# ADVISORY COMMITTEE ON HERITABLE DISORDERS IN NEWBORNS AND CHILDREN

DAY 2

HRSA Headquarters

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ALSO PRESENT:

DR. ROBERT OSTRANDER

DR. DEBORA FREEDENBERG

DEAN SHUR

KIM TUMINELLO

MICHAEL WATSON

BRITTON RINK

JED MILLER

MELISSA PARISI

SUSAN TANKSLEY

CHRIS KUS

ADAM KANIS

JACKIE SEISMAN

SHEVAN DOLAN

CATE WALSH BUCKLEY

CAROL GREENE

# C O N T E N T S

## DAY 2


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P R O C E E D I N G S

[9:30 a.m.]

DR. JOSEPH BOCCHINI: I want to welcome everyone to day two of the May 2018 Advisory Committee on Heritable Disorders in Newborns and Children meeting. I want to thank everybody for all of the presentations and the discussion from yesterday and look forward to another very productive day.

We're going to start with roll call and so we'll go through committee members first. Kamila Mistry?

MS. KAMILA MISTRY: Here.

DR. JOSEPH BOCCHINI: Mei Baker?

MEI WANG BAKER, M.D.: Here.

JOSEPH A. BOCCHINI: Susan Berry?

SUSAN BERRY, M.D.: Here.

DR. JOSEPH BOCCHINI: I'm here. Jeff Brosco?

JEFFREY P. BROSCO, M.D.: Here

DR. JOSEPH BOCCHINI: Carla Cuthbert?

CARLA CUTHBERT: Here.

DR. JOSEPH BOCCHINI: Kellie Kelm?

MS. KELLIE KELM: Here.

DR. JOSEPH BOCCHINI: Joan Scott?

MS. JOAN SCOTT: Here.

DR. JOSEPH BOCCHINI: Dieter Matern?

DIETER MATERN, MD: Here.

DR. JOSEPH BOCCHINI: Cindy Powell?

CYNTHIA M. POWELL, M.D.: Here.

DR. JOSEPH BOCCHINI: Melissa Parisi?

DR. MELISSA PARISI: Here.

DR. JOSEPH BOCCHINI: I think Annamarie is still on her way. Scott Shone?

DR. SCOTT SHONE: Here.

DR. JOSEPH BOCCHINI: And Cathy Wicklund?

DR. CATHERINE WICKLUND: Here.

DR. JOSEPH BOCCHINI: And our DFO, Catherine Riley.

DR. CATHERINE RILEY: Here.

DR. JOSEPH BOCCHINI: For organizational representatives: Robert Ostrander?

DR. ROBERT OSTRANDER: Here.

DR. JOSEPH BOCCHINI: Debra Freedenburg?

DR. DEBRA FREEDENBERG: Here.

DR. JOSEPH BOCCHINI: Michael Watson?

DR. MICHAEL WATSON: Here.

DR. JOSEPH BOCCHINI: Britton Rink by Webcast.

DR. BRITTON RINK: Here.

DR. JOSEPH BOCCHINI: Jed Miller?

DR. JED MILLER: Here.

DR. JOSEPH BOCCHINI: Susan Tanksley?

DR. SUSAN TANKSLEY: Here.

DR. JOSEPH BOCCHINI: Chris Kus by Webcast.

DR. CHRIS KUS: Here.

DR. JOSEPH BOCCHINI: Adam Kanis by Webcast.

DR. ADAM KANIS: Here.

DR. JOSEPH BOCCHINI: Jackie Seisman?

DR. JACKIE SEISMAN: Here.

DR. JOSEPH BOCCHINI: Shevon Dolan by Webcast.

DR. SHEVON DOLAN: Here.

DR. JOSEPH BOCCHINI: Cate Walsh Vockley?

DR. CATE VOCKLEY: Here.

DR. JOSEPH BOCCHINI: And Carol Greene?

DR. CAROL GREENE: Here.

DR. JOSEPH BOCCHINI: Thank you. I think the one committee correspondence that I did not mention yesterday was a report to Congress. The committee members have provided edits to that and it's in its final form and should be submitted today.

I now want to recognize two members of the committee who are rotating off the committee; this is their last meeting and, both of them, we owe a special debt of gratitude because both of them are sort of the last of the people who were on the discretionary committee so that they have extended their term for a considerable period of time and provided additional service to this committee for a number of years.

First is Cathy Wicklund. Cathy -- clearly over the years her focus is really on the patient and on the family and in every discussion that we've had she has been a contributor to those discussions. She served as our counselor on occasions as well as those for the family and children and has been a very active participant

in a number of the important initiatives that have been taken up by this committee over the term of her tenure. She also has had a signature leadership role. She took on the co-leadership position of the education and training Workgroup and I think you've seen yesterday two of the results of that and clearly in a large measure it's because of her involvement, her organizational skills and her ability to kind of bring things to closure. So, for many of the accomplishments that have occurred because of her involvement we want to thank you go forward. Here is a small token of our gratitude for you to take with you today.

Next is Dieter Matern. Dieter has brought all of his skills as a physician, as a laboratorian, as a newborn screening advocate, as a researcher, to the fore in this committee. He has served this committee well, always willing to tackle the hardest projects, always willing to be a voice for things that are really important to be discussed that sometimes get left behind, so

he has really served this committee very well and we're going to miss all of the expertise that he provides the committee. He has served on the laboratory workgroup. He was the senior author on the report that this committee put together on succinylacetone to direct laboratories to understand that this was the primary market, the best market, to detect Tyrosinemia type I. He contributed to the pilot study report. He's had a lot of accomplishments while he's been a member of this committee. You heard him yesterday make a number of important comments as we discussed important issues in the committee.

So, again, Dieter we want to thank you for all of your contributions to this committee over the years and look forward to hearing from you again and again as we move forward with newborn screening. Thank you. I know both of you are pretty shy and often at a loss for words, but if you would like to say anything, I'm more than happy to give you this opportunity.

DR. DIETER MATERN: Thank you, Dr. Bocchini

and committee members and colleagues. It's certainly been a major honor to serve on this committee. I mentioned earlier to Debbie that growing up in Germany, the last thing that came to mind was that I would ever sit so close to an important person in a government, and particularly of the United States. I think that we all sitting here at the table have a significant responsibility to the populations that we serve. We're not here because of our own personal agenda; it's about the babies and the families.

As I mentioned yesterday, the committee's mission is about babies, children, who have heritable conditions, which is certainly important, but I think as this is a public health program you have to consider all of the public and also the one that is not affected with these conditions and you have to protect those as well. And again as a taxpayer I think we should all look for ways to not waste any money. So, with that again, thank you for allowing me to serve on

this committee and I will see if I can help you in the future in any way if you like it or not.

MS. CATHY WICKLUND: I should've went first so I didn't have to -- I agree with Dieter on all of his points. This has been a great honor to serve on this committee. I grew up in northern Wisconsin, not Germany, but still never thought I would be sitting here. Maybe it's just northern Wisconsin. It is really truly an honor to be on this committee. It's probably been the hardest committee I've ever sat on, I have to say. God, I'm getting verklempt. These decisions I think are just so critical and require so much time and attention and energy, and I commend everybody who puts the energy into this.

As Scott said after the last meeting -- it was your first meeting -- that it was probably the most emotional meeting that he's ever been to and I completely agree with that but I think it's because we're taking this very seriously, it's really important, and I just want to commend everybody in this room and everybody a part of

this process for all the energy and time they put into it. So, thank you so much.

DR. JOSEPH BOCCHINI: Thank you both again for those comments. So, next on the agenda is an update on newborn screening pilot studies for GAMT deficiency. GAMT has previously been nominated for addition to the rest but after consideration of the nomination, the committee voted not to move it forward for full evidence review due to the lack of available pilot study data. The committee wants to continue to track efforts made in the field and has asked Dr. Carla Cuthbert, from the CDC, to provide us with an update on where the field is related to GAMT. In particular, we wanted to learn about current pilot studies in the United States and in other countries as well. Dr. Cuthbert is the chief of the newborn screening molecular biology branch in the division of laboratory sciences at the Centers for Disease Control and Prevention and has been in that position since December of 2009 and serves as an ex-officio CDC representative to

this committee. So, Carla, thank you.

DR. CARLA CUTHBERT: -- [missing audio] -- the enzymes involved in biosynthetic pathway for creatine. The first step involves a transfer of the amandine group from argentine to glycine, to create guanidinoacetate, and that occurs with the enzyme arginine glycine aminidinotransferase and the next step is where GAMT has its role in methylating guanidinoacetates from creatine. Now, half of the creatine in your body is not just synthesized. You get it from dietary sources: Meat and fish primarily. And any circulating creatine is picked up by your tissues with the creatine transporter. When there is a deficiency or defect in the GAMT enzyme there is a decrease in the amount of creatine, and so creatine deficiency occurs with an accumulation of the neurotoxic guanidinoacetate, so the treatment rationale is to restore the creatine pool.

So, to restore that creatine pool here you want to supplement with creatine in high doses

and s-adenosylmethionine is also supplemented to reduce the guanidinoacetate that accumulates. You want to supplement with Ornithine, reduce the amount of arginine, and give sodium benzoate to bind up the glycine which gets converted to hippurate and that gets excreted in your urine.

Clinical presentation of these patients reflects the importance of creatine in the central nervous system. Symptoms generally occur during infancy and early childhood and include cognitive impairment, development and speech delays, muscle hypotonia, seizures, movement disorders and behavioral abnormalities.

The treatment outcomes when patients are caught early: Symptomatic patients improve, the earlier you treat the better the impact and the outcome and any sort of treatment interruption they found results -- can result in irreversible damage.

In terms of the biochemical markers that are of interest, the key biomarkers that we would be looking at during newborn screening would be

guanidinoacetate which is elevated in both plasma and in the urine, and so that forms the basis of a biochemical test, once you identify these patients as well. Creatine, of course, is decreased in the plasma. It could be normal or decreased in the urine. Creatinine is also looked at and that could either be decreased or normal in both plasma and urine.

For the newborn screening programs that are evaluating GAMT deficiency, generally the principles for testing involve the following: The primary biochemical assay, or the primary newborn screening assay, generally involves fluid injection and generally what they do is they multiplex the guanidinoacetate, and some programs include creatine as well; they multiplex guanidinoacetate together with the acylcarnitine amino acid assay. Currently there is no FDA-approved test -- or sorry, FDA-approved kit -- that’s available for programs and any program that is interested or thinking about doing this would have to modify a laboratory-developed test

to include these markers.

As a second tier test, we would introduce liquid chromatography into the test and that's done with LC-MS/MS, and, again, by incorporating a guanidinoacetate, creatine -- some programs may include creatine as well. That is sometimes done as a stand-alone test or it could be multiplexed with other second-tier markers. Some programs may also choose to do Sanger sequencing once they have had a sample that screens positive in both of these tests.

So, in terms of the nomination for GAMT deficiency, the nominator was Nicola Longo. It was co-sponsored by Marzia Pasquali, both from the University of Utah and the advocate organization is the Association for Creatine Deficiencies.

As part of the discussion and deliberation by the ACHDNC. There was a natural history that was well understood, treatment was found to be very similar to many classic cases of metabolism. The outcomes, of course, were best when started

early. The newborn screening assay for this could be multiplexed with existing tests in the form of a laboratory-developed test and the newborn screening strategy had high sensitivity and was found to have a low false positive rate. On the other side, what was found to be lacking or found to be needing more work, was that the understanding of the natural history was just based on 110 patients worldwide; there was no real agreed-upon strategy for treatment, metabolic control must be strict; there was no FDA-approved newborn screening kit or test for either newborn screening or a diagnostic assay, and, of course, the biggest challenge was that there was no patient identified through a newborn screening program.

So, as part of the very vigorous discussions, this was the recommendation from the nomination committee to the SACDNC, that we not initiate external evidence review at this point because no case had been identified prospectively through newborn screening which would certainly hamper

any kind of evidence review and treatment guidelines we were hoping that they would continue to be in development, they had not yet been finalized. So, the recommendation was the proponents work toward formalizing treatment guidelines and encouraged continuation of newborn screening for GAMT deficiency in both Utah, Australia and our friends in British Columbia in Canada and to report as soon as possible when any patient had been identified.

So, right now I'm just going to -- I had some conversations with some of the newborn screening programs, the three main ones, to just find out where they were and whether or not they'd identified any patient and just see how screening was actually going. Again, these are not actual pilots, these are programs that have GAMT deficiency screening as part of their routine screening list.

So, from the State of Victoria in Australia, I was able to speak to Dr. James Pitt, and he gave me a bit of an update about how things were

going in Australia. He put out an update in 2014, and I just wanted to remind you of that, that between April of 2002 and 2013, they had screened for over 770,000 newborns, and of those screened, they found that 127 screened positive for elevated guanidinoacetate. Repeat testing resulted in three newborns still having an increased GAA, and follow-up testing showed that these were false positives and this was evidenced through evaluation of urine levels for guanidinoacetate, creatine and Creatinine and the pattern in the concentrations in the urine were not found to be consistent with GAMT deficiency.

