THE ADVISORY COMMITTEE ON HERITABLE DISORDERS IN NEWBORNS AND CHILDREN

IN-PERSON/WEBINAR

HRSA HEADQUARTERS 5600 FISHERS LANE

ROCKVILLE, MARYLAND 20852 (Pavilion)

Thursday August 10, 2023

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P R O C E E D I N G S

Welcome and Opening Remarks

DR. CALONGE: I want to welcome everyone to the third meeting of the Advisory Committee on Heritable Disorders in Newborns and Children in 2023. The next slide please. As you may recall during our last meeting and thank you Dr. Kellie Kelm for her service to the ACHDNC. We're excited to welcome the new FDA Federal Official Dr. Paula Caposino.

Dr. Caposino is the Acting Deputy Director of her the Division of Chemistry and Toxicology. Dr. Caposino has over 14 years of experience at the FDA that includes working on or supervising the review of numerous newborn screening assays and newborn genomic and genetic testing.

Since 2020, Dr. Caposino has served as the FDA contributor to several standards on newborn screening topics and is currently a member of the Clinical and Laboratory Standards Institute's Expert Panel on newborn screening. Go to the next screen please.

I'm very pleased to share that Commander Leticia Manning has accepted the position of Designated Federal Officer for this Committee. You may remember she was serving in her role until recently, and now she

has the position outright. Additionally, Commander Manning was recently promoted from Lieutenant Commander to Commander in the Public Health Service. Congratulations.

Commander Manning also serves as a Senior Public Health Analyst in the Maternal and Child Health Bureau, Division of Services for Children and Youth with Special Needs, the Genetic Services Branch. She joined the division in December of 2013, and until recently served as a Project Officer for autism, and the Family-to-Family Health Information Center Program.

Prior to joining MCHB, Leticia worked for HRSA's Federal Office of Rural Health Policy, as a Program Director for the Rural Health Network Development Program. Commander Manning worked as a Public Health Educator in Tanzania, focusing on HIV/AIDS prevention, health promotion, reproductive health and maternal and child health.

Commander Manning holds a master's degree in public health from Boston's University School of Public Health, and a Bachelor of Science in neuroscience from the University of Rochester. Please join me in officially welcoming Commander Manning in her role as DFO, and in congratulating her on her well-deserved- promotion.

Commander Manning, we're excited that you're here. If Dr. Caposino has joined us, I should, if she just wants to make a remark or two? You're on mute.

DR. CAPOSINO: I'm very excited to be here, so thank you for the nice introduction.

DR. CALONGE: Thanks, and we're really pleased to have you here as well. I'm going to turn to Leticia, who is going to call and record attendance.

COMMANDER MANNING: Thank you Ned and thank you for those kind remarks. So now I'm going to begin with the Agency for Healthcare Research and Quality, Kamila Mistry? Michele Caggana?

DR. CAGGANA: I'm here.

COMMANDER MANNING: From the Centers for Disease Control and Prevention Cynthia Hinton?

DR. HINTON: Here.

COMMANDER MANNING: Jannine Cody?

DR. CODY: I'm here.

COMMANDER MANNING: From the Food and Drug Administration Paula Caposino?

DR. CAPOSINO: I'm here.

COMMANDER MANNING: Welcome. From the Health Resources and Services Administration, Dr. Michael Warren?

DR. WARREN: Here.

COMMANDER MANNING: Jennifer Kwon?
DR. KWON: Here.
COMMANDER MANNING: Lal Ashutosh?
DR. LAL: Present.
COMMANDER MANNING: Shawn McCandless?
DR. MCCANDLESS: Here.
COMMANDER MANNING: From the National Institute of Health, Melissa Parisi.
DR. PARISI: Here.
COMMANDER MANNING: Chanika Phornphutkul?
DR. PHORNPHUTKUL: Here.
COMMANDER MANNING: And for organizational representatives, from the American Academy of Family Physicians, Robert Ostrander?
DR. OSTRANDER: Here.
COMMANDER MANNING: From the American Academy of Pediatrics, Debra Freedenberg?
DR. FREEDENBERG: Here.
COMMANDER MANNING: From the American College of Medical Genetics Robert Best?
DR. POWELL: This is Cynthia Powell. I'll be the new organizational representative for the American College of Medical Genetics and Genomics.
COMMANDER MANNING: Thank you. And if you can please email me with that information.

DR. POWELL: Yes. I'll be glad to do that. The college was supposed to be doing that, but I'll be glad to take care of it. Thank you. Nice to see many familiar faces.

COMMANDER MANNING: From the American College of Obstetricians and Gynecologists, Steven Ralston? The Association of Maternal and Child Health Programs, Sabra Anckner. From the Association of Public Health Laboratories, Susan Tanksley?

DR. TANKSLEY: Hello. I'm here.

COMMANDER MANNING: From the Association of State and Territorial Health Officials, Scott Shone?

DR. SHONE: Here.

COMMANDER MANNING: From the Association of Women's Health, Obstetric and Neonatal Nurses, Shakira Henderson? From the Child Neurology Society Margie Ream? From the Department of Defense Jacob Hogue?

DR. HOGUE: Here.

COMMANDER MANNING: From the Genetic Alliance, Natasha Bonhomme?

MS. BONHOMME: Here.

COMMANDER MANNING: From the March of Dimes, Siobhan Dolan?

DR. DOLAN: Here.

COMMANDER MANNING: From the National Society

of Genetic Counselors, Cate Walsh Vockley.

DR. WRIGHT: Cate was unable to make it, so I'm Erica Wright, and will be subbing for her today.

COMMANDER MANNING: Thank you. And from the Society for Inherited Metabolic Disorders, Gerard Berry.

DR. BERRY: Nope, not Gerard. Gerard isn't doing it anymore. I'm Sue Berry.

COMMANDER MANNING: Oh yes, yes. Thank you.

DR. BERRY: It's confusing because we have the same last name. We are not related, just so you know. Thank you.

COMMANDER MANNING: Thank you.

DR. CALONGE: Next slide please.

[crosstalk]

DR. DOWNS: Leticia, this is Karin Downs. I am representing MCHP rather than Sabra. I should have corrected you when you were doing roll call, sorry.

COMMANDER MANNING: Noted. I'll make that correction.

DR. DOWNS: Sure.

DR. POWELL: We can't hear you.

COMMANDER MANNING: (Speaker on mute.)....or a general partner unless you are also an employee of the organization, or unless you have received a waiver from HHS authorizing you to participate. As in the case

today when a vote is scheduled, or an activity is proposed, and you have a question about a potential conflict of interest, please notify me immediately, and you can email me at lmanning@hrsa.gov.

And now I just want to go over meeting participation. So, according to ACHDNC, all committee meetings are open to the public, and if the public wished to participate in the discussion the procedures for doing so are published in the Federal Register, and/or are announced at the opening of a meeting. For the August meeting in the Federal Register notice, we said that there would be a public comment period.

There are two public comment periods. Only with advanced approval of the Chair or myself, may public participants question Committee members or other presenters. Public participants may submit written statements. Also, public participants should be advised that Committee members are given copies of all written statements submitted by the public.

As a reminder, it is stated in the FRN or the Federal Register Notice, as well as the registration website, that all written public comments are part of the official meeting record and are shared with Committee members. Any further public participation will be solely at the discretion of the Chair, or the

Designated Federal Official, which is myself.

And now I just want to go over some webinar instructions. You all are already logged on, so just note this if you have to logout and log back in. When you login to Zoom, you'll be prompted to enter your name as you would like it to appear in the Zoom display name to assure the meeting host can easily identify you in the audience.

Please use your first and last name, along with any relevant organization name. If this screen does not appear for you, and your name is not clearly conveyed in the display name, please email Emma Kelly at ekelly@lrginc.com. Also note that when you are promoted to panelist, the system will briefly log you out of the meeting, and then you will automatically rejoin within ten seconds.

And lastly, I want to remind you, to give you some dates for our upcoming meetings. We'll have an in-person meeting November 2 through the 3rd. It will be located at the HRSA headquarters in Rockville, Maryland. We'll have a virtual meeting February 8th through 9th, and then we'll have an in--person- meeting May 9th through 10th. And now I turn it over to Ned.

DR. CALONGE: Thanks. Before we turn to the Committee, I just want to update you all on two

important grants recently awarded to the Maternal and Child Health Bureau Newborn Screening Propel and Newborn Screening Excel. Next slide please. Oh, this is the project map. This is the Propel Map. There are 28 newborn screening programs that have been awarded as NBS Propel recipients.

They are shown here color coded by HRSA region. The state newborn screening systems priorities or NBS Propel program is a five-year program that began July 1, 2023, and is expected to continue through June 30, 2028. Each recipient was awarded up to $345,000.00 per year during the five- year project period. -Next slide please.

This slide goes over the NBS Propel focus areas. Focus area one includes activities related to improving collection of specimens, testing of specimens, and reporting out results, including improving the timeliness of these activities, and implementing screening for newly added RUSP conditions.

Focus area two includes activities related to improving short-term follow-up through long--term follow- up, and helping families understand and navigate the process from confirmation of the diagnosed treatment, and then follow- up through follow- up across the lifespan. -Next slide.

And again, this is a continuum. So, let's turn now to NBS Excel. The National Center for Newborn Screening Excellence, or NBS Excel Cooperative Agreement recipient is APHL. This program is funded at $2.3 million a year for up to five years. NBS Excel supports the funded Propel grantees, and all other NBS programs by providing leadership, technical assistance, and quality improvement expertise.

We want also to emphasize that subject matter expertise technical assistance, training and education includes those for youth and families to promote meaningful engagement, active participation with, and leadership by families and individuals with terrible disorders at all levels of the newborn screening program. Next slide.

Sorry. I just need to finish up and go back one. As part of HRSA's demonstrated commitment to support state territorial newborn screening programs in FY 24, HRSA will be funding a new NBS program Co-Propel.

NBS Co-Propel builds on previously funded HRSA grants to strengthen collaborations between state and territorial public health agencies, and with NDS partners such as universities, non-profits, or other institutions with expertise in newborn screening to achieve a common goal, to improve access to services and

outcomes for children identified with a heritable condition identified through NBS, so they are healthy, growing and thriving.

Now we're going to turn to Committee business. Next slide. So, we're talking about the ad hoc topic groups that we have been working on for the last meeting and a half I would say. I'm going to start with the -- it's listed as counting conditions. This is a condition naming, secondary conditions, second or higher tier testing group, and previously described the work of HRSA's NBS Excel program, which received a supplemental funding for leverage efforts described by Susan Tanksley ad others during the May meeting.

The NBS Excel grantee will coordinate the work of three ad hoc work groups, condition naming, secondary conditions and second or higher tier testing. These ad hoc topic groups include stakeholders with varied -- sorry, various expertise in specialty areas. As far as conflict of interest, I presented to the Committee at the last meeting a proposal to address COI for both Committee members and organizational representatives.

I've been working closely with HRSA on the COI policy to ensure that we are abiding by all of the Federal Advisory Committee Act policies, and we hope to

bring an updated proposal to the Committee for consideration and possible vote at our next meeting in November.

Next, I would like to talk a little bit about, both nomination and prioritization and decision matrix, before we get to GAMT, so if we can go back one slide. Sorry. Thank you. During the May meeting we discussed possible revisions to the decision matrix, and decision making for the Advisory Committee on Voting to add conditions to the RUSP.

In regard to the decision making, our intent is to update the 2013 version of the matrix to match what is actually the current practice of the Committee. This is not an attempt to move the goal post, or change criteria for nominating conditions, but it's to ensure that the decision matrix reflects how the Committee has actually functioned over the past decade.

For example, B ratings sometimes are recommended for the RUSP, which the existing decision matrix does not support. Now we have thought about, and spent a lot of time thinking about, the best way to do this. We want to include a large amount of stakeholder input at all levels from families to actually, and advocacy groups -- the experts and advocates in the field.

And the issue is that the matrix itself is only a guideline for the Committee to think about structuring how it makes decisions. And I think even as we've elevated some of these to be added to the RUSP, we've shown that we make decisions that are supported by the matrix but aren't dictated by the matrix.

Being that it's a pretty straightforward structure, and decision support to all, we figured we would do better if we modified the RUSP -- I'm sorry, the decision matrix, and a smaller group of those who actually helped create it. A committee that would include subject matter experts and previous Committee members who have wrestled with the different categorizations.

And using the simplification I presented at the last meeting, see if we can strengthen the actual tool, make it more straightforward and transparent. On the other hand, implementation of the matrix, and how we make decisions within it, is where we really need enhanced participation and stakeholder work.

And to that degree, we're really hoping to open up a wide approach to gathering information from families and advocacy groups, as well as subject matter experts. We're going to ask Dr. Kemper and his group to talk about how the Committee should approach nominations

and prioritization, and how we should start thinking about what do harms really look like, and how do we best quantify those, and think about those?

