with a large
19 percentage of those being children under age four.
20 The next largest piece of the pie would be
21 retirees and their family members making up
22 fifteen percent and seventeen percent. They

1 divide it by age sixty-five, because that's where
2 they turn over to what's called TRICARE for Life
3 when individuals are eligible for Medicare.

4 There are a total of about 120,000
5 births per year in the Military Health System.
6 About half of those occur at military treatment
7 facilities, with the other half occurring at
8 civilian hospitals.

9 Where our service members are located.
10 I couldn't find better breakdown of where all of
11 our beneficiaries are. So, this is just the
12 active-duty service members themselves. Eighty-
13 seven percent are located within the US and
14 territories, but we have a substantial proportion
15 of active duty that is stationed at places outside
16 of the United States, which is an important
17 component of the medical care that we provide and
18 how we design that medical care.

19 Another program that I thought I would
20 share with you that people may not be familiar
21 with, but I think is important related to
22 conditions identified by newborn screening, is the

1 Exceptional Family Member Program. This program
2 was established in the early eighties. It covers
3 all of the services of the Department of Defense.
4 Spouses, children, and dependent adults are
5 included in the system, and really, individuals
6 are required to be enrolled in the EFMP program if
7 they have any special medical -- any condition
8 that requires special -- specialty medical care
9 for a chronic condition where those specialty
10 services may not be available everywhere. Also
11 for significant behavioral health concerns and for
12 children receiving early intervention or special
13 education services. And what the EFMP System
14 primarily does is it controls assignments. So,
15 the goal is to only station individuals at
16 locations where their family member's medical
17 needs and educational needs can be met. So, it
18 will control and not allow someone to go to a
19 location where those needs cannot be met. About
20 ten percent of military families are enrolled.
21 So, a substantial proportion of the military have
22 at least one family member who's enrolled in the

1 EFMP program.

2 We have a long history of providing care
3 for dependents, including children, in the
4 military. In terms of laws covering that, that
5 goes all the way back to 1884.

6 The military service members would bring
7 families with them. There wasn't really any other
8 medical care available and the medical care that
9 was available through the military was often
10 seeing family members and charging them for that.
11 So, it was actually more of a response where they
12 didn't want them to be charging those service
13 members for that. But that was the first law
14 mandating military to take care of dependents'
15 medical care.

16 As World War II winded down, and we kept
17 the larger standing military force than we had
18 previously done outside of any active military
19 conflict, there became quite a need to take care
20 of service members, families, family members. And
21 so, in 1943, Congress approved funding.
22 Initially, it was only to care for maternity care

1 find numbers for how many civilian pediatricians
2 there are. In total, across all the services,
3 there's about two hundred pediatric
4 subspecialists, including all the pediatric
5 specialists. So, a fairly small, small number,
6 but it gives you an idea of how much direct care
7 we're able to provide for pediatric patients.

8 That's a lot of background for you to
9 kind of talk relatively quickly about newborn
10 screening in the Military Health System. I took
11 the timeline that is on the ACHDNC website and put
12 that on the bottom of this related to important
13 time points related to this Committee and
14 Recommended Uniform Screening Panel. And on the
15 top, I put some timeline related to policy and
16 contracting issues that have arisen in the -- in
17 the military related to that.

18 So, the first actual policy related to
19 newborn screening in the military was an Army
20 Policy in 2002 that required military treatment
21 facilities to provide newborn screening. At the
22 time, the policy required a total of four tests --

1 at least four tests had to be -- that had to be
2 done. That obviously became an issue through the
3 subsequent following years with the formation of
4 this -- this Committee and ACMG Expert Panel and
5 the recommendation for twenty-nine primary
6 conditions and twenty-five additional secondary
7 conditions, and there became quite a disparity
8 between states. And because we have babies in the
9 Military Health Care System across all of those
10 states, there became a major concern that there
11 was a major difference in what we were providing
12 from one location to another across the military.

13 There was a TRICARE Management Agency
14 requested study for this in 2005, and there was a
15 recommendation to make sure that there was
16 adoption of expanded screening. As I said,
17 sometimes things move quickly in the military,
18 sometimes they move slowly. And so, you can see
19 the first time that actually led to any policy
20 change was in 2011. And at that time, there was
21 actually a central contract that was put into
22 place that was with PerkinElmer Genetics. And the

1 intention of that contract was to move all newborn
2 screening in the military to that contract. So,
3 rather than utilizing state laboratories, it was a
4 move to using one central laboratory. The
5 intention of that was to ensure that babies across
6 the Military Health Care System were having the
7 same screening. So, as children moved from one
8 location to another, that we would ensure that
9 everyone was getting the same screening and that
10 information on the results would be available,
11 regardless of where someone moved.

12 That contract expired in 2016. A number
13 of concerns arose during that time period that led
14 to allowing that contract to expire. Some of the
15 main ones were the implementation of a broader set
16 of tests across multiple states. So, the major
17 disparity from one state to another of what
18 testing was done was reduced during that time
19 period.

20 The other issues were related to, as
21 we've talked about many times in this Committee,
22 the newborn screening follow-up and subsequent

1 treatment is a major component of what occurs in a
2 Newborn Screening System, not just the testing.
3 And the contract with PerkinElmer covered the
4 testing. It didn't really cover follow-up. And
5 so, particularly in remote locations where there
6 was not pediatric specialists available in the
7 direct care system, some challenges of ensuring
8 appropriate follow-up testing and subsequent
9 required care when it was not done as a part of
10 the state system. And primarily for those
11 reasons, the decision was made to move newborn
12 screening back to the state programs with the
13 expiration of that contract.

14 So, as it relates to current newborn
15 screening policy in the Military Health System, I
16 would say, there is currently, again, we just
17 transitioned to the Defense Health Agency very
18 recently. So previously, there's policies that
19 are under the Army, the Air Force, and the Navy.
20 They're separate policies. There's been no
21 pooled-together unified policy under Defense
22 Health Agency. That is a discussion that's

1 happening right now within the DHA Women and
2 Children's Clinical Support Group of DHA. The
3 policies are essentially the same. There's some
4 minor differences, but essentially, with the
5 expiration of the central contract, CONUS is
6 continental United States. So, that's a term that
7 gets used within the Defense Health within the
8 Department of Defense for OCONUS is out of the
9 continental United States and CONUS is within the
10 continental US.

11 MTFs are strongly encouraged to utilize
12 their State Newborn Screening Program. And if
13 they continue to use the central contract, they
14 had to establish a formal plan for confirmatory
15 testing, follow-up, and specialty care referrals.
16 A little bit more vague as it relates to OCONUS
17 sites. So, they were encouraged to contract with
18 state programs, but were able to still utilize the
19 central PerkinElmer contract. So, that's where
20 things currently stand.

21 I thought I'd give you a couple examples
22 of sites that are considered OCONUS by the

1 military and what is currently happening at those
2 locations. I pulled Alaska first. So, while, you
3 know, Alaska is a state, it's considered OCONUS by
4 the military. In Alaska, I put the locations of
5 military treatment facilities here in red is Coast
6 Guard and blue is Air Force and the green are
7 where Army sites are. There's two major military
8 treatment facilities that care for children within
9 Alaska and Bassett Army Hospital is in Fairbanks
10 and JBER is outside of Anchorage. They utilize
11 the state program within Alaska currently, and
12 Alaska is sending their newborn screening to the
13 state of Iowa at this time. So, that is what is
14 happening within the Alaska military treatment
15 facilities.

16 Their newborn screens are going to Iowa.
17 They get recommendations back from the Iowa
18 program. I would say that they then often contact
19 -- so a couple of examples. More recently, we had
20 identification of a child with cystic fibrosis
21 that was in Alaska. That child received care
22 through a pulmonologist who was in Anchorage, we

1 provided telemedicine genetics for that child, and
2 that was all in the terms of getting EFMP started,
3 and then that child was subsequently moved to a
4 different location.

5 Similarly, the last one we had that
6 turned out having to get transferred down to
7 Madigan from Alaska was a child who had SCID that
8 was identified by a newborn screen, got
9 transferred down to Madigan, confirmatory testing
10 done at Madigan, and then went to Seattle
11 Children's for a bone marrow transplant as a part
12 of the care there. So, those are a couple
13 examples from Alaska.

14 Within the United Kingdom, mostly we
15 have Air Force Bases within the United Kingdom.
16 The main Air Force Base that cares for children,
17 there is RAF Lakenheath. It's outside of
18 Cambridge. They are contracted with the state of
19 Wisconsin. So, they send their newborn screens to
20 the state of Wisconsin, and when they get
21 abnormal, they get recommendations back from the
22 Wisconsin Newborn Screening Program. When they

1 have to then access care for follow-up or for
2 treatment, mostly they're able to do that through
3 specialists in Cambridge, but occasionally have to
4 go to Great Ormond Street Hospital in London. And
5 then they've also had some children that were
6 identified that then were enrolled in EFMP and
7 then were moved back to the to the United States.

8 They do have a couple of children, they
9 told me, that have stayed there who have MCAD
10 Deficiency that has not required substantial
11 treatment, and they're cared for by specialty
12 providers at Great Ormond Street.

13 And lastly, in Germany, we have a number
14 of centers in Germany. The main one that provides
15 direct care for children is Landstuhl. There is
16 still a small NICU and neonatologist at Landstuhl.
17 They also have they call it stork nesting where
18 mothers who are pregnant and are set to deliver
19 but are stationed at other more remote locations
20 will be brought to Landstuhl and live in that
21 region and then deliver at Landstuhl. The baby
22 receives care there for a period before they go

1 back to where they're -- where they're living.

2 So, they have those come in as well.

3 Landstuhl has continued to utilize the
4 PerkinElmer contracts. So, their newborn
5 screening is occurring through PerkinElmer, and
6 they get results back through them. They then
7 have to access care in the in the German medical
8 system for follow-up. So, those are a couple
9 examples related to how that's occurring.

10 And Korea is another location we have a
11 large -- I didn't -- I felt like you saw enough
12 maps of locations that I didn't need to include
13 more -- but Korea is another one that's still
14 continuing to use the PerkinElmer contract. I was
15 actually contacted about a positive screen for
16 galactosemia there yesterday that we're working
17 through follow-up for.

18 I'm going to shift a little bit just to
19 kind of tell you about what do we have for direct
20 care as it relates to genetics. Again, I'm at
21 Madigan Army Medical Center. So, you can see the
22 one there. That's where I'm the chief of myself.

1 These are the locations where we have a genetics
2 provider. Currently, we have a total of eleven
3 geneticists within the Military Health System and
4 fourteen genetic counselors. Now, not all of
5 these are full time genetics providers. Keesler,
6 I'll talk about in a little bit, has -- we have a
7 genetics lab that that does a lot of the genetic
8 testing within the direct system within the
9 military. And there are three geneticists
10 primarily, our molecular and cytogeneticists.

11 These are the locations, kind of the
12 same map, just kind of showing where we all are.
13 So, we're mostly where we have the major treatment
14 facilities within the Military Health Care System.
15 I would say that these are similar locations where
16 other pediatric specialists are. So, in terms of
17 the other specialists that we've discussed in
18 these meetings of there being shortages of related
19 to newborn screening, follow-up, pediatric
20 endocrinologist, child neurologist, these are all
21 the same locations where we have those specialties
22 within the direct care system as well.

1 Questions I'm frequently asked about
2 when I see -- when I meet with people outside the
3 military and they're asking about how they've
4 navigated TRICARE related to the coverage of
5 genetic counseling and genetic testing within the
6 TRICARE system. So, I thought I'd touch on that
7 real quick and some challenges that arise related
8 to that.

9 So, this is from the TRICARE manual,
10 what TRICARE lists as authorized providers. And I
11 would just say, genetic counselors are currently
12 not considered authorized providers within the
13 TRICARE system. Again, TRICARE is closely aligned
14 to Medicare. And so, Medicare does not consider
15 genetic counselors to be authorized providers, and
16 so, TRICARE follows that policy. What that means
17 is some challenges related to when we don't have
18 those services directly available at military
19 treatment facilities and people are sent to the
20 network. It's very challenging to actually access
21 care through a genetic counselor in the system
22 because they can't bill TRICARE for that.

1 In terms of genetic testing, this is
2 what's in the TRICARE policy as it relates to
3 genetic testing. I hear from lots of individuals
4 outside the military about challenges that they've
5 had with trying to get genetic testing covered for
6 TRICARE patients. So, this is -- it's, you know,
7 TRICARE says it covers genetic counseling, again,
8 provided by an authorized provider. So, it's
9 written in the TRICARE policy is basically anyone
10 who's an authorized provider, which could be a
11 physician, a nurse practitioner, a PA, those are
12 authorized, right, are the people that TRICARE
13 says should be providing the genetic counseling,
14 and that's a circle that we go into not
15 uncommonly.

16 So, I feel fortunate that we were able
17 to have some genetic counselors within the direct
18 care system that kind of fall outside of this
19 policy that we're able to utilize for that. But
20 it's a challenge for -- for access for areas that
21 don't have that directly available.

22 We do have the ability to add a military

1 treatment facility. I'm not really bound by the
2 rules of TRICARE, nothing that I do actually gets
3 TRICARE approval. So, it's a little bit outside
4 of the insurance access component of that. So,
5 it's a matter of my hospital paying for things.
6 We actually have a reference laboratory that does
7 genetic testing, that anybody -- anyone who's at a
8 military treatment facility can use.
9 Unfortunately, civilian providers are not able to
10 send to this, even for TRICARE patients.

11 They have a fairly broad genetic testing
12 menu, actually, so cytogenetics and broad number
13 of next-generation sequencing panels like some
14 sequencing, and a number of other things that have
15 come up as it relates to newborn screening are
16 included in newborn screening to include spinal
17 muscular atrophy that are covered there.

18 With the formation of DHA, I am hopeful
19 that we will get some traction with making some
20 changes both in policy and expanding the services
21 that we're able to provide directly for families
22 and within the military. This year, DHA created a

1 Clinical Genomics and Precision Medicine Clinical
2 Support Service, that we're outlining some goals
3 over the next few years.

4 Some of those near-term goals are to
5 expand the laboratory services for direct testing
6 that we're able to do, addressing issues related
7 to the clinical genetics workforce and genetic
8 counselors in particular, some issues related to
9 pharmacogenomics and how that information is put
10 into MHS Genesis and translated across the system.
11 And then we're working some -- there's some unique
12 issues related to policy as it relates to genetic
13 testing and active-duty service members that we're
14 trying to address as well.

15 So, in summary, so I would say, another
16 thing I'm asked about not uncommonly is how much
17 is the military going to continue to provide
18 medical care for -- For pediatrics? How much are
19 we going to send out to the -- to the community
20 versus providing direct care, and I think
21 everything right now is we're continuing to train
22 the same number of pediatricians, we're sending

1 the same number of people to pediatric specialty
2 care, we're continuing to provide really the same
3 amount of direct care for complex specialty needs
4 within the military system. And I think that, at
5 least in the near future, is going to continue to
6 be the case. There are a number of changes
7 related to the DHA transition, both in terms of
8 this push/pull between direct care that we provide
9 and the contract care, and that does relate to
10 where children are -- where babies are born, and
11 then therefore where their newborn screening is
12 done.

13 The MHS Genesis transition and how that
14 information will be seen visible across the DHS,
15 Department of Defense, as well as some issues
16 related to newborn screening are related to that.
17 I've had a request to try and work towards
18 electronic order entry and results return within
19 MHS Genesis since we have a single system with
20 newborn screening labs. The current priorities as
21 it relates to MHS Genesis changes have to align
22 with both a VA and DoD goal, and the VA does not

1 provide care for newborns. So, it is not an early
2 change that will occur. But it's something that
3 I'm hoping we can get.

4 As of right now, the Newborn Screening
5 Program is primarily aligned with states. There
6 likely will be a DHA policy update related to
7 newborn screening within the next year. I expect
8 that it will align with that. And I've given you
9 some information both about clinical genetics,
10 availability, and genetic testing coverage within
11 the Military Health System.

12 And that's all I have. Any questions
13 for me?

14 NED CALONGE: Thanks so much, Lieutenant
15 Colonel Hogue. That was a great presentation and
16 very informative. And I'm wondering if maybe I
17 could ask you to stay at the podium while we have
18 questions and discussion?

19 JACOB HOGUE: Sure.

20 NED CALONGE: That would be great. So,
21 I'm looking at the room and reminding you that
22 we're going to talk to Committee members first, as

1 far as questions and discussion, and then we'll
2 ask our organizational representatives for
3 additional comments, discussion, and questions. I
4 realize that there are folks on the phone. I'm
5 going to ask you to use the raise hand function on
6 your Zoom screen. For those folks in the room,
7 you'll notice you have a microphone in front of
8 you, and there's a little button on it. So, if
9 you're not using the microphone, could you push
10 the button so that it's not red? And Dr. Lal, I'm
11 going to ask you to unmute, or mute your -- yours,
12 and then when you speak, unmute, and we'll kind of
13 go from there.

14 The last thing for people in the room is
15 if you have a question, if you could let me know
16 by just putting your name card on it's side, that
17 would be most helpful.

18 So, I'm going to start Lieutenant
19 Colonel off, if that's okay, and just ask a couple
20 of questions. So, we know there is variation by
21 State Newborn Screening Programs, in terms of
22 implementation on conditions added to the RUSP,

1 and I wondered how that shows up across the
2 active-duty families. Does that influence what
3 families are screened for on items of the RUSP?

4 JACOB HOGUE: Absolutely. I mean, so
5 most of them are aligned with the state where
6 they're born. So, an example would be between
7 Washington state where we have added some of the
8 newer disorders to include XALD and MPS 1 versus a
9 child who's born in Hawaii, that we then have
10 moving, where they have not added those disorders.
11 So, there are some differences absolutely state to
12 state, and those are reflected in the newborn
13 screening that's occurring, I think.

14 How does -- how will that influence how
15 we move forward as it relates to policy? I think
16 it's unlikely that we move back to a centralized
17 contract. While those differences are important,
18 I think the other differences or the challenges
19 that we saw arise from moving to a centralized
20 contract kind of balancing the issues related to
21 follow-up and treatment versus the differences of
22 what is tested from one state to another will be

1 how that is looked at is looking at that balance.
2 And I foresee that those differences will not
3 outweigh the challenges related to follow-up and
4 treatment to change that policy back to what it
5 was.

6 NED CALONGE: I appreciate that. And I
7 understand that, you know, it's a -- it's a
8 current hot topic here for the Committee and for,
9 I think, newborn screening across the country and
10 appreciate you kind of highlighting the reason
11 that's an issue.

12 The other question has to do with, I
13 would think that DoD and the military families
14 system would be an ideal place to think about
15 quality improvement metrics, specifically thinking
16 about the time to screening positivity, time to
17 confirmatory testing, and time to treatment. I'm
18 wondering if -- if -- if you have, I guess the way
19 I'd say, the resources, and the direction to kind
20 of do that quality improvement for newborn
21 screening, across the DoD?

22 JACOB HOGUE: I would say it would be a

1 very good place for us to look because we're so
2 broad on what we collect or where we're treating
3 children. But I would not say that we have any
4 unified policy or place to look for that. It's
5 been very -- examples would be where we've looked
6 closer into newborn screening sent from OCONUS
7 regions with concerns that there might be delays
8 in those coming and there have been some
9 challenges related to both timing and then issues
10 getting through customs actually where newborn
11 screens and had to be repeated.

12 So, I think kind of looking at where we
13 think the most substantial challenges will be, is
14 where we've been able to put some priorities, but
15 you're kind of looking at the -- the newborn
16 screening. Anybody who's looking at the newborn
17 screening system in a particular way, I would not
18 say that that's been a, you know, a major
19 centralized plan for addressing that in a way that
20 that would be better addressed.

21 NED CALONGE: Well, I have to say I
22 appreciate that. I guess it's also important to

1 tell you, I appreciate that you're there and
2 taking on the service responsibility and I just --
3 I'm always looking for, you know, what -- what
4 folks in general could do to make things better,
5 and I think when you're -- when you're a
6 department of only one, your personal resources,
7 especially if it's spread over so many other
8 duties, I think is tough. I hope you hear that
9 we're very appreciative you're there.

10 JACOB HOGUE: Thank you.

11 NED CALONGE: I'm going go next to Kyle.

12 KYLE BROTHERS: Yeah. I just wanted to
13 ask about timelines and turnaround time. I just
14 know in Kentucky, we have, you know, a few-hour
15 drive, and that creates all kinds of barriers and
16 sending samples across the Atlantic Ocean seems
17 like it could really create remarkable delays.
18 I'm just curious about that.

19 JACOB HOGUE: Yeah. So, that was when I
20 was speaking to the people in Korea, Germany, and
21 England that I've spoken to recently about this.
22 It's -- so, this kind of comes a little bit to the

1 direct and indirect system and what happens kind
2 of uniquely in those situations, because they're
3 actually not delivering many babies at those
4 military treatment facilities anymore. So, what
5 frequently happens in Korea is -- and Germany
6 other than Landstuhl, most of the babies are
7 actually born out in the network here, and they
8 have a newborn screen that is there that is in the
9 Korean system or in the German system. So, they
10 may get that back. And then it's actually only on
11 their follow-up, they come a few days after, or
12 they will then send the screen to the state of
13 Wisconsin or PerkinElmer genetics. And so, where
14 they will often get the screen back, they'll be
15 contacted by the German or the Korean hospital
16 letting them know that they had this abnormal
17 around the same time that they're getting a result
18 back.