In terms of where they were now, we estimated that the number of newborns screened from the time that they started in April 2002 to about April 2018, it would just be over one million newborns who would have been screened and, again, he said that the numbers were pretty much very similar to what was published, his experience was very similar. To date, there have been no true positive cases identified. Specifically, he

wanted to point out that he was not aware of any false negatives. He said that he was reasonably confident that if there was a positive case of GAMT deficiency, that that newborn would have been picked up symptomatically and, since the newborn screening program is down the hall from the biochemical genetics laboratory, he oversees both of these programs, he would certainly know whether or not any case was missed.

So, again, GAMT he said in this particular population seems to be very rare. He pointed out that it was very fortuitous that he decided to add this biomarker in 2002 when he was setting up this program. As a biochemical geneticist he was just looking around at the sorts of markers he thought that would be helpful, and chose to put this in, and so it continues to run in the background and, yes, they will continue to screen for GAMT deficiency.

Okay, so that's the State of Victoria in Australia. I also spoke to Graham Sinclair, in British Columbia, Canada and they started

population-wide screening about ten years after our friends in Australia started screening. So, they started in 2012 in September. They had a pilot that ran for three years and they screened all of the infants in B.C. during that period of time. Currently, as I said, newborn screening for GAMT deficiency is part of a routine test in British Columbia. The screening algorithm I have depicted here just so you can see it; I know that it shows up very lightly, so you may not be able to distinguish everything, but essentially, as I said in a previous slide, the first tier involves just incorporation of the guanidinoacetate marker into the acylcarnitine amino acid assay and that's run if there's an elevation that exceeds 3.5 micromolar. It gets run as a second tier test with LC-MS/MS and that’s coupled to an MS/UD second tier assay that also includes markers for GAA. If there is an elevation here, then they actually do sequencing of the exons for the GAMT gene, and if they find one or more pathogenic variant, they call that a screen-positive;

otherwise, they would call it a screen-negative.

So, they identified for the time that they were screening from September of 2012 to April of this year, they've identified just under 250,000 -- or screened 250,000 newborns. Out of those newborns they identified two screen-positive cases. Both were found to be false positive when they investigated the urine for key markers. So, the number of true positives that they've identified still remain zero. They are not aware of any false negatives. In British Columbia as well, the biochemical genetics laboratory is also in the same building as the newborn screening laboratory so they would be aware of any cases that they may have missed and would have picked up clinically.

In Utah, newborn GAMT deficiency is part of their routine screen. As of the end of February this year, they have screened for 139,000 and they have identified two false positives. Both were NICU babies, and again, no false negatives identified. There's one children's hospital and

one metabolic center and, again, any symptomatic case would have been picked up and their program would've been notified and to date, no true positive case has been identified.

So, those are all of the programs that I'm aware of that are actively engaged in screening. The state of Michigan, has received approval after, really, a journey, and they're excited about being the second state in the U.S. to begin screening. They expect that screening will begin sometime later in 2018, and, CDC is going to be ready to help them if they need any assistance in bringing on that particular test.

So, as far as our program at CDC goes, we are available to provide technical assistance, if needed, to any state program that is interested in bringing on this test. We can help with method development, any sort of validation, implementation of testing, and as we do with every other condition, provide assistance with data review conference calls, on-site visits and so on.

Two weeks ago, we had a training course in mass spectrometry and all of the students -- I think that there were ten or twelve states represented, and they all learned how to do screening for GAMT deficiency as well. That was included as one of the markers that they were trained on.

We published a method non-derivatized assay to detect GAA and creatine. A derivatized assay had been previously published and we wanted to make sure any program who was interested at least had an approach to actually do so.

With respect to our materials, our quality assurance materials, we have materials that are enriched with guanidinoacetic acid so any program that just wants materials that they can work with, that’s available to them. Currently there are eight laboratories world-wide participating in our QC program and beginning in 2019, we’re going to be incorporating these two markers for GAMT deficiency into the aminoacetylcarnitine referenced PT materials, so if you are a program

and you are screening for GAMT deficiency, you would be able to identify the markers appropriately because they are integrated within that panel already.

I think that that's it, so GAMT deficiency remains a serious medical condition but seems to be very rare in the populations that are currently screening for them. Treatment follows the same principle as many of the other RUSP conditions. Approximately 1.4 million newborns have been screened in the newborn screening programs in Victoria, British Columbia, and in Utah. To date there have been no newborns that have been pre-symptomatically identified through these screening programs.

Additional programs are considering the addition of GAMT deficiency to their newborn screening panel and the CDC is available to provide any sort of technical support for programs who seek to implement screening for GAMT deficiency. That’s it, thank you.

DR. JOSEPH BOCCHINI: Thank you, Carla, for

this excellent review. Have you had any additional states inquire about the possibility of including GAMT?

DR. CARLA CUTHBERT: Not to me personally, although I understand, and I haven't been able to verify, that there may be one or two others that are thinking about it, so I think that Georgia might be interested as well, and there may be one or two others.

DR. JOSEPH BOCCHINI: Let's open the questions and comments from the members of the committee. DIETER?

DR. DIETER MATERN: Thanks, Carla. Just a couple of things. One, when we discussed GAMT here, at least the second time, we had a longer discussion about the one case that actually was picked up by newborn screening in Australia in a kind of odd pilot study, but that patient then kind of, the ball was dropped during the follow-up because they didn't think it was a true positive and then the patient presented later with symptoms, so we felt it was not a pilot

study that showed any benefit for the patient. So, I think the screening test seems to work.

Now, the other thing, it's great that you guys are providing the materials already and the training but I would really recommend that you add Creatinine to your panel. We use it primarily as a second tier test for Pompe screening so any state, like Michigan, they could stop sending us the second tier for POMPE disease if they did Creatinine in-house and it wouldn't even be a second tier test at that point because if you measure creatine and Creatinine in every baby anyway, along with GAA activity, the second tier test is already built in. So, it would help a lot in follow-up in getting a lot of anxiety out of it, and it also might help you identify at screening whether a baby has the infantile onset Pompe disease or later onset.

DR. CARLA CUTHBERT: Thank you, DIETER. I was just mentioning that to _____ and _____ has already agreed that we're going to be adding creatine and Creatinine to the panel so that will

be included as well. Thank you for that.

DR. JOSEPH BOCCHINI: Cindy?

DR. CYNTHIA POWELL: Are there any estimates as to the additional cost per infant screened from any of the programs that are currently running this?

DR. CARLA CUTHBERT: I don't have any numbers that I can offer you. I'm sorry.

DR. JED MILLER: Cynthia's question raises an important idea and what's sort of curious about this is usually when we start doing population-based screening we find lots of cases that we didn't know we would find, and many of them are variants, and so on, so to now have 1.4 million and not have a single case suggests that it's really hard to find, of course. I'll point out that historically PKU kind of got lucky because we found a case almost right away and it could also have been that you went 50 or 60 or 90,000 cases before you found one, so just because we haven't found one doesn't mean the incidence is that low.

But, again, it raises the issue of how much money can we put into a screening test that maybe one in a million children in many states may never see, and it raises again what we'll probably get to a little bit later about the public health implications, not just for the health system but health implications of what we should do with our limited resources. Thank you.

DR. MELISSA PARISI: So, based on the cases that have been ascertained thus far, is there any knowledge about any particular populations that might have a higher prevalence? I'm just wondering if we're screening the wrong people or the wrong ethnic groups or if there is any evidence that would suggest that there might be some groups that might be -- there might be a higher chance and would take fewer than 1.4 million?

DR. CARLA CUTHBERT: Well, I can't speak for Marzia Pasquali, but I know that she feels that they're probably getting close possibly. Again, it's not something that you wish for so I just

need to be very careful in terms of how we temper this, but, again, you know, there might be a population within Utah that may allow for identification of newborns, but, again, that's hard to say. I can't speak to that.

DR. JED MILLER: So from a diagnostics lab perspective, we -- it's not a high volume assay that we do, so people probably don't think about it often enough, maybe, but certainly we also don't have a lot of positives, and I'm not aware of any ethnic specifics. Now back to the cost. The cost is basically adding a couple internal standards to your aminoacinacytel carnitine so in your sample prep there's no difference when you measure aminoacinacytel carnitines already, to it's just reagent cost, the false positive rate apparently is very low, so I don't think there's a lot of follow-up cost that is unnecessary either and, again, any state that screens for the full RUSP, and therefore, for Pompe disease, would benefit and save money in the follow-up of Pompe, which they can easily recapture the money

and put the investment into _____ screening.

DR. CARLA CUTHBERT: Marzia indicated that there is a higher level of false positives in the NICU population and I understand both from Marzia and from Graham in Vancouver, that it's really, really helpful to have the second tier tests, so, you know, you really don't want to have the first tier test operating alone, you really want to include the LC-MS/MS to reduce that number of false positives as well. And, again, just to remind people that if you have an FDA-approved kit that does not have the test, it becomes a bit of a challenge, so if they are planning on bringing a test along they'd have to modify an FDA-approved kit and then be responsible for doing that validation themselves, so just to be mindful of that. DIETER?

DR. DIETER MATERN: Going out on my usual limb, so there's already a clear application for diagnostic labs and there is actually the paper that describes clear quite in detail and how it works when it comes to the co-variates, so

there's no newborn screening data as far as I know that has been captured from either Utah or British Columbia. Probably something they might want to look at because the second tier test may not be needed if you include the covariates of birth weight and everything else that you have on a screening card.

DR. JOSEPH BOCCHINI: Are there any comments or questions from the Org reps?

DR. ROBERT OSTRANDER: Bob Ostrander, AFP. I just want to go back to the very beginning couple of slides where you were talking about the background to be sure that it’s clear in my mind, and everybody’s mind, and my understanding is that the treatment for this is, number one, fairly clearly effective and, number two, fairly low risk, but what I wasn’t clear on is whether, other than protein restriction and creatine supplements, whether these patients need special amino acid modified foods or if they could get away with just a protein restriction.

The reason I’m bringing this up is because

although it’s a little past your subject of the pilot studies, it certainly will go toward the evidence review and I think it's helpful for us to start to think about this globally, and again, have a sense as to harms and costs versus benefits, even for rare conditions. So, if folks have the answer to those things or could help me understand it a little better, I’d appreciate it.

DR. CARLA CUTHBERT: I don't have very much more to add apart from what was there. I know that there was a paper that described the experience of those who were treating and managing these patients, but at the end they came up with principles but no defined series of guidelines, so I would defer to any physician who has handled GAMT deficiency patients.

DR. CAROL GREEN: Carol Green, SIMD. I have not cared for a patient yet, or found one. I’m one of the people who sends the samples. It is my understanding that you can treat with just the creatine; the diet does give you better outcomes for some of the forms, so I don't know that

there's enough experience to say how hard that's going to be but, I've got to say it doesn't seem hard at all, looking at what's being required, and it's one of those where, unlike some of our disorders, you have to be incredibly strict about the diet, or people end up in the ICU and this is one where I think the diet is important, but if you're not as careful about it you're still getting a lot of benefit from the treatment is my understanding. And I'm not so sure we lack guidelines. I mean, there are things where somebody would hand me a patient and I would look and say, "what do I do now?" and this is one where if we don't have formal guidelines that have gone through a review process, I still will feel, once I get my first case, I'm not going to have any trouble knowing what to do.

MS. DEBBIE FRIEDENBERG: Debbie Friedenberg, AAP. I have taken care of two patients with GAMT deficiency, and it goes back a little ways, and they were pretty easy to manage compared to some of the other inborn errors in metabolism that we

were managing, so I would think that would be much of a challenge for the family and the cost of treatment compared to some of the other conditions on the RUSP is pretty minor compared to some of the other interventions we do for kids.

DR. JOSEPH BOCCHINI: Thank you. Any other questions or comments? How about from individuals that are on the webcast on the phone? Hearing none, Carla, I thank you for the presentation and the update and we look forward to continuing merging data. Thank you.

So, next on the agenda is public comment. So, just as a reminder, when you are speaking, either here in person, or on the phone line, please state your first and last name each time, and indicate if you have any conflicts.

So, the first person who will make a public comment today is Mr. Dean Shur. Mr. Shur is President of the MLD Foundation and he'll be providing a report and from the round table discussion that he and other stakeholders have

held and host to discuss the RUSP. Mr. Shur.

MR. DEAN SHUR: Good morning. Thank you, Mr. Chairman, and the committee and those watching. Actually our scope is a little broader than just the RUSP, in spite of the name, as is consistent with the committee. This was our fifth meeting of the RUSP roundtable. We typically meet the day before this meeting since many of you are in town. And I just want to repeat, because I haven't said this in a while, the purpose is to create an open and well-informed space to share perspectives and insights from key experts in the newborn screening space, expand the common knowledge base, and identify opportunities for both coalition-building and collaboration across sectors to innovate and accelerate programs to make newborn screening more robust and equitable. So that's a big mouthful. Really what we're doing is bringing together a whole variety of different perspectives from the newborn screening ecosystem, and we are not thinking outside of the box, we are kind of thinking and talking as if

there was no box. We're in a time where technology, where medical science, both the basic science and understanding, as well as the clinical care and therapies are really changing dramatically. Fifty years of history with newborn screening, we're thrilled with where we are. But what if there was no box? So, that's where our conversations lead us.