What do benefits look like? And how do we deal with the fact that often benefits and harms are not in the same currency? It may be very different than the way we look at them. Hence, can we use stakeholder input, and subject matter experts to come up with a more transparent system, and I would say flexible way to make sure that we're thinking about the balances of harms and benefits in the right setting.

I would also say the same thing is true of certainty. Certainty is the other part of the matrix, which is our certainty that we're doing the right thing. I often think of certainty as the inverse, the other side is the risk of being wrong, so the higher certainty, the less there is to being wrong.

And so, I think it's in the implementation of how we think about this decision tool where we need stakeholder input and continued work. And so, we're going to reach out, talk about the core issues around how the Committee operationalizes that's not only in the decision matrix, but also how we can better support the entire newborn screening community in the nomination and prioritization of topics.

Provisions to the N&P process need to consider these reducing the burden on the nominators but assuring that they have sufficient input in the process, and then identifying the information most needed for the Committee who make the evidence based decisions that we are charged with.

We want to make sure that our Committee review process is efficient, it can address multiple nominations at once, and that it always includes supports and lifts up the voice of the stakeholder. I think the next best step is to build upon Dr. Kemper's work, and for the Committee to solicit feedback from a large stakeholder group, so rather than picking from folks who self-nominated from their interest to be on such a Committee, really trying to be strategic of including the voice of families, advocacy groups, subject matter experts and others. We will then bring this information back to the Committee to discuss.

We will also do a Federal Registry process for those who are unable to participate in subgroups but have the opportunity to contribute their thoughts and suggestions, creating the various subgroups will allow more people to participate. This is in response to the overwhelming interest we received in May for participation in the ad

hoc groups.

Leticia received names in May of several individuals interested in supporting this work, and we will reach out to you soon. If you're still interested, please email Leticia at lmanning@hrsa.com. I do want to note that many of you know that Congress authorized the National Academies of Science, Engineering and Medicine to explore options for the future of newborn screening programs.

We understand the process is continuing to have more information in the future. We think this is important work that any radical change to the way we approach assessment of evidence, assignment of harms and benefits, thinking about the balance of those, and going to a recommendation. We think that the work of the National Academies is to really inform the Committee in making the best decisions.

Now I'd like to move on to GAMT. Next slide. As a reminder GAMT was approved by Secretary Becerra on January 4 of '23 to be added to the RUSP. The addition of GAMT deficiency to the RUSP is a recommendation. Noted that does not constitute a requirement for states to implement screening.

I'd also like to point out that the GAMT evidence review report was published last month in

Pediatrics. And I want to thank the evidence review team for making sure that that happens. Next slide.

I want to thank the Committee members and organizational reps for reviewing the May 2023 meeting summary. Leticia received some corrections and sent out revised minutes on Wednesday. I want to ask first if there are additional corrections to the meeting summary before we vote to approve?

Seeing none, I wonder if I could ask for a Committee member to unmute, and move to approve, and then someone else second. Please say your name and unmute.

DR. KWON: This is Jennifer Kwon. Hi. This is Jennifer Kwon, Committee member. I move to approve the May 23 meetings.

DR. CALONGE: We have a motion to approve. Is there a second?

DR. CODY: This is Jannine Cody, I vote to second.

DR. CALONGE: Now if I could ask all Committee members to unmute and signify approval by saying aye.

CHORUS: Aye.

DR. CALONGE: Are there any opposed? Unmute and signify by saying no. Minutes passed, thank you very much. Okay.

The public comment session today will be dedicated to DMD, and then we will have DMD nomination summary and Committee discussion, and the idea is hopefully we will move forward through that in an efficient manner.

The last topic for today will be presenting the concept and the methods for expedited evidence review. You will remember that we have talked about this at the last meeting. We had come up with a process that we distributed in the meeting materials. I will present those. We'll ask for comments, and then hold the vote to approve the expedited evidence review tomorrow.

We're going to transition, I'm sorry, the meeting topics for tomorrow include -- if I can have the next slide. Thank you. Focusing on health equity after newborn screening. There will be a special presentation I'm really looking forward to. Then we'll have additional public comment.

At that point, assuming we can approve the expedited evidence review process today, we will have a presentation discussion and potential vote to move Krabbe to the expedited evidence review, and so that hopefully will finish up our meeting for August.

Now at this point I'd like to move into Committee discussion, our next slide please, and see if

there are issues that Committee members would like to discuss based on my opening comments and initial presentations. I promise you, you will have more time to talk if you don't talk now.

Public Comment

DR. CALONGE: So what I'd like to do now is go to the next slide, and move into public comment. We received five requests by individuals to provide oral public comments, specifically related to DMD. They will provide their comments in the following order:

Emma Ciafaloni, sorry Ciafaloni, Jason Dempsey, Paul Melmeyer, Michelle Rengarajan and Niki Armstrong. And Emma, I wonder if you can unmute and get us started, please.

DR. CIAFALONI: On behalf of the Duchenne clinician community, thank you for the opportunity to speak today. My name is Dr. Emma Ciafaloni, and I'm a Professor of Neurology and Pediatrics, Associate Chair of Research, and the Director of Pediatric Neuromuscular Medicine at the University of Rochester.

I lead our certified Duchenne Care Center, which follows approximately 140 patients with Duchenne and Becker. I have chaired for many years, and currently serve as a member of the Clinical Research

Committee of the Muscular Dystrophy Surveillance Tracking and Research Network, MD STARnet, a CDC funded surveillance project on Becker Duchenne muscular dystrophy, and I'm an advisor for the New York State Duchenne Newborn Screening pilot.

I have diagnosed and cared for children with Duchenne for more than two decades, and improving the age of diagnosis has been a focus of my clinical research, and a passion of mine because I have witnessed first-hand the devastating consequences of the late diagnosis and care.

Using MD STARnet data, we published in 2009 the typical age of diagnosis of Duchenne in boys with no known family history was 4.9 years, a delay of two and a half years after symptoms are noted. Following this publication, multiple efforts were made with support by the CDC, an advocacy organization, to reduce the age of diagnosis.

These efforts included the convening of a National Task Force for Early Identification of Childhood Neurological Disorders. The task force developed a tool kit for healthcare providers to aid in early diagnosis.

The American Academy of Pediatrics published a complimentary algorithm and developed a patient facing

side about physical developmental delays to help educate families. These were broad efforts endorsed by key players in Duchenne in pediatrics. Unfortunately, they did not result in improvement in age of diagnosis. Ten years later our follow-up study looking at boys born after 2000 at the MD STARnet sites had identical findings.

The mean age of diagnosis is still 4.9, and diagnosis is persistently later in underserved minority groups. It has been confirmed in multiple other studies. After three decades, and significant effort to reduce the age of diagnosis, children with Duchenne are diagnosed too late, and their age of diagnosis is unchanged.

What has changed is that Duchenne is no longer an untreatable disease, and the number of therapeutic interventions available to our patients has grown significantly. We now have five FDA appointed gene-based drugs, two drugs with downstream mechanism of action, mostly likely to be FDA approved by the end of this year, and several other disease modifying therapeutics that are in late phase clinical trials.

By age 5, irreversible muscle damage and muscle tissue replacement by fat and fibrosis as already occurred and cannot be undone. All scientific evidence

points to the likely benefit of initiating therapeutic interventions well before age 5, and as early as possible.

Newborn screening will provide a timely and equitable diagnosis, and they'll be permitted to receive lifechanging multidisciplinary standard of care. It will also result in proactive planning for, and timely initiation of the best available disease modifying therapeutic intervention, including exon-skipping, gene therapy, new anti-inflammatory and anti-fibrotic and cortical steroids.

Initiation of such therapeutics at an optimal age, and without delay at the time when there is less muscle damage will result in a better outcome and quality of life. There are more significant benefits of newborn screening for Duchenne. Avoid the diagnostic odyssey and its deleterious consequences, including unnecessary invasive tests in children.

Since children will have the diagnosis prior to entering the school system, this will facilitate timely evaluations and identification of the Duchenne associated learning disability, and access to support services. For the family, newborn screening allows timely genetic counseling, identification of carriers who are at risk for cardiomyopathy, earlier

developmental social support, and time to consider how to best incorporate the diagnosis into the family, which can affect so many downstream choices, including housing, that will maximize the children's chance for a better quality of life.

Most importantly, we need to keep in mind that Duchenne is no longer a non-treatable disease. The most important principle of newborn screening is to positively affect children's health. And I strongly, but humbly, believe newborn screening will improve Duchenne children's health and quality of life.

I greatly appreciate the opportunity for Duchenne to be discussed again today, and we urge the Committee to move Duchenne newborn screening forward to evidence review. Thank you.

DR. CALONGE: Thank you. I'd now like to turn to Jason Dempsey.

MR. DEMPSEY: Good morning. I hope everyone can hear me okay. Good morning, Dr. Calonge and Committee members. My name is Jason Dempsey, I am from Mason, Ohio. I'm here to talk about my eight-year-old son, Jude. This is Jude here. I brought a picture. Jude does share a name with a very popular song you may have heard of if I have any Beatles fans in the room, you may know “Hey Jude.”

I'm very excited to talk about the importance of adding Duchenne muscular dystrophy to newborn screening panels, and how it could have helped in our journey, so early diagnosis of DMD is very significant to us because we were not blessed with an early, or an easy diagnosis. Just quickly, to tell our story.

In December of 2020, in the midst of a pandemic, and the week before Christmas, Judge was diagnosed with Duchenne muscular dystrophy at age 6. Not long before that we had noticed that Jude had missed some developmental milestones around a year and a half year's old, such as crawling, walking, talking.

And although he finally did hit those milestones, a little bit late for our liking, we did notice that at two and a half years old he started toe walking. And this started us on a two plus year journey that included leg braces, intense physical therapy, all this was just an effort to try to resolve his toe walking by improving his range of motion and strengthening his legs and his core.

But after two years of physical therapy and not getting the results that we had hoped for, it was suggested that we have a CK blood test to rule out any type of muscular dystrophy. Sadly, this test did not rule out muscular dystrophy, and we were sent to the

world renown Neuromuscular Clinic at Cincinnati Children's Hospital where Jude underwent a full evaluation in genetic testing, and that brings me back to that week before Christmas in 2020, when Jude was diagnosed with Duchenne muscular dystrophy at age 6.

So now Jude is about to be a third grader. He rides his mobility scooter around school because unfortunately he doesn't have the strength and stamina in his legs to be able to walk to the lunchroom or to recess, or to the art class that he loves so much. But I've often wondered, you know, would his daily life be any different now, if we would have known sooner?

I mean what if we had tested him at two and a half years old when we first noticed his toe walking? Or maybe, what if we would have tested when he missed his initial developmental milestones at age a year and a half? Or, what if we had tested him as a newborn, long before we even noticed anything was different?

I don't know exactly how it would have worked out, but I do know that if Jude was diagnosed at birth, we could have started him on muscular dystrophy protocols immediately, some steroids, things of that nature. And also, we wouldn't have spent two years in physical therapy, which was actually hurting him and damaging his muscles.

We would have also had the ability to participate in potentially life-altering clinical trials that unfortunately by the time he was diagnosed, he had already aged out of most of those trials.

So I am happy that right now, as mentioned previously, there are lots of gene therapies in development for DMD. One that was recently approved by the FDA for children ages 4 and 5. And it's so exciting that we are close to seeing a terminal illness potentially turn into a manageable chronic condition. So I'm very thankful to this Committee for looking into this topic, and getting us a little step closer.

In summary, I do want to make a quick reference back to the famous song that shares Jude's name. If you're familiar with that song you know the first line in that song goes like this, "Hey Jude, don't make it bad, take a sad song and make it better." And that's the life lesson that I'm trying to teach Jude, and that's why I'm sharing with you today.

We want to take our sad song and just try and make it a little bit better for someone else. So please strongly consider moving Duchenne muscular dystrophy forward to evidence review, so that we can take one step closer to ensuring that no American babies have to endure a long and painful diagnosis like Jude did.

Thank you for your time, and I'll welcome any questions you may have.

DR. CALONGE: Thanks so much. We appreciate your time today, and I'd like to now turn to Paul Melmeyer.

MR. MELMEYER: All right. Well thank you for the opportunity to comment on today's deliberations on Duchenne muscular dystrophy for the full evidence review. I am Paul Melmeyer, Vice President of Public Policy and Advocacy at the Muscular Dystrophy Association.

MDA is proud to serve the Duchenne's bio-muscular atrophy and Pompe communities along with many other rare neuromuscular disease communities. Today we once again request that the Committee vote to move the Duchenne muscular dystrophy nomination forward to full evidence review.

MDA was proud to cosponsor the nomination of Duchenne last summer, as well as the renomination in the spring. And under the leadership of Parent Project Muscular Dystrophy, provide the evidence to the Committee required for consideration. We understand that one of the main concerns the Committee may have with moving the nomination forward pertains to evidence of effectiveness of earlier administration of available

therapies.