19 My understanding is that the turnaround
20 has been fairly good for those. I mean, they go
21 overnight, the same way as they often go other
22 places and the turnaround -- the challenges have

1 really been those smaller numbers that get held up
2 in some way by shipping problems or customs
3 problems. Those have been the ones that really
4 are a holdover for what the difference is. But
5 otherwise, I think it's not been as much of a
6 challenge. But again, in a lot of those places,
7 it's actually -- it's actually a second screen
8 that's occurring that's going there and sort of
9 ensuring that that's done within the auspices of
10 the US health care system, I guess is the goal
11 from that rather than having those contracts be
12 with health care resources within another country.

13 NED CALONGE: Thanks. I just thought
14 I'd just take one second to talk about social
15 issues. So, the National Academies, a long time
16 ago, abandoned the use of honorifics or degrees
17 and calling on people thinking that from an
18 equitable standpoint, not using the doctor, or
19 designation was something that made communication
20 a little bit more easy flowing. I do think
21 Lieutenant Colonel is one I'd like to keep, if
22 that's okay with Lieutenant Colonel, but if I call

1 you by your first name, I hope that's acceptable.
2 And I would kind of like that to be the norm for
3 the Committee moving forward, unless someone has a
4 strong objection. And given that preamble, I'd
5 like to call on Michael.

6 MICHAEL WARREN: Thank you. The
7 question I had was related to timeliness. So,
8 it's been covered. Thank you.

9 NED CALONGE: Thank you. I'm going to
10 go to Jennifer.

11 JENNIFER KWON: Thank you so much. I
12 have to say, Lieutenant Colonel, I have a hard
13 time picturing sort of what short-term follow-up
14 looks like. You've done a really nice job talking
15 about newborn screening and the identification
16 maybe of screen positives. But I was wondering if
17 you could share an anecdote maybe about how short-
18 term follow-up works. I think you touched upon it
19 by talking about your call. But let's say you
20 want to initiate treatment or want to do
21 confirmatory testing, I was wondering how that
22 works within the military system.

1 JACOB HOGUE: It's really going to
2 depend on where you are and what resources are
3 there. So, I think there's -- there's no unified
4 answer to that. So, if someone -- if a baby is
5 born at Madigan Army Medical Center, where I am,
6 it's going to occur very similar to how it does at
7 your hospital. So, they have me there, we have a
8 pediatric endocrinologist, we have hematology
9 oncology, we have all the ability to send any
10 confirmatory testing. Often, we turn out sending
11 that testing through the same laboratories as the
12 state of Washington Newborn Screening Program is
13 recommending so that it's aligned with that
14 program as compared to where I would otherwise
15 send genetic test results or metabolic tests to
16 provide confirmatory results. So, that part will
17 look very similar to any other particular
18 location.

19 Where that becomes more unique is in
20 locations where there are no pediatric specialty
21 providers related to follow-up. So, a lot of that
22 falls harder on the general pediatrician, and it's

1 part of why we try to have general pediatrics
2 providers at many of those locations. And that's
3 one of the goals of having that aligned with the
4 state programs is they often will facilitate
5 earlier access to specialty care providers.
6 Within state programs, that works fairly well.
7 Overseas, it's more of a challenge, and I think
8 it's kind of -- what frequently happens is reach
9 backs to those of us that are at military
10 treatment facilities. So, all of the
11 pediatricians that are in those locations trained
12 at facilities where they have all those pediatric
13 specialists, and they reach back all the time so
14 that I might get contacted from -- even though I
15 have no control, I'm directly responsible for the
16 care that occurs in Korea -- they will reach back
17 to me as soon as I get that abnormal and we'll
18 work together to work towards a follow-up.

19 JENNIFER KWON: And just to follow with
20 a question to that, so how are treatments
21 reimbursed? Like, are -- do you feel like that's
22 a challenge through TRICARE? Do families have to

1 use, let's say, State Medicaid as a secondary for
2 reimbursement?

3 JACOB HOGUE: I would say that I
4 probably don't have as much of a direct eye on how
5 TRICARE provides coverage for pharmacy benefits.
6 It's similar to any other insurance plan. So,
7 there is coverage for those. I know that we've
8 had challenges with quick, particularly newer,
9 very expensive treatments. I'm assuming that SMA
10 treatment is on your -- your mind, as it relates
11 to that. And we've seen that be a challenge that
12 I've seen come up. We have a challenge, you know,
13 often that is an example of something that even
14 though we might have providers to care for in the
15 acute time period, our hospital has a budget that
16 it has given us. There is no special pharmacy
17 budget, for example. So, if there's something
18 that arises, that's over a million dollar-
19 treatment that comes up as a one time, we would
20 have to come up with that out of our hospital
21 pharmacy budget, which is relatively small, in
22 order to get that in the short term. So, that

1 would be example even where I am located, where we
2 might have the individuals available to provide
3 that treatment. That might actually go out to the
4 network to be able to get that care on a quicker
5 access. But, in general, that's not the case. We
6 usually -- I don't usually have to. Again, what
7 we do at a direct care facility doesn't have to
8 get TRICARE authorization in the same way that you
9 were if you were taking care of a TRICARE patient.
10 So, it's really just internal, within the hospital
11 decisions about how the budget is utilized. And
12 usually, that's not a challenge for me, as it
13 relates to pharmacy. The one offs are the ones
14 where the pharmacy doesn't have the budget to get
15 that in the short term. If that answers your
16 question.

17 JENNIFER KWON: It does, thank you.

18 NED CALONGE: Chanika.

19 CHANIKA PHORNPHTKUL: Thank you very
20 much. I have a question about how can we at the
21 medical facility -- I'm practicing in Rhode Island
22 -- so, Newport is a big Navy station, and we do

1 see patients that have TRICARE. And how -- and
2 the family moved, and I always have a hard time
3 trying to connect the patient back to the
4 community of, you know, where I could, you know,
5 send them back. That's sort of, how can we help?
6 And how can we -- where's the access to that?

7 And sort of a follow-up to that, the
8 situation that I have dealt with is the shortage
9 of metabolic formula that happened, you know, in
10 the last six months or so. And what we have found
11 is that working with TRICARE specialty pharmacy
12 was really challenging. It's, I think, it's
13 challenging all over the country, but I need some
14 guidance so I can take that back home. Thank you.

15 JACOB HOGUE: I wish I could provide you
16 with more specific guidance on how to navigate
17 TRICARE. I would say I've heard similar things
18 from a variety of civilian providers of challenges
19 navigating TRICARE, both in terms of specialty
20 pharmacy and genetic testing is probably where I
21 hear about that the most where people run into
22 challenges with coverage of that through TRICARE.

1 Again, those -- TRICARE itself is administered
2 through the secondary contractor. So, that's --
3 while we may have some influence over what is in
4 TRICARE policy, and therefore how that comes
5 through related to how the contractors interpret
6 that, you know, we don't actually have any control
7 over what -- what is covered necessarily beyond
8 our influence on policy. So, I don't know if that
9 gives you a very clear answer for how to get
10 things better covered through TRICARE and to
11 navigate discussions with the TRICARE
12 administrators to ensure that coverage occurs.

13 I think in terms of connecting with
14 military specific resources, I think usually
15 having contacts with the closest pediatrician is
16 probably the best contact. And so, we're a fairly
17 small system, and they often will have broader
18 context. And so, you know, an example would be
19 when I was a fellow at UCSF, Travis Air Force Base
20 frequently referred patients to us to San
21 Francisco for specialty care. We had challenges
22 with navigating TRICARE as well, that they were

1 able to navigate better from inside the system for
2 testing that we wanted to do or follow-up and
3 those sorts of things. And really, maintaining a
4 good relationship with the active-duty Air Force
5 pediatricians who were at Travis Air Force Base,
6 who were the referring providers and reaching back
7 to them and having a direct discussion, rather
8 than just sending my note, they were frequently
9 able to facilitate getting care, ensuring that
10 they're connected internally to the special
11 systems within the military is usually the best
12 way to do that. People are certainly welcome to
13 reach out to me as well. But I probably don't
14 know the direct contacts there, as well as a
15 general pediatrician that who's stationed there.

16 NED CALONGE: Ash.

17 ASHTOUSH LAL: Thank you. I'm also from
18 UCSF, and in hematology, we have also seen some
19 patients from Travis. I appreciate what you have
20 presented. My question is, it's really a follow-
21 up to some of the other discussions that have
22 taken place. For some of these rare disorders,

1 the centers that excel in those conditions or are
2 doing active research maybe just in a few places
3 around the country, how do you view -- is there
4 support for families to form some relationships
5 with those centers so they can both obtain current
6 advice on standard of care as well as be eligible
7 for any advances in management that may happen in
8 the future?

9 JACOB HOGUE: Yeah. The short answer is
10 yes. It depends on regionally and what the goals
11 of care are. So, similar to -- so, there are
12 abilities to provide for both travel as well as
13 insurance authorization for children within the
14 Military Health System to travel and be seen by
15 specialists and receive treatment that is uniquely
16 available at certain locations. So, the short
17 answer is yes, absolutely.

18 What happens sometimes is where, you
19 know, a family identifies, and they say I want to
20 go see this expert on this disorder and trying to
21 convince TRICARE that that's really a need that
22 needs to be addressed versus a want or a desire

1 because they don't just provide insurance
2 authorization, they provide travel for both that
3 individual and their family members to that
4 location for a period of time. And so, the short
5 answer is yes, absolutely, if it's -- if it's a
6 fair need that truly needs to be addressed, that
7 happens fairly regularly.

8 The -- again, some of that goes through
9 TRICARE and the regions get involved in that issue
10 as well. So, they try and say, is there someone
11 who's regionally able to provide that care rather
12 than traveling from where I am to, you know, Duke
13 or to Children's National, or whatever the case
14 may be? Is there somebody who's on the West
15 Coast? Can we send them to Seattle Children's?
16 Can we send them to OHSU? Can we send them down
17 to San Francisco for that care? So, there are
18 some components of the logistics. But the short
19 answer is, yes, that can occur.

20 Now, they won't send for clinical
21 trials, for example, right? So, if it's for
22 clinical treatment, the same as any other insurer,

1 clinical trials are not inherently a part of
2 clinical treatment that insurance is covering.
3 And so, that comes up sometimes where people say I
4 want to go to UCSF to be a part of this clinical
5 trial and TRICARE Insurance won't pay for someone
6 to travel there to participate in a clinical
7 trial, if that answers some of your question.

8 NED CALONGE: Thanks. I'd like to
9 now turn to our organizational representatives.
10 I'd like to ask those org reps on the phone, if
11 it's possible to turn your camera on, it helps us
12 see your hands a little bit better, and I'm going
13 to start with Cate.

14 CATE WALSH VOCKLEY: Hi, thank you.
15 Cate Walsh Vockley, National Society of Genetic
16 Counselors. First of all, thanks for the great
17 overview and for your acknowledgement of some of
18 the challenges related to access to genetic
19 counseling services. I think it's important to
20 acknowledge that the members of the National
21 Society of Genetic Counselors have been working
22 diligently for quite a number of years to try and

1 become approved providers or recognized providers
2 by Medicare, Medicaid, and that if that happens,
3 that will improve some of your access issues.

4 My question relates to whether or not --
5 you mentioned that APPs, nurse practitioners and
6 others, it's okay for them to provide genetic
7 counseling, and I'm wondering whether or not
8 they're actually doing that? And if so, have you
9 looked at what the genetic counseling licensing
10 laws say in the states where they're practicing in
11 terms of who is able to provide genetic
12 counseling?

13 JACOB HOGUE: An answer to the first
14 question of whether we've looked at that, or I
15 would say, anecdotally, we've looked at it many
16 times, there have been some more different ways to
17 look at that as well. There was actually a study
18 the group was involved in related to a formal
19 program of trying to train primary care providers
20 to provide some basic genetic counseling
21 surrounding genetic testing that was being
22 performed. And that essentially worked okay, in

1 the short term and not well, in the long term,
2 even with substantial training for those
3 providers. So, and in terms of a more objective,
4 formal way of studying that, I would say, limited,
5 I'd say my, my incidental experience -- so what --
6 what frequently occurs is that that those
7 providers don't feel comfortable providing that.
8 So, that's sort of a TRICARE ask them to provide
9 that genetic counseling. That is not something
10 that they feel comfortable doing most frequently.
11 So, it's not so much a situation where we have
12 individuals who are PAs or nurse practitioners,
13 particularly and specifically put in places to
14 provide genetic counseling in place of genetic
15 counseling. I didn't want to give you that as the
16 impression because that is not at all the case.
17 It's more than the circumstances where providers
18 are in a place where they feel genetic testing is
19 warranted and they don't really feel that they
20 have access to reach out to someone or to get
21 genetic counseling in some other ways. And so,
22 they provide the best counseling that they can

1 surrounding that is what I've seen more commonly.

2 But I think, particularly where I where
3 I am, where we have genetic counselors and where
4 I'm there, people reach out to us all the time and
5 would like us to serve that function as much as we
6 possibly can. So, I would say, in general, people
7 are not comfortable providing that. I think the
8 situations surrounding the policy doesn't --
9 doesn't really match where people's knowledge and
10 comfort level is providing that care.

11 CATE WALSH VOCKLEY: Well, and as
12 genetic counselors become acknowledged providers,
13 there's so much access to virtual genetic
14 counseling that might be able to support your
15 patient population. Thank you.

16 NED CALONGE: Debra.

17 DEBRA FREEDENBERG: Hi. Thank you for
18 all of the work you're doing on behalf of newborn
19 screening in children. My question really relates
20 to continuity in short-term follow-up. As part of
21 my -- I'm also in Texas State Newborn Screening
22 Program, and we have a large number of military

1 facilities within the state, and we've had
2 challenges on continuity in which when we do the
3 screens and our follow-up folks are trying to call
4 back the person, we identify someone within the
5 facility as a contact, but they've been
6 transferred or deployed or whatever, and then
7 there appears to be no one that can do that
8 follow-up, and we spend hours trying to figure out
9 how to get the child appropriately cared for and I
10 was wondering if there was any overarching within
11 those providing those services, the pediatric
12 services, to have some sort of continuity, because
13 it seemed like there was very, very limited
14 continuity happening.

15 JACOB HOGUE: I'd be curious to know
16 what your experience is, you know, navigating that
17 for other facilities outside the military. We
18 certainly have that as a challenge. We have -- at
19 Madigan, we have -- the goal is we have one person
20 who's in charge of all the -- and so, what happens
21 frequently as compared to services provided
22 outside the military, is that it's a large system

1 and people are sort of assigned their pediatrician
2 or that -- but they are not able to do that -- or
3 pediatrician or family medicine provider to care
4 for the baby after birth. And that's not really
5 done until the baby's enrolled in the system. The
6 baby can't be enrolled until the baby's born. So,
7 as compared to where individuals might identify
8 who's going to be the care provider for their baby
9 before they're born and then, that can be written
10 on the newborn screening card. So, that's the
11 person that they have a contact for an abnormal
12 result. Our system inherently creates a challenge
13 related to that, I would say.

14 The ways that we've tried to address
15 that are probably different at every facility.
16 So, it may be a facility specific challenge that
17 you're dealing with there. It's absolutely, it's
18 certainly a problem. We have mobility of our
19 providers, as well as our families that move, and
20 I think that does create certain challenges and
21 that would relate to that as well. We've tried to
22 address that at certain facilities by having one

1 number for the state screen lab to call. So,
2 that's what we have at Madigan, where regardless
3 of who the baby is, or who their primary care
4 provider is, it all filters through that
5 individual, who then establishes the follow-up
6 care to do that. And so that's what we've --
7 again, as we move to DHA, and we're trying to push
8 out best practices.

9 Right now, it's -- what happens at each
10 military treatment facility as it relates to
11 something like this, is going to be individual to
12 that particular military treatment facility,
13 similar to the way it's going to be at any other
14 hospital that's inside or outside of the military.
15 And so, I would imagine that there's many
16 challenges at specific facilities of navigating
17 that type of situation.

18 I think the best practice is to have,
19 again, given those inherent challenges with who
20 the babies are seeing after birth and not having
21 continuity to that it's established before the
22 baby is born, is having one sort of in-road to the

1 system that then can push that. But there is no
2 unified policy related to that or particular
3 something that would push that to be a requirement
4 at all military treatment facilities.

5 NED CALONGE: Thanks. I want to ask our
6 organizational reps in the room to -- I know you
7 have to share microphones, but the closer you can
8 get to it, the better folks, especially online,
9 can hear. And Natasha, you're next.

10 NATASHA BONHOMME: Hi, I'm Natasha
11 Bonhomme with Genetic Alliance. Do you have any
12 policies or recommendations around education
13 either on the front end in terms of having people
14 be aware that this is going to happen and how it
15 will happen, depending on their location, or on
16 the, I guess you could say, back end if there's a
17 diagnosis and more condition-specific education or
18 resources? Or is that then kind of just out of
19 your hands?

20 JACOB HOGUE: I would say that there is
21 policy surrounding one, the requirement to perform
22 newborn screening and what the approach is if a

1 family is declining newborn screening, there's
2 some policies surrounding that. In terms of other
3 components, the policy is really to align with the
4 state programs. And so, there is some reliance in
5 that some of the benefit of aligning with the
6 state programs is relying on those programs and
7 the components of follow-up related to those
8 programs in terms of what is -- what is both
9 required at the front end about counseling
10 surrounding newborn screening, as well as
11 education surrounding conditions that are -- that
12 are identified. And so, that's one of the goals
13 of aligning with those with those state programs.
14 I would not say that there's any broader DHA or
15 Department of Defense Policy surrounding those --
16 those requirements.

17 NATASHA BONHOMME: Okay. So, does that
18 mean there's any education coming from your huge
19 team of one out to those families about newborn
20 screening, or is that -- is that meant for them to
21 get that information in other ways?

22 JACOB HOGUE: I'd say there's a large

1 amount of care that's provided that is not
2 necessarily captured by policy. And so, yes,
3 there's lots of education and follow-up that
4 occurs for children, and I think we do -- I like
5 to think that we do a very good job of providing
6 education for families after we identify some of
7 the conditions and get them into care and those
8 kinds of components. But is that covered by
9 policy? No, that's just providing good -- what I
10 would think of as being very good medical care as
11 it relates to follow-up for substantial disorders.

12 NED CALONGE: So, we just have a couple
13 of minutes left. I'm going to go to Marc on the
14 phone.

15 MARC WILLIAMS: Thank you, Marc Williams
16 representing ACMG. Thanks very much for the
17 presentation. I have two brief questions just to
18 follow up and expand on some prior questions that
19 were asked, the first relating to acute care with
20 a positive newborn screen. I'm curious, in
21 military facilities, whether there is access to
22 the ACMG Newborn Screening Act sheets for the

1 providers to kind of assist with that.

2 And then, the second question is
3 specific to treatment, which is if you're aware of
4 whether or not TRICARE covers medical foods. This
5 is unfortunately, as this group is well aware, a
6 very common exclusion in most commercial insurance
7 plans, and so, I was just curious to see if
8 TRICARE is essentially the same as other
9 commercial insurers or whether they have a
10 specific policy on them.

11 JACOB HOGUE: The first answer, yes,
12 absolutely. We have access to the to the ACT
13 sheets to the ACMG and would say they're regularly
14 utilized, probably depending on which state and
15 how to get results back through PerkinElmer, for
16 example, are more reliant on those versus reliant
17 on the program to give them the follow-up
18 information.

19 As it relates to the medical foods, I
20 don't know that I know the specific details
21 related to that. I know that there were major
22 challenges a few years ago when there was a change

1 in the TRICARE contracts with coverage,
2 particularly even if formulas for inborn errors of
3 metabolism and medical foods were captured as a
4 component of that. I believe that there is some
5 coverage, but I know that it is imperfect and
6 incomplete. That would be my short answer to
7 that.

8 MARC WILLIAMS: Thank you.

9 NED CALONGE: And Margie, you have the
10 last question.

11 MARGIE REAM: Margie Ream with Child
12 Neurology Society. There are some situations with
13 private or state-insured individuals that need
14 out-of-state subspeciality care, particularly, you
15 know, maybe very urgent, but getting approval for
16 payment for out-of-state care can be a delay. Has
17 TRICARE or the Military Health Service come up with
18 a way to provide timely approval or very quick
19 approval for out-of-system or network care in
20 those sorts of situations that maybe the outsider
21 military system might learn from?

22 JACOB HOGUE: I think the short answer

1 is yes, but it's inherent to our system being a
2 federal system. We're actually -- that kind of
3 aligns with some of the questions earlier related
4 to some policy components where we aren't
5 necessarily obligated to follow the state
6 regulations or how that works within states. We,
7 in general, try to follow those, but there's times
8 where the federal rules might be a little
9 different than the state rules in some way or what
10 is mandated through the DoD. We are not -- the
11 DoD is not at all bound by state boundaries. So,
12 we -- we -- I would say that wherever the
13 specialty care needs to be for follow-up and
14 treatment is not really a challenge as it relates
15 to approval. I would say more of the -- the --
16 the little line that showed the regions between
17 the TRICARE regions is probably more of a
18 challenge than the state-to-state lines more just
19 navigating payment, and who's going to pay for
20 that, and how does it actually shift over to this
21 other, or can we pay for something that's
22 occurring in that region that's occurring here.

1 But in general, that is not an issue that arises
2 in the DoD system.

3 NED CALONGE: I hope everyone can join
4 me in thanking Lieutenant Colonel Hogue for an
5 excellent presentation and standing up there in
6 the hot podium for a good discussion and it's very
7 useful. Again, thanks for all you do for our
8 active-duty military and their families. Thanks a
9 lot.

10 JACOB HOGUE: Thank you.

11 **Implementation of Conditions Recently Added to the**
12 **Recommended Uniform Screening Panel**

13 NED CALONGE: You'll remember that we
14 had what I thought was a rich discussion, talking
15 about the enabling factors and challenges to
16 implementation of conditions added to the routine
17 screening panel across the country. And we also
18 discussed the complexity of the system, as it
19 varies as well.