On Tuesday, we had advocacy, state and federal public health, Pharma, technology and services and a payer was present as well, so, again, a wide variety of participants and great discussion. Some of the things that we touched on were definition and application of benefit, the words and the meanings of therapy, cure and clinical care and where does that fit and/or be a result of what happens in newborn screening, the Wilson-Younger criteria which is the root of most newborn screening programs, international newborn screening, molecular screening and diagnostics, state and federal RUSP disconnect. The great work that you all do ends up being, in many

cases, repeated or questioned by some of the state programs, and I know, Dr. Bocchini, you talked about how in some of the future discussions you're going to be looking into that, but it's really important that the states be able to leverage the benefit of the great work that's done by you and particularly by the work on the review committee.

I just wanted to say one comment that was just so profound, or repeat one comment. It says: "I need to find babies in some way different than having their older sibling die first." And, you know, we just talked about that here: Screening 1.4 million and not finding any cases. It's kind of a chicken and the egg situation, and sometimes the chicken and the egg don't match up as we've seen in just the data from a moment ago. So, this challenge of how do we validate the screens and identify the public health programs to support them when it's so challenging to put pilot studies in place and to go through that process, so it's that chicken and

egg kind of circular challenge. So, we're dealing with those kind of topics. Many of you have been invited. We have a changing attendance at the meetings which is awesome. There's consistency which is good, and just encourage you if you want to learn more and you're here today, come see me. Newborn Screening dot US is the website where we are posting updates.

Our next focus is to be better about sharing data out and so we agreed yesterday, or day before yesterday, to start to develop white papers, be focused in some of our discussions, develop white papers with pros and cons and maybe some recommendations, but to help you and committees and groups like you that are doing great work to kind of invigorate discussions and to be creative and help guide us five-ten years down the road as to where the programs are.

I also wanted to mention very briefly a second initiative which is not MLD Foundation based, which is an initiative that I've started called Rare Army, and one of the legs of Rare

Army is a policy initiative and we know that Newborn Screening Saves Lives Act is going to be up for reauthorization next year. Certainly at the state levels there are a lot of policy issues related to newborn screening. There's regulatory issues and so on and what we're doing is taking existing policy, good stuff that other people are putting together, and helping disseminate that down so that we can get good, solid public education, engagement and then involvement, so that the things that we need -- the appropriations, the legislation, the regulatory feedback -- can help move forward the good work that you all are doing. Thank you very much.

DR. JOSEPH BOCCHINI: Thank you, Dean, and thank you for giving a much better explanation of your scope of work than I did. Thank you. Our second public comment will be given by Ms. Heidi Wallace. Ms. Wallace is the vice president of the Association of Creatine Deficiencies and will be offering comments on GAMT. Thank you for being here.

MS. HEIDI WALLACE: Thank you so much for having me. I really appreciate it and it's an honor to be here and to have a few minutes of your time. I am with the Association for Creatine Deficiencies, as Dr. Bocchini mentioned, and I also am the parent of two children with GAMT deficiency, and listening to everything before I am now feeling like I need to re-plan my entire presentation. So hopefully I answer the questions that came up but if there are more questions, please let me know. Someone mentioned the cost of testing. Marzia Pasquali, has spoken of it being around under fifty cents per child for the reagents, factoring in secondary testing when needed, it's still under a dollar, so, hopefully, you'll leave this meeting going 'this is pretty easy to screen for.' As far as the diet and metabolic formulas or foods, now my children are on no metabolic formulas. Early on the treatment has evolved a little thanks to our children who they experiment with and see how it goes, and diet has really come to be not a big

issue. Even when it was controlled it was pretty moderate. My son, when he was three years old, could have 16 grams of protein which is a pretty decent amount of protein, but now it's not a focus and what they measure to see how your child is doing is their creatine, are we giving them enough creatine that have a good supply constantly, and their GAA and is it being kept low because it is neurotoxic at a certain level. We don't know what that level is quite yet because it's a rare disease, but one thing I wanted to mention was that with the newborn screening blood spots that have been found from children with GAMT, they've gone back and pulled them -- the GA level has been seven and higher and you and I, we would all have about a one, so it's a really big marker. I know there are the NICU children that throw things off a little, but even with that if you notice the false positive rate was 0.0002, I think. So, very, very reliable testing.

I want to show you my children and tell you

just a little bit about them. This is Samantha. She was diagnosed with GAMT at five and she had had developmental delays for years, she had an autism diagnosis that just didn't quite fit. Teacher after teacher said, "there's something, you know, she doesn't fit the autism bill," and she started to have seizures. We got lucky and a neurologist said, "let's do spectroscopy while we're looking for any possible tumors or anything," and they saw that there was not a creatine peak. So, she has been treated for nine years and she is intellectually disabled. She will not recover. She's improved. It has helped her health to some degree but she continues to have recurrent seizures and she will need care for her whole life. And, when we talk about the price of these tests, we talk about the price of treatment, I just strongly want everyone here to realize how affordable the testing is for this, how affordable the treatment is, and the cost of a lost life. If the higher -- sorry, the lower incidence rate of one in 250,000 were to be true

and it were a dollar a child, I would pay that ten times over to go back in time and save this child. And that probably only matters to me, but taxpayers, healthcare system -- what is the cost of an intellectually disabled individual? School systems. It's through the roof. I did see a report from the CDC at one time and it was in the tens of millions, so I have a hard time accepting that money is an issue on adopting GAMT.

Now, six years ago, my son was born and we knew we had a one in four chance of having a child with GAMT and he was diagnosed a couple of days after birth. He started treatment. This is his kindergarten picture, he’s graduating in a couple of weeks, and this kid is just, amazing. There's not a single beat he's missed, he is in no therapies, he is in the higher level kindergarten class. He is doing phenomenal. And his diet is relaxed. He takes his creatine, ornithine and sodium benzoate three times a day. The cost of each treatment each dose a day is around .30, so we're talking about taking tens of

millions of dollars in costs to society and instead spending a few cents and treating a kid. This is what he takes. Mom makes it. I buy the supplements over the counter, mix them up and draw them into three syringes and he takes them through his mouth and goes about his day. He knows he takes creatine; he understands it, tells his friends and of all the disorders, we feel fortunate to be living with this disorder. It's the poster child for newborn screening. I tell people where I'm going and what I'm speaking about and just give them a snapshot explanation and no one can understand why this is not on newborn screening. I can't understand. And, after listening to Carla explain that the CDC is being so helpful and forward thinking, which we really appreciate the support, that training of people of how to screen for GAMT tells me you know you can screen for GAMT, yet the reason we were turned down two years ago was because there wasn't evidence we could screen for GAMT, but now we're saying, "here, we'll show you how to do

it." We all know how to do it. It's really simple. This is not CH, we're not going to miss children, the cutoff levels aren't scary, it's very straightforward and treatment is cheap, effective as can be. I think that's all I've got. If anybody has any questions, I'd love to answer them.

DR. JOSEPH BOCCHINI: Thank you very much for your presentation. Thank you. Next, we have Ms. Kim Tuminello. Ms. Tuminello is the Director of Advocacy for the Association for Creatine Deficiencies. She will also be providing comments on GAMT. Thank you.

MS. KIM TUMINELLO: Hi, good morning. Thank you for the opportunity to be back and speak with you all. My name is Kim Tuminello and I am the cofounder of Association for Creatine Deficiencies. I'm here speaking on the behalf of all the families and children that have been diagnosed with GAMT. I'm currently serving as the Director of Advocacy and I personally began my quest to get GAMT on newborn screening in 2006

when I first learned that my son had been diagnosed with this severe, ultra-rare, metabolic disorder.

At the time, Ty was already ten months old and could not sit up. He could not play like other babies and he was dangerously underweight. He had been diagnosed with global developmental delay by the time he was seven months old, but we now know that GAMT could have easily been detected by his newborn blood spot and effectively and safely treated. I also have a daughter, eight-year-old, who was treated from birth and, like Heidi’s Louie, she has had completely normal development with no therapy needed.

These days I spend much of my free time talking to other parents that have just learned about their own children’s heartbreaking and preventable tragedy. I’ve told them about our own personal struggles with our son: The years and years and years of physical therapy, occupational therapy, speech therapy and then

some. I attend conferences such as ACMG, DIA, CNS, SIMD, Gatlinburg, the Global Gene Summit, and many others. I talk about GAMT and what said here two years ago and what our own doctor, Bruce Barshop in San Diego called the term “the no brainer” of a disease to have on newborn screening. When I was here exactly two years ago for the first time, many of you may know or remember that GAMT lost by just one vote. It was a split of six to seven to be moved forward to the Evidence Review Board. There had been a fierce debate that day on the vote for GAMT, about whether a new requirement should be that to get added to the RUSP there should be one prospective find during a newborn screen. It was argued that this was another roadblock of getting GAMT and other treatable, ultra-rare disorders from being included on the RUSP.

Since then, I've had the opportunity to meet many of you, and some of you have said that this is a no brainer of a disease for RUSP, but I’ve also been told that GAMT could be paying the

price of not being added because of some of the previously approved diseases that are more complicated, costly, and treatment may or may not be as effective. And I get it. We all understand that there needs to be a process, requirements, protocol, but I want to simply remind you that we are talking about lives, the most innocent lives that you, this committee, could save. We are talking about infant, newborn babies, children and their families. And who knows? Maybe one will show up in Utah or next year when Michigan and New York start their testing. Or maybe they won't, maybe it will be like Australia who have already tested over a million babies and still have not had a positive.

And then there's Austria. They found one. Had they just done a confirmatory test with blood, instead of with urine, on that newborn baby years ago, I guess we would have had that one prospective find that we need to satisfy that requirement. But can't it be a lesson learned? We know that it can be detected in a newborn

blood spot and needs to be confirmed with blood. That could be written and published in a GAMT newborn screening protocol today and never questioned again.

These past two years we've done what you've told us to do: Go and get it on newborn screening in other states. I personally have had the chance to go to Georgia to talk to them about adding GAMT also. I asked a fellow mom, Glenda, just one of our many community members, and her 18-year-old daughter, Carly, to come tell their story. Carly was not diagnosed until she was nine years old. At the time of Carly’s diagnosis she was having almost 200 seizures per day. She couldn’t walk and she had never spoken a word. When her mom, Glenda, got the diagnosis and started that simple treatment of a creatine cocktail three times a day, Carly immediately stopped having seizures. Carly is the sweetest girl. She absolutely adores her mom and smiles at her all the time. But Carly cannot speak a single word. She never has and she probably

never will. Not one word. And at times she has to get around with her wheelchair and will be cared for for the rest of her life and her mom will never hear the words, “I love you.” But, all of this could have been avoided. It’s preventable. But we have to test for it. This test that costs a state lab less than a dollar could have saved this poor girl and her family this ridiculously unnecessary tragedy. And Carly is not the only one. There are dozens out there like this. Who knows how many? Safe, affordable, effective treatment: GAMT has that. This is the no brainer.

This past year, Quest Diagnostics has started testing for elevated guanidinoacetate and in just the last two months they have found three cases of GAMT.

And we have new families who are added to our community all the time. So, realistically, by the time this committee meets again, next quarter in August, on average there could be another four to eight families that learn of this devastating

diagnosis of lifelong intellectual disabilities, seizures, wheelchairs, nonverbal children and all of it could have been prevented with a safe, affordable, and effective treatment. If we were to sit around and debate GAMT for another two years, there will be as many as 20 to 60 families who will find out that they are too late in finding out the diagnosis of their child, their, grandchild or their sister or brother. Why? Why are we preventing screening from happening? How much longer can we justify being a gatekeeper versus a committee that can make the ethical and moral judgment to test and treat.

This last week I received something from the Becker's Hospital Review E-Weekly and it gives a viewpoint, how diagnostic test delays are harming babies and families. They gave seven points to this article and I'll summarize them for you:

1. Currently, newborn screening programs monitor for 60 rare and genetic conditions but we all know that there are 350 that are treatable.

2. Despite the significance of these

programs, there's a lack of comprehensive data on program adoption since they are managed by individual states.

3. After investigating newborn screening programs, the authors express concern of how testing delays harm patients, their families, and health care providers.

4. The authors noted that complex and time-consuming process of developing a reliable and economically viable screening test, which GAMT already has, and must be reviewed by various committee members and the Secretary of Health And Human Services before being approved in the recommended uniform screening panel.

5. Their research indicates that it typically takes ten years or more before a new screening test reaches all U.S. newborns, and it didn't say this, but I would guess that, again, it would be after this committee would approve that newborn screening.

6. Additionally, the authors argue that families who are affected by rare diseases not

included in screening panels, must seek out testing on their own and often lack the resources necessary to get a diagnosis. They quote: "It is inefficient and arguably cruel, to place responsibility for advancing screening tests on affected families and their physicians who are grappling with the hard realities of caring for children with often devastating and poorly understood disease.