Included in the nomination package are several studies showing early effectiveness of treatment that now I wish to reemphasize. First, cortical steroids are recommended to be considered at time of diagnosis, regardless of any evidence of physical decline. And steroids had been administered as young as the first year of life complying with this standard of care.

The data showing effectiveness of steroids is unequivocal. Boys given steroids had statistically significant better scores on standing from a supine position, 9-meter walk time, or stair climb lifting a weight and force capacity compared to boys not given steroids.

We are also expecting a new steroid option for boys with Duchenne called Demoralon to be approved this fall. Second, four exon skipping treatments have been approved by the FDA with no age restriction on the label. Consequently, boys could start the treatment upon diagnosis. While approved, accelerated approval, the evidence of effectiveness continues to grow.

A recent retrospective and perspective comparison on long term outcomes showed the delayed loss of ambulation and pulmonary decline for those using Eteplirsen compared to natural history. An additional

study published within the last year showed a significant extended survival time in this study, five years longer for those who took Eteplirsen compared to those who did not.

Both younger initiation and longer exposure time to Eteplirsen were tied to better outcomes. Finally, an additional study published in 2021 showed delayed loss of ambulation of an average of four years for patients on Eteplirsen compared to natural history controls.

Finally, while it's always difficult to predict when clinical trial readouts will occur, we understand there's a chance we will see data from Sarepta's EMBARK trial on the efficacy of ELEVIDYS, on ambulatory boys with Duchenne, including boys younger than four years old around this end of this year.

In addition to these efficacy data, we wish to further emphasize several points that Niki Armstrong of PPMD will soon be making about the importance of an earlier diagnosis when accessing ELEVIDYS. As this Committee knows, the FDA approved ELEVIDYS for boys ages 4 and 5 with Duchenne in June, via accelerated approval.

In just the last week or two, the first boy with Duchenne was commercially dosed shortly before his sixth birthday. This rush to dose him was due to him

soon becoming ineligible to receive the therapy under its current label. This situation is reflective of the challenge many boys with Duchenne face in obtaining this gene therapy prior to their sixth birthday.

With newborn screening providing a diagnosis at birth under the current label, boys with Duchenne would have a full two years to obtain the therapy, and not only have to rush to receive the treatment, but also not risk potentially being diagnosed at six years or older, which still happens to many boys with Duchenne.

Newborn screening for Duchenne would allow access to ELEVIDYS for all eligible boys born with Duchenne, rather than just those privileged enough to be diagnosed prior to their sixth birthday.

Finally, we understand that some still may question the utility of diagnosis at birth for those with Duchenne, as treatments traditionally that have not been administered, excuse me, until later in childhood. Not only do we believe corticosteroids, exon-skipping therapies, and hopefully soon gene therapies may be prescribed to boys as early as the first year of life, much more frequently if newborn screening is adopted. But non-pharmaceutical interventions are also critically important, including speech and physical therapy, as these services are optimized, the earlier they are

administered in childhood development. For recent treatment guidelines, interventions from physical, speech and occupational therapists are recommended as soon after diagnosis as possible.

We believe that all of these reasons and more, within our nomination package, justified the Duchenne muscular dystrophy nomination moving forward to full evidence review, and we urge the Committee to vote to do so today. Thank you.

DR. CALONGE: Thank you, Paul. At this time, I'd like to turn to Michelle Rengarajan.

DR. RENGARAJAN: Thank you. My name is Michelle Rengarajan, and I'm an Academic Physician Scientist, and a mom of two boys, ages 1 and 3 with Duchenne's muscular dystrophy. And I'd like to tell the Committee about my family's experience.

First, what has been available to us because our sons were diagnosed early. Second, what will be available to children diagnosed with Duchenne's through the newborn screen, and finally how expanded the important screening is, and opportunity to enhance equity in the diagnosis and treatment of Duchenne's.

For the first nine months of my older son's life he was a motor first kid. His head control was fast. He sat with confidence, and he pulled to stand on

anything he could find. But then everything stopped. For seven months he tried and tried, but just couldn't seem to get his feet off the ground to take a step. It was as if his legs were weighed down.

I knew something was wrong when my son was 12 months old, but when I brought up my concerns to family and friends and doctors, I kept getting told that this was all normal. It took another 18 months for him to be diagnosed, and during that time our second son was born.

In those 18 months when I knew something was wrong, but nobody else believed it, a simple blood test could have diagnosed his disease. Instead, we started strength-based physical therapy, and kept watching for improvement. Last fall, our son's wonderful PT expressed concerns about his slow progress, and my father-in-law, a general pediatrician, suggested that we should test to confirm that this was not muscular dystrophy.

Our pediatrician, and the pediatric neurologist, again reassured us that this was not Duchenne's, but that they would check just to make sure. Actually, like Jude, one week before Christmas our older son's tests came back positive. Because this is a genetic disease, we tested our baby too, and found that he was also positive. He was then 7 months old.

We had no family history of this disease. Within days of the diagnosis our son's care changed. Our now 3-year-olds PT immediately stopped repetitive strength-based exercises, which can exacerbate muscle damage for boys with Duchenne's, and instead started stretching-focused exercise, aiming to maintain ambulation for as long as possible. He started two additional life changing interventions a couple months later.

First, occupational therapy through our local public schools. Second, a steroid medication that is truly disease modifying and proven to prolong walking by on average two years, meaning he might make it through the challenging years of middle school before he needs a wheelchair.

Within days of starting steroids, my son climbed a ladder on a playground, and could join a friend inside a playhouse for the first time. We and experts around the country believe that starting this medication early will give him the best chance of slowing the ongoing damage to his muscles. And clinical trials are now testing the use of steroids for Duchenne's in infants.

Our younger son, who is now 1, immediately enrolled in early intervention, and is followed weekly

by a physical therapist, as well as his speech pathologist, to help him achieve developmental milestones without putting his muscles at risk. Speech delays can be a part of Duchenne's, and because our baby was diagnosed early, we're able to monitor proactively, and intervene at the earliest signs of delay.

In addition to steroids, there are currently five other FDA approved drugs to treat Duchenne's, four of which are mutation specific and have no lower age limit. Universal and newborn screening will diagnose newborns with mutations amenable to these drives, and they could start on therapy right away.

The newest drug, ELEVIDYS, is a gene therapy, and is approved for almost all Duchenne's mutations, but only for boys who are 4 or 5. We were told about this treatment on the day of our diagnosis, and we feel extraordinary relief that our sons were diagnosed early, when they are young enough to be eligible for ELEVIDYS, which may further prolong their motor abilities.

Perhaps these early therapeutic interventions will help my sons be part of the first generation of boys with Duchenne who are able to walk across the stage when they graduate from high school. When I was in medical school just ten years ago, we were taught that Duchenne's was a death sentence.

Nobody believed it could become a chronic, manageable condition, and yet we are almost there. But despite massive advances in therapy, the average age of diagnosis for Duchenne's has not changed in 30 years. If we are to have any hope of getting current treatment to boys with Duchenne's, and curing children born with this disease in the future we need universal screening. There's simply no other way.

My sons were diagnosed with Duchenne's when they were unusually young. As you've heard, the average age of diagnosis is closer to 5. We've met families whose sons were not diagnosed until they were 6 or 8, or even 10, by which time they missed a critical window to intervene and prolong their children's ability to walk, breathe and live.

Hospitals, universities and companies are leading the way to treatments and cures for Duchenne's, and every boy with Duchenne's should have a shot at those treatments, regardless of who their parents are, or what they luck into.

Universal newborn screening for Duchenne's would mean that every child born with this disease will have access to treatments that will prolong their abilities to play with their friends and love and spend time with their families. Finally, I want to end by

sharing that before our diagnosis when my toddler refused to walk home from the park and begged to be carried, my husband and I thought that we were being good parents when we told him to keep on walking.

Now we know that we couldn't have been more wrong. He was trying to tell us that his muscles had reached their limit. When we learned eight months ago what our two loving, joyful and brilliant little boys were dealing with we were immediately able to better support our sons, give them the help they need, and build them a better future.

Thank you so much for considering moving Duchenne's forward, and I'm happy to answer any questions.

DR. CALONGE: Thank you, Michelle. And finally, we have Niki Armstrong.

MS. ARMSTRONG: Thank you. On behalf of Parent Project Muscular Dystrophy and the Duchenne patient community, thank you for the opportunity to speak today. My name is Niki Armstrong, and I am the Associate Vice President of Community Research and Genetic Services at PPMD.

I also serve as the Newborn Screening Program Manager and have had the honor of updating this Committee for the last several years now on our work in

Duchenne newborn screening. The last few months have been a very exciting time in the world of Duchenne.

As you all know, we resubmitted our Duchenne nomination package at the end of May, and that is up for discussion later in today's meeting. In addition, in June, we had our first FDA approval of the gene therapy, ELEVIDYS, which is a transformative therapy for Duchenne. An addendum to the RUSP package was submitted and is included in this briefing book.

ELEVIDYS was approved to children 4 to 5 years of age, which is the youngest age group that was included in the clinical trials that were submitted to the FDA. Available data and modeling using ELEVIDYS suggests Duchenne's could include an additional decade of walking, and potentially two decades of life expectancy, which is amazing.

Unfortunately, a sizeable percentage of the Duchenne population is not eligible because they are diagnosed too late. As you've heard multiple times today, the average age of diagnoses in Duchenne is around 5 years of age, and that is despite nearly decades of efforts that Dr. Ciafaloni outlined in order to try to decrease that age.

Data from the Duchenne Registry, and from the CDC's MD Starnet show that 26 to 33 percent, that's a

quarter to a third of all boys with Duchenne are diagnosed after their sixth birthday and will therefore be ineligible for ELEVIDYS at the time of their diagnosis.

Newborn screening will mean that no child is ineligible because their diagnosis was just slightly later than average. We know that age of diagnosis varies based upon race and socioeconomic factors, disproportionally affecting underserved minorities, and whom the average age of diagnosis is already more than a year later. All children should have access to transformative therapies.

This is the purpose of newborn screening, to make sure children are identified in time to benefit from the available treatments. There are now six FDA approved therapies, including ELEVIDYS, that are specific to Duchenne, as well as the commonly used corticosteroid Prednisone. All four exon skipping therapies are FDA approved for all ages, and data suggests increased benefits when initiated earlier.

Corticosteroids are also associated with increased benefits when initiated earlier. There are two additional, excuse me, investigational therapies that are currently under review by the FDA, with decisions expected later this year. In addition, there

are multiple other ongoing products and clinical trials that will help this Committee understand the benefits of Duchenne in newborn screening.

A retrospective sibling chart review is underway at one of our certified Duchenne care centers, results which are expected later this year. As is a qualitative study of clinical experiences with siblings diagnosed at different ages, again with results expected later this year.

Clinical trials are ongoing looking at once weekly steroids in infants, and a gene therapy trial for 2- to 3-year-olds has identified all participants. The bottom line is that while we already know there is benefit to Duchenne in newborn screening, even more evidence will be available in the near future.

Duchenne is a progressive condition that results in irreversible muscle loss over time. It has an FDA authorized newborn screening assay, multiple pilots that effectively identified babies with the condition, and multiple approved therapies that are more effective when there is more remaining muscle tissue.

It is time for Duchenne newborn screening. We greatly appreciate the opportunity for Duchenne to be discussed again today and urge the Committee to move Duchenne forward to evidence review. Thank you.

Duchenne Muscular Dystrophy (DMD) Nomination Summary

DR. CALONGE: Thanks Niki, and thanks to all of our participants in the public comment period today. We appreciate your commitment of time, energy and passion helping in informing the Committee and moving forward. Before we move on to discuss the nomination package a second time, I wanted to just go over the background a little bit to remind folks where we're at.

We received a nomination to include Duchenne's muscular dystrophy to the Recommended Uniform Screening Panel in June of 2022. The package was reviewed by the Nomination and Prioritization workgroup, and the Committee voted not -- I'm sorry, voted on whether to recommend the condition move forward to evidence review in February.

The Committee voted against assigning DMD to the full evidence review at that meeting, and after the meeting I provided a letter to the nominators advising them of the outcome and next steps. That letter is available on the Committee website. The DMD nominators submitted a revised package, as you heard, at the end of May or in June of 2023.

The nomination and prioritization workgroup has reviewed the resubmission. Today, on behalf of the nomination and prioritization workgroup, Dr. Chanika

Phornphutkul will present the summary and the N&P workgroup's recommendation to the Committee.

Dr. Phornphutkul joined the Committee in January of 2022. She's the Director of the Division of Human Genetics, Department of Pediatrics at the Warren Alpert Medical School at Brown University in Providence, Rhode Island. She has practiced genetics and metabolism for the past 16 years. Dr. Phornphutkul is the Course Director of the Medical School of Genetics Curriculum at Brown University, and a longtime member of the Newborn Screening and Advisory Committee to the Rhode Island Department of Health. And with that, Dr. Phornphutkul, I'd like to turn things over to you.