20 So, for this roundtable session, we've
21 invited, and we'll hear directly from states that
22 range in size, location, program structure, and

1 legislative requirements about their processes and
2 experiences and implementation.

3 I'd like to introduce the panel now and
4 then we'll get started. So, the first one I'm
5 going to introduce is Lisa Caton, who is the
6 Director of Screening and Special Services at the
7 Oklahoma State Department of Health. Here she
8 oversees the Newborn Screening Program, the
9 Newborn Hearing Screening Program, the Pediatric
10 Audiology Program, the Birth Defects Registry, and
11 the Oklahoma Childhood Lead Poisoning and
12 Prevention Program. She received her Bachelor's
13 in Nursing from the University of Oklahoma in
14 2002, and a Master's in Science from Southern
15 Nazarene University in 2014.

16 Early in her career, she worked as a
17 charge nurse in a Level 2 Nursery, a quality
18 improvement nurse, and a public health nurse. In
19 2009, she accepted a position in the Oklahoma
20 Newborn Screening Program as the Newborn Screening
21 Quality Assurance and Education Coordinator.
22 Here, she had the opportunity to lead quality

1 we've had either parent advocates or specialty
2 care physician advocates who have recommended a
3 any evaluation of a candidate condition for
4 inclusion into our screening panel. It can also
5 happen through the spring boarding off the work
6 from the Federal Advisory Committee and the
7 recommendations for adding to the RUSP. So, it
8 happens both ways.

9 For example, a few weeks ago, when MPS
10 II was signed by the Secretary, I sent an email to
11 my liaison at the board and said, "Hey, this is,
12 you know, this is now part of the RUSP and to get
13 on to the agenda for our consideration, within our
14 -- at least put it on the radar for the board, who
15 has the authority for the rulemaking, and then
16 also alerted our internal policy people at the
17 Department of Health in my division that this is
18 happening." If you could advance.

19 The board has five criteria to evaluate
20 candidate conditions. And so, they're listed
21 here. Available screening technologies. So,
22 there needs to be a sensitive specific test that

1 can be done for the whole population.

2 The next is that diagnostic testing and
3 treatment is available. So, once they're tested,
4 is there infrastructure to take it to the next
5 step for a diagnosis and treatment.

6 Prevention potential and medical
7 rationale. That identification in the newborn
8 period provides benefit to the baby.

9 Public Health rationale is that the --
10 like, the condition is, like something that all
11 babies should be screened for rather than targeted
12 screening.

13 And then the final is cost benefit/cost
14 effectiveness, and the benefits need to outweigh
15 the costs. And that's a real interesting
16 challenge to quantify.

17 And so, I think this is a part of what's
18 unique about Washington's process is that there's
19 formal economic analyses that are made for any
20 candidate condition. This dovetails the last --
21 advance please.

22 This dovetails with a separate

1 requirement. If you can advance the slide,
2 please. Washington has an Administrative
3 Procedure Act. And so, I'll just read what a
4 portion of that says. It says "before adopting a
5 rule, an agency shall determine that the probable
6 benefits of the rule are greater than its probable
7 costs, taking into account both the qualitative
8 and quantitative benefits and costs and the
9 specific directives of the statute being
10 implemented." So, we have a process in which the
11 condition will be evaluated. We'll take a look at
12 -- we basically do a decision tree analysis where
13 we compare the outcomes for no screening model,
14 which is the status quo, with a screening model.
15 And so, we look at the differences in mortality
16 and morbidity, the differences in the costs of
17 treating, and costs of screening and diagnostic
18 testing, and make a final determination in the
19 form of a benefit cost ratio and then net benefit
20 for the screening programs, and those are helpful
21 information for the Advisory Board to understand
22 when they make recommendations to the Board of

1 Health.

2 So, what's difficult and, well,
3 impossible to do in the in the system that we have
4 currently is to evaluate some of the intangible
5 challenges and both benefits and costs of adding
6 new conditions. Like, how do you measure the,
7 like, how do you put a dollar figure on the
8 confusion and stress that's caused by a diagnostic
9 odyssey, for example, compared with perhaps a
10 screening test that doesn't perform super well,
11 and creates a large number of false positives?
12 Like so, how do you compare those, and how do you
13 put a dollar figure on those? So, there's some
14 things that just can't be done, but they are part
15 of the discussion amongst the Advisory Panel, and
16 amongst the Board of Health when making decisions.

17 Let's see, in this, kind of from an
18 overall perspective, from the time that a
19 condition is either brought to the board's
20 attention from, like, wherever this process starts
21 to actual implementation usually takes about two
22 to three years, which is similar to what we've

1 heard from our other states today. And one of the
2 big pieces, as Susan mentioned, is, can you
3 piggyback this technology? Like, can you add this
4 to an existing infrastructure in our laboratory,
5 and if not, that adds time.

6 For our standpoint, as a fee for service
7 setup that we have in Washington, we need to have
8 legislative approval to increase our spending
9 authority. So, anytime that we need to increase
10 our fee, it needs to be approved by the
11 legislature. And so, as you can imagine, with
12 them meeting only once each year, the timing of
13 that request and whether it's granted, will play
14 significantly into how quickly we can implement
15 screening for a new condition. Thank you.

16 NED CALONGE: Thanks so much, John. And
17 now if we could turn to Roberto and Florida. And
18 you're on mute, Roberto. Oh, he's coming up with
19 slides.

20 ROBERTO ZORI: Sorry, yeah, thank you.
21 So, thank you, more than thank you, I need to say.
22 This is a bit apprehensive. I'm very apprehensive

1 of this in order to be able to do justice to the
2 Florida Screening Program, and at the same time,
3 give you information that might be useful.

4 So, I thought I'd start with the
5 Commandments, which we live under. This is the
6 Florida Statutes, and it really says a couple of
7 things. It really says that as soon as a
8 condition is approved by the Federal Advisory
9 Program on the screening panel, the clock starts.
10 So, the Newborn Screening Committee -- Newborn
11 Screening Section has then a year to prepare to
12 present to the Advisory Council, and I'll go into
13 what that means in a minute.

14 The second part of this gives the role
15 of the Advisory Council, which looks at that -- at
16 that work done by the Section, and then gives the
17 up or down or I need more information answer. So,
18 at that point, if it's approved, like most of them
19 are immediately, then there's a year and a half
20 before the screening is mandated to start. So,
21 there's a two-and-a-half-year maximum -- two and a
22 half year max time, unless the Advisory Committee

1 sends it back for more information. So, if I
2 could have the next slide. Next slide, please.
3 Yeah. So, here is the -- here's the
4 roadmap for this. So, we've divided it up just in
5 like four quarters. But the first is that a
6 condition is on the screening panel and added to
7 the RUSP. That sets in play -- in motion to
8 mainly two people, the coordinators of the Newborn
9 Screening Plan, Emily Reeves and Dusty Stern.
10 They are the heart and brains of the screening
11 program. I don't know how they stay sane in
12 getting this all together and getting everyone to
13 work together. But they do an incredible job.
14 So, it is very operator dependent. That then has
15 to be presented. They also do the budget. So,
16 they do budget and assessment of what's needed.
17 They start drafting the budget, and that's in the
18 second quarter. And then in the third quarter,
19 then, we say that that's when it's presented to
20 the Advisory Council, that's within a year. At
21 that point, the Advisory Council, if they approve
22 it, then they have another year and a half to

1 start screening, and so, screening is mandated to
2 start within that -- after the approval, within a
3 year and a half. And that sort of ensures at one
4 point that that there is immediacy, that this is
5 taken and done as quickly as possible. The
6 problem with this is that we, in doing so, we have
7 to maintain precision and accuracy, and it feels
8 frequently like that scene in Home Alone where
9 everyone is running to get on the bus in a certain
10 amount of time. And I feel frequently that I may
11 end up as the boy that's left behind because
12 there's so many moving parts done within that
13 timeframe.

14 So, if I can just tell you what that
15 timeframe is just give me a second there. All
16 right. So, when that goes into effect, the
17 Secretary recommends two routes that this will be
18 done, and the Newborn Screening Program starts.
19 And what they do evaluate is the cost per
20 screening tests, methods, compatibility with LIMS,
21 space, staffing, data system updates, contracted
22 providers that may be needed, provider education

1 that has to be done for the specialists and for
2 the individuals, technical assistance needed for
3 the birthing facilities, follow-up process,
4 updated rules, website updates, updated education
5 material, and then complete the framework for the
6 added newborn screening conditions in Florida that
7 we have to fill in and send to us.

8 Now, so, that's all done within a year
9 and even the budget. The legislature budget
10 request begins also during this period for a vote.
11 So, within one year of the action by any routes,
12 the program presents the framework for added
13 newborn screening conditions to the Florida
14 Advisory Council for an official vote.

15 Now, again, there is an enormous push to
16 get this approved at that level. The Advisory
17 Council can request additional information if
18 they're uneasy because all this is presented at
19 that one meeting when meetings are held twice a
20 year. So, there's a lot of information to
21 present, and if the council doesn't feel that this
22 safeguards all accuracy, they could theoretically

1 send it back for new information, and this has
2 been done recently twice for MPS I and Pompe. And
3 then we re-reviewed it at six months, the
4 information was given. Again, the people in
5 counsel are not always -- usually, most of them
6 don't know what MPS I is or Pompe. They're not
7 geneticists, and so that has to be presented in
8 the assessment done during that meeting. And in
9 each of these two cases, we sent it back for a
10 vote. And on the other hand -- and then we voted
11 on it after six months. So, in essence it delayed
12 this process.

13 If the Advisory Council votes favorably,
14 then the clock starts again at eighteen months,
15 then implements -- then screening must be
16 implemented within the eighteen months. During
17 those eighteen months, the legislature budget has
18 to be submitted during the appropriate legislative
19 cycle to ensure that funding is available.
20 Nothing can be bought or done until that money is
21 in place, and that has to also be done within the
22 eighteen-month framework. And so, and until the

1 funding is received, the isn't able to procure any
2 resources, reagents, equipment, staffing
3 contracts, until that's done. All right. And
4 that's again within the eighteen months.

5 And really, that is the program. The
6 problem has been recently that the push to get
7 this moving faster and faster is there. There are
8 four lobbyist entities that have made this
9 sometimes difficult. The -- it's not that their
10 reasons for lobbying are well understood and
11 appropriate. So, parents, the researchers, the
12 companies involved with a screening program, a
13 screening reagent for testing, and then the
14 legislators themselves, they all feel strongly
15 that this should be done and have been lobbying
16 for this process to go faster and even faster than
17 we're able to do. The problem with that is
18 appropriate, to go as fast as possible. Our
19 concern at the Advisory Council is we're all
20 physicians is, as you know, we swear by the same
21 thing, first do no harm, and that this procedure
22 is done with minimal risks to patients. In other

1 words, that patients be identified positively and
2 correctly with treatment, that's appropriate. And
3 secondly, that stress is caused by the parents by
4 being screened with waiting for confirmatory
5 testing, and we're afraid that we miss someone.
6 So, all of those three things have to be
7 considered. They're in the process and that's
8 where the delay comes in if we do not think that
9 the conditions are in place, as presented, that
10 safeguard those three risks. And I think that's
11 all I've got for now.

12 NED CALONGE: Thanks, Roberto, and I
13 want to thank each one of the speakers for such
14 great outlines of your program overall. I think
15 maybe one more question before we open it up for
16 discussion and that's to see if there is like a
17 certain step or part of the process that was the
18 most challenging or takes the longest to get over,
19 and if there are resources or strategies that help
20 your program get past those most challenging
21 steps. And Susan, I'm going to turn to you again
22 to lead us off.

1 SUSAN TANKSLEY: All right, thanks.
2 Giving kind of the overview, funding really has
3 been the biggest issue for us. So, when we do the
4 cost estimate and, you know, looking -- so, I gave
5 Pompe, MPS I, and MPS II as an example. And so,
6 our cost to implement is on the order of like \$7
7 million. It's a lot of money. And our annual
8 ongoing costs are expected to be over that. So,
9 you know when we get seed funding from grants,
10 it's very helpful. But unless we have funding
11 already in the works, there's no point in even
12 applying for the seed funding, because 300,000-
13 400, you know, that's not going to get us anywhere
14 in implementation.

15 We were able to apply and we're very
16 thankful to get some of the funding through CDC
17 through the latest round of funding. And we wrote
18 it up as implementing or developing our second
19 tier and third-tier testing. So, it's not nearly
20 enough to do all the work on like the tandem mass
21 spec piece. But it's enough for us to be able to
22 do some of that work that's going to take longer.

1 So, the development of a second tier LCMS, MSSA,
2 and the development of that third tier, as I
3 mentioned next gen sequencing of a panel,
4 essentially, of all of the genes for all of the
5 newborn screening disorders. And so, you know,
6 the seed funding is definitely helpful. I'm not
7 saying don't do that, please continue to do that.
8 Because I think that's helpful for a lot of
9 states.

10 But that really has been our issue is
11 funding. And as I mentioned, we do have, I call
12 it a Newborn Screening Savings Account, and I know
13 there are some states who have that. It's a
14 valuable asset. When we get a deposit, it will be
15 nice, because that should set us up for the future
16 to be able to not have that as an impediment.

17 NED CALONGE: Thanks, Susan. Lisa,
18 could I ask you to go next?

19 LISA CATON: Absolutely. So, I would
20 say previous to our statute language being
21 updated, the most timely thing that took for us as
22 far as the length of time, would have been going

1 through the role change process, because that
2 would take us a year and a half to two years just
3 to get through that. So, that was a barrier and
4 that's been removed, which is -- that is one very
5 positive thing.

6 I think moving forward, what's going to
7 be most likely going to be our barrier is going to
8 be the lab capacity to be able to add those
9 conditions depending on the methodologies
10 available, the equipment, is it included, and, you
11 know, can we run it with another condition that
12 we're testing for? Those factors can be very
13 complicated if you're talking about bringing on an
14 entire new equipment because you need space to do
15 that. And it's also getting the staff and getting
16 staff trained to proficiently be able to run the
17 tests and reduce false positives and stuff like
18 that. So, I think previously, it was the roles
19 was the most challenging part. Going forward, I
20 think it's going to be just the implementation in
21 the lab. It's going to be more challenging for us
22 if I had to rank it right now.

1 NED CALONGE: Thanks, Lisa. Thank you.
2 Richard, could you go next?

3 RICHARD OLNEY: Yeah. I mentioned
4 before that staffing is a major challenge for us
5 and as many programs, not just, you know, getting
6 money for a position, that takes time, but the
7 actual hiring process and in finding people to do
8 that. When we implemented screening for adrenal
9 leukodystrophy, we did get over some of that by
10 doing a contracting process to hire contract
11 staff. That, in itself takes time, but that that
12 was one solution we had.

13 Funding is not as much of an issue
14 apparently, as in Texas. And in fact, the mandate
15 and statute has been kind of, I think, accelerates
16 or puts more weight on our requests for funding
17 just because, you know, we have to do it and so,
18 that allows us to do it.

19 And finally, I just wanted to mention, I
20 noticed in the in the Florida statute, that
21 there's a mention of having an FDA approval of an
22 assay. And, of course, laboratory developed

1 testing can be a prolonged process, and not just
2 capacity for the lab, but, you know, developing
3 new processes, and having that available would
4 certainly facilitate things in California, but
5 that's not part of our statute.

6 NED CALONGE: Thanks, Richard. John.

7 JOHN THOMPSON: Yeah. So, I think, from
8 our standpoint, the part of the process that takes
9 the longest time is the budget piece and that's
10 sort of tied, like the rulemaking won't start
11 until the budget is approved. So, put together
12 those are the longest. But the budget is
13 definitely the longest.

14 So, for example, our Advisory Committee
15 last year considered ornithine transcarbamylase
16 deficiency as a candidate that was recommended,
17 put forward by a family who lost a child to OTC
18 deficiency. And so, the Advisory Committee met
19 last summer, early fall, and then I think in
20 November of last year, the Board of Health
21 approved OTC deficiency for our adding to our
22 panel.

1 And so, immediately, I started the
2 internal policy process for greasing the skids, so
3 to speak, because I knew that we needed to
4 increase our fee in order to be able to do that.
5 And so, I started talking with our divisional
6 management team and saying, okay, next May when we
7 do our proposals to the Governor's office, we need
8 to add OTC deficiency and then, this is what that
9 looks like. And so, we're in that process. It's
10 going -- so far, we're in good shape and there
11 have, like, in that process, like internally,
12 there's always chances that it might not be
13 approved, or it might be delayed and then once it
14 gets to the governor's office, it needs to show up
15 in his budget and then when the session starts in
16 January, it needs to show up in both the House and
17 the Senate budget. So, there's all these hurdles
18 that need to happen in order for that fee increase
19 to move forward.

20 And so, the like there's a pretty decent
21 amount of preparation and communication that goes
22 into making that happen so that when the

1 legislators or the staff for the Senate contact
2 our DOH policy person, they'll say, well, why do
3 you need to do this, and they'll have an answer.
4 That's ready. So, that's what we're facing.

5 NED CALONGE: Thanks, John. And
6 Roberto.

7 ROBERTO ZORI: Yes. So, like anyone
8 else, it's money, and in Florida, there's money
9 and time. And so, setting a time clock may
10 actually force legislators to approve it since
11 there is a time clock. But there is nothing in
12 place that says if they did not approve it, what
13 do we do then because the time clock doesn't stop.
14 So, that's sort of an intrinsic problem with the
15 system. Though, the problem is that there's a lot
16 of work to be done in one year. Everything's
17 prepared, including the budget within the year.
18 The Advisory Council then doesn't have like a lot
19 of time to assess their preparedness, and they're
20 pushed very hard to, because of the time, to
21 approve it. There is -- how could you deal with
22 that? I mean, one, I think it would be helpful if

1 we had guidelines at the federal level for what
2 needs to be in place for each condition or
3 suggestions, so they'd have something to work
4 with. Because we -- this is all new to us. We're
5 building a cathedral without ever haven't built a
6 church.

7 And so, the other thing is that it's
8 very important to get it right the first time
9 despite the low amount of time we have to do it.
10 If there was the ability to review this so there
11 would be a second review, to pick up the things or
12 go back and pick up the things we forgot, or there
13 are new things done. So, there's no automatic
14 review process for the individual conditions where
15 you could go back and say, well, we did things
16 quickly, forgot about this. For example, with CF,
17 we passed it for CF, but there is no provision for
18 genetic counseling, and I think that should have
19 been considered. You know, there is no re-review.
20 There -- we can sort of go back to the legislative
21 too, but that's a difficult issue, because it's
22 for extra money.

1 So, I would really appreciate, when we
2 have the accepted condition, that we go back and
3 review it in terms of is it doing what we presumed
4 or are there risk factors, like I said before, too
5 many false positives, false negatives, prolonged
6 wait for parents that make the system not optimal,
7 so we could optimize the system in place. You
8 know, we declared victory as soon as we put this
9 on the list. But there's, you know, I don't know
10 if the casualties are too high that I don't think
11 that this should be a victory. So, I think that a
12 review process has to be in place with the
13 automatic review for extra legislative --
14 legislative monies to be released to fix what we
15 didn't do, because of the timeframe.

16 Anyway, that's really all I got. Oh,
17 yeah, like I said, if it's not approved, the
18 budget, then we don't really know what would
19 happen next.

20 NED CALONGE: Thanks. Thanks, Roberto,
21 and thanks to all the panelist members. I'm going
22 to open it up. We have about a half hour for

1 discussion, starting with questions and comments
2 from the Advisory Panel. I do really appreciate
3 Roberto for reminding us, and Susan, you did at
4 the very beginning, that there's a lot more to the
5 implementation of a new condition other than the
6 laboratory. So, we talked a lot about laboratory
7 challenges in terms of equipment, space,
8 personnel, reagents, tests, but the issues about
9 the other parts of the system like counseling,
10 treatment, confirmatory testing, diagnostics,
11 especially at the molecular level, where does that
12 occur, in the state lab, outside of the state lab,
13 who interprets those? The complexity of the
14 system is great, and funding will always, I mean,
15 it's interesting to say, well, that's not so much
16 of a problem. It's almost inconceivable for me to
17 think about that, as the general fund dollar is
18 the most precious dollar in Colorado, because it's
19 the only dollar that one hundred different
20 legislators trying to control.

21 So, with that kind of preamble, I wonder
22 if we could start with Michael.

1 MICHAEL WARREN: Thank you all for these
2 insightful comments. I just wanted to make folks
3 aware, we're going to be releasing a funding
4 opportunity that's forecasted to release on
5 November 10th. That is subject to change. But,
6 Susan, to your point, it won't be \$7 million.
7 It's \$345,000 per state, but we're anticipating
8 funding twenty-five states. That's new for us and
9 it's to be able to support states really wherever
10 they are, as we think about that continuum newborn
11 screening, whether you're focusing on quality
12 metrics, whether you think about building state
13 capacity to be able to bring on some of these new
14 conditions that are added. And so, I hope we will
15 have more than twenty-five applications and can
16 later make the case for more funding, but excited
17 to have that 345 a year for five years.

18 NED CALONGE: Thanks, Michael. Shawn.

19 SHAWN MCCANDLESS: Thank you. I'd like
20 to thank all of the speakers as well. That was
21 really fascinating and insightful. And it points
22 -- it points to something I think is really a huge

1 problem for newborn screening as a system, and
2 that is that people do things with the very best
3 of intentions, advocacy groups, state legislators,
4 but without understanding what they're actually
5 doing and the unintended consequences of the
6 decisions they make. For instance, we've heard
7 about today in Texas a mandate to screen for, not
8 just the RUSP, but the secondary conditions,
9 which, if anybody had even looked at the website
10 for ACHDNC, they would recognize that they are
11 specifically not intended to be targets of newborn
12 screening. They're intended to be reminders for
13 clinicians that these are other conditions you may
14 encounter when you're working up a kid for one of
15 the primary conditions or Washington state where
16 Dr. Thompson told us that you have a mandate to
17 screen for OTC in spite of the fact that the data
18 show that we don't have an appropriate screening
19 test for OTC and that the test that's available is
20 neither sensitive nor specific.