7. And the final point, number seven, to address this issue, the authors offered these suggestion: Raising awareness among families, physicians and advocacy groups of diseases that could be included in the newborn screening panel, increasing funding for test development and improvement, and petitioning advisory committee quickly, even if the Advisory Committee on Heritable Disorders in Newborns and Children rejects a new test.

What this says to me and everyone else is that it is up to you, the ACHDNC, and the voting members, that you are capable of saving these

lives right now. This article could've started and stopped with the last point. It is up to the ACHDNC. It is up to you to not put these children and families through this, as they said, cruel process.

This seems like it is coming down to something else. What is really the problem here with adding GAMT? I've talked to physicians, researchers, state labs, pharmaceutical executives and business and community leaders and no one thinks this makes any sense and that we have a moral obligation to test for it. GAMT is the perfect candidate for newborn screening. It is the no brainer. I have a question: If we knew there was going to be a mass shooting in the next two years and anywhere between 20 to 64 children and their families would lose their lives as they know it, wouldn't we do everything in our power to stop it?

We all know that Perkin Elmer also plays a big role in the state's ability to be able to test. We had a meeting with them about a year

ago. We talked about GAMT, and the fact that their latest test kit had come out and GAMT wasn't on it. Why? I'm sure it's because it cost money. It wasn't required, or even asked of them. Why not? States have figured out that they can do their own GAMT testing without Perkin Elmer kit for less than a dollar.

I am sure Perkin Elmer can get it done. I'm sure there's another profit company that could do it. But, we know that it's not just because Perkin Elmer doesn't have it on their newborn screening kit that we aren't testing for it. I'm sure if GAMT was added to the RUSP they would figure it out.

It has been said that it is the perfect disease for newborn screening and the committee wants to see it added. So, I say do it. I say put it up for another vote. Let's get it to the evidence review board. Let them do their job. GAMT has a proven, easily detectable newborn screen. It has a safe, affordable and effective treatment that could save a life destined to be

full of disabilities and their and their family's suffering. It is my job to advocate for this disease, but it is your job to vote it through.

I would like each of you to consider the good you could do as a committee, restore the faith of the public and help save the lives of these children. GAMT really is a no-brainer. Thank you for listening to me. Thank you for giving me the opportunity to be here. I appreciate all of you. Thank you.

DR. JOSEPH BOCCHINI: Thank you very much. Thank you, we appreciate your presentation and advocacy. Next, we have Dr. Mariza Pasquali, Professor of Pathology, Medical Director and Section Chief of Biochemical Genetics, Supplemental Newborn Screening, at the University of Utah School of Medicine. Dr. Pasquali was one of the experts on the nominating team for the GAMT nomination. I think we have her on the telephone. Dr. Pasquali, your line should be open.

DR. MARIZA PASQUALI: Can you hear me?

DR. JOSEPH BOCCHINI: Can we increase the volume? Go ahead and speak, we should be able to hear you.

DR. MARIZA PASQUALI: Thank you, Dr. Bocchini, and thanks to all the committee members for allowing comments. In our experience with newborn screening the GAMT deficiency. Our group in Utah, together with the Association For Creatine Deficiency has nominated this condition for including on RUSP. At the time, the recommendation of the committee was to wait until a patient could be prospectively identified through newborn screening before advancing the condition to full review. So far, we have screened probably over 140,000 babies. Even though we have not found a true positive yet I think I can speak about our experience and the screening test.

The screening works very well. The method is robust. Our false positive rate to date is less than .002%. The cost is minimal because it's integrated with the routine screening. The

increase in cost is really reflecting only the cost of the reagent. We don't think we have had any false negatives in the three years that we are performing the screening. In Utah, as Dr. Cuthbert highlighted, there is only one children's hospital, there is only one genetic center, and we would know if a patient had been clinically diagnosed and missed by the screening.

At the time of the committee discussion two years ago, there were a few concerns from the committee. One was, do we know whether the test will work and can identify patients during the newborn screening? I think we had the most ____ of these. We have analyzed the blood spot, retrospectively, but nevertheless these were true blood spots from two positive cases. These were the same spots that were collected for the routine screen, so the marker for GAMT Deficiency undetectable through newborn screening. Another concern was about the reliability of confirmatory tests in a symptomatic patient. We have demonstrated the reliability by testing the

sibling of patients. They were symptomatic, they were tested when they were a couple of days older, and the result of the diagnostics test was very, very clear. If you perform the correct diagnostic test, you will identify, you will confirm the result of the screening. And then the other concern was about treatment and the consensus on the treatment. There are numerous publications describing the treatment of GAMT deficiency and the outcome. Currently, some of the world experts on creatine deficiency syndromes have gotten together to draft a consensus document. As far as _____ is concerned, the demonstration is the outcome of the patient identified and treated at birth because of family history, like Ms. Wallace has demonstrated. In other words, we feel that we have all the evidence that newborn screening for GAMT deficiency works, we feel that all of the criteria are met, perhaps they have not been collected in the order that the committee is used to see them, but nevertheless they are valued.

In the meantime, while we are waiting to demonstrate that the laws of probability and statistics are true, or for the manufacturer of a newborn screening kit to modify products, several patients in the U.S. are born with GAMT deficiency, they are not identified early and they suffer irreversible damage. Please consider screening for GAMT deficiency and its addition to the RUSP. Thank you.

DR. JOSEPH BOCCHINI: Thank you Dr. Pasquali. Thank you for your comments. We appreciate them. Now, Dr. Longo, who also was a lead on the nomination packet, is traveling but was going to try to be on the call to make the next comment. Dr. Longo, have you been able to join us? So, apparently not. He was in transit and indicated that he might not be able to be on the call. So, based on that, we've concluded the public comment section. We now have a scheduled 15-minute, I guess we need to be back here at 11 o'clock so we have a little over 15 minute break. So, if you'll all be back promptly at 11:00 we'll start

the next segment of the meeting. Thank you.

DR. JOSEPH BOCCHINI: We have two items on the agenda for the rest of the morning and into the early afternoon and that's reports from each of the three workgroups that met yesterday afternoon and then a review of the surveys that are part of the process for evaluating public health impact. So, we asked each of the workgroups to discuss the surveys and make sort of high level comments about them and we decided that we will divide the presentations of each of the workgroups so that they can talk first about other things that they discussed on their agendas during the initial presentations of workgroup activities, and then have each of the workgroup leadership present what they talked about with the public health impact surveys so that they'll all be at the same time as we begin to discuss whether there need to be modifications to those surveys.

So, first up is the education and training workgroup update and Cathy Wicklund will provide

that presentation.

MS. CATHERINE WICKLUND: Thank you. I think ours will be relatively quick just because we spent yesterday talking about the education guide and communication guide as well, so I'll give you just some updates of what we continue to talk about during our workgroup. We have new members joining our group. We have a really nice group of individuals coming together and had a really good discussion yesterday and I just want to thank everybody for all of their input and hard work on all of our projects. Again, this is our workgroup charge that I already talked about yesterday. And just to be clear, again, the newborn screening education planning guide is the one that looks like the table. There’s an example in the briefing book where it’s a matrix that has stakeholders on one side of it, and also content, different types of content, across the top and it helps people who are going to produce educational materials to think about what content should be included in those materials, so, again,

that's just what we're talking about now. What we spent the time in the committee talking about was what was brought up by our larger discussion here, which was how to validate the actual tool itself.

We heard from Erin who had a student who is trying to utilize it within some of the state newborn screening programs and the educational materials they produced. Also, Kate had gotten some feedback from individuals who reviewed the tool that they were unsure about maybe some of the content areas so that led us to think that we needed to create a legend or definition of the different content areas, so we'll be doing that.

And we do feel like we need to have a little bit more feedback and validation before we disseminate and publish this, so we're going to explore validation methods used with similar tools and we're going to do a literature review, we're going to talk to some experts in the educational field who have done this before so we can figure out a way to do this, and then

dissemination we will do after and we also are really cognizant of not spending so much time on this that it's another year or two years and that we don’t actually get it out to people to utilize. So we will look at what is necessary to do to validate it and look at our resources that we have as well, but try not to go overboard on this.

We have been trying to complete a list of groups that we want to think about contacting for dissemination, and what I realized yesterday in thinking about these long lists that we’re creating, is how much time and resources that is going to take as well, to try to contact these organizations so I think it would be good for us to prioritize the different organizations that we’re going to work with, some that might be more receptive to our efforts or have a bigger bang for our buck. You know, really thinking about who should we target first and be thoughtful about how we work through these organizational lists, so we're going to be able to do that as

well.

Let me switch topics. This is now the Communication Guide. This is the guide to help providers talk about out-of-range results. So, what we're going to do is -- we talked about the goal of the document yesterday. Again, it's to help clinicians talk about how they communicate these results. It's not specific to any disorder and it's meant to be used in conjunction sometimes with the Act Sheets through ACMG.

So, what we want to do is right now it's in a Word document and we want to go ahead and improve the design and formatting of the actual document itself, so Catherine is going to think about this from the HRSA perspective and see if we have some resources here that can help us do that.

We also talked about maybe measuring the utility -- so, not so much validation of the actual communication guide, but how useful is it to a provider? Obviously, our end point is that patient, the family and whether or not they feel things are communicated better because of this

tool. That's a very hard population to get to and think about measuring success in that way, so we are going to have some more conversations about what utility is the provider and think about whether or not we can maybe collaborate with some individuals about piloting this and get that feedback in that way.

Also, Jackie talked about baby's first test, having some language and questions already that they use on their providers when they're assessing the utility of some of their tools, and we're going to hopefully collaborate with them and lift some material from them so we're not reinventing the wheel.

I think also we need to reach out to -- we're going to reach back out to our communication health expert, Courtney Shur [phonetic] at Northwestern, who helped us also give feedback on this guide and see if she has any ideas. And also, we are going to ask some of our broader ENT workgroup members to join this small workgroup. We have some new members that bring in some

expertise that we think would be very helpful for us to have in this and this dissemination we feel like can happen after we get it formatted and a little bit prettier. We don't necessarily have to wait for the pilot study or the measuring the effectiveness or how useful it is. We're going to go ahead and work on dissemination and building a comprehensive list. I know we got a lot of really good suggestions yesterday from members of the group and we're going to add that to the list but then also really prioritize the organizations to contact.

We had a little discussion about some other projects but we feel like we still needed to focus on the two that we have on the table right now and bring those to the end. The communication guide for normal results or typical results, we wanted to talk about that. Luckily, we have some members of our workgroup who are actually already tackling some of these issues, so what we're going to do is see where their work takes them and think about how our workgroup can

provide feedback to them, just kind of help them move their projects along.

We also were asked yesterday to think about how we can support the issue of educating about basic concepts around screening and risk assessment. Also, we have some workgroup members who are working on these initiatives already and we are going to try to piggyback with them and just see how we can help them move their projects forward. Any questions?

DR. JOSEPH BOCCHINI: Any questions or comments from committee members? If not, then organization representatives? Telephone? Thank you, Catherine, for a clear and concise presentation.

Now, Dr. Brosco, Chair of the follow-up and treatment workgroup will give us an update from activities yesterday. Thank you, Jeff.

DR. JEFFREY BROSCO: Thank you very much. So yes, we met yesterday, and first I want to recognize all the members of our workgroup, and note that we have a couple of new members:

Ackner, who works in newborn screening in Alaska, and Dawn Heck. They both joined us yesterday by phone and it was great to have them in our meeting. We hope to meet them in person at the next one. We have one person who is rotating off, Carol Greene, and her institutional position is rotating off our workgroup and I just spent the last 20 minutes trying to twist her arm to keep her coming back and we'll see if that works. Because we have a very broad group of input and it's helpful to have folks there that are part of the workgroup and even beyond that.

So, just to remind everyone that we have this vision for what long-term follow-up and treatment should look like and it's probably worth just reminding ourselves that the outcomes are meant to be broad, so there is improved survival but also well-being for individuals who are screened for congenital conditions. It's a wide range of measures from the obvious for things like mortality, all the way through the patient and family experience, quality of life, well-being,

graduating high school, and making sure that disparities are reduced. So, we have very broad outcomes and previous members of the workgroup, previous iterations of the workgroup, have gone through what those drivers should be. What are the things that should happen over time and what are some of the ways we might measure that? So, this is sort of a vision that's out there, and what we've been working toward, really, over the last ten years through this workgroup.

So, what are some of the things we're doing to get there? I think you'll all remember that our Quality Measures Report is now complete and will be posted. They are doing the last couple of edits but basically it is all done. We spent a fair amount of time over the last couple of months really talking about dissemination plans and we're very lucky that Allen is willing to continue helping us figure out exactly what those dissemination plans will be.

One thing I do want to say in particular is that we have decided not to try to publish the

report itself which allows it to be immediately put up on our website, so it should be available, right Catherine? Within a week or something like that. So it will be available right away. If you look at our website it's not clear that that happens with our reports as often or as quickly as it should.

Within terms of dissemination, we're working on having at least the Executive Summary come out in a journal and various members of our workgroup and outside of that are looking at their specific groups. So, should pediatric neurology and child neurology be one group that can learn more about newborn screening and quality measures in particular?