DR. PHORNPHUTKUL: Thank you. Thank you very much. Thanks for the kind introduction. I'm glad to be a representative of our committee, subcommittee to discuss the nomination, and prioritization workgroup reports on Duchenne muscular dystrophy.

As you could see the list of the workgroup, obviously at the bottom of the slide. Next slide please. So the nominators listed as Niki Armstrong, Pat Furlong and the advocate organization is PPMD and MDA. Next slide please.

So DMD condition information. DMD is an X-linked neuromuscular disease with progressive muscle

damage and weakness in both skeletal and heart muscle; and primarily affects males, although females can be variable affected.

Associated with high level of creatine-kinase. Diagnoses is based on genetic testing to identify the likely disease-causing variants in the *DMD* gene or muscle biopsy showing decreased dystrophins. Deleterious variants in *DMD* are associated with other forms of disease, including Becker muscular dystrophy, *DMD*-associated dilated cardiomyopathy.

Currently, it is known to occur in 1 in 5,000 male live births, female with pathogenic variant can be clinically affected, about 30 percent. Next slide please.

DMD is a progressive neuromuscular disease of childhood. Patients with DMD experience loss of ambulation, followed by loss of upper limb use, progressive impairment of pulmonary function, and progressive cardiomyopathy. Children affected with DMD often have significantly delayed developmental milestones, including motor function, global delays, and delayed onset of ambulation and other early motor skills.

It is noted that irreversible muscle damage begins as early as fetal life. Typically, the diagnosis

is 4 to 5 years, with loss of ambulation in early adolescence, and death related to pulmonary or cardiac disease often in their 30's. Next slide please.

In terms of DMD treatment and management, currently there are four FDA exon skipping therapies available, which accounts for 30 percent of children and adults with DMD. Therapies are provided weekly and by intravenous infusion. The optimal age to initiate this treatment is not established. Experts recommend offering at the time of diagnosis, even if corticosteroids are not yet appropriate.

Corticosteroids are the standard of care and recommended to begin prior to the onset of physical decline. However, the average initiation is at 5.9 years. The optimal age to initiate the use is not established. Current practice guidelines recommend discussing the use at the time of diagnosis.

Additional therapies in development in various stages of clinical trial, which is very exciting. Next slide please. So the treatment typically begins as clinically indicated, at the time of diagnosis, which is 4 to 5 years. There's limited evidence on early treatment benefit because of the diagnosis delay, clinical course, heterogeneous nature of DMD, and the rarity of the conditions.

As mentioned earlier, FDA recently approved a new gene Therapy, ELEVIDYS. Next slide. Management. DMD requires a multidisciplinary team led by a neurologist, physical medicine rehab specialist, which includes cardiologists, therapists, genetic counselors, pulmonologists, orthopedists and others on the team.

Physical language and speech therapy and early intervention services have been shown to improve quality of life and early functioning. Next slide. So the core requirements for nomination. Number one, validity of the laboratory test. Our answer is yes.

Second, widely available confirmatory testing with a sensitive and specific diagnostic tests, which include this FDA-approved screening test, CK. There is a processor that's high throughput and similar to other GSP tests used, commonly in newborn screening. Confirmatory testing requires Next Gen sequencing, which is not necessarily widely available, but it is available, so the answer is yes.

Third, a prospective population-based pilot study, and the answer is yes from New York, North Carolina, and China. Next slide.

So the summary of the resubmission. This is a new slide. Additional information that was provided. Number one includes new case definition. Highly

elevated levels of CK-MM, followed by persistent elevation of CK level, and a pathogenic, or likely pathogenic variant in the *DMD* gene.

Second, specific treatment is available for 30 percent of DMD cases. Third, gene therapy age of treatment is 4 to 5 years, but the average age of diagnosis without family history is 6.9 years. And fourth, one sibling outcomes study. Next slide.

The key questions to address. I'm not going to read through all since we will go through one by one, but there are eight questions to be addressed. Next slide. Key question 1 is the nominating condition medically serious? The answer is yes, as we discussed earlier. Next slide.

Key question 2 is the case definition and the spectrum of this condition well described to help predict the phenotype range of those children who will be identified based on population-based screening. We thought the answer was yes. This is an X-linked disorder, primarily affecting males although females can be affected.

One third of the male with DMD have a de novo pathogenic variant. Genetic testing could identify pathogenic and likely pathogenic variants, and/or a muscle biopsy could confirm the diagnosis. There are

other variants including Becker's muscular dystrophy that may also be diagnosed and could benefit from early detection. Patients are typically clinically identified between the age of 4 to 5 years. Next slide.

Key question 3, are prospective pilot study in the U.S. or other international countries from population-based assessment available for this disorder? And the answer is yes, as you can see in this table. Next slide.

Key question 4, does the screening test have established analytic validity? Our answer is yes, screening tests for DMD. The primary screening assay would be measurements of creatine Kinase MM or CK-MM. Assay performed using genetic screening processor instrument. Second tier test would be genetic analysis of *DMD* gene via next gen sequencing. Next slide.

Key question 5, are the characteristics of the screening tests reasonable for the newborn screening system among other aspects, a low rate of false negatives? Our answer is yes, based on the updated information on the right side of the slide.

State labs will need to define and optimize cut-offs to reduce false negative and false positives. Second tier molecular testing should be required. Technology continues to evolve so newborn screening for

DMD would likely result in less false positives. Next slide.

Key question 6, is there a widely available and CLIA and/or FDA approved confirmatory testing diagnostic process? The answer is no. It's not FDA approved, however 194 labs across the U.S. are able to provide confirmatory testing for DMD. Next slide.

Key question 7, are there define treatment protocols, FDA approved drugs if applicable, and is there treatment available? The answer is yes. As we mentioned earlier the treatment includes exon-skipping therapies, gene therapies, corticosteroid therapy, speech and physical therapy. However, evidence of treatment prior to the usual clinical diagnosis is still limited.

Key question 8, next slide please. Key question 8, do the results have clinical utility? If the spectrum of disease is broad, will the screening and/or diagnostic test identify who is most likely to benefit from treatment, especially if the treatment is onerous or risky?

Our conclusion, there are benefits from available therapy as noted in the slide from question 7. The benefits are significant and described as delayed in the loss of motor function, and delay in loss of

ambulation. The longest follow-up reported 4 years for exon-skipping therapy, and 20 years for corticosteroids.

It is likely that the harms from therapy are outweighed by benefits. However, long-term data, and data quantifying the frequency and severity of the harm appear to be sparse. There remain questions regarding variance of uncertain significance. Next slide.

There are potential harms of a population-based screening program that must be considered in determining the balance of benefits and harms in clinical utility. There was insufficient evidence provided on potential harm to make a decision on clinical utility based on balancing harms and benefits.

There is some evidence that newborn screening detected cases that access early intervention and therapies may improve the outcomes. So our answer for key question 8 is yes/no. Next slide.

This is the summary of all the key questions, as we've been through in detail. Next slide. So the Nominations and Prioritization Group Recommendation, the Advisory Committee should move the nomination of Duchenne muscular dystrophy forward for a full evidence-based review.

So the additional recommendation from the group include recommended that DMD be defined as an elevated

CK-MM and subsequent molecular testing to avoid/limit false positives. Provide evidence/data of clinical utility from pilot studies, or retrospective sibling case studies. Next slide. I think that's it.

DR. CALONGE: Thank you very much Chanika. That is a wonderful summary, well presented, and I appreciate the time. We're going to open the floor in discussion, questions and comments from Committee members and organizational representatives. Just as a reminder Committee members have the opportunity to discuss first, followed by organizational representatives, and I need to ask you to raise your hand in the raise hand function in Zoom, to put you in the queue for an answer.

When you speak, please remember to unmute yourself, and state your first and last name when you ask a question or provide a comment, so that we have proper reporting of who said what. I think I would like to start with asking, are there any members of the Nomination and Prioritization Committee who would like to add any comments to Chanika's presentation?

Not seeing anyone rush to raise your hand or unmute, I will open it up to questions from Committee members. Jennifer Kwon?

Committee Discussion

DR. KWON: So, it's Jennifer Kwon, Committee member. And I was going to be slow about raising my hand because I wanted to give others a chance to ask questions. I appreciate Chanika's great presentation. Thank you so much. And I appreciated you stating the differences between this nomination package and the presentation that was given before.

And I wanted to make sure I understood that the primary difference in this nomination that is causing the Committee to approve the nomination is the change in the testing, which includes second tier testing for DMD mutational analysis. The fact that the treatment landscape is exciting and evolving and is likely to make earlier treatments available.

And the sort of the hope that even though those treatments don't have a clear protocol for infants, or children, you know, even let's say under 2, that there's hope that infants can benefit from early intervention programs. Like those are the sort of major differences.

DR. CALONGE: Thanks for that summary, Jennifer. Next, I have Cynthia from CDC.

DR. HINTON: Hi. Yes, Cynthia Hinton from CDC. And I just wanted to follow-up on what Jennifer was commenting on. I think another key difference if I'm

correct is that the case definition has changed. The case definition has become more targeted, and I think that has also clarified some issues, so I just want to make sure that I have that correct as well. Thank you.

DR. CALONGE: Yes. Chanika, I don't know if you want to answer that?

DR. PHORNPHUTKUL: Sure, yes, that's correct.

DR. CALONGE: I wanted to make sure I involved a Committee member. Ash Lal, have a comment or a question?

DR. LAL: Just a comment. Thanks Ned. So the evidence gathered for the treatment is really -- it seems has been created by the delay in diagnosis as it currently happens, so I think that with newborn screening it would allow, would be for those that evidence has been accumulated by clinical trials that have been issued. And I think it's not something that can be answered by some product and clinical trials at the moment, so the registries, but eventually the implementation of the newborn screening is the one thing that's most likely to answer that question for me. Thanks.

DR. CALONGE: Thanks, thanks Ash. Now I'll turn to our organizational representatives. I'm sorry, Shawn, I saw your hand go up, so let me move to Shawn

first.

DR. MCCANDLESS: Thanks Ned. I just wanted to add a few comments that I know will be unpopular in some quarters, but the reality is that this Committee is charged with considering implications of adding conditions to the RUSP based on the entire population of the infants born in the United States who undergo compulsory, which is non-voluntary population-based, universal newborn screen, which is relatively, if not completely a unique process in the United States. There are very few other things that one can point to that every person born is required to do except pay taxes. And some people are very good at finding ways to not do that.

As a result, this Committee's charge is much more extensive, and we have to consider many things that are not necessarily of interest or concern to individuals who are living with a particular disease or are advocating for the treatment of a particular disease that are not of particular importance or interest to a pharmaceutical company that has developed a therapeutic for a rare disease.

And I just want to remind everyone listening that this Committee takes very seriously this charge of protecting the integrity of compulsory population base

newborn screening in the United States and making sure that we are really being thoughtful about the evidence of benefit of treatment, the evidence of effectiveness of the screening tools and the diagnostic tools, about the clarity of the case definition to minimize people that end up in a diagnostic odyssey that is not caused by symptoms, but is caused by screening tests that are ineffective, at clearly distinguishing affected individuals from unaffected individuals.

There is no advocacy group. There is no parent support group. There is no pharmaceutical company that is interested or is supporting research in the harms of newborn screening. And therefore, there is very little data about the harms of newborn screening, and so those people who follow-up patients identified by newborn screening, or individuals who have newborn screening results that are not interpretable, and lead to diagnostic uncertainty have experience that makes us feel concerned about potential harms, maybe in a way that's difficult for others to understand because they haven't walked in our shoes.

And I say that specifically that way because the Committee is often reminded that we have not walked in the shoes of the individuals that are affected by these rare diseases, which is very true, and of which I

think all of the Committee members are very sensitive.

Finally, I would say that I just want to speak for myself. As a member of the Nomination and Prioritization Subcommittee now twice, this nomination package is a very challenging one to evaluate. And there are -- we're now up to 197 attached references, thousands of pages of attached documentation.

Each of us has a full-time job. Each of us has -- none of us are able to drop everything for two weeks and read thousands of pages of scientific data. So we're forced to accept what's in the nomination package as being representative of what's in the references that are attached.

And I think that it's important for nominators to be really sensitive to that and understand that it's important that when a reference is referred to in a nomination package, that it actually clearly supports the statement that's being made in the nomination package. And there are multiple examples in this nomination package where that is not necessarily the case, and I haven't read all of the references, but there were several points that came to my attention that I said, well that's very interesting. I'm going to go look at the reference.

And the reference was I don't want to say that

it was a misrepresentation of what was in the actual reference, but it was clearly an interpretation that was one interpretation of several possible interpretations, and where I felt that the nominators had overstated the strength of the evidence in the nomination package.

That was a concern that I had the first time. It was a concern that I had this time. The difference between the two, and the reason that I voted to move this forward this time and not the last time is that there is additional information as has been referred to earlier regarding efficacy of the therapy, and by the nominator's responsiveness to the question about why there are no data provided about earlier treatment of affected siblings when an older child has been diagnosed, which I still find hard to understand with a disorder this common why this has not been previously published.