21 So, we're going to be spending a lot of
22 money for a completely ineffective program. And

1 as somebody who has spent the last ten years
2 researching that particular question, how do we
3 screen for OTC deficiency, I'm particularly
4 perturbed by that. And there have been other
5 examples. And so, I have three questions for the
6 speakers related to this, and the first is a
7 simple one. Should this Committee consider
8 eliminating the terminology around the secondary
9 screening panel? Should we just get rid of the
10 secondary? Would that be helpful in any way? The
11 second question, so first question is should we
12 eliminate the secondary panel?

13 Secondly, the second question is what
14 would be the impact on state Newborn Screening
15 Programs if this Committee were to make a
16 recommendation to the Secretary for a -- to add a
17 condition only if an appropriate secondary tier
18 test was required to be available to minimize
19 false positives? And I don't know that this
20 Committee actually has the ability to do that.
21 But what would be the impact on states if there
22 were a mandate to -- if we're going to implement

1 testing that you implement a second-tier test to
2 minimize false positives?

3 So, the first question is eliminating a
4 secondary panel and the second question is a
5 mandate to do second-tier testing.

6 And the third question is recognizing
7 the limited options for action that are available
8 to this Committee, what can we do to improve your
9 state's ability to implement recommendations
10 regarding newborn screening? Thank you.

11 NED CALONGE: So, I'm going to take the
12 same order if that's okay, and if any panelist
13 wants to defer, just let me know. But I'm going
14 to see if Susan has an answer she'd like to offer
15 to Shawn's questions.

16 SUSAN TANKSLEY: All right.

17 SHAWN MCCANDLESS: And you can answer
18 any or all of the questions.

19 SUSAN TANKSLEY: Okay. Thank you,
20 Shawn. Those are really great questions. So, I
21 have -- in regards to your first question, so, I
22 have been chairing a condition counting task

1 force, through Association of Public Health Labs
2 for the last about a year and a half. And at the
3 Newborn Screening Symposium two weeks ago in
4 Tacoma, I gave the recommendations from that
5 Committee, one of which includes an evaluation of
6 the secondary conditions, perhaps to see if they
7 need to be on the core, or if it needs to be
8 eliminated altogether. And so, I do think that
9 that needs to be evaluated and considered. It
10 does have unintended consequences, and there's a
11 lot of confusion over the intent of the secondary
12 targets. And you're correct, it's absolutely
13 spelled out in the ACMG paper. It's absolutely
14 spelled out on the website. There's not
15 conflicting information there, but it has been
16 interpreted differently, and it's not just in
17 Texas that it's been interpreted differently.
18 Ours just happens to be in statute.

19 In regard to the impact on state Newborn
20 Screening Programs, if it was required to have a
21 second-tier test. So, I think, as we -- as the
22 Committee has considered new conditions, since the

1 original conditions from ACMG, I think there's
2 been a lot of emphasis on minimizing false
3 positives, and, you know, it has to -- there has
4 to be a really good test. And a lot of programs
5 tried to implement that second-tier testing or
6 some way to reduce false positives. So, moving
7 forward, and even in the existing ones, I don't
8 know how big of a problem that would be in in
9 Texas itself, just speaking for Texas, that's
10 something we seek to do. Unfortunately, the same
11 cannot be said for the original panel. And, you
12 know, that's really, if you look at the endocrine
13 disorders in particular, that's where most of the
14 false positives are coming out of, I would say,
15 most Newborn Screening Programs. Even if you look
16 at the disorders coming out of tandem mass spec in
17 comparison, so many more disorders, but so many
18 fewer positives reported out with much better
19 positive predictive values. And so, one of the
20 things that we've talked about on the lab
21 workgroup, over the years even has been
22 improvement of existing, you know, the conditions

1 on the panel, and we really haven't gotten much
2 traction there or moved forward with that. But
3 that's another thing is just looking at what we're
4 already doing and quality improvement
5 opportunities there.

6 So, as Dr. Warren spoke about the
7 additional funding coming out, you know, something
8 at the top of my mind is, is there something
9 quality improvement related that might fit in
10 there that we could definitely use that funding
11 for? I'm going to think more on your third
12 question.

13 NED CALONGE: Thanks. Lisa.

14 LISA CATON: Yeah. So, I would probably
15 echo a lot of what Susan said as well. I think
16 there's a lot of confusion between the primary and
17 the secondary panel and what that really means.
18 Even though we understand it, the general public
19 does not. For our legislation, or our statute
20 that was updated, it does not differentiate. It
21 just says it will align with the RUSP. And so,
22 that makes it challenging because there are a

1 couple of conditions on the secondary panel that
2 we do not screen for. So, then the question was,
3 well, when are you adding those? And it's like, I
4 don't know if we are. And so, then it goes back
5 to looking at that. So, I think definitely
6 reevaluating that is great.

7 I think as far as the second-tier
8 testing, I love the idea of second-tier testing to
9 reduce false positives. But we also need to make
10 sure that that first-tier testing is still a
11 really good solid test as well, because the costs
12 that can incur if you're spending a lot of
13 specimens for second-tier testing can be a huge
14 burden for the program as well. So, that's a, I
15 don't know, that's a double-edged sword. I don't
16 know quite the answer to that on that one.

17 And, I would say things to pay -- and
18 this is -- this is really out there and stretching
19 a little bit, but, you know, the -- what the
20 Committee has seen and been going through over the
21 years has changed, and you're getting more and
22 more conditions quicker and quicker and getting

1 added in the capacity for the lab to be able to do
2 that is challenging. But if we're so busy doing
3 that, we can't go back and refine and even make
4 improvements on what we've already been screening
5 for, and we're just caught in this vicious cycle.
6 So, I would almost consider maybe adding like,
7 maybe when conditions get added, they're not
8 necessarily added to the RUSP, but they're in like
9 a trial period, like a holding period, where we're
10 gathering data from states that are expanding
11 long-term data, it's contributing, really what the
12 feasibility is that's appropriate to truly go on
13 to the RUSP, and then it can get slid on to the
14 RUSP or something. And then, it's not so much a
15 state just trying to scramble and add if they have
16 a statute or some kind of requirement to align
17 with the RUSP. That gives some time to those
18 states that can move forward that do not have
19 maybe as many challenges with funding or something
20 else or the expertise within the laboratory or
21 specialist within your state, whatever the error
22 may be. It provides a little bit of, I guess, a

1 little bit of cushion to try to figure that out
2 and to see really what a screening for that
3 condition look like long term. Just a suggestion.

4 NED CALONGE: Thanks, Lisa. Richard.

5 RICHARD OLNEY: Yeah, I also would
6 really support reexamination of the secondary
7 conditions on the RUSP and that term and what it
8 means and what it means for RUSP legislation in
9 particular. And I know that Susan will be coming
10 back to you with the recommendations from APHL and
11 I would listen closely to those because they've
12 been vetted quite a bit among many of us.

13 I'm going to skip over the second
14 question but go right to what the Committee can
15 do. And I already mentioned, in California, we
16 pay a lot of attention to FDA approval and
17 availability of test kits because we use regional
18 labs for a lot of our first-tier screening, and
19 with the neuro conditions, we've not been able to
20 do that. The laboratory developed them and that
21 means, you know, hiring in-house resources, hiring
22 and other resources for in-house testing, which is

1 a bit burdensome. And then, I would -- I know,
2 it's been talked about in the past about
3 reexamining conditions that are already on the
4 RUSP as to whether they are -- and really should
5 stay on there, what's -- what's the data after in
6 the real world, and we've heard about states that
7 have dropped conditions that they were previously
8 screening for. And it seems like once they're on
9 the RUSP currently, they haven't been dropped.
10 So, you know, I think it's important for the
11 Committee to think about a reevaluation process
12 for existing conditions. I'll throw it over to
13 John.

14 JOHN THOMPSON: Thanks. Great advise
15 from everybody so far. I'll jump to the second
16 question. I think that having a requirement for
17 only if a second-tier test is available would be
18 great for some programs. I think that not all of
19 our newborn screening laboratories have the
20 capacity or expertise or space in their laboratory
21 to do second-tier testing. A lot of the tests
22 that are being done as second or third tier are

1 molecular, and I just was on a webinar yesterday
2 talking about the, like, the status of, like, very
3 not many Newborn Screening Programs have a strong
4 molecular component to them currently. So, that
5 might tie in to your third question.

6 But also, like, we were taking advantage
7 of an opportunity from the Association of Public
8 Health Laboratories. We have a fellow. That was
9 the first time we've been able to host a fellow
10 and we are doing -- like, his job is method
11 development and we've got a tandem mass spec that
12 we purchased just for this project and it's not
13 going to be borrowed for regular testing, like
14 every other time we've ever had to bring on a new
15 test. Like, we're really focusing on, like, what
16 can we do to better improve what we're already
17 assigned to do with the work that he's doing? And
18 second-tier testing is part of what we're hoping
19 he can do during his two-year tenure with us.

20 The -- your third question, the funding
21 that was mentioned by Dr. Warren, like, I could
22 think of so many different ways that we could use

1 that type of funding, especially since it's a
2 significant amount per award over several years'
3 time. That's really critical for us. A lot of
4 the funding opportunities seem to be either
5 smaller dollar figures or for shorter durations,
6 and it's been difficult for us to justify the
7 amount of time and energy to get a contract
8 established, wherein we've used a lot of the
9 resources just in establishing that. So, the
10 long-term piece is really helpful for states. So,
11 we appreciate that level of support. And building
12 infrastructure, quality improvement efforts,
13 health information exchange, data analysis,
14 education, follow-up, like, there's so much that
15 we could use that type of funding to do over a
16 period of five years. So that's really exciting
17 to us. Thank you.

18 NED CALONGE: And Roberto.

19 ROBERTO ZORI: Yeah. The problem with
20 being last is I don't remember the questions, but
21 I'm going to try. But the first one has to do
22 with the secondary criteria, and that's a big

1 problem. In our state, we tried to be more
2 involved with decision-making and the information
3 we need to approve a program. I think the results
4 of that may have been negative because we saw in
5 the last recently, one SMA, we had a year and a
6 half, but legislature decided that we should move
7 faster on that and so, not slower, so we had less
8 time to review.

9 The other thing is that CMV, since it
10 was a secondary criteria -- fit the secondary
11 criteria, they just went around -- they went
12 straight to the legislature. But there's nothing
13 in the statute that says other things can't be
14 taken up. So, it wasn't presented to the Advisory
15 Committee, it went straight to the legislature for
16 funding. And so, that's another door that's open
17 now that we had never seen before.

18 So, I think with the effectiveness of
19 the lobbies, again, they all have good intentions,
20 but they're starting to make work difficult if you
21 want to be analyze -- do a fair amount of analysis
22 on precision, and again, not doing any harm.

1 I think that I don't -- the second
2 question was the -- the removing the -- oh, the
3 second tier. Now, you know, a tent is not a tent.
4 I think there's too many places where the devils
5 can hide in those details. So, I think that
6 that's not going to work, and there are ways to
7 get around it.

8 Finally, the third one, you know, I
9 don't understand how we have a program, that's --
10 you know, when you make a comment or put down some
11 roots, then that's done. That's sort of where
12 states have to be mobilized. But there's nothing
13 at the end of it to say, a quality improvement
14 program, I mean, there's no analysis of are we
15 doing the right thing, are we actually doing what
16 we intend to do, to improve the health of our
17 infants, and not cause too many issues with that.

18 So, I would say that it's time to, like
19 I did once in the Advisory Council I voted for,
20 that we stop adding new things unless we fix what
21 we have. There are too many holes in our -- in
22 our present screening systems that we should fix.

1 And in fixing those systems, we make things better
2 for the next one.

3 So, I think it's time to have a Quality
4 Improvement/Quality Assessment Program, and that
5 should be maybe at the federal level that does and
6 says -- that makes a comment, and that would allow
7 us to have some ammunition with legislatures that
8 we can make the arguments that precision and
9 accuracy matters. Because at the moment, there's
10 no way for us to actually -- not -- very little
11 way for us to convince anyone to take this up
12 seriously. But again, the quality that each state
13 sort of reports back.

14 In terms of the twenty-five grants, I
15 don't get it, why not fifty. I would say that
16 shouldn't be based on a number of competition.
17 All the states have problems. Some of us are more
18 awake than others. But it should be based on a
19 good project. So, there should be fifty of them,
20 and what you could do is reject the ones that
21 don't seem to have -- to have enough teeth and
22 help them get to a better project so they get that

1 money. So, the incentive should be that each
2 state comes up with a good project, not that we
3 award the twenty-five. I mean, come on. It's not
4 a race. We're all -- so, yes, I need more money,
5 and I think it needs to be in place.

6 I need some guidelines. I mean, again,
7 these are so complicated. You know, the rare
8 diseases, we have guidelines. We create
9 guidelines for rare diseases and what we should do
10 A, B and C. Why shouldn't there be a guideline
11 for any condition you have and then have a
12 Committee set up what is the optimal guidelines so
13 that we have something that the Advisory
14 Committees has some push and say that these
15 guidelines aren't met, and we believe in those
16 guidelines.

17 NED CALONGE: Thanks. I appreciate your
18 passion. Okay, I'd like to turn now -- oh, I'm
19 sorry, Jennifer.

20 JENNIFER KWON: Hi, Jennifer Kwon. I --
21 just a quick comment. I was just thinking for
22 those states where RUSP recommendations are sort

1 of a requirement for adding to their state newborn
2 screening panel, I was wondering if there was a
3 way that the Committee could phrase a
4 recommendation in such a way for quality
5 evaluation or quality improvement or review of
6 some past added condition so that that would --
7 that state -- that same state language could push
8 those recommendations through as quickly as
9 nominated conditions are pushed through. It was
10 just a thought as a way to help states like
11 Oklahoma and Florida institute some of the looking
12 back quality improvement measures without having
13 to scramble to just introduce a new condition.

14 NED CALONGE: Thanks, Jennifer. I think
15 it's a really interesting, great discussion. I
16 will say that in our last letter, for me, it would
17 be my first letter from the Secretary accepting
18 the last condition we added, not the one that's
19 still pending, that the charge back to the
20 Committee was to report on kind of the quality
21 improvement finding and what happened after we
22 implemented it. And so, clearly, that's an

1 expectation of the Secretary moving forward, and I
2 think thinking about how to make sure that we're
3 thinking about quality improvement and quality
4 assessment at the state level is key.

5 Let me turn now to our organizational
6 representatives with Debra going first.

7 DEBRA FREEDENBERG: All right, thank
8 you. So, I'm really -- my comment is really
9 related more as a state newborn screening program,
10 then from the pediatrician aspect and when you
11 start thinking about secondary conditions, we're
12 an integrated program, but you need to be cautious
13 about what you're going to do. For instance, in
14 our state, we can't provide resources or benefits,
15 clinical help, to any child unless it is a
16 screened condition. So, for instance, if you were
17 to look at secondaries versus primaries, we could
18 provide services to a child with cobalamin A or B
19 but not C or D. So, I think you need to -- there
20 may be unintended consequences you need to think
21 through what that might mean. And I don't know if
22 we're unusual in that, but that's the way it is

1 for us.

2 And then the other comment that I have
3 is, you really need to be careful in defining what
4 secondary conditions are. Because we have heard
5 that there are some state programs that would
6 consider a late onset of a screen condition a
7 secondary condition, because it doesn't happen in
8 the newborn screening period. And so, I think
9 those are challenges, you know. For me, as a
10 geneticist, it doesn't make much sense to think of
11 it in that form. But there are -- that is one of
12 the thought processes that's out there around the
13 country. And so, I think you really need to be
14 very careful in your definition of what you're
15 calling and what your aims are.

16 And then my last comment is, we are, I
17 think, one of the few programs that's really an
18 integrated program in both the laboratory and
19 follow up component. And within that -- even
20 within that, although we're one integrated
21 program, we do have challenges between the two
22 parts of it. Susan's laughing continuously. And

1 so, there are a lot of Ying and Yangs and
2 pressures within programs in terms of their
3 abilities to both implement, you know, educational
4 aspects of it. And so, I think you kind of --
5 there's nothing that's perfect and that there are,
6 in theory, we're a model of an integrated program,
7 but in reality, we have lots of holes in it. So,
8 I just wanted to put that out there.

9 NED CALONGE: Thanks, Debra. Natasha.

10 NATASHA BONHOMME: Thank you. Natasha
11 Bonhomme of the Genetic Alliance. I have a couple
12 of things.

13 One is, you know, I understand and hear
14 the call for wanting the public to be better
15 informed and more aware and act accordingly to
16 that. But, I mean, we can't even decide amongst
17 experts around these things. So, I think we have
18 to kind of pivot that a bit. You know, I think
19 about some of my very early conversations with
20 Susan fifteen or so years ago about counting
21 conditions, and we are now having a workgroup
22 after a year and a half thinking about that. And

1 so, we all know, I'm going to, you know, stand up
2 for parents and the public, and I think, yes,
3 there's a lot to be learned, but we have to be
4 better communicators. If we can't even agree, you
5 know, how can we expect that from families and
6 advocates and clinicians, right? It's not just
7 families who are advocating for the addition of
8 these conditions.

9 Also, to go along with that, newborn
10 screening is the only system that catches at this
11 level. You know, I think back to the work that
12 Don Bailey did when he was on this Committee
13 really asking the question around, what would it
14 look like if we had pediatric screening just as a
15 way to try to take -- I don't think he would
16 necessarily frame it this way -- but take some
17 pressure off of the Newborn Screening System. We
18 had those activities. They were very interesting
19 presentations, and then that was that. So, I
20 think there are lots of reasons why people may be
21 adding conditions or wanting to add conditions at
22 a level that may not necessarily fit what some in

1 this room think is appropriate, but it's what's
2 there. So that's one.

3 Another piece is, and this has come up a
4 bit in some of the responses, which I'm really
5 happy about is, you know, as there's all this
6 attention to adding conditions, I think it would
7 be really helpful to hear, you know, clearly, from
8 state programs, what they are not able to do
9 because of this. And again, that's come up a bit
10 in some of these responses. I think that would be
11 really helpful for the larger Newborn Screening
12 System stakeholders to really understand. You
13 know, there have been mentioned around QI, there's
14 been mentions about just reviewing what we're
15 already doing. I really encourage, if that is a
16 pressure that states are feeling, which I know it
17 is, because I hear it in conversation, but to
18 think about how to communicate that out. All
19 stakeholders want to have a sense of what's really
20 going on.

21 And lastly, with all these pressures, I
22 think really thinking also about what are the

1 things that can be done across states, not just
2 every state having to reinvent its same wheel. I
3 think about that, particularly around education.
4 I mean, it still really surprises me how often
5 I'll hear from three states who are building the
6 same educational materials, and, you know, asking
7 us to review them at the end of the process, and I
8 say, you know, you could have saved a lot of time
9 coming either to us or to a patient advocacy
10 organization or some other group because that
11 information is eighty to ninety percent the same.
12 So again, just really encouraging to use the
13 resources that that are there. Thanks.

14 NED CALONGE: Thanks, Natasha. I
15 appreciate your comments. And I want to be really
16 clear, I'm -- it was not my intention to criticize
17 parents or advocacy groups or say that they need
18 to be doing better. And certainly, it's not my
19 intention to say that any group of parents or
20 advocates or researchers should be an expert in
21 how the Public Health System of newborn screening
22 works. My point is a little bit more directed

1 towards legislators. I do think legislators and
2 state legislations have an obligation to have
3 their staff dig into the -- to the implications of
4 what they're proposing, and I've seen several
5 examples where that has specifically not happened,
6 and that's not the fault of the advocates who are
7 bringing it to the attention of the legislators.
8 That is a fault with the legislators. And so, I
9 speak only for myself when I say this, but I think
10 that there is a real responsibility that is often
11 neglected on the part of state legislators to do
12 their due diligence before bringing these things
13 forward. I think that your -- I think you very
14 eloquently stated what I feel, which is that we
15 all need to work together, and the point that you
16 made at the end about programs developing the same
17 tools independently, that's exactly the point I'm
18 making about making these decisions about how to
19 move forward. We just -- if we don't act
20 together, public health people, clinical
21 specialists, advocacy groups, if we don't act
22 together, if we don't listen to each other, the

1 system is going to collapse. The Newborn
2 Screening System will collapse under its own
3 weight and under the problem -- the unanticipated
4 problems that we create if we don't work together.
5 So, we all have to take advantage of opportunities
6 like this, to listen to each other, to talk to
7 each other, and to understand the realities of the
8 situation. So, thank you for your comments.

9 Roberto.

10 ROBERTO ZORI: Yeah. Just quickly,
11 during expanded screening, we were in bad shape,
12 we were not ready at any level for a metabolic
13 disease. And so, what we did was exactly what I
14 think Lisa's referred to is we went to three
15 states, and we brought three states in and looked
16 at their program and presented. Our workgroup
17 worked over a year, we looked at every aspect, and
18 actually the end result I sent to you. So, I'd
19 like you to, maybe if you have time, to look at
20 that. I think that's what should be done, that
21 sort of that sort of detail for every newborn
22 screening. It took a while. But we had a

1 workgroup, and we went to other states, and we put
2 together, I think, the only document out there for
3 how to do expanded newborn screening, first.