The Medical Foods For Inborn Errors In Metabolism report is also complete. We're in the final stages of editing. Just the last paragraph really needs to be cleaned up a little bit. That report we're not going to immediately put up. Sue and her co-authors are going to publish, we hope, in an abbreviated form and so they are

already working on drafts of that and since it's abbreviated it’s not really changed in content, this should be relatively easy to get through our group.

We spent a good deal of time yesterday speaking with Alex and K.K. about the environmental scan that they’re doing and I think they are likely to present to the entire group in August, if not November, and it was a lot of back and forth dialogue about who’s doing what, who’s using which tools, and how do all the things fit in that vision? I’m going to go back to it for one second because I think it’s worth it: Saying, so this thing is our vision but who is really doing some of this? So, the California newborn screening program, are they doing some of these things? Are there examples around the country or outside of the country where we can say here’s one of the ways we can do it, because clearly this is not happening yet. So, we spent some time talking about what Alex and K.K. are doing and how our work might inform theirs, and

theirs informing ours.

And then last we talked about this idea of a road map which is how do we get from here to that vision of what long-term follow-up and treatment should look like. And, by the way, the “L” we keep talking about, how this means long-term but also longitudinal and life span.

So, the road map is probably what we'll be focusing our workgroup on a lot over the next six months and the idea is to provide stakeholders with a road map to achieving some kind of federated system that makes sense. We know there won’t be any simple solutions to this.

The barrier is that there are so many follow-up activities, but also a lot of gaps and no system that connects all of it. So, the idea is maybe we can work with stakeholders to develop a report and consider interim steps and during the break, we had Joe and Bob volunteer to try to put together an initial kind of paper or statement of intention I guess would be the best thing to say, that we can respond to as a workgroup on our next

call. And I'm putting December 28th, even though that's completely crazy. I can't imagine we'll be done by then but it's nice to have a timeline that pushes us. We can do it. Excellent. And that's it. I think, he meant singular. Any questions for us?

DR. JOSEPH BOCCHINI: Questions from the committee? SID?

UNKNOWN SPEAKER: Jeff, thank you for that summary because I think it's incredibly difficult to contain the conversation we had yesterday, so one of the things I'm just going to ask about is what role do we see for larger scale advocacy organizations such as The National Organization For Rare Diseases in particularly working with patients and patient registries? Is there a way that we can engage them in some of this process as well?

DR. JEFFREY BROSCO: Absolutely, and I think that's part of engaging at every level so as our next -- probably on our next call we'll talk about who should be part of this in terms of how

do we create this road map to the future? Because we're going to want to include patients, families and consumers right from the very beginning. And then obviously as an advocacy group at the end, whenever we come up with specific steps, that will be critical as well.

DR. DIETER MATERN: Can you quickly define the federated system that you talked about in your group meeting?

DR. JEFFREY BROSCO: No.

DR. DIETER MATERN: Can you take a moderate deliberation?

DR. JEFFREY BROSCO: The reason why I said federated system was because it sounds a lot better than “we have no idea how this is going to work.” But, I think the point is we are not a healthcare system in the United States that has a single electronic medical record that can easily say, “okay, here's how this whole thing is going to come together.” It has to be some sort of federated system. So, some of the ideas we were floating are, can you have--does it start with

families and patients entering data into patient registries? Is it population specific? Are all the SMA going to have one system? Is it going to be run out of a university? Would it be part of the American Academy of Pediatrics, which is now talking about a special health care needs data set.

So, that's just the data part of it that would have to be federated. How does the quality improvement part of it work? Again, that’s going to be so newborn screening programs -- state newborn screening programs -- will have some quality improvement part of that, but so will specific disease groups. So, you can imagine cystic fibrosis or sickle cell disease are already doing things to build quality improvement. So, when we say federated systems what we mean is there are going to be lots of things happening in different places and we’re going to put a sort of dotted line around the whole thing and say “See? We have this beautiful federated system.”

I think the other thing that's important, and sort of a big question for us to deal with, is should this be newborn screening specific and we build a new system or do we make sure that the systems that are happening and in place have a newborn screening component? So, when we do the National Survey Of Child Health, if we added a newborn screening question, well then suddenly we'd have a whole dataset about newborn screening conditions, and we don't have to create a whole data system for it. So, those are the kinds of things we're struggling with.

MS. CAROL GREEN: To maybe remind people that this is tied, or historically was tied, to some discussions about getting all of the stakeholders into a room and exploring -- not saying what people's responsibilities should be, because that's not the purview of a committee, but exploring what people, what are their current roles and responsibilities and what do the stakeholders think their responsibilities should be? And the answer that was just given about the

federated system had some really good examples, and it's so easy to talk about the data and, again, all the examples were about the data.

This idea of this road map in the federated system includes the hospitals that are involved in doing the newborn screening, the insurance companies that pay for the treatment, the professionals, the families -- it's just not about the data and not just about using the data for quality improvement, but it's actually delivery of the care. And we all know that, we all believe that, and then we start talking about what we can do which ends up talking about the lab and the front end and the data on the back end and we want to not lose sight of all the stuff in the middle and the people.

DR. ANNAMARIE SAARINEN: I'm on the committee, and thanks for the summary -- the federated summary. So, I wonder if I could call on Dr. Ostrander to give his hypersimplified suggestions of how we might not reinvent the wheel here, just because this was part of our

discussion yesterday, even though we're road mapping, we're trying to figure out a pathway, but at the end of the day we're really trying -- so there's kids identified by newborn screening that we don't know what's happened to them over time, even in short term, two or three years out, but then even farther out than that.

But the NICU model and CF model seemed like things to look to that also have had to address the complications of payers, providers, specialists, but somehow with just a few short questions every year going to that primary care provider, that medical home, has been a really foundational starting point to capture what you need. And we already know which kids are identified by newborn screening, we already know that, so it's just figuring out how to tie in those gaps. So, I don't know if you have a few comments, Dr. Ostrander.

DR. ROBERT OSTRANDER: Hi, I'm Bob Ostrander with the Academy of Family Physicians. So, what I brought up yesterday was that perhaps we -- I

may disagree with Carol a little bit because I think we need to get out of the weeds and, you know, stop asking everybody how they're doing it and talk about how we could make the recommendation, I guess, though maybe it's not in our purview to do that, about a system that might move us forward. And, my experience with and my thought would be, to model it on the NICU graduate kind of follow-up programs that most university programs and NICUs have, where they send out an annual follow-up. Cancer registries do this a lot, both for kids and adults, as well, to the primary care physician and probably to the specialty clinic that diagnoses, with, again, a handful of our most fundamental questions about: "Are you getting care? Are you still alive? Are you getting extra help in school? Do you still see this patient? If not, do you know where that patient is?"

And if we could encourage or recommend that this be replicated for kids with special healthcare needs and in the subset of kids with

confirmed positive or newborn screens, that might be a way to move the needle forward. Granted, we wouldn't get 100% of the kids with positive newborn screens but since, especially with kids, the large proportion of kids with serious or complex illnesses are connected to a specialty center, my thought was that perhaps the specialty centers doing what they already know how to do, having technology in place, could be the center in the sorts of primary responsibility and then figure out how to link and network them in a way that the data could be shared and done nationally, rather than having it be done in parallel, in a whole bunch of clouds. So, that was my initial discussion and I know Joe and I are going to try to flesh out some straw man version of what might look like a recommendation for the subcommittee to look at.

UNKNOWN SPEAKER: Thanks, Bob. I think that gives us a good example of the kinds of things that we talk about in our workgroup and as Bob ended up saying, he and Joe Schneider are going

to work to put something together that we can respond to in our next workgroup call.

MS. CAROL GREEN: That's great. It's still the data. I'm still interested in making sure that somebody's there to provide the care. We just got cut again from the state of Maryland, not because the state of Maryland wants us to, but we haven't had an increase in the funds that allow us to provide services for about 20 years, and they managed to keep the cut to four percent but that's a cut of four percent plus raises that people get and I think that's an issue and I think we need to tackle it.

DR. JOSEPH BOCCHINI: Thank you. Other questions or comments around the table? How about on the telephone?

MR. CHRIS KUS: This is Chris Kus.

DR. JOSEPH BOCCHINI: Yes, Mr. Kus, go ahead.

MR. CHRIS KUS: I represent ASHTO and I guess one of my comments, and it really goes toward the environmental scan and whether Alex or K.K. are going to look at the issue of current resources

devoted to long-term follow-up? And where do those resources come from? Are they federal dollars? Are they state dollars? And I suspect there's a real difference across the country about that with some states committing more toward long term follow-up, but I think that, to me, is one of the limiting factors in doing long follow-up.

DR. JOSEPH BOCCHINI: Thank you for that comment. Other comments from the telephone?

MR. CHRIS KUS: This is Chris Kus again from ASHTO. I just have one comment and it relates to Bob's comment, because I'm from New York State and when he talks about the NICU model, the one thing about it is it's really specific to the center as to how they decide how they're going to follow up infants in the NICU. There isn't, to my knowledge, kind of a model that goes across those centers. We work with NICUs in quality improvement but I'm not aware that there is a common model for follow-up.

DR. JOSEPH BOCCHINI: All right, if there are

no other comments. Again, thank you Jeff. I look forward to this coming through.

DR. JEFFREY BROSCO: Thank you.

DR. JOSEPH BOCCHINI: Next is the Laboratory Standards And Procedures Workgroup update and Kellie Kelm, the Chair, co-chair.

DR. KELLIE KELM: Thank you for fixing the date too. Good morning. So, Lab Standards And Procedures Workgroup: We had a lively meeting yesterday and really our focus was on just two topics, but to start, we did have new members for the workgroup and I have them start here: Rosemary Hage was able to join us from Ohio, Bonnie Taffe from Florida was not able to join us yesterday but she is a new addition, and, Liz Amos is replacing Rebecca Goodwin from NLM. So, we're happy to have the new folks. As I said during yesterday's discussion about -- talked to Dr. Bocchini about -- ongoing discussion on risk assessment and cut-offs, so we spent about half of our time talking about that. The question was whether or not the workgroup would have

recommendations for the committee to consider and chew on, on whether there's policies to talk about that states should consider regarding the risk assessment and cutoffs.

And, so these were after our discussion went around and around. I think these were the things that we had currently based on discussions amongst the group as well as the presentation yesterday by CDC.

So, number one, we thought that states should have written processes in place and so this is a robust process, or SOP, the idea that they should have something written down about how they will go about the rigorous validation of the test systems to determine if a newborn is -- and obviously people have many different terms -- normal in-range low risk, versus abnormal out-of-range high risk. Also, they should have a written process in place for how they're going to revisit cut offs in algorithms and that should include how often they're going to reassess their cutoffs in algorithms. Some states say that they

do it twice a year, but I think we've heard quarterly. So, once again, states should have their process written down and they should obviously follow it.

And, lastly, states should have a written process in place for how they're going to go back and review missed cases when they're brought to their attention and assess their program.

Another item that had come up, I believe during discussion yesterday as well in our group is that states should disclose available -- transparently somewhere, for example on a website or with their program materials -- what the targets are for their newborn screening programs. So, we have heard that states sit down and figure out what they're screening for and not all states screen for the same things with each analyte. So, that should be transparent and available for the public, for physicians or anybody to find out.

And lastly, obviously talking about the normalization work at CDC which is going to be

moving forward, we would love to encourage participation in the normalization process whether at CDC or others, and what can come from that would be some downstream QA/QI efforts. Once we can normalize the data across the states then we can do a lot of work comparing but then also QA/QI efforts can come from that. So, that's only just starting and I think that it'll be great to see where that goes. I think that's really it for our slides -- oh, I think we do have -- that was related to the other topic. So, we do want to go back to the APHL Risk Assessment Guidance document. We heard that APHL has still been working on it and plans to finalize it next month and I do think that we want to circulate it to the workgroup and probably have a call in between now and the August meeting of the committee, to see whether or not, after revisions are done, see whether or not there are any recommendations regarding that document that we would have for the committee and talk to you guys about that either in August or whenever that

would be appropriate. We, I know, had just gotten a draft the night before, it would actually make more sense to wait until APHL has finalized it. So, I think that's it for us. The rest of the discussion was on the public health system impact survey.

DR. JOSEPH BOCCHINI: Thank you, Kellie, very much. Questions or comments? I certainly think that the development of a process and policy for states sounds like a very reasonable thing to pursue and, in tandem with the APHL document, I think would potentially be very helpful . So, questions or comments, committee members? Cindy?

DR. CYNTHIA POWELL: I applaud your including that states should state what their targets are. I think there's a tremendous amount of misunderstanding on the part of the public when you look at, you know, how many conditions the state lists and that one state might list 55 conditions that they're screening for and others, you know, 30-some, and often it's based on sort of a theoretical that we, you know, should be

able to detect this condition but, in reality, they never have and it's probably unlikely that they would.

But, really, the public views it as "well, why is such and such a state screening for 22 more conditions than my state is?" So, I think that would be very helpful to be more specific about it because some states really just include conditions that they know they've been able to detect through their methodology.