But that's beside the point. That's not the nominator's responsibility. It's not my responsibility. It's just hard to understand. Anyways, there is additional information now, but the concerns that I had the first time about the package that the members of the N&P Committee, just really, it's not in our charge to do the full evidence review.

Those concerns persist. And so, I want to be

clear that while I am going to vote to move this toward -- forward, to full evidence review, that should not imply that I think the evidence is as strong as is indicated in the nomination package, although it may be. I'll await anxiously for the result of the evidence review, but I still have some concerns about the quality of evidence, and the evidence for efficacy, as well as the evidence about harms.

That I think it's going to be very important for us to think about very, very carefully, and ask a lot of really hard questions. Not because I don't think DMD should be on newborn screening, it's just that there are 10,000 additional genetic disorders that one could make similar arguments for, and for which there will be a growing number of therapies in the near future.

That we're going to have to be really careful of as we go back to where I started, which is protecting or following the charge that we've been given, which is to think clearly about the population based newborn screening process. I apologize that these were very long comments. I'm sorry for that, but I wanted to be really clear about why I'm voting the way I'm voting today, and why my vote is changing from the last time we discussed this. Thank you.

DR. CALONGE: Thanks Shawn. I'm going back to

Jennifer.

DR. KWON: Jennifer Kwon, Committee member. So just very quickly, Shawn, I have probably read a lot of those references as a Director of an MDA certified clinic, and as somebody who cares for a number of Duchenne boys. And I will say that I agree with your concerns, and that's why I will say upfront that I don't think my vote will be changing.

DR. CALONGE: Melissa?

DR. KWON: Oh, I think you're on mute.

DR. CALONGE: Melissa?

DR. KWON: You're still on mute, Melissa.

DR. CALONGE: You need to unmute, Melissa. There you go. We can't hear you. As you work on your audio, I'm going to move to Robert.

DR. OSTRANDER: Oh, thank you. I'm Robert Ostrander, AAFP representative. I was a coauthor on a paper that MBA did in gene neurology in 2019 promoting the addition of neuromuscular conditions for the RUSP. And it was because of our discussions at those meetings that I have become such an advocate for including the potential EI benefit in our decision making.

I think it's especially an entry with this condition where the clinical diagnosis time and the symptom time are so widely gapped. I think it's

important to point out that as of the first presenter discussed, there have been efforts to move clinical diagnosis closer to symptom onset through other means, and they have not been as successful.

And I think, you know, that should be considered. I mean is there some other way to get people diagnosed earlier when treatment might be beneficial, and other efforts have not been useful, at least based on the data that was presented.

And my third comment is in this case, you know, variants of uncertain significance are typically considered by the Committee as a potential harm, because of the psychological distress, and so on and so forth. My own, again there's no data on this yet because there can't be until there is, but my thought about Duchenne muscular dystrophy for the same reason about the gap between symptom onset, which is where certainly there may be good reason to start treatment.

And clinical diagnosis is so wide that VOUS is number one, may allow for closer monitoring in those early symptoms that have been written off won't be written off, and treatment considered. And number two, as a side benefit, I know it's not one of our criteria, but you know, new knowledge generation because we will figure out if these VOUS(s)s are indeed pathogenic or

not.

So, I think this sort of perspective I guess on both the EI and the time between symptom onset and clinical diagnosis, I think I would encourage people to consider seriously as the evidence review moves on, gets moved to evidence review. Thank you.

DR. MCCANDLESS: Ned, can I just respond to one thing Robert -- I'm sorry Ned, I'm presuming that you're going to say yes. I apologize for that. But Robert, I just want to be clear that the nominators were responsive to the concerns of the N&P Committee in terms of definition of the disorder, and I think I want to be very clear that a VOUS that is not associated with a persistent elevation CK-MB would not be considered a positive screen, and that patient would be -- if I'm understanding the nominator's proposal, their recommendation is that that patient would not be followed further as being at risk of having Duchenne muscular dystrophy.

So if I'm understanding it correctly, the VOUS issue would not add, would not really change the follow-up. The follow-up would be based on the persistence of the elevation of the CK-MB, and that would be the defining characteristic for the purposes of newborn screening. And if that's an incorrect

perception, I'm happy to be corrected by someone who's more knowledgeable than me.

DR. CALONGE: I think you're correct in that interpretation Shawn. Melissa, I see you're back on, so I'm going to go to you next, and we still can't hear you. So Michele Caggana is up.

DR. CAGGANA: That's okay. Hi everybody. I just had a couple comments. Thanks for the re-review of the Nomination and Prioritization workgroup for the re-review of this. It was a very long reapplication. I just had a couple comments. One is that for this condition I think unlike so many other newborn screening conditions that we deal with, the actual diagnosis for this is pretty straightforward.

These kids will have a persistent, as just said, CK-MM value. The Committee, as part of the definition of the test, once molecular diagnosis a very certain significance in this instance could cause both benefit in harm in the way that you would have, you know, and without persistent CK-MM, you could sort of be a little bit more dismissive. You could undergo another diagnostic biopsy, or something like that. On the other hand, it could point you towards the follow-up to make sure that these kids do have elevated CK-MM that holds.

Related to the question about the improved

technology. I just want to clarify that the assay in our hands works quite well from our pilot study, but the issue for the newborn screening perspective is really just establishing your cut-off values, which newborn screening programs do whenever we start with a new test, even in cases where it's an FDA approved test.

You have to do these biomarkers and analyte tests and establish you cut-offs based on your population within your state. And so in that instance, that doesn't seem to be as much of a concern, at least from the newborn screening program perspective.

And then lastly, the idea that we're going to -- I just want to be careful that we don't dictate necessarily that we make molecular part of the newborn screening piece that we actually have a means to separate that out, or give programs the ability to parse out a molecular test as part of the affirmatory post-screening, rather than part of the newborn screen because this is a very large gene, and programs are probably not going to be able to do the sequencing in house.

And so, I just want to make sure that folks understand sort of that when we talk about how we're going to define what we're actually screening for. So I am in favor of service elevated CK-MM, and then

potentially having a model where perhaps a program could ask for a second CK-MM, or a repeat specimen, as we know the factors that are considered when birth factors that elevate CK-MM early on, and shortly after birth.

So, that's what I would like people to hear. Thanks.

DR. CALONGE: Michele, what is the process for states setting its own levels? I mean how do you codify it to analytic validity, and how long does that take? And is there a process, is there a time period where you get that, children might be misidentified until the calibration is correct?

DR. CAGGANA: Well as we heard the last time, a lot of the pilot studies had their cut-offs quite conservatively. So in New York we did time of collection cut-offs, how old the baby was when the specimen was collected. Because in our hands that seemed to be the strongest factor.

But typically, what people do is they will screen specimens coming in the door for the test, whether they're doing it in a pilot phase, or as part of the validation study. They will look at their population parameters, and then in that we also make sure we sort of enrich that validation population with any of the parameters we're concerned about, whether it

be birth weight, age at collection.

We do this for other assays that we have already. So you basically create your dataset. You make sure that you have representations from these different groups that are known to have variations in analytes. You then also have positive controls from the newborn period that you get from kids who you know had a Duchenne diagnosis and try and get consent from parents to use their newborn screening specimens.

You put those in. You see how that falls out. And then you set the threshold based on insuring that you're going to catch all those children we know had Duchenne when they were born, but undiagnosed. And then also you can do a 3 SD, you can do different types of things to set your cut-off to start.

And then as time goes on, you can change them. We did find from our repeat testing that CK-MM does go down over time, and so you may put a model in place like that where you would just request a repeat sample. And so typically, you know, typically that's what we would do.

DR. CALONGE: Thank you. Melissa, do you want to try again?

DR. PARISI: I'm hoping that the third time is a charm. Can you hear me?

DR. CALONGE: Yes, yes.

DR. PARISI: All right. Thank you for your patience. So I just wanted to make a couple comments, and I had a question as well. So my first comments just to echo what was said earlier, and Cindy Hinton mentioned as well that the changes to the nomination really include the fact that there are new treatments available, including the gene therapy, that has been described, ELEVIDYS, and then the revised case definition that really helps to refine how we characterize what Duchenne muscular dystrophy should look like on newborn screening. And then, of course, additional information about improved outcomes for those with earlier diagnosis.

And I think as many of the public commenters stated earlier today, there are many value-added benefits to early diagnosis that include treatment strategies, treatments that can be avoided, such as damaging physical therapy when that's really not going to be in the best interest of these boys who may have this diagnosis.

And the ability for families to get support services, be able to plan their life, and plan their housing, and do a lot of additional planning. In addition to, of course, the goal of creating strategies

and treatments that are medication-based that can improve long-term outcomes for this condition.

So those are just my comments about the revised case definition, and the revised application nomination proposal I should say. And why I think that there is value in considering moving this to evidence review.

My one question for the group, and maybe someone can answer this, is with the revised case definition does that mean that mutations that are associated more with Becker muscular dystrophy would not be reported, or would they still be reported under this revised case definition? I just want a case clarification on that. Thank you.

DR. CALONGE: Chanika, do you have an answer for Melissa?

DR. PHORNPHUTKUL: I did think it was clear. I think being really focused on pathogenic variant, and you know, sort of looking at the literature. But I think that is something that is -- that needs to be discussed.

DR. MCCANDLESS: My read of the nomination package though was that they would be reported that they were clinically relevant, that it's a severe disorder and that it was appropriate to include. I may be misinterpreting what I read.

DR. CALONGE: Yeah, I believe that's correct, that we wouldn't not report them because of the implications of a positive test, or a positive presence of Becker's.

DR. PARISI: Thank you.

DR. CALONGE: Melissa, does that answer your question?

DR. PARISI: Yeah. I think so. That was my impression as well, but I wasn't quite 100 percent clear on that, so I just wanted to hear if other people read it and interpreted it the same way. Thank you.

DR. CALONGE: Jennifer?

DR. KWON: I just wanted to also respond to something that Robert was saying. I think it's a goal for all of us who care for boys with Duchenne, and should be able to offer lifelong care, and to be able to really stimulate children early in life.

We, I think all clinics have examples of children who have been identified for all kinds of reasons in infancy, or in the first year, or in the first or second year of life who we can't get them into early intervention services because these are county-based services, and they set their own rules, and many of them use their resources to only serve patients who have disabilities that fall below a certain level.

And so we have boys with Duchenne who probably could benefit from services, but they just don't quality because their deficits aren't that obvious.

DR. CALONGE: Natasha?

MS. BONHOMME: Great, thank you. Natasha Bonhomme, Genetic Alliance. My comments are in reference to some comments that Shawn McCandless made. As the organizational rep for an organization that serves those rare disease groups, many of whom will never be eligible for a newborn screening, as well as really committed to the families that go through genetic services as just part of their routine care, like prenatal care and others.

The characterization that no family or patient group is interested in looking at the harms, is frankly inaccurate. I can show you references to work that we have done looking at the impact of false positives, that were published with our partners, the University of Maryland in 2012.

If there are other opportunities for us to partner and look at that work, we'd be very interested. But I just wanted to call that out because the same way that no bio ethicists would want to be painted with a broad-brush stroke and compared to others. The same goes for family organizations and patient groups who are

committed to making the system better, so thank you.

DR. CALONGE: Thank you, Debra?

DR. FREEDENBERG: Thank you. Debbie Freedenberg, AAP. I just wanted to comment on the kind of false positives, and clearly this is going to touch on our condition counting issues. So in this particular scenario, if you have a child that has two positive CKs, you know, second thing, and then you know, your molecular testing is negative, there's a whole broad spectrum of what that could be, including nothing.

And so I think that that should be considered as well because I know that there is some programs that say well, it's not what we're screening for. We don't care what it is out there, and I think in the best interests of the child if we're going to go through the testing, we should kind of broaden our horizons a little bit and be concerned about what else is in there within the differential.

DR. CALONGE: Thank you, Debra. Well, this has been an excellent discussion. I appreciate the engagement of everyone around the screen who worked with the Committee to help us make the best decisions. As we were planning the session today, we decided we would put a lunch break now, and let folks have time to digest what you've heard, information. You can go back and

look at the slides as you wish, and then we'll bring up the potential vote when we reconvene in about a half an hour.

We're right on time. I appreciate again the thoughtfulness folks have put into the discussion, and we'll see you back then. Thanks.

(Lunch break.)

Lunch Break

DR. CALONGE: Ready to go. Welcome back. Let me just pause for a moment and make sure that there weren't additional questions or comments that came up from Committee members and organizational representatives during the break, which I realize was actually an hour ahead of time.

I think you were doing well on our agenda for today. Michele?

DR. CAGGANA: Hi again. I just wanted to add one more comment for people to consider when talking about newborn screening for this condition. So our publications from the pilot study were in the briefing book. And we have a forum to talk about different aspects of the pilots.