4 The second is I agree about the
5 lobbyists. I've got my good friend. His -- his
6 child has Pompe. We were on the other sides of
7 the -- of the -- of the argument in this and he
8 was a lobbyist also. I understand why he did
9 that. I would do the same thing. But again,
10 there are priorities, and we have to sometimes
11 make them, and it's his job to lobby for
12 institution of Pompe today, and it's mine to see
13 whether that can be done safely, and we don't
14 agree on a timeframe, but we did have a
15 conversation over time. And I think that
16 lobbyists of any sort, we need to engage them with
17 an advisor counselor or something to put that in
18 perspective. I've found that all the lobbyists
19 have good points, but at the -- actually, the
20 timeframe and what we need to be in place, that
21 may differ in terms of what their timeframe is.

22 NED CALONGE: Thanks, Roberto.

1 So, I want to make sure that I respect
2 the time of the panelists and recognize you may
3 have something that follows on quickly if you need
4 to drop off. I understand that I have two more
5 comments from organizational representatives, and
6 if we can be brief, that would be great. I'm
7 going to start with Marc Williams.

8 MARC WILLIAMS: Thank you. Yes, this
9 will be brief. First of all, I want -- I share
10 everybody's dismay and despair about the inclusion
11 of secondary findings. We've tried to be as clear
12 about that as we can, and that's not working,
13 obviously.

14 I wanted to extend, though, on what
15 Roberto had recommended about quality improvement,
16 and I think that the point I would bring up is
17 that we really need more than that. I think we
18 need to begin to look at implementation of science
19 frameworks to evaluate the implementation of these
20 Newborn Screening Programs, and the reason I say
21 that is because, as we've heard this morning,
22 there's been so much -- there is so much

1 heterogeneity about the conditions and the
2 individual states and territories that are
3 implementing them, that using a formal framework
4 to gather the information is going to be much more
5 successful than quality improvement, which tends
6 to really work much better in more homogeneous
7 types of settings. So, I think that's a really
8 exciting thing to do. It's something I'm very
9 interested in, and I hope we can pursue that at
10 some point in the future.

11 NED CALONGE: Thanks, Marc. Gerry.

12 GERARD BERRY: Yes. Gerry Barry, I'm
13 representing the Society for Inherited Metabolic
14 Disorders, and my home is Boston Children's
15 Hospital and Harvard Medical School.

16 I'm usually a very positive person, but
17 I think there's a need here to be really
18 transparent and I have to say that, at this point
19 in time, our individuals who are caring for
20 patients with positive newborn screens are really
21 struggling, and this is not even with the addition
22 of new materials. Part of this has to do with the

1 with the pandemic and the changes that have
2 occurred. But this is really a very dicey
3 situation right now, in terms of providing
4 adequate care. It's a real struggle. So, I think
5 -- I think we have to keep this in mind with these
6 discussions.

7 NED CALONGE: Yeah, Gerry. I really
8 appreciate your comment. I think as Natasha was
9 talking, I was thinking about state labs do things
10 other than newborn screenings. So, you took us up
11 a level and I would take us up even a level higher
12 and recognize that state labs responding to COVID
13 testing and Monkeypox testing plus other additions
14 to their strategies and things they have to do all
15 have to work within the same physical environment
16 and the same budget and the same legislative
17 priorities. And so, always keeping in mind that
18 we are looking at a very important part of a very
19 important part of public health is important, and
20 now it's interesting because I think we are now
21 competing for the same workforce amongst several
22 different programs in state laboratories and

1 health care delivery systems and in public health.
2 And so, it doesn't mean we need to take our eye
3 off of our focus, and I do think trying to be
4 understanding and look for ways that we can
5 facilitate, and support implementation will really
6 be key to the success. And I take Shawn's warning
7 about collapse about Gerry's comment very
8 seriously because I think we want to be very
9 careful as we move forward and add conditions
10 always with the concept of how do we improve
11 implementation, long-term follow-up, and
12 contribute to the health of the population moving
13 forward. So, with that, I know we're over time,
14 but I'm going to hold us to just a shorter lunch
15 break, if that's okay, and ask you all to come
16 back at 1:30. I'm going to turn things over to
17 Soohyun who is going to say even though it's a
18 lovely day in Washington, all the doors lock
19 behind you. So. I'll turn that over to Soohyun.

20 SOOHYUN KIM: For our virtual attendees,
21 I just want to let you know we will be restarting
22 our meeting to help us troubleshoot some of our

1 technical difficulties. So, please rejoin the
2 meeting before 1:30 using the same link that you
3 used to join this morning.

4 And then, for our in-person attendees,
5 just a gentle reminder that you only have access
6 to the pavilion area and the lovely cafeteria. If
7 you are going to leave the building, you are going
8 to have to come to security, so please plan
9 accordingly. With that.

10 NED CALONGE: We'll see you all at 1:30.

11 SOOHYUN KIM: See you at 1:30. Thank
12 you.

13 **Lunch Break**

14 NED CALONGE: This afternoon, we have our
15 usual public comment period, and then we're going
16 to have our first Phase 2 to update on Krabbe
17 Disease Evidence Review. That will kind of close
18 out our all-person meeting, and then we're going
19 to end the day with workgroup meetings in the
20 three standing workgroups, and I'll give you more
21 information about that later. Do you have any
22 other announcements, Soohyun? She says no, so,

1 let us please turn to our comment period.

2 **Public Comment**

3 We received eleven requests for public
4 comments. We received two written versions of the
5 oral testimony that was shared with the Committee
6 in the meeting materials, and I know that we read
7 those and look forward to those comments from
8 their authors. And I have a list, and I'll just
9 proceed with the list as we go. And my request is
10 that you come up and speak at the podium.

11 So, Marianna Raia from Expecting Health
12 will be first.

13 MARIANNA RAI: Can you hear me okay?
14 Great, thank you. Thank you, Dr. Calonge and
15 thank you to the Committee for the opportunity to
16 share with you today three key updates related to
17 our Newborn Screening Education and Engagement
18 Initiatives. My name is Marianna Raia and I have
19 the privilege of working as the Associate Director
20 of Programs at Expecting Health. Our programs are
21 driving by clear vision that the fear and
22 confusions individuals and families face during

1 pregnancy and parenting is replaced by confidence
2 in agency to make the best health care decisions
3 for their lives. We do this through a variety of
4 programs that center around education, engagement,
5 and partnership with key system stakeholders.

6 The Newborn Screening Family Education
7 Program is a HRSA-funded program dedicated to
8 developing opportunities for all families to learn
9 about newborn screening and to develop training
10 and education resources that build confidence for
11 families to become leaders in the Newborn
12 Screening System.

13 As this Committee knows well, newborn
14 screening is more than just a screen at birth, but
15 a complex system with many stakeholders. We
16 believe that families are integral to driving
17 system change and supporting positive family
18 experiences within the Newborn Screening System.
19 We focus on supporting families through their
20 newborn screening journeys and create tools and
21 resources that support families before, during,
22 and after screening.

1 We would like to take a moment to thank
2 HRSA for their partnership and support to fund
3 this work.

4 To date, we have engaged over 18,000
5 families through a combination of efforts
6 including online training and education modules,
7 which are available in both English and Spanish,
8 online video education, and targeted initiatives
9 to raise awareness and knowledge of newborn
10 screening during the prenatal period specifically.

11 Additionally, the program has developed
12 an extensive partnership network of forty-five
13 organizational and individual partnership
14 relationships, which are integral to the
15 dissemination and connection to families.

16 The network is invited to participate in
17 biannual community of practice forums, where all
18 have the opportunity to share more about their
19 work, key problems, and the strategies to engage
20 families in the newborn screening community.

21 In collaboration with the University of
22 Texas Health Science Center at Huston, as well as

1 the Indiana Community Clinic, we conducted two
2 pilot programs to increase awareness and knowledge
3 of newborn screening during pregnancy among
4 medically underserved populations. Through the
5 initial success of this program, we've seen an
6 increase in the number of states directly reaching
7 out to us for technical assistance and support to
8 develop and implement newborn screening education
9 initiatives during pregnancy.

10 As a result, we have formed a workgroup
11 including representatives from nine state
12 laboratory and follow-up programs as well as
13 family representatives from three different
14 states. This group will meet four to six times
15 between October of 2022 and July of 2023 with the
16 aim to create and design a family-informed
17 resource that will be shared with all state
18 programs to support implementation of prenatal
19 education at the state level.

20 Secondly, the Navigate Newborn Screening
21 Ambassador Program, which launched in October of
22 2021, represents a network of trained family

1 leaders interested and engaged in the Newborn
2 Screening System. Participating individuals
3 commit to join a yearlong program, which includes
4 online and virtual live training modules,
5 quarterly group learning and discussion sessions,
6 and various other opportunities to connect and
7 share their stories with others in the newborn
8 screening community. We successfully completed
9 our first year of this program in August of 2022
10 and have ten ambassadors representing ten
11 different states who received certificates of
12 program completion and are actively working with
13 other newborn screening stakeholders.

14 In an effort to quantify the impacts of
15 this program, we asked ambassadors to share
16 feedback through both a baseline and post-program
17 evaluation and were able to measure noticeable
18 increases in knowledge about the Newborn Screening
19 System as well as confidence in their leadership
20 abilities.

21 Since completing the program, trained
22 ambassadors have provided input and support at

1 both the state and national levels including
2 contributions to national survey designs, state
3 advisory Committees, genetic counseling training,
4 and most recently attendance in speaking
5 opportunities at the APHL Newborn Screening
6 Symposium.

7 We are looking forward to expanding this
8 network of family ambassadors and launched a new
9 cohort with thirteen new families, including
10 diverse perspectives from a range of geographic
11 locations, condition groups, and various
12 perspectives.

13 We would like to take this time to share
14 with the Committee and other attendees that this
15 training network is available, interested, and
16 eager to collaborate. We encourage you all to
17 reach out directly to us if you wish to connect
18 with this network of family leaders.

19 And finally, in partnership with the
20 EveryLife Foundation, Expecting Health recently
21 cohosted the 4th Annual Newborn Screening Boot
22 Camp. This event is designed to educate and

1 engage participants on the latest newborn
2 screening updates and best practices, and to build
3 relationships between stakeholders from all
4 aspects of the Newborn Screening System. We had
5 over forty live attendees and roughly twenty-six
6 virtual attendees with many more that have
7 registered. The agenda included three key
8 sessions, including a presentation and panel
9 discussions regarding updates from this Committee,
10 changes from the ACHDNC, data and patient
11 perspectives, and equity in newborn screening.
12 This event continues to support and validate the
13 need for coordinated efforts across stakeholders
14 to build relationships, increase communication,
15 and generate opportunities for advocates to engage
16 in the Newborn Screening System.

17 In closing, I'd like to thank the
18 Committee again for allowing me the opportunity to
19 share these updates in this important work with
20 you all. Through these efforts and with the
21 experiences of the families we have the privilege
22 of working with, we've identified several helpful

1 strategies for education and engagement that we
2 will apply to existing and future programs.

3 As this group knows very well, the
4 landscape of newborn screening continues to
5 evolve, and this work highlights the utmost
6 importance of ensuring families are not just a
7 part of the discussion but are given the
8 opportunity to share their insights, experiences,
9 and ideas for solutions to help improve the
10 Newborn Screening System for all who are a part of
11 it. Thank you.

12 NED CALONGE: Thanks, Marianna, and
13 thanks for all the work at Expecting Health.

14 Next, I'd like to welcome Dylan Simon
15 from the EveryLife Foundation for Rare Diseases.

16 DYLAN SIMON: Good afternoon and thank
17 you all for having me today. My name is Dylan
18 Simon and I serve as the Director of Policy for
19 the EveryLife Foundation for Rare Diseases.

20 The patient community and the Committee
21 here find strong alignment in our commitment
22 ensuring the timely implementation of conditions

1 that have been nominated for addition to the RUSP.
2 And while we appreciate the Committee's
3 discussions in the previous two meetings on how to
4 strengthen newborn screening, we feel that
5 discussion may have conflated the many legislative
6 approaches underway, and thus we feel it is
7 important to provide some clarity into our
8 legislative process and the legislation that we
9 seek.

10 Since 2016, the EveryLife Foundation has
11 been working with the rare disease community and
12 state leaders to pass state RUSP alignment
13 legislation to ensure that state health
14 departments are resourced, implementation
15 timelines are reduced, and patient access
16 organizations can focus precious resources on
17 community follow-up. Our collaborative and
18 systemic approach has resulted in our community
19 helping to pass legislation in eight states and
20 consulting in two additional states to pass RUSP
21 alignment legislation. Those states include
22 California and Florida who you heard from today,

1 in addition, Georgia, Ohio, North Carolina,
2 Arizona, Pennsylvania, Iowa, Mississippi, and
3 Maryland. In addition, in Oklahoma, while
4 Oklahoma does not meet -- does not have all the
5 aspects of RUSP alignment legislation, which I'll
6 go into momentarily, we did help to consult with
7 both a state advocate as well as the state
8 legislator and the legislation that was passed
9 last session to help reduce the rulemaking process
10 for the state.

11 When we begin RUSP realignment efforts
12 in every state, we seek to engage newborn
13 screening stakeholders including patient
14 advocates, policymakers, public health labs and
15 department officials. We work with these
16 stakeholders to craft legislation or regulation
17 that ensures that each state can successfully add
18 new RUSP conditions within a predictable timeline.
19 In every state we work in, we reach out to both
20 the department as well as local advocates to
21 ensure -- to aid in the development of the
22 legislation to ensure the fact that that

1 legislation will work best for that state. We are
2 also aware that we are not the only community
3 members advocating for newborn screening
4 legislation within states, which is why we think
5 is important today to talk to you about what we
6 consider state RUSP alignment legislation, and
7 that contains three components.

8 The first component is auto-inclusion or
9 vote for inclusion, either requiring the state to
10 add a new RUSP condition or requiring the state's
11 Newborn Screening Advisory Council or Department
12 of Health to consider a new RUSP condition for
13 their state panel. The bill does not name
14 specific conditions, nor do they allow for
15 conditions that have not met the evidentiary
16 criteria of the federal RUSP to be required to be
17 added by the state.

18 The second component of RUSP alignment
19 is the timeline, which requires the state to add
20 or consider adding a new RUSP condition within a
21 stated period of time. Depending on the state,
22 that period is typically two to three years.

1 Finally, the third component of RUSP
2 alignment legislation is the allocation of
3 resources. While different in every state, this
4 typically includes the ability for the department
5 or Public Health Lab to raise the fee as they see
6 fit, or the creation of a newborn screening line
7 item within the budget. Essentially, if we're
8 going to ask the state to add a condition, we're
9 going to ask them to in a certain amount of time.
10 We want to make sure that the funding is that we
11 want to make sure that the state has the resources
12 to implement this condition properly.

13 We're committed to ensuring that the
14 conditions which have been nominated for inclusion
15 on the RUSP have pathways that are timely and
16 resource implementation in all fifty states. As
17 an organization, we are engaging with stakeholders
18 every day to determine the best way to enhance
19 policy efforts that improve and strengthen newborn
20 screening.

21 Thank you again for the opportunity to
22 speak with you today. I'm happy to answer any

1 questions about this at any time, so please do not
2 hesitate to reach out and have a great rest of
3 your day. Thank you.

4 NED CALONGE: Thanks to EveryLife
5 Foundation for Rare Diseases for your work.

6 And now, Kim Stephens from Project
7 Alive.

8 KIM STEPHENS: Chairman and members of
9 the Advisory Committee, my name is Dr. Kim
10 Stephens, and I'm pleased to offer comments on
11 behalf of over thirty million Americans living
12 with rare diseases as President of Project Alive,
13 the co-chair of EveryLife Foundation Newborn
14 Screening Diagnostics Working Group, and as a
15 parent advocate.

16 The EveryLife Foundation for Rare
17 Diseases is a nonprofit, nonpartisan organization
18 dedicated to empowering the rare disease patient
19 community. Through our newborn screening efforts,
20 the EveryLife Foundation works with many diverse
21 stakeholders that comprise the newborn screening
22 ecosystem every day. To ensure the Committee

1 remains representative of these stakeholders, we
2 encourage the Committee to provide more formalized
3 opportunities for engagement. To this end, we
4 have the following suggestions for consideration
5 of the Committee.

6 We recommend that as the composition of
7 the Committee is considered, professional
8 diversity among Committee members and
9 representation of the ecosystem be reflected. We
10 request that the Committee once again add a
11 patient advocate as a Committee member so that
12 they may properly represent the patient experience
13 on the Committee.

14 We ask the Committee take time to
15 respond to public testimony, to develop a deeper
16 dialogue between the Committee and the various
17 stakeholders that make up the Newborn Screening
18 System, and we request that the Committee add a
19 public comments section to their quarterly
20 meetings dedicated to advocates speaking about
21 conditions currently within the RUSP nomination
22 review process.

1 And finally, we ask that the Committee
2 include patient advocates and panel presentations
3 to ensure presentations and subsequent
4 conversations that occur at the Committee meetings
5 are properly represented by the patient
6 experience.

7 We ask that as you continue forward, you
8 actively communicate your concerns regarding
9 resources and other limitations with newborn
10 screening, but not allow those concerns to
11 dominate conversations.

12 In turn, as a patient advocacy
13 community, we will continue to work with policy
14 makers to provide more resources and reduce
15 workforce barriers so that all know newborns may
16 realize the lifesaving benefits of newborn
17 screening.

18 Thank you for the opportunity to speak
19 with you today.

20 NED CALONGE: Thanks, Kim. And also our
21 thanks to Project Alive.

22 Next, I'd like to welcome Heidi Wallis

1 from the Association for Creatine Deficiencies.

2 HEIDI WALLIS: Good afternoon. It's
3 nice to see everybody in person, not on a Zoom
4 screen. It's great to be here. I'll be really
5 brief. I want to leave this stand with everyone
6 here remembering I'm representing GAMT Deficiency,
7 GAMT. I hear people go that one deficiency, it's
8 really rare. But I also want to bring up the
9 patients that I'm talking about, and my kids are
10 the poster kids. My nineteen-year-old daughter is
11 severely intellectually disabled. She was
12 diagnosed at five-and-a-half, and my son was
13 diagnosed at birth, thanks to his big sister, and
14 he is a typical fifth grader, doing fantastic.
15 All of this because of a supplement they could get
16 over Amazon and measure in the kitchen on a scale,
17 and that's it.

18 So, you know, I've heard -- we first
19 were here in May 2016, and I'll just say for the
20 comments, we've kind of gone around about the
21 advocates and they can be a real pain. We've
22 waited six and a half years very patiently and you

1 know, heard from a lot of experts, this is the no
2 brainer condition. This is multiplexed with amino
3 acids, and acylcarnitines that the labs are
4 already screening for, the treatment is safe,
5 effective. There's just nothing holding us back.
6 And so, I'm just here to say GAMT Deficiency
7 Association for Creatine Deficiencies, we've got a
8 strong network of researchers, we have expert
9 panel meetings where we bring these rare disease
10 folks together, and they talk about treatment and
11 care, and they connect with each other and support
12 each other. So, the follow-up piece is taken care
13 of, and we've got a strong patient registry.
14 We're developing core outcome sets where we're
15 here and we're here for the patient. Please don't
16 forget us. And if you're in a lab, reach out. We
17 would love to share a presentation that we created
18 with laboratorians and experts on the disease, how
19 it manifests, how the treatment easily addresses
20 those issues, and how this screening can be put
21 into your lab.

22 I also want to throw out I spent three

1 years working in my home state's public health lab
2 in newborn screening, and maybe unpopular to some
3 of the advocates, I will say it's hard to add a
4 disorder. I know that process. We added disorder
5 while I was there, and it's not simple. So, this
6 is a long, hard process, and I appreciate
7 everyone's work. I appreciate the struggles to
8 communicate things like primary conditions and
9 secondary and this is hard. But I know that
10 working together, we all are doing great things,
11 and I appreciate your support. I am hoping in
12 nine days or less, we've got a signature on GAMT
13 from Secretary Becerra. And again, reach out.
14 GAMT Deficiency, my name is Heidi Wallis, and I'd
15 love to talk to you. Thank you.

16 NED CALONGE: Thanks so much, Heidi, and
17 thanks to the Association for Creatine
18 Deficiencies.

19 Next up, I'd like to invite Niki
20 Armstrong from Patient Project Muscular Dystrophy.

21 NIKI ARMSTRONG: On behalf of Parent
22 Project Muscular Dystrophy and the Duchenne

1 Patient Community, thank you for the opportunity
2 to speak today. My name is Niki Armstrong. Are
3 you guys getting that? Yeah. Better? Perfect,
4 okay. And I am the Newborn Screening Program
5 Manager for Duchenne Newborn Screening. I'm
6 pleased to provide an update about our efforts.

7 As you know, because I've been telling
8 you for the last few years that Nancy Kennedy told
9 you before that, we have been working on Duchenne
10 newborn screening and the infrastructure for more
11 than ten years. The learnings from our efforts
12 and the efforts of everyone that came before us,
13 were compiled into a RUSP nomination package that
14 is currently in review, and we look forward to
15 discussions of that in future meetings.

16 Today, I wanted to give you a quick
17 update of some of our efforts to prepare for
18 Duchenne newborn screening and advances in
19 Duchenne treatment. We understand, as we
20 discussed at length today, that this is way more
21 than just a lab test that needs to be validated.
22 And so, one of the pieces that we wanted to learn

1 more about was how providers feel about Duchenne
2 newborn screening and specifically the providers
3 that would be seeing these kids in clinic. So,
4 those are the neuromuscular physicians and the
5 rehab specialists.

6 So, as part of that process, we
7 developed a survey -- we used a steering
8 Committee, developed a survey that was then sent
9 out to the professionals that would be seeing
10 these kids. So, we used our certified Duchenne
11 Care Center Network and asked providers for their
12 opinions on the benefit of Duchenne newborn
13 screening and whether or not the care community
14 was ready for Duchenne newborn screening, and then
15 what they would do afterwards -- what they would
16 do at those initial visits after those babies were
17 diagnosed, and that work has now been published.
18 So, I'm happy to share that publication. But
19 today, I'm going to give you just some of the
20 highlights.