DR. DIETER MATERN: So, when it comes to listing what the targets are we talked about this not only in terms of the conditions that are screened for but, maybe also moving to a way that we can come up with -- or every state could come up with -- what are the targets and false positive rates and false negative rates of basic performance metrics. I was a little bit naïve in just saying why don't we just do it all the same way, but then we moved to where we said well maybe we can put those performance metrics up as targets, and try to really come to a uniform

screening panel not only in terms of what conditions are included, but also how the performance is across the country. It was asked about a federated system and how that discussion went because it was vivid in our workgroup.

DR. JOSEPH BOCCHINI: Good, some overlap. Other questions, comments? Telephone? Thank you, Kellie, very much. Appreciate it.

Okay, next we're going to hear from each of the workgroups, some of the key issues that were discussed and comments made related to the process for assessing public health impacts, specifically looking at the surveys and whether there are things that we're missing. So, here's the guidance that we gave the workgroup: High level revisions for the next iterations of surveys: Are there gaps in information collected which could be addressed by the surveys that are not being evaluated? And specific recommendations for adding or removing or, as we heard in education and training, maybe modifying some of those questions. So, we are in the same

order, so education and training first.

MS. CATHERINE WICKLUND: I'd welcome any comments from people who were in the ENT workgroup yesterday, too, as I try to go through this. I think it’s a little hard unless you have the survey right in front of you, so we’ll see how this goes. I think a couple of things came up and there are some specific things and also just some general comments that we had about the surveys themselves and we were lucky to have some people in our group who are on the public health side and were able to give us some feedback from their perspective in trying to answer some of these questions from their state perspective, so I think just in general some comment was to clarify the purpose again, that it really is an assessment of the newborn screening program itself, not the public health system, which is just the title of the actual survey, The Public Health System, and I think that there were a couple of clarity things making sure that the questions, when they were asking about screening

or if it was on the RUSP, was it really more than was on that state RUSP at that point or was it that they actually had started screening for that condition at that time, and we thought it really was about screening for that condition, so to just clarify that.

If you look at the survey itself there is a question that goes over funding and whether or not there are funding challenges with particular categories and the funding level of challenge -- it's like, major challenge, minor challenge and not a challenge -- and with those they're tied closely to the year. So, less than one year would be a minor challenge, two to three -- I'm just kind of -- I think that's what it is -- three or more would be a major challenge and I think what we were thinking of is the time always directly related to the fact that it's a challenge? You know, something could be not a challenge but take time just because there might be a lot of paperwork or processes that you have to go through, but you know you can do it, it's

just going to take some time.

So, we were kind of questioning the validity of tying the extent of the challenge directly to the time it would take and thought maybe those were two different questions. And again, I think if we are going to ask major challenge versus -- what does that actually mean for some people? So, to get a little bit more nuanced about that might be helpful. Not-knowns should be an option. That's not really up there. And there was a suggestion that maybe taking those funding questions and maybe simplifying just to, like, is there funding for this, yes or no? Is there funding for this thing? Yes or no? And that might help us get a better handle on the funding issues.

The other thing that came up is whether or not -- and I know this has come up in our conversations before -- about whether the Public Health Department is the best person to be asking questions about the availability of specialists or impact on the clinicians, and I think that

that varies probably state by state. Amy, who was on our call, felt like she reached out to a lot of the specialists and providers and had a good handle as to the wait times and how that was affecting the providers and the access to treatment, but I think that probably might be state dependent, so just considering whether or not we are actually the right person the question and that they can actually answer it was something we thought to consider.

So, 6B, what was that about? I think we had somebody on our committee or workgroup that was also just looking at the usefulness of using some of the Likert scales that we use so there's five different categories for 6B, and I guess it's a question to Alex and K.K., like how is that data used? And I can't remember if it's collapsed ultimately in the long run, you know in different Likert categories, or is it truly helpful to have as many as we do? So, that was just probably more of a data analysis question that we asked.

And then I think question seven, too, which

is on how long, again, will it take to do these things? Thinking about reframing it from how long to startup to implementation because I guess also we were wondering the accuracy or validity of these answers. These are all hypothetical and I think people do their best guess, but we don't really know, obviously, how long it really is going to take. Do we need more choices or just ask specific numbers because right now they're categorized in different years? And then we had a suggestion that maybe asking about things that may inhibit you from reaching that goal, so unforeseen circumstances that might happen that would interfere with your ability to reach the goal that you have, so again, just some ideas.

The general thoughts we had is whether or not we should expand questions to include issues of equity and disparity. Should we expand and address sustainability of the program? There was a comment, too, that the initial survey is hypothetical, the follow-up survey might be more important because I think that captures a little

bit more hard data as to what is actually happening.

Then the other issue that we had a conversation about was just the transparency about how this information is actually weighted within the decision matrix when we're thinking about adding things to the RUSP and making that more transparent to the Public Health Department. What we don't want to do is get into a situation where we're asking all these questions and then Public Health Departments feel like, "well, it doesn't really matter what we say about the readiness or the feasibility of this, it doesn't matter in the ultimate decision of the committee." And that might be true or not true, I don't know. I just think we need to be -- and you guys are a great direction in reviewing the evidence matrix and I think that this is a good one to really examine a little bit more carefully as to how much is this really weighted in that matrix?

The other thing -- so this is more specific

on the actual second survey, the follow-up survey, and probably just more comments about the questions themselves, as just trying to specify the various phases of implementation a little bit better, maybe add some more specific probes under the questions if there are certain things that you want to get at. The methodology questions, we wondered if they were beyond the scope of the actual survey. This is becoming, it seems like, a bigger issue when we were talking about normalization and harmonization, and there's methodology questions on there and I guess the question is are we really getting the data about the methodology from those set of questions? Is that good enough or are there other ways now to get that data and more focus that we're going to get about that? So, we wondered if that should just actually be a part of this or not. There was also a suggestion to assess downstream impact or unintended consequences and whether or not we should have other stakeholders that we're interviewing, either, again, going back to the

specialists who are providing care that can talk a little bit more about the impact on their practice, or the families themselves, but again we know that we have a limited amount of time in which to do this review, so that was also an issue that was brought up. And I think that's it for us.

DR. JOSEPH BOCCHINI: Thank you, yeah, I think if anybody has any quick questions they could do that, but I think it would probably be better to see everybody first, and then any -- let's do all presentations and then we'll talk, thank you.

DR. JEFFREY BROSCO: So, the things that we're going to present -- I think it was better for me to sit down and do it from here because they're not really that we decided and came to a consensus and here are clear recommendations from our workgroup, it's more like "here are some of the ideas that we came up with and observations we made as part of our group discussion."

So, one of the things you see we underlined

and bolded “system” because as Cathy pointed out this really is about the public health system impact and not really about opportunity costs, public health and broader population issues. One of the things we did was similar to Cathy and her group is who exactly is answering this? One of the things that came up, I think it was Sue, said “look, when you ask lab people, they’re like, ‘good people want to take care of babies,’ so you say, ‘can you screen for this?’ They say yes, because they really want to. So she wondered, are there ways to think about who exactly we’re asking so that we get a range of answers and, of course, the way it’s done -- you see the wording on it, it says, “please ask other people in your state so you get broad answers.” It’s not mean to be just one newborn screening person.

Another thing that came up was, is there a way to distinguish between early adopter states and more conservative states? The ones that immediately are always excited about the newest thing on the RUSP, and the other states that are

sort of holding back and if that's a useful kind of distinction to make in figuring things out. A lot of states have advisory boards. Should they be part of answering these? And particularly, the very last question, which is about what the public health opportunity costs -- and we'll come back to that -- should that be a place where the public health leadership is involved and not just the newborn screening because it's harder for them to judge that?

Another big theme that came out of our discussions was the idea of time and how this might be a less useful kind of way of figuring things out and Cathy mentioned question five where it said, 'how hard is it to get funding? Less than one year, one to three, and so on? But for a lot of states now there's a mandate that says that as soon as it's on the RUSP you have to do it and in our state is that as soon as it's on the RUSP you have a year to decide and then 18 months to implement, whether you have money or not. And so a lot of labs just have to do it,

and so money is not necessarily tied to time and we'll come back to that at the end.

The other thing is that if something's politically important, then time suddenly contracts, right? If it becomes an important thing then you're going to do it tomorrow because that's what whomever in the state thinks it's really important suddenly.

And the last thing about time is that the answers on this survey we would have to acknowledge it's just a snapshot in time that can change.

Another set of things that came up really from our group that was sort of a big theme was, yes, the questions about follow-up and treatment are there but it feels like they're hidden. It feels like they're not really part of it because of the way they have a sort of different line and tables, I think five and six. So, one of the questions we had was could we separate out those survey sections so there's a lab section and maybe a section about clinical resources and

follow-up in that so it's clear that there's sort of a separate set of issues there for us to focus on.

One of the other quick points is don't forget point of care is also newborn screening. It's very lab-oriented but if you're doing hearing screening then a lot of the questions seem less applicable or another.

Then to sort of try and put some of this together, as Cathy was talking about a little bit, really what's the purpose of this and who are the different audiences? Yes, on one hand it's about for our committee to help decide about new conditions and maybe we have some discussion about that and how important it is, but it also can be helpful for stakeholders to understand how easy or hard it is to implement a new condition. So, yesterday as soon as it hits the RUSP you can implement as a state but some things may be harder or easier, so getting a time line, sort of, "here's what the 50 states say is how long it's going to take," can help temper expectations

and give people a sense of how long something will take.

A lot of it, of course, is the big question: How hard is it? How painful is it? How much burden is it to take on this new condition? And you can imagine that that bigger question is made up of a lot of the littler ones. So, in those tables where they have all the different rows, it's not so much that the specific answers matter in those rows but that it gives the people answering the survey a chance to think, "aha, yeah, I have to think about lab testing, I have to think about follow-up, how many false positives would I have?" and then going through an exercise and at the end of it you can then say, "okay, how hard is it really going to be?"

So, what is that global question exactly? We'll come back to it, but it probably is a few different components. They're numbered there one through four. So, technically how hard or easy is it to scan, to screen? And it seems like, for example, that GAMT is relatively easy because

you're adding to MS/MS, but there might be things that it's an entirely new technology the state has no experience with and it's going to be a huge amount of work for them to do it. So, you'd like to have a sense of that obviously. And then how many infants will need follow-up? What's the prevalence of the condition? How many false positives, how many indeterminates? So, that could be a huge issue for your follow-up program or it might be very small. Clinical resources similarly: Are there specialists readily available? There's lots of pediatric cardiologists that are eager to take on kids, or there's three clinical geneticists in your state and they're already overwhelmed.

And this last thing, it's hidden in there in the last line, is "is it a public health priority? So, is this new condition part of what your public health strategic plan is? For example, a lot of our states are dealing with the opioid crisis, so if you add a newborn screening condition related to that, that would fit in well

with what your public health system is already doing and so, therefore, would really be consonant with what your public health system is there for. Otherwise, there may be opportunity costs. A lot of state programs don't get any additional resources. They just get a mandate to add something, so there's a true opportunity cost. That means they have to stop doing something that was a priority before in order to do this.

Then, if you take those four sort of things where it might be easier or hard on that scale for all of them, it then gets into the real "practical" issues if the resources are available; because most state newborn screening programs would say, "well, if you gave me all the resources and all the FTE's I needed, of course we can screen for it and we can start right away. And if you're not going to give me the resources, then we're going to have to figure it out as we go." So this makes it really hard the way the questions are worded about -- "how many years

will it take you to implement this?" Well, in some states it's like "well, we have to do it within one year, will we have resources or not?" So, trying to figure out what that big question may be is hard to figure out. I think we tried one version of it here but we didn't get to the point of figuring it out, which is, I think, something like in the middle there: "Given your state's experience with adding new conditions, how hard will it be to add this new condition?" So, given what your experience has been like the last few years, you know, how much of a burden will this be? But that's just one sample of what it might be like and it's kind of where we ended. Thank you.

DR. JOSEPH BOCCHINI: Great, thank you. Kellie?

MS. KELLIE KELM: So, let me look at my notes again. I think a lot of the discussion that we had, and I'd really like some of your feedback on pulling some of the other factors out, but I do think that one of things that came up was the

fact that a lot of the questions actually ask you to say you already have authority and you have funding. And I think what we heard from a lot of the people in our group, is that that actually can be one of the biggest issues. So, a lot of the answers to the questions tend to be the same in terms of timeline from state to state, but I think many people thought that we actually do need to capture better how long it takes and how hard it is to secure funding and/or authorization which can also vary state by state by a lot.

So, we do think the survey should capture the impact of securing funding and authorization to screen for a new condition.

In general, our thoughts were that a lot of the factors and activities in those tables are a little bit too much method specific and so you could, especially since it's going to be used potentially for a lot of surveys, it should become method agnostic. So, instead of onsite genotyping as part of the second tier test you should just state second tier tests available

onsite if needed.