But one thing that we actually have worked on, and Norma Tapa Cooley has an abstract for that APHL

meeting coming up in October, is that we actually ran their pilot data through the Clear tool from the Mayo Clinic and found out that we really could reduce the number of borderlines, because that was sort of the most troubling part.

As I said we had these conservative cut-offs to begin the pilot because we weren't sure what the, you know, with the slack would be. And so, we found out that we would be able to reduce the number of babies that we had to recall with the borderline result with about 80 to 90 percent just on a quick pass through.

And so, this is part of what I was talking about earlier on how we refine the assay over time. So the goal is to impact as few families as possible while not missing one, obviously. So I just wanted to add that.

DR. CALONGE: Thanks so much, Michele. Melissa?

DR. PARISI: Michele, can I ask you just a follow-up question then? So were you also picking up Becker cases as well through your screening, or did you have any that were picked up even when you refined your cut-offs you didn't have any?

DR. CAGGANA: No. We didn't have any, but as part of this we certainly if the pathogenic variant for

Becker was kicked up, we would certainly report it.

DR. PARISI: Okay. Thank you.

DR. CAGGANA: Um-hmm.

Vote on Moving DMD Forward to Full Evidence Review

DR. CALONGE: I think at this time it would be appropriate to ask with a motion on whether to move Duchenne muscular dystrophy forward to a full evidence-based review.

DR. CAGGANA: I would make a motion to move it forward. Michele Caggana, Committee member.

DR. CALONGE: Thanks Michele. There's a motion. Is there a second?

DR. DORLEY: I second the motion. This is Chris Dorley.

DR. CALONGE: Thanks Chris. It's been moved and seconded to move the condition of Duchenne muscular dystrophy forward to a full evidence review. Any additional comments before we vote? Seeing none, Leticia, I wonder if you could do a roll call vote?

COMMANDER MANNING: Thank you.

DR. CALONGE: Please remember to unmute when your name is called.

COMMANDER MANNING: Okay. Michele Caggana?

DR. CAGGANA: I approve.

COMMANDER MANNING: You can just respond yes or no.

DR. CAGGANA: Yes.

COMMANDER MANNING: Ned Calonge?

DR. CALONGE: But just put me at the end this time.

COMMANDER MANNING: Okay. Sorry. Jannine Cody?

DR. CODY: Yes.

COMMANDER MANNING: Representative from CDC, Cynthia Hinton?

DR. HINTON: Yes.

COMMANDER MANNING: Paula Caposino?

DR. CAPOSINO: Yes.

COMMANDER MANNING: Christine Dorley?

DR. DORLEY: Yes.

COMMANDER MANNING: Jennifer Kwon?

DR. CALONGE: She may not have rejoined.

COMMANDER MANNING: Ash Lal?

DR. LAL: Yes.

COMMANDER MANNING: Shawn McCandless?

DR. MCCANDLESS: Yes.

COMMANDER MANNING: Kamila Mistry?

DR. MISTRY: Yes.

COMMANDER MANNING: Melissa Parisi?

DR. PARISI: Yes.
COMMANDER MANNING: Chanika Phornphutkul?
DR. PHORNPHUTKUL: Yes.
COMMANDER MANNING: Michael Warren?
DR. WARREN: Yes.
COMMANDER MANNING: And Ned Calonge?
DR. CALONGE: Yes. Just checking, is Jennifer on?
COMMANDER MANNING: I don't know.
DR. CALONGE: Mark her as absent, and what is the final vote count? 12 yes.
COMMANDER MANNING: Yes.
DR. CALONGE: One absent. That's an aye vote, and moves us forward. So we will now assign DMD to the Evidence Review Group, and they'll start their process immediately. I do want to remind Committee members and members of the public, and our organizational reps, that moving to an organization to a full review is just that, a full review. It does not anticipate ahead of time or prejudice vote on adding the condition to the RUSP. That will depend on work by the ERG and the group that helps advise them moving forward.
And then the Committee's review of the completed evidence review, before we decide whether or not to add the condition. So thanks everyone for a

really thoughtful discussion, and vote. And we will proceed.

Expedited Review Process

During the new business at the May meeting, it was mentioned that the Committee should consider to wait for nominators to resubmit additional evidence for information without having to redo the entire nomination process. So working with others, we have come together to put a proposal for this process, which I would like to present at this time.

I hope someone can bring the slides up. Could I have the next slide please? Just by way of background the final step in the process of deciding to recommend adding a new condition to the RUSP involves Committee review, and the discussion of evidence review and synthesis, and at least one vote, if not multiple votes. If the vote does not result in a recommendation to add, there may be specific evidence asked, or other issues that could be addressed in a short timeframe, which we would define as within a calendar year, next slide.

In such instances the nominators may choose to respond to address issues and submit new evidence and/or other revisions within that one-year timeframe. It is

expected that in these cases the Evidence Review Group could do an expedited review, incorporating new evidence, or addressing other revisions, such as a change of the scope without starting evidence review process over. Next slide please.

So I'd like to present a proposal for an expedited review process. First, if the Committee vote results in not recommending a commission to the RUSP, the Chair sends a letter to the nominators summarizing the issues leading to the decision. Two, within one year of the Chair's letter, nominators may resubmit a renomination package for expedited review, that outlines at least one material change to the recommendation -- I'm sorry, to the nomination, and the supporting data for documents.

Three, the Chair reviews the renomination package, and with input as necessary from the ERG and N&P workgroup determines if it qualifies as a material change, which we define in the next slide. Next slide please.

We propose to define a material change as such, it must be a change in scope of the condition nominated, and/or substantial new evidence for the nominated condition. If there is a change in scope, it is preferrable that there is also new evidence provided in

support.

The nomination package resubmission should address, maybe questions and comments described in the Chair letter to the nominators. Next slide.

Four, if renomination constitutes a material change the package will be presented and be discussed by the full ACHDNC for consideration for expedited review. The Committee votes whether to move the condition nomination to expedited review conducted by the Evidence Review Group.

Six. If that vote fails, the Chair summarizes the issues leading to the decision in the letter to the nomination group, and the condition returns to the list of conditions for future nomination and prioritization. Next slide.

Eight, if the vote passes, if necessary, N&P workgroup prioritizes the review considering other topics in the prioritization queue to determine timelines and deadlines. Nine, the ERG works with the technical evaluation panel and revises the review to include the new evidence and/or address the revised scope, note that this may involve additional modeling.

Ten, the condition is scheduled for presentation, discussion and vote for recommendation for inclusion on the RUSP at a full Committee meeting. Next

slide please. So I would like to open the floor up again starting with Committee members, and then to our organizational reps for questions and comments. And the first hand up I see is Shawn.

Committee Discussion

DR. MCCANDLESS: Yeah, sorry about that. Shawn McCandless, Committee member. I think this is a very thoughtful approach, and it makes a lot of sense. The only concern I have is I think we need to be really careful that this, either the decision about adding a condition to the RUSP, has a lot of moving parts.

And there's not sort of a checklist that the Committee goes down and says okay, check this, check this, check this. Oops, this is missing, check this, this is missing. And my concern is that we want to be careful to recognize that a re-evaluation, even with new evidence that's responsive to one specific concern that was raised earlier may not lead to a different result.

Anybody who writes NIH grants is familiar with this. You submit a grant. You get feedback on your grant. You respond to that feedback and resubmit, and you get a worse score the second time than you did the first time, and there are a variety of reasons for that. And they're not bad things, they're frustrating, and

it's annoying if you're the person who submitted the grant.

But it's part of the process, and there's many reasons why that happens, not the least of which is that sometimes there's different people involved in the decision making. It seems to me the same will be true in this situation, and so if we do adopt this approach, which I think is very logical, we also need to be really careful around the communication to ensure that it is very clear that this is not sort of -- that there may be other concerns that will come up in the second review, and that being responsive to a specific concern, or two specific concerns, or three specific concerns, is not a guarantee that the condition will be voted to be added when it is brought back to the full Committee.

DR. CALONGE: Shawn, do you think that should be explicit? Like an explicit line in the process? Or can we just understand that as a normal part of expedited reviews?

DR. MCCANDLESS: That's a great question. My opinion would be that it should be explicit, it should be stated upfront that this -- that here are specific concerns that were raised by the Committee at this time, but that the new evaluation will be a new evaluation, and that there's no guarantee of what the outcome of

that will be.

And you know, I understand people's concerns that it feels like the goalposts are moving. And that's because this is not a static process, it's a dynamic process.

DR. CALONGE: Thanks Shawn. Ash?

DR. LAL: Not being terribly familiar with the process you're doing, I just wanted to ask if once the nomination packet is submitted does the Committee, then work in affirmation, or is there a pronged mechanism to reach out to the nominators to ask missing or corroborating information without having to go to a full vote, and then return the package to the nominators?

And I say this because I think the nominators, one could not assume that every nomination group has a similar level of capacity to put together a comprehensive package that you can expect from that.

DR. CALONGE: Thanks Ash, for the question. And I think that's one of the things that we're trying to address in opening up the nomination process because there's a better way to do it with resources that are more available across topics, and not dependent on the resources available to a certain advocacy group, or other considerations.

There is a technical expert panel that may

include members of the nomination group that provide input. Questions are asked regularly. I can tell you that Alex's group returned to the subject matter experts, which are often participating in a nomination package submission to gain more information, and to clarify. So that's a very dynamic and not a closed process. Scott?

DR. SHONE: Thank you, Scott Shone, org rep from ASTO. So I want to go back to what Shawn said because I think there's some really critical details in his question that I'd like to delve in on, and I'm wondering. I'll start with where this comes from when I was a grad student at Hopkins, I had a professor who if you challenged a grade on a test, he would regrade the entire test.

Inevitably I thought I would get five points back, and I would get those five points back, but he would find five points elsewhere that I had missed, and I suddenly had the same grade. And I learned after I graduated and talked to him about that process, it was a way to dissuade students from challenging the grade because he inevitably regraded the whole thing.

I don't mean to be bring light to this conversation, but I'm wondering do you imagine that an expedited review would presuppose that everything

already reviewed hasn't changed and there's no new evidence to suggest there's changes to that, and that you move on with just the rescoped and new evidence that has been presented, and it's kind of like what Shawn said of this being a dynamic process.

Is you know that the initial evidence review, at least per the original Newborn Screening Saves Lives Act was guided by nine months. And so, there's no timeframe here to what this re-review would take, so I wonder about that, and that goes into what is the scope? What's the bounds? How far will the ERG go in terms of just assessing the response to the feedback in question, but also new evidence that might weigh on other parts of the robust review that was done initially, so I'd like to throw that out there for consideration and comment.

DR. CALONGE: Sure. And in the areas where expedited reviews I've experienced, so this is not a novel concept. The USPSTF uses an expedited review of the process as does the CPSTF, and it's not exactly in the area where new evidence is becoming available or needs to be considered.

Usually, an Evidence Review Group when given even expedited review will do a gap survey, an update survey to relook at what new literature pool has been

published since the former review was done, so that the review is as complete as it would be, were it submitted for the first time. We have not talked about timeframes, and that's something we probably need to discuss with Alex's group to kind of put parameters around how long the ERG might have to do an expedited review.

Inherent in the word expedited is expedited, so the idea is that it would be more rapid than original review where all of the literature had been looked at once before. Usually gap analyses turn up only new things that should inform the overall decision. So I think those are both your points and Shawn's, were great points.

And I think it's the Committee's job to do the best job with the best evidence that's available. That being said, I would say that that opens up the review to any new evidence that would be on one side or the other, or on questions not answered in the renomination package.

It may not happen very quickly. I have now paid more attention to the pace of new research publications and newborn screening, and so within a one-year period of time I do expect there to be some, but I think a manageable amount. Thank you for those

questions. Bob?

DR. OSTRANDER: Yeah, hi. Robert Ostrander, AAFP. And this is very much an open-ended question. When the nominator resubmits for expedited review, may they in addition to answering the concerns raised in the letter to them, discuss other topics, or is there request to the expedited review confine only those issues that were raised in that letter?

DR. CALONGE: Thanks for that question, and I think we can be explicit about that too. That needing new information, that the nominators want to provide would be fair in the submission for expedited review. Any further questions?

What I would propose, I know we just got off a break, but if you all can give us about a minute to make a revision to the process that incorporates this concept of gap analysis and other issues may come up beyond the question set itself, and other information might be addressed.

We can do that I think in about 10 minutes, and then come back. Present that change to you and see if the Committee is ready to vote. I'm not seeing any objections to that proposition. So if those with more nimble fingers than I, can go ahead and pause the call, give us 10 minutes, and we'll reconvene with those

changes.

(Pause.)

DR. CALONGE: I appreciate everyone's patience. Thanks. I must admit I'm suffering a little from my Boomer inability to use a touch pad on a computer. I am mouse dependent, I apologize.