21 So, our first question asked them for
22 their view on Duchenne newborn screening, and

1 whether they thought the care community was ready
2 for this, and the answer was a resounding yes.
3 They felt that there was benefit to Duchenne
4 newborn screening and the care community was
5 ready.

6 We then asked what they would do with
7 those initial visits when they saw the infants
8 that were diagnosed with Duchenne because, of
9 course, we want to make sure that there's
10 something that we're doing for these babies. And
11 the providers answered many, many different
12 responses, things like genetic counseling,
13 referral to early intervention services, screening
14 siblings, maternal carrier screening, assessment
15 of social and language developments, discussion of
16 clinical trials, and, of course, initiating the
17 FDA-approved exon skipping therapies. Overall,
18 the physicians reported believing that the optimal
19 time to start those exon skipping therapies was
20 before age two, with the vast majority wanting to
21 start them as soon as possible. But
22 unfortunately, right now, Duchenne is not

1 typically diagnosed until after age four, and at
2 that point, there is significant irreversible
3 muscle damage that we do not have a way to fix or
4 to change. And of our list of care
5 recommendations that the experts endorsed, every
6 single one of them is time sensitive with benefit
7 to being initiated early, social and language
8 skills, physical therapy and occupational therapy,
9 even screening mothers and siblings. There is a
10 benefit to doing all of those things earlier.

11 Right now, Duchenne has five FDA-
12 approved therapies and two potential therapies,
13 including gene therapy that are under FDA review.
14 We expect responses on those two additional
15 therapies next year. In addition, our research
16 pipeline has more than twenty different potential
17 therapies in clinical trials, and even more in
18 preclinical research. But for the best outcomes,
19 we have to identify these babies and treat these
20 babies before there's irreversible muscle damage,
21 and newborn screening will provide the opportunity
22 to do that. Thank you.

1 NED CALONGE: Thanks, and, of course,
2 thanks for the work of Parent Project Muscular
3 Dystrophy.

4 I would now like to invite Amanda
5 DeRossett up -- oh no, I'm sorry, she's virtual.
6 So, Amanda.

7 AMANDA DEROSSETT: Can you all hear me?

8 NED CALONGE: We can.

9 AMANDA DEROSSETT: Okay. Hi, everybody.
10 My name is Amanda DeRossett. My son, Ty, screened
11 positive for Krabbe disease in 2016.

12 NED CALONGE: Amanda?

13 AMANDA DEROSSETT: Yes?

14 NED CALONGE: Is it possible for you to
15 turn on your video?

16 AMANDA DEROSSETT: Oh, yes.

17 NED CALONGE: Thank you, go ahead. I'm
18 sorry to slow you down.

19 NED CALONGE: You're good.

20 AMANDA DEROSSETT: So again, my name is
21 Amanda DeRossett. My son, Ty, screened positive
22 for Krabbe disease in 2016. On our second day at

1 home with our perfect newborn, we headed to his
2 first doctor's appointment. He was just five days
3 old. The doctor walked in with his assistant and
4 sat down. He looked at us and said, I'm sorry to
5 tell you, but your son has a metabolic disease.
6 What does that mean? He proceeds to inform us
7 that Ty has Krabbe disease, which is fatal and
8 there is no cure. He did get us in contact with a
9 specialist who explained to us he had a chance to
10 be transplanted. My husband and I chose to
11 transplant, and there's yet to be a day that we
12 regret that decision. I can't imagine if we
13 weren't given that option. Ty was the first child
14 found on newborn screening in Kentucky and one of
15 the quickest ever to be transplanted.

16 Fast forward to today. Ty will be six
17 years old at the end of November. He embraces
18 life and everything he does. Ty, just like most
19 six-year-olds, he loves books, especially Pete the
20 Cat, driving his jeep, playing his tablet,
21 swinging at the park, and watching movies. We
22 cannot imagine our life without Ty.

1 Sorry. What you aren't aware of is we
2 actually lived in Tennessee when Ty was born. We
3 chose to have Ty at a Kentucky hospital because we
4 lived on the state line. We were unaware that
5 every state did not test for all the same
6 diseases. Had we have chosen for him to be born
7 in Tennessee, he unfortunately would not likely be
8 with us today because in 2016, Tennessee did not
9 test for Krabbe disease. Today it does.

10 I believe that every parent regardless
11 of their state should have the ability to choose
12 whether or not they want their child to be treated
13 for this vital disease.

14 The biggest thing I can ask each of you
15 in deciding whether or not you will recommend
16 Krabbe is to put yourself in our family shoes.
17 Would you want that choice to save your child's
18 life? Sorry, but I got it said. But thank you
19 all so much for allowing me to tell our family
20 story.

21 NED CALONGE: Thank you so much, Amanda.

22 I recognize these are difficult

1 opportunities and it means a lot to us all for you
2 to have the courage and ability to present to us
3 today. It's a gift that we appreciate. Thank
4 you.

5 I wonder if we could now turn to Kelly
6 Denora Bonacoursa.

7 KELLY DENORA BONACORSA: Good afternoon.
8 My name is Kelly Denora Bonacorsa, and this is my
9 daughter, and this is my daughter Sophia. Sophia
10 has Krabbe disease. She was diagnosed in March at
11 age six months, following back-to-back emergency
12 room visits, invasive medical procedures, long
13 hospital stays, and multiple misdiagnoses. Her
14 diagnosis of Krabbe Disease blindsided us. Our
15 lives have ended. Our active-duty military move
16 overseas canceled, our careers halted, and our
17 family plans extremely complicated. Sophia was
18 born a seemingly healthy child, but in the months
19 preceding her diagnosis, Sophia didn't reach
20 important milestones, even losing some skills she
21 once had. She became irritable and rigid. She
22 plateaued in length and weight. Sophia spent five

1 weeks inpatient for failure to thrive and to
2 understand why she stopped developing and started
3 deteriorating. She saw countless physicians,
4 underwent endless scans and tests, and even
5 endured a failed gastrostomy tube procedure that
6 required intensive wound care. Our situation went
7 from devastating to tragic when we learned that
8 the commonwealth of Virginia determines Sophia's
9 chance at life. You see, we live in a state that
10 doesn't screen for Krabbe disease at birth,
11 largely because the disease isn't on the
12 Recommended Uniform Screening Panel. Sadly,
13 Sophia's diagnosis came too late, and treatment
14 couldn't help her.

15 Sophia is one year old, and she is
16 dying. Her life is limited. She's impacted by
17 hearing loss, muscle weakness, difficulty
18 swallowing, seizures, stiff posture, and
19 significant developmental delay. She's legally
20 blind. Sophia can't walk, sit, talk, or eat.
21 She's unable to smile. She requires in-home
22 nursing services and around-the-clock medications.

1 She's dependent on special equipment like a
2 feeding pump and a suction machine since she can't
3 safely swallow. She needs continual supportive
4 treatments to help her perform functions that you
5 and I take for granted like looking at an object
6 or moving an arm. She receives hospice and
7 palliative care for pain management and other
8 physical symptoms.

9 In the seven months since Sophia's
10 diagnosis, her medical care amounts to over half a
11 million dollars in expenses. And as Krabbe
12 progresses, Sophia's health will worsen, and her
13 care will become more complicated.

14 Today, I want you to see Sophia --
15 really see her. She's a beautiful, sweet, little
16 girl. She's fond of the outdoors and likes music.
17 She loves to taste the apples. We tried to give
18 her a full life even in the face of her disability
19 and her very short life expectancy, including
20 trips to the farm and daily walks and playtime
21 with her cousins.

22 The Virginia Newborn Screening Advisory

1 Board voted against adding Krabbe to the
2 commonwealth's panel of conditions in November
3 2020. My daughter was born ten months later.

4 I need you to remember Sophia and
5 recognize that you, the Committee, can create
6 change so that no other child suffers an early
7 unnecessary death and no other family misses
8 precious moments. Newborn screening for Krabbe
9 disease is critical because early diagnosis and
10 intervention make a difference in the life of the
11 child and the family. And I know because it would
12 have drastically altered the course of our lives.
13 Thank you for your time today. Thank you.

14 NED CALONGE: Thank you, Kelly.

15 Next virtually, we're going to hear from
16 Hema Rangarajan from the Nationwide Children's
17 Hospital.

18 HEMA RANGARAJAN: Good afternoon,
19 Chairman and members. Can you hear me okay?

20 NED CALONGE: We can indeed.

21 HEMA RANGARAJAN: Thank you. So, good
22 afternoon, everyone. Obviously, I was very

1 touched by the last two comments, something that's
2 very close to our heart here at Nationwide.

3 So, my name is Hema Rangarajan and I'm a
4 physician who specializes in bone marrow
5 transplant for children. I'm an Associate
6 Professor of Pediatrics at Nationwide Children's
7 Hospital, Columbus and the Ohio State University
8 here in Columbus, Ohio.

9 So today, I would like to take this
10 opportunity to briefly describe my team's
11 experience -- the BMT team at Nationwide's
12 experience in the care and transplant for newborns
13 with Krabbe disease, and thereby demonstrate to
14 you how transplant for these infants can actually
15 be done within state without having to go out of
16 state to another transplant center.

17 So, over the last five years, with the
18 implementation of the newborn screening for Krabbe
19 disease in Ohio, the bone marrow transplant team
20 at Nationwide, we have the unique opportunity to
21 take care of two infants with Krabbe, who are
22 diagnosed by the newborn screening.

1 The first infant is -- was -- is a
2 newborn girl who was diagnosed in April of 2017.
3 Immediately following her abnormal screen, we were
4 alerted, and she was seen by a multidisciplinary
5 team comprised of ourselves, the BMT team, the
6 genetics, neurology on day nine of life. So, her
7 result came on day five or six, and we saw her on
8 day nine as soon as we could.

9 As this was our first infant with
10 newborn Krabbe that we were considering
11 transplant, we immediately reached out to our
12 colleagues at Duke University, because we knew
13 they had vast experience in transplanting such
14 infants and sought their guidance and
15 collaboration, and this was a very successful
16 partnership because with the team at Duke led by
17 Dr. Joanne Kurtzberg, we immediately initiated the
18 process of transplant for our patient.

19 We first had to work with the National
20 Marrow Donor Program that is the NMDP, and we
21 rapidly identified suitable cord blood units in a
22 matter of just few days, like one or three days.

1 It didn't take us that long. And with the same
2 help provided by Dr. Kurtzberg at Duke, we
3 actually tested the levels of enzymes in the
4 cords, and we chose the most suitable and
5 appropriate cord. Usually, when we take patients
6 to transplant using a cord blood, we cannot start
7 chemotherapy for transplant until the cord blood
8 arrives at the center. But that would have meant
9 we would have lost some days.

10 So, again with Dukes guidance, we sought
11 special approval from the National Marrow Donor
12 Program to actually start chemotherapy even before
13 the cord arrived at our center so that we could
14 expedite the process of transplant in our patient.

15 We took our first patient to transplant
16 in May of 2017, and we started therapy -- that is
17 chemotherapy -- on day twenty-six of life -- of
18 the child's life and did the transplant on day
19 thirty-five. So, this was then followed
20 surprising and a year and four months later, our
21 team actually took another male infant with an
22 infantile Krabbe disease once again diagnosed with

1 an abnormal newborn screen in August of 2018.
2 This patient came to us after he was actually
3 diagnosed at a local children's hospital, which
4 was not transplant -- did not have a transplant
5 team there. And therefore, we were alerted about
6 him on day -- his day nineteen of life and the
7 Nationwide Multidisciplinary Team immediately met
8 with the family when the child was twenty-one days
9 of age. I remember that distinctly because it was
10 over a weekend, and we could not bring on Saturday
11 and Sunday. So, we said please, please, come to
12 us on that Monday.

13 And using the same steps I previously
14 described, and because we've had the experience,
15 we were able to expedite the process and this baby
16 actually started chemotherapy on day twenty-nine
17 of life and received his cord blood transplant on
18 date thirty-eight of life.

19 So, during this entire process, we
20 frequently communicated with our team at Duke to
21 make sure we're taking the right steps and we also
22 monitored the neurodevelopmental progress of our

1 patients posttransplant over several months and
2 years.

3 As of today, both patients are alive,
4 with the first patient being nearly five-and-a-
5 half years posttransplant and the second patient
6 being four years, two months posttransplant, and
7 I'm happy to say that both are free from
8 transplant-related complications. Both children
9 are making steady developmental gains with strong
10 cognitive, receptive, and expressive language
11 skills, and as expected, their motor skills is a
12 little bit lagging behind.

13 But to conclude, I think I would like to
14 take this opportunity to say that our experience
15 is actually an important and highly successful
16 example of how in-state pediatric transplant
17 centers are able to perform transplants for
18 infants with Krabbe disease diagnosed by an
19 abnormal newborn screen through an expedited
20 process. And I can confidently state that this
21 process was made possible because of our
22 collaboration with our colleagues at a center

1 which had more experience in this area.

2 Thank you. I'm happy to take any
3 questions.

4 NED CALONGE: Thanks so much.

5 Next, I'd welcome Stacy Pike Langenfeld
6 from Krabbe Connect.

7 STACY PIKE LANGENFELD: Thank you so
8 much for this opportunity to speak today. I am
9 Stacy Pike Langenfeld, Co-Founder and President of
10 Krabbe Connect.

11 I want to take a moment to review the
12 2009 RUSP submission that didn't get approved.
13 Concerns around the disease not being well
14 defined, concerns about the screening method, and
15 uncertainty on the benefits of treatment. I'm
16 going to take a moment to tell you about three --
17 those three items today.

18 The disease is broken down into four
19 categories: early infantile, late infantile,
20 juvenile onset, and adult onset. Truthfully, I
21 knew these categories back in 2001 when my
22 daughter was diagnosed. We've known for quite

1 some time the most severe forms are early
2 infantile and late infantile subgroups. Many
3 publications have identified early infantile as
4 accounting for nearly ninety percent of the cases.

5 But to be clear, I want you to hear me
6 out on how our community sees the subgroups of
7 Krabbe disease. Early and late infantile, no
8 chance of quality of life without access to
9 newborn screening. Juvenile and adult onset have
10 the option to treat with or without access to
11 newborn screening, however, prefer to know sooner
12 than later to have the ability to treat at the
13 most optimal time.

14 Well, let's talk about screening method.
15 Over the past three years or more, we've proven
16 that if a low GALC enzyme activity is identified
17 through an infant's dried blood spot, the sample
18 is moved on to second-tier testing to test for the
19 biomarker psychosine. Published studies have
20 validated that the use of psychosine assay can
21 identify a patient as having severe Krabbe disease
22 with onset in infancy, or later onset variant.

1 Studies have also proven that psychosine can
2 assist in monitoring the later onset subgroups.
3 But to be clear -- oh, sorry about that.
4 Onto treatment. Today, the standard of
5 care is transplant. Many stories exist on the
6 internet on Krabbe disease patients living well
7 with transplants. Transplant kids attend school
8 and dress up for Halloween. Oh my gosh, you
9 should have seen the photos this year. They were
10 so cute. Eat on their own, manipulate objects,
11 navigate their wheelchair, and so much more. The
12 development of children post-Krabbe disease
13 transplant is widely available through several
14 peer-reviewed articles. When reviewing these
15 publications, don't make the mistake of comparing
16 them to normal children born without disease. The
17 only fair and equitable comparison that should be
18 made is between patients born with Krabbe disease
19 who were transplanted, and patients born with
20 Krabbe disease who were not transplanted. The
21 difference between the quality of life for the
22 transplanted versus the non-transplant patients is

1 crystal clear.

2 We also now have gene therapy clinical
3 trials; however, only patients identified through
4 newborn screening will have access to the current
5 clinical trials.

6 Now let's talk about the other stories.
7 A majority of the stories that exist on social
8 media can be summed up by one father's statement
9 in a todayshow.com article. Buying a 3'6" coffin
10 is at the bottom of every parent's to do list.
11 Five months ago, my kindergartner, Emmett, took
12 his last breath. This is this is because only
13 nine states currently test for Krabbe disease.

14 As I close out, I truly believe I'm very
15 thankful for this opportunity to be in front of
16 you today and you continue your evaluation of
17 Krabbe disease. Please remember to keep the
18 mission of newborn screening at the top of
19 everything you discuss. The reason Dr. Robert
20 Guthrie pioneered this health care program was to
21 help identify disease at the earliest point to
22 allow for early intervention and to decrease the

1 morbidity and mortality of infants born. I
2 believe the mission remains the same today and I
3 believe Krabbe disease can be safely screened.
4 Thank you so much.

5 NED CALONGE: Thank you, Stacy. Again,
6 we appreciate all the work by Krabbe Connect.

7 And next I have Lisa Brackbill from the
8 Leukodystrophy Newborn Screening Action Network.

9 LISA BRACKBILL: Good afternoon. It is
10 such an honor to be here with you today. My name
11 is Lisa Brackbill, and I live in Hershey,
12 Pennsylvania. My daughter, Tori, was diagnosed
13 with Krabbe disease at six-and-a-half months and
14 died at twenty months of age because she wasn't
15 eligible for treatment. It is because of Tori and
16 our great loss that I advocate. I advocate so
17 that other parents can seek treatment or take
18 advantage of gene therapy clinical trials, and not
19 be told there's nothing we can do because those
20 are the worst words a person and parent can hear
21 on diagnosis day.

22 I have lived and breathed both Krabbe

1 and newborn screening for seven and a half years
2 now, and I understand the disease, I understand
3 the assay, and I understand the newborn screening
4 system and the treatment options. In fact, I know
5 more about Krabbe and newborn screening than I
6 know about my daughter. I spent five years
7 advocating in Pennsylvania for a stronger, more
8 equitable newborn screening program, and if you
9 have any questions, I'm happy to share our success
10 because we took the legislature and funding out of
11 the equation entirely, and I think our system is a
12 great model, as a side note.

13 I saw great success with Act 133 of
14 2020. Because of the mounting evidence and my
15 persistence as a member of the LSD subcommittee,
16 the Pennsylvania Newborn Screening Advisory Board
17 added Krabbe at that time and we found four babies
18 in our first seven months of screening. Those
19 parents were given an opportunity that we were
20 denied, which is the opportunity to even try to
21 save our child's life.

22 I have encountered many common

1 objections to screening for Krabbe and I've even
2 created a frequently asked question/ objections
3 document because there are scientifically backed
4 answers to every question I've heard raised.

5 We as a community of scientists,
6 clinicians, advocacy groups, and families are
7 ready to see every baby screened for Krabbe
8 disease. The ten states already screening paved
9 the way and solved the problems. Those who know
10 the disease best believe it is time for Krabbe to
11 be added to the RUSP.

12 These babies will be born with Krabbe
13 whether they are screened for it at birth or not,
14 and it's time to give them the best possible
15 opportunity to actually live, no matter where they
16 are born. No parent should have to bury their
17 child, especially when newborn screening gives
18 them the opportunity to treat it. I've seen both
19 versions of the Krabbe story, one of despair like
20 mine, and one of hope, like Ty's. Let's give
21 these families hope. Thank you.

22 NED CALONGE: Thank you, Lisa and thanks

1 for the Action Network.

2 I want to thank again and recognize the
3 contributions of all our public commenters today
4 and thanks for sharing your stories, your passion,
5 and your worries, and life journeys with us.

6 Thank you.

7 So, in July of 2021, the Committee
8 received a nomination for Krabbe disease for
9 inclusion on the RUSP. And you've heard, it was
10 the second nomination that the Committee has
11 considered. At the May 2022 meeting, the
12 Nomination and Prioritization Workgroup presented
13 an overview and the Committee voted to move Krabbe
14 disease forward to a full evidence-based review.
15 In our August meeting, the Committee reviewed the
16 Phase 1 update on the evidence-based review, and
17 today, Dr. Kemper -- Dr. Alex Kemper, lead for the
18 Evidence-based Review Group, and Dr. Lisa Prosser,
19 ERG member, will provide the Committee with the
20 Phase 2 update.

21 Dr. Kemper is the Division Chief of
22 Primary Care Pediatrics at Nationwide Children's

1 Hospital and Professor of Pediatrics at The Ohio
2 State University College of Medicine. Dr.
3 Kemper's research focuses on the delivery of
4 preventive care services including newborn
5 screening. Since 2013, Dr. Kemper has also served
6 as the Deputy Editor of Pediatrics.

7 Dr. Lisa Prosser is the Maryland Fisher
8 Blanch Research Professor of Pediatrics and
9 Director of the Susan B. Meister Child Health
10 Evaluation and Research Center. Dr. Prosser also
11 holds an adjunct faculty appointment at the
12 Harvard School of Public Health.

13 Her research focuses on measuring the
14 value of childhood health interventions using
15 methods of decision, sciences, and economics.
16 Current research topics include newborn screening
17 programs, vaccination programs, and methods for
18 valuing family spillover effects of illness.

19 With those introductions, I'd like to
20 ask Dr. Kemper up to the podium. Thanks, Alex.

21 **Krabbe Disease Evidence-Based Review**

22 **Phase 2 Update**

1 ALEX KEMPER: Good afternoon, everyone.
2 I'm pleased to be able to present this interim
3 summary of the Krabbe Disease Evidence-Based
4 Review.

5 So, this is a list of the Evidence
6 Review Group members. In the interest of time,
7 I'm not going to read through them all. But I
8 would like to thank Dr. Kwon and Dr. McCandless
9 for their work serving as the liaison from the
10 Advisory Committee to our Evidence Review Troup.
11 Next slide, please.

12 As we do with all of our projects, we
13 have a series of technical expert panels, panel
14 members, these are experts in issues related to
15 Krabbe disease, who we work closely with, and
16 we'll have them evaluate the report before it's
17 finalized and submitted to the Advisory Committee.
18 Next slide, please.