I think, in terms of we had one question we thought we could remove which was, “how long have you had this position?” and the other thing that we thought -- you know I think a lot of the discussion has been about what has state experience been and have we captured that? And so we heard that NewSTEPS has a readiness tool which has a lot of the questions from the survey but the idea is to actually go to states and ask them to look back, so it’s a retrospective look at how they’re doing in terms of implementation of things that have been added to the RUSP. So, first of all, we actually think that information that NewSTEPS has been collecting would be very useful for the community here, but the other question was whether some of those questions would be useful for us to look at as we craft the survey, and I did have that back a few pages so I might make everybody dizzy as I go back and show you a picture. So, this is just a snapshot of the authority questions and the funding questions

from the NewSTEPS readiness tool, and let me tell you that right now NewSTEPS has actually gotten it for three conditions: So, for X-ALD, Pompe and MPS I. They actually have gotten survey results from 45 states. Once again, this is a snapshot looking backwards at them implementing screening for those three conditions. And so we can find about, for those three, what has their experience been in terms of -- and there's more to the right here, I had to cut it off to put it on, so we could find out about states that haven't started screening, what ones have started screening, how long it took and what were the gaps and barriers for the ones that aren't screening and what they thought about this whole thing. And NewSTEPS has gotten surveys from two states on SMA, so they're starting to collect that information for SMA as well. So, I do think that finding out about what these 45 states have responded to in terms of these three conditions on and looking back and telling us what the issues have been also could help inform the

survey, but also I think the committee would love to see the snapshot and see what the experience has been because they have that data and I think it would be useful to have it.

Those are just the thoughts, high-level thoughts from the committee and I do think that what we heard was that most of them do reach out and talk to other people in their group so most of them know that it's coming and when they hear that it's gone to evidence review, they know that they're going to be asked to do this survey for their state and most of them will take the time to reach out to experts, the downstream, the follow-up, and get them involved in the survey, so most of the time it's not just the lab people filling out the survey. That's it from us.

DR. JOSEPH BOCCHINI: Thank you very much. So, clearly there's some similar things from each of the workgroups and then some very specific differences in some of the aspects were covered. All of this is very, very helpful, so let's open this up for discussion and some views from

committee members first on where we are and potentially other things related to these surveys. Scott?

MR. SCOTT JONES: I think a couple different items, some of the guidance from _____ were around trying to keep it more high level because of the OMB process and I think what we're hearing is that there's potentially more depth that we need to get into on this document and I want to make sure that it's clear in terms of what is being asked of the committee and how much opportunity for change there is and that goes into my next two points which is everybody brought up, every workgroup brought up the idea of this system, that system's the name but that we're not really evaluating the system and so I think Cathy's point of defining the first -- I don't remember what the first bullet was -- but my recollection that this is supposed to be looking at the system and why everybody asked who's being -- where's this data coming from? Who's asking whom? Are we getting an accurate

picture and I think that needs to be the focus. But it's only worth the effort if we do decide that this is going to play a role in our decision, and to the transparency issue Cathy said that we need to be transparent to the Public Health Department; I think we need to be transparent to the committee because it's not clear. I don't think -- as a member of this committee it's not clear how much this is supposed to be weighted. I think it needs to be part of the process. It's a little unfortunate that we're now embarking on a review of the evidence review process at the same time that we're talking about this, and so I think that's going to make it hard because you're trying to decide how much a document that's currently being revised should play a role in the process. But I think we have to decide if it's going to be part of the process; otherwise this is just an exercise in an exercise and why are we wasting everybody's time? Throughout the last two days it's been a discussion of where are we gaining?

Are we burdening the system with activities that don't actually have a net contribution and this is just one of them? And it's almost like an overall number of false positives, using a survey to fill out but we're not going to actually take it to heart and use it in part of a decision. So, I think we need to decide that -- my recommendation is that it is part of the review process, it has weight, and that the time and effort it's for the public health programs to put into it to assess their system, not just a test and not just an individual program, is crucial.

DR. JOSEPH BOCCHINI: Yeah, that's a very important comment and I think there's no question that the goal here was to see if we could get better results. I mean, we clearly need an understanding of the impact on states when we make a recommendation, and having the data to help understand feasibility, readiness, total impact is incredibly important and so, no matter what we do in terms of making sure that it's transparent and plays a role as we do the

evidence review, we need to see whether we've got gaps in the information that we are now collecting and I think it's clear that it's important that we develop an approach for the system rather than just the lab or one part. So, I think you're absolutely right, Scott.

MR. SCOTT JONES: Can I make just one clarification about the language that I was using? Because you're right, there's the lab and then the public health system program, but I was also talking about broader things. Because if you said to me "what's the public health impact of vaccinations?" I would think about the entire population and how that changes morbidity and mortality for a population, so typically when we say what's the public health impact? You mean at a broad population level and we're not really saying what the public health impact of SCID, right? We're not saying, "well, we found three kids last year in our state and there's four million -- we're not doing that kind of calculation, so when I say the "public health

system" I meant more of the newborn screening public health system. What's the impact on that system? So, just to be clear what my language was.

DR. JOSEPH BOCCHINI: DIETER?

DR. DIETER MATERN: So, it's no secret that I have never been a great fan of the matrix because I always thought that if you determine the readiness and we get those results back and then it doesn't meet higher readiness, then nothing would get added on the RUSP anymore. Now, that hasn't happened and we'll see what happens to SMA. I think it is important to get that information from the states otherwise because if there are roadblocks that the states experience, individual states, because of funding, because of whatever it may be, it's important to identify those so that also those stakeholders that actually came to the committee to nominate a condition or to get it on the RUSP, so all you patient advocacy people out there, can identify which states you should go next to to make sure

that what this committee recommends and where the secretary might agree with us is actually getting on the state's RUSP. So, from that perspective I think it's important to know where are the hurdles.

MR. SCOTT JONES: If I could follow up on that, I think it's really important what Dieter's saying, because if you think about the entire system that we're working in, at some point someone does have to say, "well, is it worth it for us as a society to screen for this condition if it happens one in 200,000 times?" And at the end of the day that's the responsibility of a legislature and an executive branch to decide how we do that. By having a really clear idea of what it's going to cost our state to do it -- you know, this is what we would have to do, how many FTE's, what lab would we need, what we need in terms of treatment and follow-up, then there can be a rational decision about that. It's not for us to decide it, so that's a corporate, political kind of decision in each state. So, I think

you're right, this information from that point of view is very helpful too.

DR. JOSEPH BOCCHINI: Other comments? Any discussion from APHL, or states' representation or evidence review workgroup that might help with additional comments?

MR. ALEX KEMPER: I'll start. So, let me just state first of all I think this is an incredibly important conversation to have. As far as I understand, the authorizing language for the work that we do states that there has to be a public health impact assessment, and in thinking through how we do the evidence review, we've really separated out the public health impact that Dr. Brosco talked about in terms of if you were to adopt screening what would be the impact on the population? So, if you were to adopt SMA screening, how many newborns with SMA would be detected and what would be the expected outcome on their health? That's the kind of thing that we presented through decision analysis with Lisa Prosser.

And then separate from this we've done the public health system impact assessment so the impact on the newborn screening programs and we've really been challenged to set this up in a way where we have a tool that we can use each time, because of the OMB requirements and to get the nuance that you all have been talking about and I personally don't feel like we're there yet, and so I really appreciate the conversation.

So, there have been things that have been brought up like you know this issue about funding. Well, when we initially put it together we were concerned that we said if we included the process for getting funded everyone would say "well, that's the major barrier and we'd never get to these other issues" but I realized that we've sort of swung too far by excluding the funding question, but I'm not sure how we do that in a way that really gets to what we need.

The other thing, and this is from the people that -- I think the people that run newborn screening programs are real heroes, so if we ask

can you do something and can you do it in a short period of time, the answer is inevitably yes, so how do we get to a meaningful expectation of how long it takes to do things, I'm not really sure. So, the bottom line I guess I'd like to express to the committee and everyone else is that we really, really appreciate that you all are struggling with these questions and I look forward to getting to 2.0 of this instrument, but I have no doubt that there's going to need to be a 3.0 and a 4.0 as we refine this and as what newborn screening is becomes more and more complicated and there's more point of care tests and that kind of thing, so let me just finish by saying again, I don't think we're really there yet and I appreciate any input that we can get in terms of how to get to where we want to go.

DR. JOSEPH BOCCHINI: Thank you Alex. Sue?

DR. SUSAN BERRY: Alex, thank you, but I just want to reiterate something Jeff said, I don't think -- this is Sue Berry and thank you -- I love this sign, we should have a happy face on it

though, please -- or maybe an unhappy face. So, when Jeff talked about the system, yes he was talking about public health in the global sense, like vaccinations, but I think what we were really trying to focus on and point out is that it's more than just the public health laboratory that encompasses the newborn screening system. And that's been reiterated in what the newborn screening process is, it's a process, not an event, and then the follow-up team is part of it, and then you start moving a little further away from the public health laboratory in a state to the resources that are required to actually manage another condition, which is all of the providers, the facility for being able to have enough -- I don't know the things that come into the related activities, and we just don't touch on that if we focus only -- as much as we love our public health laboratories -- if we only focus on them we're underestimating the system costs, and I would really like us to make sure we at least pay some attention to that impact as

well.

MR. ALEX KEMPER: Can I just add in? I mean, I 100% agree with you and then you get into all these complicated challenges too where a lot of these children, and some cases adults if you're talking about late onset diseases, are going to find their way to care anyway and so you end up having to think about the delta as well. So, going back to SMA, the treatment for SMA is complicated and expensive but at which point do they interact with the healthcare system comparing newborn screening relative to what would happen with public care, so it becomes very, very complicated quickly, and I 100% agree with you that it would be nice to look at all these downstream effects, but the one other plea that I would put in is to remember that under the current legislative rules for how we operate that this has to be done within the nine months, and so that includes all the up front evidence review as well as this part.

DR. SUSAN BERRY: So, an element in this then

also becomes the speed with which you can approve outcomes. A late onset disorder, while I will be happy if that will be helpful to somebody eventually in their life that we know that, the real impact for newborn screening is how does it impact immediate outcomes for kids? And that does have an immediate downstream effect. It is temporally discoverable, I think.

MS. CAROL GREEN: I wanted to focus on the process. So, it sounds like lots of input and I'm struck by the 3.0 and the 4.0 and, of course, we know everything changes, and one of the things that I think I've seen over the years the committee struggle with is the challenge of, and sometimes getting criticized for, a continually changing -- like "we did it with these rules and now we've got our experience and we realize that the rules or the protocol or the practice or how we judge, needs to be improved and then we do the next two or three with another set of rules, and there's a sense in the community that it's a moving target and that's hard.

And it’s also not possible to get away from that because newborn screening is a moving target and healthcare is a moving target and everything is changing, and you do want to do quality improvement, the committee with its practices just as much as healthcare and the labs and everything else, but you do want to try to get it as right as you can the first time. And I don’t know, I assume most people in the room know that if you ask more than -- I think it’s nine people -- the same question, then you have to go through OMB to get permission, so you can't even change a period. You can't change anything and once you’ve got it, it’s stuck. So, I wonder if in the process with all of these ideas of improvements if there's any way for somebody like APHL or NewSTEPS or somebody to pilot a new draft and get a sense from people, does this improve their ability to communicate what they feel? Does it make it more clear what’s being asked? Does it make it more clear what questions you -- and that it's not about a three month

study to get input from everybody, that it's trying to get a snapshot right now of, if we told you right now, how hard would it be? But, without going into any more details, is there a way to get somebody to pilot it?

DR. JOSEPH BOCCHINI: I think that's certainly an important potential step that we could take to pilot and get a better understanding and I think certainly -- are there people in the audience from the states that have either filled out one of these forms? Or been involved with it that want to speak to whether you believe that it addresses the issues that we are talking about appropriate, or what gaps you feel that it is not addressing, that might, again, be helpful as we put this together? So, Debbie and then Susan.

DR. SUSAN BERRY: So you're gonna get two perspectives from the same state. We have filled these out and we have tried to disseminate them as broadly as possible. We do share it with whatever specialty is involved as well as a

variety of other folks; however, the feedback we get from sort of outside of our internal system is limited. I mean, you have short time frames, you don't get large response rates as with any survey. So, it still feels like for us, or from my standpoint, that presumption of if funding was available really changed the whole tenor of how you would answer this because obviously if you had funding and you had space and you had FTE's, everybody's going to say, "yes, we can do it," but the reality is that that funding is that big hurdle and also from my standpoint it seemed like this still was focused mainly on the laboratory aspect, that it did not encompass the follow-up, and granted there are some issues we can't address, like work force issues. We know there's nothing as a public health program right now you can do about what's out there in the work force to be able to take care of these kids, and the lack of geneticists and metabolic docs and all of that. I mean, we're well aware of that, but it seemed like this was really just focused on more

of the laboratory aspect and that the follow-up was almost like an afterthought and the broader system really wasn't being addressed and it may be beyond the scope of the committee, but that's kind of where my thoughts are on filling this out.

DR. JOSEPH BOCCHINI: Thank you, Susan.