Here are the additions for the process we have considered. The first is around timeline, a vote must be held on the condition within 9 months of the approval of expedited review. Now it doesn't mean it has to wait for 9 months, it's best applying the criteria for the most amount of time that might occur if there is new evidence, new study, or another material change, it certainly does not have to take nine months, but it shouldn't take longer than that.

And we do have to recognize that there might be other conditions in the queue, but some vote on the condition needs to occur within 9 months. The next point is the expedited review should include responses to the Chair's letter and may include additional new evidence or information on other issues.

This is a change to give the nominators to open the door to evidence that strengthens their case in other parts of the nomination package and help ERG in making the decision or a good review. The ERG can also

find additional research on issues not included in the original discussion and Chair's letter that may impact the decision to recommend the condition be added to the RUSP.

So we're trying to make sure that any new evidence that should be included to inform the Committee in making a decision is included in the review. Next slide. Since we couldn't quite get it all under one.

It should be clear that a topic of proof or expedited review may still end in the decision not to recommend addition to the RUSP. So with that we believe we have covered the issues that we brought up, and I'll open it up to discussion again by the Committee and organizational representatives.

If the Committee is comfortable at this point in approving the expedited review process, which I assure you we will clean up in terms of the order of the bullet points, I would entertain a motion to do so. Ash, do you have a question, or are you making a motion?

DR. LAL: I have a question, thanks Ned.

DR. CALONGE: Yes, sir.

DR. LAL: Thank you. I just wanted to ask about the timeframe of resubmission, and what was, how that was arrived at for logistical reasons to keep the evidence in the same composition as before? Because I

feel one thing is strategy, and some questions could be addressed right away if there was new evidence that may be forthcoming of any pending studies and so on.

That could come outside of the timeframe of the one here. Just to ask for some clarification.

DR. CALONGE: Yes, thank you. It was experience based, and the fact that other evidence-based review groups included ACIP feel that an evidence review becomes too stale after a one-year period of time.

So, the Committee guide at CDC will use somebody else's systematic evidence review, but not if it's over a year old. And again, the idea is that too many new things have happened, knowledge moves at a quick pace, and that seemed like a reasonable timeframe.

I would say it's a reasonable thing to ask, and to keep an eye on. We have to start with a timeframe. That's the one I proposed in terms of experience, and if it appears like that is too restrictive, or too permissive, I think we could change the timeframe if necessary. Shawn?

DR. MCCANDLESS: Thank you. I think this is the right thing to do, but I also think that there's a lot of potential for unintended consequences based on the language that we use around it, and the expectations that we create. And so, I think the language is going

to be really, really important, and I would be a little hesitant to vote on something right now without having in front of me that I can ponder for a few minutes, the actual language.

And so, I had a few questions that came up with those slides and I just don't -- I just think slowly I guess, and so I can identify a couple of concerns. The first is it wasn't clear to me who was responsible for each of those bullet points, whether that was the nominators, whether that was the Evidence Review Group, whether that was the Committee, so I think we need clarification there.

I also think that we need to be really clear that there's no may about it. If there's going to be a re-evaluation there's going to be a re-evaluation. The re-evaluation should look at all of the available data, including all of the new data, and it shouldn't be "may include new data." It should be "will include all new data" because that just seems absolutely mandatory to me.

And I would like to see the language that we're voting on, and have a few minutes to ponder it, to try to anticipate if there may be unintended consequences based on the way we framed the statement.

DR. CALONGE: Well Shawn, we anticipated that

might be the case, and so what we are proposing if that sentiment is shared by the Committee members that we postpone the vote on this until we can distribute the language in order, and we would thing would be ideal, and have everyone have the opportunity to look at it, and dwell on it before a formal vote.

But you know I had to ask. Jennifer?

DR. KWON: Hi. Sorry I was having some technical difficulties, but I did hear much of the conversation by phone. It's just that none of you could hear me, which I can't help but think might have been on purpose. But if you're going to postpone the vote does that mean that does that affect what's happening tomorrow?

DR. CALONGE: Yeah, great question. It depends.

DR. KWON: That wasn't my original question, it's just a response to what you just said, sorry.

DR. CALONGE: Yeah. If we vote to approve the process tomorrow, then we plan to move ahead with consideration of Krabbe disease as the topic for -- potentially a topic for expedited review. So to change the order a little bit of the agenda tomorrow. If the Committee rejects the expedited review process, then that changes our plans for moving forward tomorrow.

DR. KWON: Okay. So I think that one of the things that we heard about the Duchenne nomination package was that there is a lot of hope, and there is a lot of potential for these treatments that are out there. You know, so there's a lot of that. And I feel like having an expedited review process in place does maybe open the door for people not waiting for evidence to become available.

The hope of today will hopefully be the evidence of tomorrow, and one of the questions that's been asked by many of us who treat patients with Duchenne for example, with the new gene therapy, is why Sarepta didn't simply wait for more data to become available, rather than to push the FDA so that the FDA in turn provided a very limited approval based on what they thought was, you know, in the best interest of what is Duchenne.

And so I was just yeah, wondering what safeguards there might be to keeping -- to maybe opening the door for there not to be enough evidence, but with an expedited review process to be able to sort of bringing the evidence in the future. And therefore, have an application be submitted a little prematurely.

DR. CALONGE: I would hope that Nomination and Prioritization workgroup wouldn't use this process as a

shortcut to their responsibilities in bringing a nomination package forward to the evidence review group. I guess that's the best answer I have for you. Chris?

DR. DORLEY: Yes, so just for my clarification with the expedited review, this is kind of like a carryover from the last meeting that we had to establish a process so that once someone submits a nomination, and it gets kicked back, that there doesn't have to be a long, extended waiting period for them to have a review again.

DR. CALONGE: Yes.

DR. DORLEY: So I'm in favor of posting, or having a vote today so that we don't delay this process any longer, and maybe having this discussion now so that we establish as Shawn mentioned, you know, whose roles and responsibilities are these, so that we can move ahead and not delay the vote tomorrow. That's my opinion.

DR. CALONGE: Thanks. We could put the slides back up. We could try to do that clarification now, or again we could revise the slides, get them to you yet today, ask you to review them, provide us with additional comments or questions. Respond to those before the meeting tomorrow, and have a vote on the process tomorrow, which would then set up the rest of

our agenda tomorrow.

But let me just go through what we were thinking about here. The vote must be held by the Commission within 9 months after the approval of an expedited review. We put that 9 month on there because it's already there for a review, or at least has been in the past. And not that we would anticipate it taking that long. But I think that's clear about who is responsible, and it would be the clock starts after the approval.

So here the expedited review should include responses to the Chair's letter and may include additional new evidence or information for other issues. I was just thinking would there be other topics that the nominators wanted to bring up. So that's a good one to say that responses to the Chair's letter may include new evidence or information on other issues submitted by the nominators. Shawn, does that make that clear?

DR. MCCANDLESS: Shawn McCandless, Committee Member. That is addressing the concern I have there is it's not clear whether I think that there's still some work that needs to be done there because if I hear what you are saying, you are suggesting that the nominators are responsible for including responses to the Chair's letter and including additional new evidence or

information. And that is a responsibility of the nominator, not the Evidence Review Committee, or as the expectation of the Evidence Review Committee will respond directly to the Chair's letter and the issues you raised by the Committee, plus additional new information.

DR. CALONGE: Right. So yeah, the Chair's letter goes to the nominators, and so it's the nominators who will review that and not the ERG.

DR. MCCANDLESS: So maybe the way -- I'm not sure you want to do wordsmithing here, but maybe the way to fix that is to say requests for expedited review.

DR. CALONGE: Got it. That change. Michael?

DR. WARREN: That's what I was going to suggest that clarification.

DR. CALONGE: Shawn, the next -- well it was kind of to your point, and so I think the ERG may find additional new research. So again, the idea is that the charge to the ERG needs to be look at what's provided to you from the nominators and expedited review package, and you should use typical search strategies to look for additional new research that may not have been included in the original discussion in the Chair's letter, but that could impact the decision to recommend the condition.

So that's basically saying there may be research that occurs in that timeframe that would either support or not support the decision of the Committee, and ERG should look at that in the traditional approach with the gap search. So we need to make that a bit more specific.

DR. MISTRY: Ned, this is Kamila. I think that what you just said I think really needs to be captured in that last bullet because I think it can be read a number of different ways. And just logically they're giving us new evidence, right? And also naming -- giving us more information.

And then we're saying on top of that we're going to look at that and then we can find even more. And so I think just kind of being more linear in laying all that out, and then we're also saying if we find something we're going to have to consider that as part of the decision making.

And so, I think just being super clear about those pieces and how they fit together I think is really important.

DR. CALONGE: Got it. And I think I understand what we want to say, and I also understand we didn't quite say that, so those were as we're catching that concept we go onto the next slide. Expedited review.

This one is pretty clear, right? Shawn, we just wanted to be -- Shawn and others, we wanted to be explicit about the fact that just because we're doing an expedited review, it doesn't prejudge the vote.

There will still need to be a presentation by the ERG, discussion and consideration by the Committee and a vote. And that the vote may be to recommend, or it may be to not recommend. So just because you get submitted for expedited review it doesn't prejudge the vote.

DR. MCCANDLESS: I think that does capture my concern there. I think there's an unspoken point about the process though, and that is that there is no requirement, nor there's no requirement for voting members of this Committee to provide their concerns for a list of the specific reasons that they vote the way that they vote, and I think that that's another thing that I don't know how to make that clear.

But that's -- my concern about this process is that it creates the expectation that there was one thing, or maybe two things that a little bit more data, one little piece of information that was missing would change a no vote to a yes vote. And we just have to be clear that that may not be the case, and probably won't be the case most of the time because we don't have a

checklist, and we don't have a requirement that Committee members sort of articulate and define their specific reasons for voting yes or no.

And so I just want to be really careful that we don't create expectations here that will then end up with people feeling nominators in particular, feeling frustrated with the process because we're trying to make it more clear, and make it appear that it's more, you know, set in stone of how decisions are made when the reality is that the data are never clean, the evidence is never entirely clear, and that there's always going to be subjective human judgment involved in the decision making, or at least through the foreseeable future.

And I don't know how to capture that in this language honestly.

DR. CALONGE: I think that yeah. I mean I hope the nominators can understand. I mean I have heard questions like so if we give you this you'll vote yes, which isn't what we're saying. It's like these are the items that the Committee discussed and said needed to be addressed. It doesn't say this is a comprehensive list of all the reasons why people might have voted one way or the other.

And I'm not certain as I say that other than the process works its way through. I understand your

point, and at the end of the day you know we want to avoid if there's a point that the Committee felt was fine, we don't necessarily want to re-educate that. I think that to make sure though that we're looking at the evidence on the whole, and are doing that balance between benefits and harms, and a level of certainty that adheres to the process is what we look to do even with an expedited review.

And I understand that if another issue comes up and says we still aren't going to vote that, that the nominators, advocates and family members need to understand that that's part of the process. Jennifer?

DR. KWON: Hi. Jennifer Kwon, Committee member. So when it goes -- so this will go back then to the ERG, and the ERG I assume will prioritize the key issues that were brought up as problematic for the application, the nomination. And so when are you envisioning -- and so, you are basically leaving it up to the ERG to decide how to approach their evidence review then?

There's no other sort of guidance that the Committee is going to give to the ERG.

DR. CALONGE: Well yeah, that's the way we envisioned it.

DR. KWON: Okay.

DR. CALONGE: Kind of the way we do it now.

DR. KWON: Yeah, sure.

DR. CALONGE: And there will still be a technical expert panel to provide input as well.

DR. KWON: So and this may lead our ERG to have the managing two issues overlapping, depending on how the vote goes tomorrow. Has there been any discussion about their bandwidth to manage this?

DR. CALONGE: I think that's why we tried to put in language that anticipated the workload of the ERG, and that we have to do prioritization of a -- sorry, an expedited review and a new review as a Committee to say this is the way we want to prioritize these. Shawn?

DR. MCCANDLESS: Shawn McCandless, Committee member. I appreciate all of this, and to respond to Dr. Dorley's concern that we do need to probably make a decision today. One possibility would be that I think a lot of the issues that are being raised here, at least the ones I've raised, could be addressed by the language in the Chair's letter to the nominator that we don't necessary -- that doesn't necessarily have to be all included in the language around the, you know, around the vote to add the expedited review process, or to make that a part of the Committee's options.

So I would be comfortable with the few changes to the language of what's on the slides that we discussed earlier, voting on this today with the understanding that there will be a work group created to help draft the language that will go in the letter to the nominators that will assuage the concerns that have been raised.

I don't want to step on anybody's toes, HRSA's toes, or your toes, Ned, but that would be one solution to allow us to move forward today. DR. CALONGE: Okay. Yeah, I think we could do that, actually, Shawn thanks. Debra?

DR. FREEDENBERG: Yeah, I just had a question, a clarification about Shawn's comments about Committee members justifying why they voted the way they voted. Maybe I misunderstood what you said, but I would think that that would not be desirable. I'm not a Committee member, from those Committee members, because people are passionate about things that are being discussed, and things that are being proposed.