19 We have had two group calls with the
20 technical expert panel. Advance, please.

21 In addition to this, we've had a series
22 of key informant interviews with experts and

1 advocates in the field. This is a really
2 important part of our process to really make sure
3 that we understand all the nuances and issues
4 related to Krabbe disease newborn screening. So.
5 I'd like to thank members of our TEP and the other
6 individuals who participated in the interviews.
7 Next slide, please.

8 So, this is obviously a very brief
9 outline of what I hope to accomplish today. We're
10 going to provide a very high-level summary of
11 where we are with the evidence-based review, and
12 I'm going to be highlighting our current progress
13 in terms of talking about some particular studies
14 and findings that I think are going to inform the
15 final report.

16 Dr. Prosser will talk about the decision
17 analytic modeling process, and I will follow up
18 with where we are with the Public Health Impact
19 Assessments, and then we'll end with next steps
20 and open the floor to conversations.

21 So, you know, you heard just a few
22 minutes ago about the 2009 review, and I just want

1 to highlight it again, although the summary of the
2 issues was excellent.

3 So, it was not recommended in 2009, and
4 there were several gaps that were identified at
5 the time, including issues related to the
6 definition of early infantile Krabbe disease.
7 There were questions at the time about the
8 screening and treatment algorithm. There were
9 questions about the benefit of stem cell
10 transplantation, including if there were
11 subpopulations of infants with Krabbe disease that
12 would benefit more than others. And then there
13 was also concern about over-referral and potential
14 burdens and follow-up for those infants who screen
15 positive. Next slide, please.

16 So, there have been obviously a lot of
17 advances since 2009, including psychosine testing,
18 in addition to screening for low enzyme activity
19 level, which can really decrease false positive
20 referrals. Next slide, please.

21 So, the reported prevalence of Krabbe
22 disease is on the order of about one per 100,000

1 with a fairly wide range based on different study
2 types. It's lysosomal storage disorder and
3 leukodystrophy, as you heard just a little bit
4 ago, it's chromosome fourteen, it's an autosomal
5 recessive disorder. There are more than two
6 hundred variants of the GALC gene, the gene that's
7 associated with Krabbe disease. Many of them are
8 private, and not all of them are pathogenic.
9 However, there are some specific variants that are
10 predictive of the outcomes, including a specific
11 thirty kilobyte deletion, which is associated with
12 the most severe form of Krabbe disease. And then,
13 it's associated with low glucocerebrosidase or
14 CALC enzyme activity and we heard about that just
15 before I came up, and elevated psychosine
16 concentrations in early infancy, as I mentioned
17 just a little bit ago as well. Next slide,
18 please.

19 So, I do want to summarize the natural
20 history of the disorder. For those who -- those
21 infants who develop symptoms before the first six
22 months of life, they present on average, around

1 four months of age. About half of them develop
2 head control, but lose milestones like head
3 control, within a very short period of time.
4 There's spasticity, early onset of severe
5 irritability, there are swallowing problems that
6 develop, and then loss of fixation. Most infants
7 who develop symptoms of Krabbe disease in the
8 first six months of life don't develop any
9 language, there's a loss of vision and hearing,
10 there's seizures, but that could be more variable,
11 and survival between ten and thirty-two months.
12 Next slide, please.

13 For those who develop symptoms later, so
14 six months to thirty-six months, those infants
15 oftentimes present with irritability and
16 developmental regression. They too have loss of
17 milestones about fourteen to sixteen months later,
18 and the median survival time is about six-and-a-
19 half half years. Next slide, please.

20 So, I want to spend some time just
21 talking about infantile Krabbe disease and some of
22 the language that we're going to be using around

1 it. So, the term infantile Krabbe disease, it's a
2 classification that's involved, and I think that
3 reflects better understanding of the epidemiology
4 and also have the term be used for different
5 clinical purposes. Next slide, please, or
6 advance.

7 So, I just want to -- I think it's
8 helpful to put up different definitions that are
9 used. So, in the article that was published in
10 2017, early infantile was described as less than
11 six months, late infantile from six to forty-eight
12 months, and the juvenile form that was about four
13 years of age. Please advance.

14 And then in 2019, there was a study that
15 described infantile as being less than six months,
16 and then described late onset as being the late
17 infantile form between six and thirty-six months,
18 and the juvenile form between three and eight
19 years. Next slide, please.

20 And then, more recently, there was a
21 study that described the early infantile as those
22 infants who, if untreated, would develop symptoms

1 within the first six months, late infantile
2 between six to twelve months, and then they
3 discuss in the article early childhood and
4 adolescents and adults who can get affected in
5 this late onset bucket. Next slide, please or
6 advance.

7 So, the condition, as nominated for the
8 Advisory Committee, really focuses on infancy
9 developed Krabbe disease in the first thirty-six
10 months, and that's how we're going to focus on it.
11 I put these definitions up just so you can
12 understand how there's, you know, the
13 terminologies evolved and sometimes when we're
14 looking at studies, things and terms can be
15 slightly different. But what we're going to do in
16 the evidence review process is to focus on the
17 infants who would be expected to develop symptoms
18 of the first thirty-six months of life. And
19 obviously, as we go along, if we find, for
20 example, from state newborn screening programs who
21 have babies who might have developed even a later
22 form of Krabbe disease, we'll summarize it. But

1 again, I just want you to understand that there's
2 some variation in how the terminologies evolved.

3 Next slide, please.

4 So, let's talk a little bit about
5 screening. So, the Tier 1 screening -- the first
6 tier for any newborn for Krabbe disease is with
7 GALC enzyme activity. And then from there, there
8 could be additional testing. So dried blood spot
9 psychosine level can reduce false positives, and
10 as I'll be talking about in a little bit, can also
11 be helpful to stratify risk for those babies who
12 are found to have low enzyme activity and an
13 elevated psychosine level. Next slide, please.

14 There's also molecular analysis. So, as
15 I talked about before, there are a large number of
16 variants, but some of those variants can be
17 predictive of the expected outcome. Next slide,
18 please.

19 So, I want to summarize this one study,
20 Expert Panel Recommendations for Follow-up After
21 Positive Newborn Screening. It's called a study,
22 but it's really a report, and it's really based on

1 dried blood spot psychosine levels.

2 So, dried psychosine level that's two or
3 greater is typically considered to be abnormal,
4 and if it's ten or above, that's strongly
5 predictive of the early infantile Krabbe disease,
6 and that's where the follow-up is time critical.

7 There are three different pathways that
8 infants can fall under based on whatever the
9 psychosine level is. Advance.

10 The first is the early infantile form,
11 and those babies require immediate referral for
12 diagnostic evaluation and treatment, and those are
13 for the babies who are above ten. And then
14 there's this at-risk for late onset Krabbe
15 disease, and those are infants who are recommended
16 to see a specialist within two to four weeks to
17 follow up and see what needs to be done. And for
18 those infants, this is, again, for the infants in
19 the two to ten range, the genotype can be helpful.
20 So, the genotype can help stratify infants into a
21 high-risk group, where they need more frequent
22 monitoring is listed on the slide or low risk,

1 where there's less need for intensive follow-up
2 during childhood and up through to adulthood.

3 So again, the psychosine level is really
4 the laboratory result that helps classify infants
5 into needing an urgent follow-up with a specialist
6 or if there can be a slight wait. Next slide,
7 please.

8 And, of course, there's going to be some
9 infants who are not going to be expected to have
10 Krabbe disease based on the psychosine level, and
11 they're not going to have -- they're not going to
12 need follow-up. So typically, that's less than
13 two. Next slide, please.

14 And, again, I just want to highlight
15 that using psychosine this way really does reduce
16 referral from newborn screening. Next slide,
17 please.

18 So, these are the states that are
19 currently offering Krabbe disease newborn
20 screening. You can see the one state in the light
21 blue, Ohio bases screening on GALC alone, the
22 other states use psychosine at some point during

1 the screening algorithm, and I'm going to be
2 talking about that a little more in a second.

3 Next slide, please.

4 So, I want to go back in time a little
5 bit and talk about this report of the first eight
6 years of newborn screening for Krabbe disease in
7 New York. This is pre-psycho-sine. They describe
8 screening from 2006 to 2004, there were
9 essentially two million infants that were
10 screened. Next slide, please.

11 And there were 620 of those infants had
12 a low GALC enzyme activity, and there were
13 ultimately 348 who were referred for follow-up
14 with others assumed to have a negative screen
15 based on the GALC polymorphisms that were found.
16 Next slide, please or advance.

17 And based on the infants that were
18 referred in these sort of early days of the New
19 York Newborn Screening Program, you can see the
20 distribution of finding including five infants who
21 were confirmed to have infantile Krabbe disease.
22 Next slide, please.

1 So, I now want to summarize a little bit
2 of a later report. This is from Illinois,
3 describing 2017 to 2020, where about half a
4 million infants were screened, and this is a
5 report of their two-tier screening. Next slide,
6 please.

7 There were -- so they -- the way the
8 program works is they looked -- they did repeat
9 testing on infants who had GALC enzyme activities
10 of sixteen percent or less, and that those on
11 repeat testing were thirteen percent or less, were
12 considered to be positive. So, there were 288 of
13 those, you know, essentially half a million that
14 were positive. Next slide, please.

15 And then they did second tier psychosine
16 level testing and GALC sequencing. And from this,
17 they identified two newborns with elevated
18 psychosine levels, so ten to thirty-five -- ten
19 and thirty-five, and obviously, that's, that's
20 above ten, and they were referred to immediately.
21 There were six newborns with psychosine levels
22 between two and five, and 178 with pseudo

1 deficiency alleles and psychosine less than two.

2 Next slide, please.

3 This is a summary of information that
4 we've gotten back covering more recent period of
5 newborn screening. The listed states were very
6 kind to provide this data to us. In working with
7 our partners at APHL, we're continuing to work
8 with the states to better define this information.
9 But you can see the referrals range from, what was
10 it, like 0.6 per 100,000 up to a high of nearly
11 13.8 per 100,000. So, there's that bimodal
12 distribution, and some of that has to do with how
13 decisions are made about referrals. So, we're
14 referring in as soon as a low GALC level is -- as
15 soon as a low GALC level was confirmed on newborn
16 screening while awaiting the psychosine or the
17 molecular testing. So, you know, states vary in
18 the point at which they make their referral.

19 You can see the range of infantile
20 Krabbe disease per 100,000 infants that were
21 identified and those who were, you know, at risk
22 for late onset, so the ones that are still in

1 follow up there. The classification of infantile
2 Krabbe disease and at-risk for late onset Krabbe
3 disease was based on information that we received
4 from the Newborn Screening Program, and we're
5 working closely with the Newborn Screening
6 Programs and their follow-up arms to really better
7 characterize those infants who were referred
8 including the status of this with Krabbe disease.
9 Next slide, please.

10 So, the diagnostic evaluation includes
11 GALC enzyme activity as a clinical test, so,
12 separate from the newborn screening dried blood
13 spot, psychosine concentration against a clinical
14 test, and then molecular analysis that had not
15 been previously done. And then, there's a lot of
16 additional information that can be collected to
17 help confirm the diagnosis. But this can be done
18 in conjunction with the work that needs to be done
19 to plan for a stem cell transplant so MRI, nerve
20 conduction studies, EEG, evoked potentials, lumbar
21 puncture for CSF, are all -- can be helpful in
22 terms of confirming the diagnosis. But really,

1 babies with very high levels of psychosine and low
2 GALC enzyme activities are the ones that need to
3 be teed up for likely stem cell transplant.

4 Oops, loo, it worked this time. There we go.

5 Now, in terms of where things are going
6 -- I'll still play to you -- so, the treatment, as
7 we've discussed, for Krabbe disease is a stem cell
8 transplant with those with suspected early
9 infantile Krabbe disease requiring urgent referral
10 and transplant goal ideally of thirty days. I'm
11 going to drill into that thirty days in a minute,
12 and then for the other phenotypes, it's still stem
13 cell transplant. But based on the development of
14 signs or symptoms, as was talked about in the
15 public comment period, there is gene therapy
16 that's being evaluated in clinical trials right
17 now, but that gene therapy isn't available for
18 clinical purposes right now.

19 So, I want to go back to this thirty-day
20 recommendation and talk about one of the studies
21 that really gave rise to this. So, this is a
22 study of nineteen subjects who received a stem

1 cell transplant for early infantile Krabbe disease
2 diagnosed by -- or not diagnosed, treated with a
3 stem cell transplant by two months of age, between
4 1996 and 2010, in a single center, and for whom at
5 least five years of follow up was available. So,
6 about sixteen percent of them were diagnosed based
7 on newborn screening, the bulk were identified by
8 family history, the median age at transplant was
9 twenty-seven days with a range of nineteen to
10 sixty-one days, and most, but not all, were
11 treated with umbilical cord blood from unrelated
12 donors. Next slide, please.

13 So, if you look at survival at five
14 years, it was eighty-four percent, and at ten
15 years, it was seventy-nine percent. And there is
16 no difference in five- or ten-year survival based
17 on if the transplant was done before thirty days
18 or after thirty days.

19 But as I drill into these numbers, I'm
20 going to remind everyone that, you know, we're
21 talking about nineteen subjects, and so I put less
22 value on the P value. Obviously, this isn't the

1 kind of thing that it's easily powered for
2 statistical significance. Please advance.

3 But I want to summarize important points
4 about the outcomes of the transplant against
5 stratifying, based on whether the transplants
6 occurred before thirty days or after thirty days.
7 So, for those and, again, follow-up was up to five
8 years, ninety percent were walking, although some
9 did need an assistive device versus seventeen
10 percent. All were "verbal", but I didn't have any
11 additional information on what that was, versus
12 about fifty percent who got transplanted after
13 thirty days. Ninety percent could feed by mouth
14 versus seventeen percent. And none of those who
15 were transplanted before thirty days had seizures
16 versus a third of those who had transplant after
17 thirty days, that statistical significance value
18 is listed as NS, not significant.

19 Again, you have to take caution when you
20 interpret studies around just around nineteen
21 subjects. Now what I can't do is go back and say,
22 well, what if you'd moved things to thirty-five

1 days or forty days and look at the outcomes that
2 way? When we talk to the experts, they really say
3 that based on this and, and their expert
4 experience, they would really like to get the
5 transplants done by thirty days. But if you can
6 get it to forty-five days, maybe that's okay. But
7 certainly, once -- and from the expert opinion
8 once you develop significant involvement, then the
9 benefit of the transplant is not going to be as
10 effective. Next slide, please.

11 So, I'm going to go back and talk about
12 more recent information from New York. So, this
13 is from 2016, where they had about two million
14 newborns that were screened. 348 newborns were
15 referred based on the screening with two lost to
16 follow-up, and of these, five had infantile --
17 early infantile Krabbe disease, of which four
18 retreated with transplant. Next slide please.

19 And these are the outcomes of those five
20 infants. So, there was an infant who was
21 transplanted twenty-four days who died at sixty-
22 nine days of age, an infant who was transplanted

1 at thirty-one days who died at eighty-four days,
2 an infant who was transplanted at thirty-two days
3 who had follow-up to eight years, who had
4 developmental delay and was non-ambulatory and did
5 have some complications related to the transplant,
6 and then another infant who was transplanted at
7 forty-one days who at forty-one days who at five
8 years of follow-up had developmental delay and
9 failure to thrive. And then there was one infant
10 where the parents refused transplant who died at
11 eighteen months.

12 So again, these are small numbers. But
13 I want to give you a sense of things. I want to
14 be clear as we go about and talk about our
15 analysis, we are going to be comparing outcomes of
16 newborn screening for Krabbe disease to infants
17 who were not detected through newborn screening.
18 That's really the comparisons that we're going to
19 be making. And I'm going to be visiting this
20 again in a second when Dr. Prosser comes and joins
21 us. Next slide, please.

22 This was a recent study, identifying the

1 age and of transplants and outcomes for infants
2 with early infantile Krabbe disease. And so, each
3 row represents a different infant, and I think
4 this slide is particularly helpful just in
5 understanding all the things that have to happen
6 to be able to get a transplant by around thirty
7 days of life.

8 So, the vertical kind of light blue line
9 is thirty days. So, you can see the first infant
10 in this study received transplant -- I can't
11 remember -- it was like forty days, you know,
12 after -- after the thirty-day mark, and you can
13 see all the things that have to happen in order to
14 be able to get the transplant done. The second
15 baby had it before, the third one a little bit
16 later, the fourth one right around the thirty-day
17 mark, and the last two after the thirty-day mark.
18 I highlighted on this slide, baby number 1 and
19 baby number 4, because these were infants who had
20 to go out of state for their -- for their
21 transplant. Next slide, please.

22 This slide describes some of the

1 outcomes for those infants who were transplanted.
2 Each colored bar represents a different infant and
3 there was variation in terms of the length of
4 follow-up, going from thirty to fifty-eight months
5 after transplant. All the infants did have
6 developmental delay, particularly related to gross
7 motor deficits, but they were -- they were still
8 alive at this thirty- to fifty-eight-month mark.
9 Next slide, please.

10 So, our ongoing focus, as I alluded to
11 before, was clarifying the screening results and
12 digging more into the outcomes of stem cell
13 transplant for early identification. And
14 ultimately, what we'd like to do, although I'm not
15 sure that we're going to be able to find the data
16 this way, is to be able to stratify things by
17 genotype and the initial GALC enzyme activity
18 level and the psychosine level. But to the degree
19 that we can put those three together that way, we
20 will. Next slide.

21 So, I'm going to be quiet for a minute
22 and have Dr. Prosser talk about the projecting

1 population health outcomes. So, Lisa, I hope
2 you're there.

3 LISA PROSSER: I am here. Are you able
4 to hear me?

5 ALEX KEMPER: Yes, we can.

6 LISA PROSSER: Terrific, great. And
7 Alex, you'll advance the slides on your side?

8 ALEX KEMPER: I -- Alisha is.

9 LISA PROSSER: Excellent. Okay, great,
10 because I don't see any controls on this side.
11 Thank you very much.

12 On the next few slides, I'll be walking
13 through the plan for evaluating population-level
14 health outcomes for newborn screening for Krabbe
15 disease.

16 So, using simulation modeling, the
17 overall objective is to be able to project
18 population-level health outcomes. So, modeling an
19 annual US newborn cohort of 3.65 million, this
20 analysis will project both newborn screening
21 outcomes as well as outcomes under clinical
22 presentation. So, under newborn screening

1 outcomes, those will include screening specific
2 outcomes such as positive screens, cases of
3 confirmed Krabbe disease, and importantly, as Dr.
4 Kemper has walked through in the previous slides,
5 the numbers of babies that will fall into the
6 various at-risk categories following the newborn
7 screening process.

8 We'll also include projections of the
9 numbers of babies who receive transplant, as well
10 as projected transplant outcomes within a short
11 timeframe, and mortality.

12 Under clinical presentation, we'll be
13 comparing these outcomes to identify cases of
14 Krabbe disease without newborn screening as well
15 as mortality without newborn screening. Next
16 slide, please.

17 So, just a step back, just for a brief
18 moment. So, the methodological approach that
19 we'll be using is decision analysis, and I know
20 this has come up a little earlier in the
21 presentations today. It's a systematic approach
22 to decision-making under conditions of

1 uncertainty, and the goal here is really to
2 project ranges of short-term outcomes for newborn
3 screening compared to clinical presentation given
4 the scarcity of the data for newborn screened
5 conditions, and particularly like for Krabbe. Our
6 goal, again, will be to project ranges to give a
7 sense of what those projected outcomes would be
8 under a national newborn screening recommendation.

9 Decision analysis will then allow the
10 decision maker to identify which alternative is
11 expected to yield the most health benefit. And
12 here, there will be a number of different outcomes
13 which can be used to measure health benefits.

14 At the same time, it can also be used to
15 identify key parameters and assumptions. So, it
16 would be possible through sensitivity analysis to
17 identify which parameters in the model are driving
18 the results and where it would be important to
19 have more information as we move forward. Next
20 slide, please.

21 So, where we are right now, the model
22 structure is in development and in the next two

1 slides, I'll walk through the current model
2 structure.

3 The second technical expert panel
4 focused on reviewing the model structure and the
5 assumptions underlying the -- underlying the
6 model, and the model went through a number of
7 revisions following that process. The time
8 horizon for the modeling analysis, right now we're
9 anticipating a three-year time horizon for the
10 overall analysis, depending on as we finalize on
11 the parameter inputs and finish reviewing
12 literature, that may only be two years, but right
13 now we're anticipating we'll be able to project
14 outcomes up to three years.

15 During the second expert panel, there
16 was a very -- a very rich and important discussion
17 about the classification and terminology of
18 screening outcomes, which is reflected in the
19 current structure of the model. That may be
20 updated as we learn more in the coming months.
21 And we've also refined the definition of the
22 timing of transplant, as well as transplant

1 complications based on the expert panel
2 discussion. Next slide, please.

3 So, this slide shows the schematic of
4 the -- of the simulation model for the newborn
5 screening arm. And so, starting on the left-hand
6 side, the analysis will use a hypothetical -- a
7 cohort of hypothetical newborns who are not at
8 higher risk for Krabbe disease and model their
9 pathway through a hypothetical screening program.

10 So, if you kind of walk through across
11 the top of the diagram, and I won't go through all
12 the detail here, but I do want to give a flavor of
13 what will be incorporated into the simulation.

14 So, following newborn screening, the
15 baby can either screen positive and be referred
16 for further diagnostic valuation or screen
17 negative. If they screen positive, it is assumed
18 again and important to characterize here that the
19 plan for the simulation modeling is to model a
20 state that is using a screening approach that
21 includes psychosine as second-tier testing or
22 evaluating whether a baby should be referred for

1 transplant evaluation. So, that's what you'll see
2 reflected here on the screen. So, important to
3 note that the screening approach depicted here in
4 this model will not match what's happening exactly
5 in every single state. But we'll be able to use
6 data from multiple states to inform this -- the
7 data underlying this model.

8 So, following a screen positive and
9 further referral for diagnostic evaluation,
10 including the results of psychosine testing, a
11 baby could then fall into one of four groups,
12 either presumed early infantile, referred for
13 transplant evaluation, at risk for late onset, and
14 within that group, they would be identified as
15 either following the low-risk follow-up pathway or
16 the high-risk follow-up pathway. They could fall
17 into the category of not recommended for regular
18 follow-up, or they may decline follow-up, and we
19 will be able to model the projected numbers that
20 fall into those two categories as well based on
21 current state level data that's been shared with
22 us.

1 So, just following along through the top
2 part of the model. So, for those that are
3 referred for transplant evaluation, then there is
4 a probability that there'll be transplanted within
5 thirty days, and Dr. Kemper has characterized that
6 this thirty days instead of thirty-ish days that
7 there's -- that within thirty to thirty-five days,
8 you may see that exact number change in the final
9 version of the model. But looking to be able to
10 identify where outcomes are likely to be different
11 beyond a certain timeframe if transplant occurs
12 after a certain timeframe, we want to be able to
13 differentiate those two categories of outcomes.
14 So, transplant either within that window or
15 outside of that window are also to capture
16 outcomes for babies that are either not
17 recommended for transplant, or if parents elect
18 not to not to follow a transplant recommendation.

19 So again, just following through the
20 very top box, and then we'll move on to the next
21 slide.

22 So, following transplant on the outcomes

1 that will be modeled here, as there's a
2 probability of either surviving or potentially
3 dying of transplant-related complications. Here,
4 we'll be modeling outcomes within a one-hundred-
5 day window following transplant. For babies that
6 survived the transplant, again, we'll be looking
7 at long-term outcomes, and looking to characterize
8 short-term outcomes over a three-year time period,
9 in terms of what their level of symptoms are at
10 the end of those three years in terms of either no
11 or few symptoms, moderate severe symptoms, or
12 having died from Krabbe or from transplant
13 complications.

14 So, I'm not going to go through any of
15 the rest of this part of the model in detail. But
16 let's move to the next slide and I'll walk through
17 a comparison which is the clinical presentation
18 arm.

19 So, here for this part of the model, the
20 simulation will evaluate the same cohort of
21 hypothetical newborns who are not at higher risk
22 for Krabbe disease. They will have some

1 probability of presenting with Krabbe disease at
2 some point due signs and symptoms that can happen
3 either within the first year of life or beyond
4 that. Here, we'll be comparing those infantile
5 Krabbe disease and again, we're using here a
6 definition of infantile Krabbe up to and through
7 twelve months of life.

8 We'll be modeling similar outcomes as
9 was seen on the previous slide. And then we'll be
10 able to compare outcomes under a hypothetical
11 newborn screening program compared to no
12 screening. Next slide, please.

13 This slide shows a table of anticipated
14 projected results from the model. So, we'll be
15 able to project the numbers of positive screens as
16 well as all the screening outcomes listed on this
17 slide comparing newborn screening, and then
18 compare it to clinical presentation just for the
19 identified early onset Krabbe disease cases. Next
20 slide, please.

21 This slide shows the anticipated health
22 outcomes that will be modeled for longer-term

1 health outcomes. So, projecting the number of
2 babies that receive transplant under newborn
3 screening compared to clinical presentation, as
4 well as longer-term projected outcomes related to
5 symptom severity or death. And then being able to
6 evaluate the number of cases or deaths that are
7 averted in those different categories. Next
8 slide, please.

9 So, in the next few months, we'll be
10 continuing to update and finalize the model
11 structure with continued conversations with
12 experts in the field as well as our liaisons. The
13 Advisory Committee will be finalizing the model
14 input using data from states with screening
15 programs that have very generously shared very
16 detailed information on their screening outcomes
17 to date, as well as incorporating additional
18 literature from literature, and then filling the
19 gaps with the with information and discussion with
20 the technical expert panel. We'll be running
21 analysis and sharing those preliminary results
22 with liaisons, the Advisory Committee, and with

1 the technical expert panel as we finalize those
2 results.

3 So, I will stop there. I'll turn it
4 back over to you Dr. Kemper, and I would be happy
5 to take questions at the end.

6 ALEX KEMPER: Okay, fantastic. Thank
7 you very much.

8 So, I'm just going to summarize by
9 talking about where we are with the Public Health
10 Impact Assessment and I should really give credit
11 to Elizabeth Jones and Jelili Ojodu, who are our
12 partners at APHL, who really do a fantastic job
13 with this part of the project and also collect
14 those data like I showed you before from the
15 newborn screening programs.

16 So again, we're collecting data from
17 states that are offering Krabbe disease screening
18 and they're conducting interviews with relevant
19 individuals within those programs. You can see
20 who's been completed by little asterisk there.
21 Next slide, please.

22 As we've talked before, GALC enzyme

1 activity can be measured by tandem mass spec or
2 fluorometry, and it can be multiplexed with other
3 liposomal storage disorders and screening tests.
4 Contracted labs are often used to measure the
5 psychosine. Although it could be done within the
6 State Newborn Screening Program, most people are
7 sending psychosine out. Please advance.

8 And so, we're continuing with the usual
9 Public Health Impact Assessment looking at the
10 usual barriers to implementing newborn screening,
11 as was talked about this morning. Next slide,
12 please.

13 And we're just about to begin the survey
14 of the newborn screening programs that are not
15 currently offering Krabbe disease newborn
16 screening. We held a webinar on October 13th to
17 begin to allow those programs to prepare to
18 respond to the survey, and the link was
19 distributed at the end of October. It's going out
20 as we speak. Next slide, please.

21 And so, with that, I'd like to stop and
22 open things up for questions.

1 NED CALONGE: Thanks so much to Lisa and
2 Alex and the entire team. I know you've worked
3 hard on this presentation. I also want to thank
4 the work of the Committee that signed on to
5 provide comments and expert guidance. It's been a
6 great experience. I apologize for having a
7 question, because I've seen it several times, but
8 it wasn't until I saw it big on the screen that it
9 came up. But way back in the early slides, you
10 were talking about the New York experience, and
11 there were nine high-risk kids for infantile
12 Krabbe and then five got transplanted or five were
13 confirmed. I was just curious about how did the
14 other four unrulid out and what was there -- and
15 was there any chance that one of them --

16 ALEX KEMPER: Yeah, yeah.

17 NED CALONGE: -- not being
18 transplanted.

19 ALEX KEMPER: I'm going to sort of
20 dance around that because we're still trying to
21 collect all that information directly from the
22 program. So, my guess is that there's probably --

1 it's been like -- this is a guess, but maybe three
2 dozen children that have been transplanted related
3 to early detection through newborn screening or
4 other ways, and I really do want to just finalize
5 it with a list and know like what happens to those
6 with later onset. So, I'm looking at Dr. Kwon.
7 She may have personal experience with some of
8 those infants. But, in terms of summarizing it,
9 I'm just -- I'm going to sort of plead the fifth
10 until we have that all organized on one table.

11 NED CALONGE: Great answer. It makes me
12 feel not bad about missing it before. Jennifer.

13 JENNIFER KWON: I'm a little removed
14 from that report. But I think none of those
15 needed to be transplanted.

16 KYLE BROTHERS: This is a somewhat
17 related question but could you -- could you just
18 confirm it sounds like with psychosine testing, we
19 now believe that there were no false positives
20 that are then making it all the way to transplant.
21 But I mean, that would be a very difficult kind of
22 thing to recognize if that was happening. But it

1 would just be good to know what information we
2 have related to that.

3 ALEX KEMPER: Yeah, I think -- I'm going
4 to turn your single question into two questions.

5 So, as we talk to the experts and we
6 look at the data that we have, it's true that
7 babies who have the early infantile Krabbe disease
8 or the kind of Krabbe disease that you would want
9 to move to transplant, they're all going to have
10 elevated psychosine levels. It's just part of the
11 condition.

12 Now there is, for example, a single case
13 report of an infant who had a psychosine level
14 that was close to two but not exactly two, who
15 turned out to have the infantile form of Krabbe
16 disease.

17 So, I think that, you know, the science
18 has really gotten around psychosine in terms of
19 when it's elevated, that it is associated with the
20 kind of disease that you'd want to transplant.
21 But one of the points that I didn't make during
22 the presentation that I probably should have made

1 stronger is that, you know, these various cutoffs
2 and stuff, to a certain degree, it's artificial,
3 because these are all spectrum diseases and it's
4 clear that there really is this spectrum of
5 psychosine levels and that kind of thing. And,
6 but I don't think that there's any infant with an
7 elevated psychosine level that didn't turn out to
8 have, you know, the kind of disease that would
9 benefit from transplant.

10 NED CALONGE: Thanks. And Soohyun was
11 reminding me just a couple of additional points.
12 So, for Committee members in the room, if you do
13 identify your first and last name, that helps with
14 the recording and the minutes, and then if you're
15 in the room, if you shut your video off, it keeps
16 the screen a little less cluttered. Oh, video on?
17 Well, I misunderstood that. So, if you'll turn
18 your video on so that we can see whose --

19 ALEX KEMPER: I'm glad their video is on
20 because it's unnerving to see a gigantic version
21 of yourself on the screen.

22 NED CALONGE: Over and over again. So,

1 I'm going to turn next to Jane.

2 JANE DELUCA: Thank you, Dr. Kemper.

3 That was a great presentation. I wanted to know a
4 little bit more about the psychosine because it
5 sounds like it's a really important measure. So,
6 you had mentioned that it's actually sent out to
7 some labs where it's performed and is it a simple
8 analysis, or is this something that's complex?

9 ALEX KEMPER: Well, I'm not a laboratory
10 person, so I sometimes think that it's all simple
11 for me because I just circle the lab that needs to
12 be ordered, and it comes back. But what I will
13 tell you is that it's more complicated, from what
14 I understand, than doing, for example, GALC enzyme
15 activities, which can, you know, easily be
16 multiplexed, and there are certain labs that are
17 doing the analysis. So, a lot of people send them
18 to Mayo. People are sending them to my home
19 institution, Nationwide Children's, and I'm
20 looking at Margie because I can't remember where
21 the other places are. But there's a handful of
22 places now that offer it.

1 NED CALONGE: Next, I'm going to Ash.

2 ASHTOUSH LAL: I'm unable to start my
3 video. It's been stuck. Slightly unrelated
4 question. My question is about late infantile and
5 later onset Krabbe. In those cases where
6 transplants are done, is the timing of the
7 transplant decided by symptomatic disease, or is
8 there pre-symptomatic MRI evaluation or other
9 indicators to decide upon the optimal time?

10 ALEX KEMPER: Yeah, I can tell you that
11 we're really, you know, all of our work so far is
12 really focused on the very youngest children. So,
13 I'm going to point to Margie, who helps me for the
14 clinical side of things and is one of the members
15 of our Evidence Review Group, that it's a
16 constellation of findings in terms of if there is
17 a, you know, change on MRI or nerve conduction,
18 those kinds of things, tied off to clinical cases,
19 clinical findings. But we've really been so
20 focused on the early infantile one, I don't know
21 if you want to add any color commentary, Margie.

22 MARGIE REAM: I was looking up the

1 other. The third lab is PerkinElmer. So,
2 PerkinElmer and Mayo.

3 ALEX KEMPER: PerkinElmer, that's right.

4 MARGIE REAM: And so, in the process of
5 looking that up, I didn't catch the beginning of
6 the question.

7 ALEX KEMPER: The question is like when
8 would you decide to do a transplant for somebody
9 with later onset Krabbe disease?

10 MARGIE REAM: Based on the symptoms.
11 So, seeing signs of active disease is usually when
12 people would consider it time to transplant. So,
13 the later onset the disease, the slower -- the
14 more slowly progressive it is. So, with very
15 early onset, it's very rapidly progressive, and
16 so, then it's, you know, if it's by genotype, then
17 we know they're going to have early infantile
18 disease and then move quickly through that
19 evaluation process. But if they seem to be late -
20 - at risk of later onset disease, then we have a
21 little more time to do the evaluations.

22 NED CALONGE: Shawn.

1 SHAWN MCCANDLESS: Thank you. Thanks,
2 Alex, for the presentation and just a couple
3 things. I want to -- I want to echo what one of
4 the speakers in the public comments earlier noted
5 about making sure that we're comparing -- using
6 the right comparison group, and I think that -- I
7 think the point was well made that, you know, the
8 right comparison group for kids who are
9 transplanted is kids who weren't transplanted, and
10 so as much as possible, we would want to see those
11 data.

12 Likewise, we would, I think, and this is
13 not news to you, but I just want to make sure that
14 everybody hears me say this, which is that we
15 really, I think, need to know as much as we can in
16 the kids who are transplanted. What was the
17 evidence that points towards the severity of
18 disease? And it comes back to that comparing
19 apples to apples argument, that if we're going to
20 compare people who were transplanted to people who
21 are not transplanted, we need to be confident that
22 the people that were transplanted have similar

1 genotypes and similar psychosine concentrations to
2 the people that were not transplanted, so that we
3 can compare the outcomes, because we've already
4 seen today that if you transplant somebody who's
5 going to present with symptoms at six months
6 rather than one month of age, that outcome without
7 treatment is going to be much different. And so,
8 we want to be really confident that we know as
9 much as we can possibly know with this very
10 limited data set. So that's my comment.

11 My question is -- maybe there's more of
12 a -- maybe this as a question, maybe it's a
13 comment. What -- could you summarize, and maybe
14 not today but next time -- could you summarize the
15 data supporting the utility of psychosine? Is it
16 -- is there -- is this like overwhelming data that
17 psychosine is a really clean marker, or is it --
18 is that still in question?

19 ALEX KEMPER: So, I'll confess to you,
20 when you said I could have this as a question or a
21 comment, if it was going to be hard, I was going
22 to take it as a comment, and if it was going to be

1 more straightforward, I was going to take his
2 question.

3 What I can say is, from the evidence
4 that I've looked at, that psychosine clearly
5 reduces the number of infants that are referred,
6 and it's really baked into the algorithms right
7 now for classification of, you know, expected type
8 and drives towards treatment as well.

9 So, psychosine, I think, is a real, if I
10 can use this term, a game changer related to how
11 newborn screening works for Krabbe disease, or at
12 least you have to get it at some point along the
13 way.

14 SHAWN MCCANDLESS: It's certainly
15 impacted decision making.

16 ALEX KEMPER: Correct.

17 SHAWN MCCANDLESS: My question is a
18 little bit different though, and that is how
19 compelling is the evidence? Because I just can't
20 find a lot of data on this.

21 ALEX KEMPER: Well, I'll take that as a
22 comment.

1 SHAWN MCCANDLESS: That is a comment.
2 There are -- I can't find a lot of papers and a
3 lot of data. So, it's small numbers, and big
4 decisions being made on small numbers.

5 ALEX KEMPER: But it's a condition
6 that's, you know, rare to start with, so.

7 NED CALONGE: Kellie.

8 KELLIE KELM: Kellie Kelm, FDA. My
9 first comment is, and looking at the entirety of
10 what you presented today and seeing a number of
11 things that I know is going to be very challenging
12 for all of us, whether, you know, seeing the
13 definitions of, I guess, onset change, in a very
14 short number of years, small numbers of people,
15 and I know you only really presented some, you
16 know, the transplant data on the on the youngest
17 kids, although I will say the nomination is for
18 kids thirty-six months and younger. So, I'm
19 assuming that means we may also get data not on
20 those kids that would be in early infantile, but
21 that we would have to consider larger than that
22 unless we want to, you know, talk about how we

1 might, you know, consider this condition.

2 But, you know, I think all of that, and
3 also looking at the difference in referrals in
4 states and stuff and, as you mentioned, the use of
5 psychosine, and we always have to deal with
6 problematic data here. I think I will harken back
7 to what Shawn said that the more that we can see
8 of the data, and because I think we're going to,
9 whether it's year-to-year, state-to-state, you
10 know, what we're going to get from each kid is
11 probably going to be very different. I think it's
12 -- since we're talking about small numbers, it's
13 going to be very important, it's going to be
14 really challenging, but that's why they pay us the
15 big bucks, right?

16 But, you know, I don't envy you. I
17 don't -- I'm interested in seeing what numbers
18 Lisa can actually plug in because I can't tell how
19 many states have the psychosine data, and we'll be
20 able to do that at one point, and how many kids we
21 can't put in there that we have experience with.
22 But that's what I'm interested in seeing in the --

1 in the final report and, I hope, more granularity
2 I think is just going to be more helpful for us to
3 get a bigger picture. Thanks.

4 ALEX KEMPER: Got it, we agree.

5 NED CALONGE: Thanks. Melissa.

6 MELISSA PARISI: Melissa Parisi, NIH. I
7 have another psychosine question. I'm just
8 curious about the stability of the measurement and
9 whether it is considered a biomarker for
10 progression of disease, or if you measured it in
11 an infant with early onset disease at two weeks
12 and at two months, assuming they hadn't gotten
13 transplanted, it would be the same or if there's
14 any -- if there are any studies that look at the
15 progression of psychosine levels over the disease
16 course.

17 ALEX KEMPER: Yeah, there are studies
18 that look at changes in psychosine over time, I
19 just don't have the date on the top of my mind,
20 but I can get back to you even before the final
21 report with that. But we'll make sure that we put
22 that in there as well because there is a change

1 with psychosine over time.

2 NED CALONGE: I'm going to turn to our
3 organizational reps now and Robert.

4 ROBERT OSTRANDER: Thank you. Robert
5 Ostrander, AAFP. On these complicated cases, I'm
6 very happy to be an organizational rep and not a
7 voting member. And great presentation, Alex, it's
8 good to be back. I'm going to step back a little
9 bit from Krabbe and just talk about our process in
10 general over the years. I'm not going to get too
11 far into the weeds. But it occurs to me that much
12 of today's conversation has been informed by
13 states that have instituted universal newborn
14 screening for Krabbe disease, and it's just
15 fortuitous that this particular nominated
16 condition has this wealth of data, relatively
17 speaking, and others don't, because they only have
18 pilot studies, and no one has done the mandatory
19 universal newborn screening in a small number of
20 states. I mean, if, you know, your disease has a
21 famous quarterback whose kid gets it, you know,
22 you get some early legislation, and you get this

1 raw data and this great source of data, and if it
2 doesn't, you know, we're way behind the eight
3 ball.

4 I wonder if it would be reasonable for
5 the Committee to consider making a recommendation
6 with some of these more complicated conditions.
7 Would the Secretary consider advocating for
8 funding a limited number of states to institute
9 universal newborn screening about a condition? I
10 mean, this is basic improvement science, you know,
11 before you dive in all the way you do a PDSA
12 cycle, essentially, do it, study it, and then move
13 forward if it confirms. And so again, that's kind
14 of my observation after having been involved with
15 this group for more than ten years and watching
16 our evidence review evolve and the difference
17 between conditions where some states have
18 instituted universal screening and other
19 conditions where that has not been an opportunity.

20 NED CALONGE: Thanks, Robert. Shawn.

21 SHAWN MCCANDLESS: I want to respond to
22 Robert. I think I love that idea except I would

1 tweak it a little bit in that first off, I'm not
2 sure we're empowered to make that kind of
3 recommendation. But if we were, I would say,
4 based on what we heard from some of the parents
5 and families today that it would be really
6 uncomfortable to me to say we're going to do it in
7 twenty-five states and not do it in fifty states.
8 So, I love the idea of a limited introduction,
9 collect data, and show that it -- show with
10 confidence that it's an effective program. But I
11 would be in favor of doing it in every state,
12 which has its own set of complications, but.

13 ROBERT OSTRANDER: Just to finish, my --
14 just to throw out the rest of my comment was, I
15 mean, the whole problem with doing that is that we
16 don't dive in about something we're not sure of.

17 NED CALONGE: Alex.

18 ALEX KEMPER: Well, I just want to
19 comment to something early on. So, you know,
20 there no doubt that, you know, there was a famous
21 football player who has, you know, had a personal
22 family attachment to Krabbe disease, but we've

1 dealt with so many other advocacy groups and
2 scientists in the field and stuff like that, I
3 don't want -- I know, that's not what you
4 intended, but for the message that it was -- that
5 that's sort of what drove us to where we are, and
6 I know you one hundred percent didn't want to say
7 that, but I just wanted to clarify that.

8 NED CALONGE: Well, I want to again,
9 give our thanks to Alex and the entire team. He's
10 one representative of an army of people.

11 ALEX KEMPER: A fantastic, wonderful
12 army. We're very lucky.

13 NED CALONGE: We want to make sure I
14 recognize all of them, and thank you for the work
15 today, and we look forward to Phase 3
16 presentations.

17 This brings us to the end of today's
18 session, but not the end of opportunities to
19 participate in thinking about the Newborn
20 Screening System. So, we are going to adjourn
21 here and then, I think, Soohyun is working on
22 putting up the workgroup meeting locations for

1 people who are here physically and the webpage
2 where you can Zoom into a workgroup if you so
3 choose. Remember, the charge for the workgroups
4 is to identify three top priority solutions and
5 action steps that the community can consider on
6 supporting state implementation of those
7 conditions added to the RUSP, and overall
8 strengthening the Newborn Screening System.

9 We'll adjourn for today. I'll tell you
10 that same place, same starting time tomorrow, so
11 9:30, and I appreciate the work of everyone today
12 and especially our folks providing public comment.
13 It's greatly appreciated. And we'll see you
14 tomorrow, I hope.

15 (THEREUPON, DAY 1 OF THE MEETING
16 CONCLUDED AT 3:00 P.M.)