And I would think that would put a Committee member at an increased risk for getting say unpleasant feedback. If you have to justify exactly why you voted this way or that way rather than just the vote, so maybe I misunderstood what you were trying to say.

DR. MCCANDLESS: Ned, may I respond?

DR. CALONGE: Yeah, of course.

DR. MCCANDLESS: Shawn McCandless. Thank you, Debra, for that. This is probably a good opportunity to say that -- just to say after the meeting where we did not move Krabbe forward, I had the opportunity to interact with a number of people who were nominators or were strong advocates.

And I can say uniformly those people's behavior was totally appropriate and professional. I never felt any blowback from anyone about that, and this is an opportunity to publicly say, that I really appreciate the way that people handled that situation. The nominators and people who are strong advocates handled that.

But I think your concern is legitimate. My point though was not so much that I think we need to force people to list their reasons, you know, the concerns that they had in a public forum. It was really just to make the point that if they're complex decisions and each person will have probably multiple points that they're concerned about that they weigh together to impact their vote.

And that makes it impossible to send a letter to a nominator that says here's the two issues that the

Committee was concerned about that if you address them we'll be able to move forward because there's no way. And even if we did ask the Committee to list every concern they had, when we go back through the evidence review, they're probably going to be new concerns.

So my point was not that we should ask the Committee members to list in detail their specific concerns. It was to say that that would be impossible, and that we want to be really clear that there's no guarantee that the concerns listed in the Chair's letter are the only concerns that impacted how people voted. Thank you though for bringing that up.

And to our friends in the Krabbe community, thank you for your kindness and tempered response after what was clearly a frustrating decision made by this Committee.

DR. CALONGE: Thanks Shawn. Michele?

DR. CAGGANA: Michele Caggana, Committee. I would agree with Shawn, you know, to the facts that these words are very heated, and they come with a lot of emotion. And so along those lines I think it would be difficult to specifically articulate a reason for, or for not voting for something because it's complicated, and a lot of factors do go into this.

And I think part of the reason we have this

Committee is so that the Chair and staff who are involved can sort of take that, all that discussion and then distill it down to something that the nominators can simply respond to. And I think that that mechanism seems to work well.

And I just want to clarify and make sure. The expedited part of this process is really that once there is an evidence review and it turns back to the nominators for whatever reasons that are given in that letter, the expedited part of that is that they do not have to go back and start from scratch with a brand-new nomination package, correct?

So I just want to make sure I think some of the discussion seemed like people might not get that, and I want to make sure I'm getting it right. And that's they can just sort of start from that letter and then move forward. And in all honesty, by the time they get through, you know, follow the timing that is laid out, it's going to be quite a period of time.

It could be another year and a half before the final vote is made. Is that correct?

DR. CALONGE: It could be, or it could be faster. I just think it's important to recognize that it gets to kind of Jennifer's issue about what if there's a study that's just about to come out? And it

answers all of the questions or provides such an overwhelming sense of benefit overall.

Or conversely, a pilot study does more -- uncovers harms that were not yet anticipated. Just because it's been longer. It could take a quicker period of time. The other part of the expedited review is that even though review committees look back at their last review, when they start a review, they almost have to start over, so they say they have to pick a new end date for the research scan.

They bring in all the studies, and actually begin a whole new review. That's what we're trying to avoid, and we can do it faster because of that. Does that help? Yeah.

DR. CAGGANA: Absolutely, thank you.

DR. CALONGE: Ash?

DR. LAL: It's a process question. Thanks Ned. So once it's determined, in response to the Chair's letter, that a material change has been submitted then it goes back to the whole Committee to vote, I mean to expedited review. But the Committee does not discuss whether the change that has been submitted is a material change or not. That determination has already been made before it comes to the Committee vote, so that's one question.

And the second is if it could be a perception that the way the Committee works to send something back to evidence review for expedited consideration, the way the Committee votes, whether it's like a unanimous vote versus a split vote, could that in any way influence the working and the discussions of the evidence review? In short, either the Committee's involvement, before the response of the material change comes into expedited review, it doesn't mean that the whole Committee vote, that's the question.

DR. CALONGE: I really appreciate those questions. I'm going to take the last one first. So I don't think ERG takes the vote count into account when they do an evidence review and synthesis. So my answer to that would be that's not a concern. The other issue is that the Chair working with others makes the Chair's decision about whether or not there is a material change.

It's still up to the Committee to decide whether or not that change is compelling enough for them to vote to move the condition on for expedited review. So, what I'm trying to say is that that material change decision by the Chair is just whether or not to bring it back and request a discussion and vote on re-review. Then it's again, entirely under the Committee's purview,

whether or not that material change as determined by the Chair is sufficient to move the condition to an expedited review.

And we did it that way to not have so, to try to do it in a way that honored the desire to be responsive to the nominators in moving forward. And the idea is the Chair could ask for ERG or input from others in saying does this feel like a material change. Ultimately, the decision to review or not review belongs to the Committee. Jannine?

DR. CODY: Jannine Cody, Committee member. What would help me a lot to clarify this is a little bit more of a specific timeline, so how long does the Chair have to submit the letter, and who's supposed to do what with each one of these steps in what amount of time, since timeliness is a key to all this process.

DR. CALONGE: Yes. So I think there is a timeline for the Chair's letter. That's within two months. So that timeline has already been set. And then that puts the decision back in the hands of the nominators to decide whether or not they want to try for an expedited review, and to assemble the additional information.

I will tell you that we are responsive in having conversations with nominators in terms of

discussing the letter, in terms of discussing what new evidence might look like, what another material change could be. So we're really, we try to be responsive. But ultimately the timeframe for the submission for expedited review is sometime within a year, and there's no other timeline associated with that. It's up to the nominators.

I suppose we could build in a, or maybe we need to build in a two-month timeframe for the Chair to make a conclusion about is this a material change at a reasonable time.

DR. MCCANDLESS: There's a lot of back and forth.

DR. CALONGE: Yeah. We spent a lot of time talking about this, so it makes me nervous cutting it too short, and I don't want to make it too long either. Maybe we just say expeditiously, and we get some experience with it, and if that's too long, we set a narrower timeline. Melissa?

DR. PARISI: Yeah, I just wanted to echo what Jannine said in that, you know, for me seeing all the words is a little bit confusing. It would be great if we could put like a diagram, or some sort of a timeline together just to help us visualize what it is we're talking about with a few parameters around the time for

each process, realizing that there's going to be a bit of a range.

DR. CALONGE: I'm sure we can do that, and we'll try to provide that to you if not tonight, tomorrow. Chris.

DR. DORLEY: Chris Dorley, member. I just wanted a little bit clarity based on a point that Dr. Kwon had made regarding the bandwidth of the Evidence Review Group. And I was thinking about a scenario where the Evidence Review Group already has a disorder that they are trying to research to get it to the point for voting.

And then we as a group, you know, push this to evidence review for an expedited review. Does the expedited review then supersede the work that the Evidence Review Group is doing? Say they have one or two conditions that have been nominated that they are reviewing, to keep within this timeframe for bringing it up to the Committee for a vote. I just need some clarification.

DR. CALONGE: I think we anticipated that if there are two conditions that the Nomination and Prioritization Committee would set the priorities about what needs to go first, and what needs to go second. There just needs to be a vote within 9 months. It might

be a vote to allow more time because of a prioritization of another topic over one that's also in the queue.

I will say that the contractor has assured us that the ERG ended two nominations at once. I just got that message, so I wasn't trying to -- I didn't want to commit them to something, and now they've committed to us.

So we can clean this up. We can provide kind of a draft, I'm sorry a broad approach and a timeline that will be kind of a guiding -- how about a guidance document for moving forward in terms of finding and other issues.

And then include Shawn's comment on working on language in the Chair's letter that brings in all of the issues that might be associated with an expedited review going forward, being presented, and the topic still not being recommended to the RUSP. So that expectations about the process, and the outcome are being prejudged, and are clear.

So those are the two things, and then we answered the issue about bandwidth. So with those issues, are those things that the Committee needs to see before they're willing to do what I would call, as a conditional vote saying we'll address all these issues, or do you want to put this vote off until tomorrow?

And the best way to answer that would be for someone to make a motion.

DR. DORLEY: I motion to approve a conditional vote, Christine Dorley, Member.

DR. PHORNPHUTKUL: This is Chanika, I second.

DR. CALONGE: It has been moved and seconded that with the caveats I have provided, the additional information we have committed to providing the Committee before tomorrow, that we go ahead and approve the expedited review process. There are no other comments or questions at this point, I would like to call for a roll call vote.

COMMANDER MANNING: And please respond with a yes or a no, or whether you're abstaining. Michele Caggana?

DR. CAGGANA: Yes.

COMMANDER MANNING: Jannine Cody?

DR. CODY: Yes.

COMMANDER MANNING: Cynthia Hinton?

DR. HINTON: Yes.

COMMANDER MANNING: Christine Dorley?

DR. DORLEY: Yes.

COMMANDER MANNING: Paula Caposino?

DR. CAPOSINO: Yes.

COMMANDER MANNING: Jennifer Kwon?

DR. KWON: Yes.
COMMANDER MANNING: Ash Lal?
DR. LAL: Yes.
COMMANDER MANNING: Shawn McCandless?
DR. MCCANDLESS: Yes.
COMMANDER MANNING: Kamila Mistry?
DR. MISTRY: Yes.
COMMANDER MANNING: Melissa Parisi?
DR. PARISI: Yes.
COMMANDER MANNING: Chanika Phornphutkul?
DR. PHORNPHUTKUL: Yes.
COMMANDER MANNING: Michael Warren?
DR. WARREN: Yes.
COMMANDER MANNING: Ned Calonge?
DR. CALONGE: Yes. Unanimous vote. We've adopted with the changes as outlined expedited review process with a commitment to provide the Committee with the revised language in order, and a timeline draft order to be for review tomorrow.
And I appreciate that discussion. This is such a strong Committee in terms of seeing what's there, and then seeing what's not there, and anticipating unintended consequences, being very deliberate about the charge of the Committee, and the importance of what we do, both in terms of making decisions to add conditions,

or recommend adding conditions to the RUSP, and to decisions where we think we have insufficient information, too much uncertainty, or the call between harms and benefits is too close.

I hope to that the community that involves those most interested and affected by the conditions understand that this is an approach to try to be more centric around the concerns of the advocacy community, to be fair, and to be more timely if we can when the evidence allows.

With that I think we're coming to a close of day one. We've done great work. Okay, and I have one other item. I said we're coming to a close. I would like to ask Susan Tanksley to say a few words about our college who recently passed away, Bonnie Taft. Susan, can you come off mute and make a few comments?

DR. TANKSLEY: Yes. Thank you so much. Can you hear me okay Dr. Calonge?

DR. CALONGE: Yes.

DR. TANKSLEY: Great, thank you. And thank you so much for this opportunity to honor and to pay tribute to the life and the work of Bonita, better known as Bonnie Taft. Bonnie was a chemist and a public health laboratory leader. She earned a Ph.D. in toxicology from Johns Hopkins School of Public Health, and a Master

of Public Health in Environmental Health from Columbia University.

Her career included time as a medical technologist, a professor, a chemist and a public health lab manager and director. In her public health career Bonnie served as the technical director for the laboratory response network chemical threat programs, in both Florida and Michigan. She also served as Director of Newborn Screening in Michigan for two years, Florida for seven years, and in Georgia from April 2022 until her death in June of this year.

Bonnie's experience in public health environmental chemistry, and across state newborn screening programs, gave her very broad perspectives, which she shared as she served on the APHL Newborn Screening Committee, as well as the Laboratory Standards and Procedures Workgroup for this Committee.

Bonnie was also a strong advocate for, and a team player in continuity of operations. And we frequently shared texts alerting each other of concerns that might lead to the need for backup testing between Texas and Florida.

On a personal note, Bonnie's coworkers in Florida shared that she was an animal lover. She always had a few cats and dogs, and she would take in rescues

and give them the love that they deserved. She also volunteered at a local rescue shelter. She also liked fixing things around the house as much as she could on her own, and on weekends she'd go to local thrift stores to see what treasures she could find, and she found many.

Bonnie will be missed by all. Thank you so much for giving me this opportunity to share that with you.

DR. CALONGE: Thanks so much for your kind words. Bonnie made a tremendous contribution to newborn screening, and I know we will all miss her, and appreciate you sharing with us. That does bring us to close.

Tomorrow, I hope you're all looking forward to hearing a presentation on equity in newborn screen from Dr. Houtrow, and a Committee discussion.

We will have a vote tomorrow on whether to move Krabbe to expedited review. At this point I will ask the Committee to look for an email with what we promised you sometime before the start of the meeting tomorrow, and we will resume tomorrow morning promptly at 10:00 a.m. Eastern Time. Thank you all for your time today.

(Whereupon the meeting adjourned at 1:50 p.m.)