DR. KELLIE KELM: I think there are a lot of really good suggestions that have been made by all three workgroups. One of the longest discussions we had in the lab workgroup was on the issue of the authority to screen itself. So, we didn't really talk about the funding so much except to say we really shouldn't assume that everybody has funding because that part really is a large -- takes a large chunk of time -- but there were a lot of comments about the authority to screen and that there are different processes in states, and although there are some states who are required to screen when it's added to the RUSP, there are probably more that are not -- that don't have that within their law, and so

there are different processes within the states for that.

In regards to the question surrounding the follow-up aspects, the condition review workgroup consults a group of experts for the particular condition, and I've had two different thoughts. One was: Should there be a separate survey that would go specifically to specialists and then you'd get a broader spectrum within -- across the state or should we have some very specific questions that get asked of the expert panel in the condition review workgroup that might also address some of these issues. We typically talk about what are the diagnostic tests and the availability of those and such, but that really is targeted to a very specific group of experts, but we may be able to broaden the questions possibly and avoid a secondary survey.

The other thought I had was using the existing survey, or the 2.0 version, you know, what are the questions that we need to expand? How would we need to reword them so that we could

get better information from each state? And, like Dr. Freedenberg said, although we send it out to our group of specialists and we also send it to our newborn screening advisory committee, we are limited on how we respond to how they respond, and

sometimes the answers we get back are completely conflicting, so then we're torn as to how to respond, because we have an opinion, we have a specialist with an opinion, and then we have another specialist with a completely opposite opinion and so having to interpret that and then fill in one blank for it is difficult as well.

DR. JOSEPH BOCCHINI: Thank you for those comments. Debbie?

DR. DEBBIE FREEDENBERG: I just wanted to add a little more. So, in our state we're large and we have multiple centers and specialists for all of these and the resources at each of these centers is not equal around the state and so we do get very discrepant responses, but those are

the realities with those particular centers, and so it may be fairly easy and one center may have capacity in the specialty group and the others are just totally overwhelmed and say “no way, nohow, don’t send me any more.” And so I think that the recognition that there is this unequal-ness of resources across the state and that when you’re trying to collate it and you have limited responses, it's difficult to come to really a consensus answer.

DR. JOSEPH BOCCHINI: Thank you. Yes, Jed?

MR. JED MILLER: Jed Miller, AMCHP. I’m going to build upon some things that were said about the authority aspect and what Jeff had mentioned earlier about context. I think that that part of it is just as important as thinking about the follow-up aspect the authority part seems like it's a challenge but it’s also very valuable. At the same time, it seemed like there were some objective elements that could be discerned from a survey. For instance, even though there is heterogeneity across states, it

could be asked about if there's an advisory board of sorts. And thinking about what Kelly shared about with that matrix, but the timing, I guess beyond that it would be interesting to know from my perspective: Number one, if an advisory board has discussed it; number two, if it's come to a vote; number three, what the results of the vote were and how often -- how many times the vote came and then at that point if a recommendation was made to the state commissioner of health or secretary of health, and then from that point if it was accepted or not. So, there's all these different elements to the authority side and that's not even thinking about if things happen via legislation. But, again, even though it's a challenge to kind of gauge the context, I'm wondering if it might be a way to expand the survey in that realm.

The other thing I noticed in the survey is that the initial survey, the first three questions essentially say stop if the answer is yes, and given the things that I just mentioned,

it might be interesting to have those folks who say yes, not stop but go through and answer some of these other questions about what was the history here? Let's think about how this came to be in your state, and I think that that could inform things just as there's an answer "no" could inform things.

DR. JOSEPH BOCCHINI: Thank you. Joan?

MS. JOAN SCOTT: Joan Scott, HRSA. Actually, I wanted to also follow up on the comments that were made about authority and then funding. And one of my questions is how much does that change over time? So, is there another way to get -- and maybe it's through the APHL, the NewSTEPS data, that shows us historically how long it takes to get authority and then, separately, funding, and does that really -- do we have to ask that question for every single new condition that comes on? Because does that really change quickly from state to state, or even if this is what we know about your state before, is there any differences?

DR. JOSEPH BOCCHINI: Let's have both, Susan, Debbie.

MS. SUSAN TANKSLEY: Susan Tanksley, Association of Public Health Labs. So, we discussed that also within our workgroup because the readiness tool and the information that's been gathered from that is fantastic, if 45 states have filled that out for at least one of the conditions. And that really does follow up on a lot of the -- how long did it -- so the readiness tool says "how long did it actually take you to do something and what are these processes in your state, length of time, etc?" And I thought, well could we just use that information? It's recorded, it's there, but it could possibly change over time, so you could possibly ask all the questions in the survey or you could say, "has your information changed since the last time you did this? If so, fill it all out again, if not we'll use the survey data from prior." I think that NewSTEPS collects that information, and so NewSTEPS retains that for

the states so, therefore, we would have a way to recover the information.

And in regards to the comment about the states who answer yes, that they're already screening, there's a follow-up survey and so it records basically that information but more in depth for those states.

DR. DEBBIE FREEDENBERG: I was going to take it from the state perspective and, yes, there is a big difference because, for instance in our state, our law says that we're authorized to screen anything on the RUSP as funding allows. And that "funding allows" is a huge part of it because if you're adding a condition that you just add on to your MS/MS, that's going to be one issue and one amount of funding and it's not going to require a huge expenditure of both work as well as funding, but if you're adding on a condition that you suddenly need for RUSP eight new MS/MS machines or how many microfluidics we need, that funding becomes very different and it includes more FTE's, more follow-up, it includes

-- it’s very different, so even though our authorizing law has not changed, the time for implementation and the time that we're going to need to do that is going to vary based on what we’re actually doing per condition.

DR. JOSEPH BOCCHINI: Carol?

MS. CAROL GREEN: Just to build on it, although it’s a small point and I think it might be in the survey, another step in the funding and the authorization is, in some states, you’ve already got your authorization to do it in accord with your funding, and then the advisory committee say yea or nay, or you can add it on RUSP, and in order to get the funding you have to change your cost for your newborn screening and you have to go to the legislature for that and they might say now. And then, even if you’ve got the money, you still have to go to the state for the budget that if the money’s there you may not be allowed to spend it. I think that's happened in Maryland.

DR. JOSEPH BOCCHINI: Sylvia?

MS. SYLVIA MANN-WHITE: Hi, Sylvia Mann-White, Department of Health. See? I said my name. So, I fill out those surveys and I also am project director of the Western States Regional Genetics Network and our states are really good people and they fill out the surveys and I had to laugh when Cathy made the comment that hopefully this will get to the point where states feel like it doesn't matter anyway, and we always discuss the fact that as soon as it gets to evidence review with this committee it doesn't matter anyway, but we still fill out the surveys because we're good people.

I think one of the things that I commented on yesterday during our workgroup, was that in order to get to the follow-up survey, you have to be a state that has either piloted or are screening. So, most of the states are not piloting or screening for these disorders that you're putting through evidence review, so that means that we never would give you information more in depth because it wasn't actually on our radar, we

didn’t have staff to do it, or whatever.

So, you’re always getting information on that second survey mostly from the same states because everybody knows there are certain states that have a research part of their newborn screening program that go there, and so you are getting information from those states. And generally they tend to be bigger states, not the smaller states that might have more issues because they are smaller states. So, there has to be some way of being able to get the information you want from more people because I think the barriers are more from the states that aren’t screening than the states that are screening, because the states that are screening obviously have put thought and money towards it, whereas the states that aren’t screening are the ones that have the biggest barriers, so they're not the ones that are giving you information from the follow-up survey, and I don't know how Alex is going to be able to do this because a lot of the states are just like “I’m not thinking about it, I don't want to know,

I don't want to go and take staff time to look up what the costs are or how this is going to happen," but just a reality of that's the information that you're getting.

DR. JOSEPH BOCCHINI: Thank you. Jeff ?

DR. JEFFREY BROSCO: I wonder if we can go back to the bigger questions that Scott and Dieter raised at the beginning and we probably can't answer this now but maybe we can begin to grapple with this idea of what are we really doing and trying to get out of this? And if we imagine a thought experiment in which a condition with A1 plus perfect for everything except for public health readiness and there it was ten years before we'd be ready to screen for it, would we as a committee then say, "okay, no, it's not going on the RUSP" or would we say, "yes, it should go on the RUSP," but recognize it may take ten years for a state to do it?

And so I think it will be worth hearing peoples' comments about that kind of issue because it may be we say "yes, this goes on the

RUSP, but we recognize it's going to take ten years" and that kind of separates out a little bit if we say yes or no based on its public health readiness and gives states and their newborn screening programs an opportunity to say, "yes we want to do it but it's going to take us a long time and a lot of work." I don't know if people have comments about that.

DR. JOSEPH BOCCHINI: Scott?

MR. SCOTT: I don't know if -- I mean, I agree with you, Jeff, but is that part of the discussion around the gaps in this or is that part of how we use it, because I think that we need to address that, but how do we do both at the same time because part of that is the evidence review process. But, just give me one more second to say I think in general some of the things that we have been discussing and teasing out in the back and forth with some of with some of this, and Debbie and Sylvia brought up and in the general realm just state processes, there are some things that are not going to change. You

know, what's the review process? What's the cost?

And that's data that I don't think we should waste time collecting on this instrument because it's already collected, or supposed to be collected, through state profiles and the NewSTEPS website, so I think perhaps an encouragement of states to maintain those profiles so we don't have to ask for that data again and again, but rather use this tool to be specific to the disorder that's of interest and say, "okay, well according to the NewSTEPS profile that you've completed, it takes this long -- this is your process, given this disorder. Is there any -- because I know we talked about being metho-diagnostic and things like that and I just wonder if we could hone what we get from this instrument by leveraging other data collection mechanisms, it saves everybody time and effort and makes the data better and it goes back to this thing that I agree with Dieter on in terms of this data sharing and the less you have

to answer the same question, the more likely people aren to contribute, and so if we could push that and complete profiles and grab data from that resource and then focus on this and put weight to it, which I think is a different topic.

DR. JOSEPH BOCCHINI: Alright, any questions or comments from those on the telephone? Any further questions, comments? Hearing none, I think this has been a very fruitful discussion and I think that we now need to take this back and start to collate all of the information that we've gotten and kind of develop a draft that I think the committee will need to kind of look at to see what we've got from that and probably some feedback back and forth with some key members to then see if we can come to a better, or more final, iteration of the surveys, certainly have the organizational reps involved in that aspect as well. Then, once the survey is drafted and in final form, it goes to the federal register, and is that when the public has an opportunity and others to comment on it? Is that correct?

So, we want to make sure that everybody who has a chance can have input into this so that we do get the best survey possible so that we can have the information that we need when the evidence review is done.

And, remember the key thing is that the evidence review workgroup has a nine month timeline within which to make a decision about a condition, that we move forward to them from this committee. So, I think standardizing things using, as Scott indicated, other databases where we don't need to repeat getting information might simplify some of the process for states and then trying to determine who are their key members and stakeholders that need to look at this to get information in a timely fashion so that the evidence review workgroup can utilize it effectively within that nine month time frame will be really important. So, thank everybody for their input. I think this has been very helpful.

Is there any new business that anyone wants

to bring forward to the committee? Carol? I saw your hand first, so go right ahead.

MS. CAROL GREEN: So, this is a suggestion for new business that's actually old business, that's something that had been worked on, I think, a few years ago and I though of this as I was listening to the testimony from the families talking about newborn screening for the creatine disorders, and not to bring back up the whole issue of creatine and newborn screening, but it brings back, I think, an open question this committee is about hereditary diseases and we have talked before about education of people in general and providers and families and one of the interesting comments was made by a couple of the people presenting summaries of their experience that we would know if there was a missed case because our newborn screening laboratory is closely tied to our biochemical laboratory, so if there was a baby who had -- if there was a two-year-old, a three-year-old, with a creatine disorder we would know and we would know that we

missed it. That assumes that somebody is sending in the kids with autism for testing and they're not. So, newborn screening now is a discussion that is -- it will be on your radar screen when it's appropriate to be on your radar screen, but in the meantime there are kids out there who are four years old and nine years old who have creatine deficiency and the examples we heard are people who were unfortunate enough to have the experience, but lucky enough to have the diagnosis made, so that the second kid would be okay, but there are still people out there -- we heard the discussion of children still being found when they're four years old or nine years old or older and those children either never were sent to somebody for a diagnostic evaluation for genetic etiology, or, if they were having a diagnostic evaluation by a neurologist or a geneticist, it was by somebody who subscribes to the belief that you don't need to look for metabolic disorders because they're so rare. And they are rare in the general population, but

they’re not a rare cause of autism and seizures. So, I want to bring back before the committee the notion that had been discussed before with maybe creatine disorder as a good example to develop some sort of a project -- what would it look like if you tried to educate people, not about the newborn screening, but about a hereditary disease that’s out there, is missed, that children can benefit from treatment even if -- we heard the example of the seizures stopping, and I think it was with Dawn Bailey that the committee had looked at from the education point of view but it is in the purview of the committee, as well all know that it’s not just a newborn screening committee, and I bring that up as new business and ask that it be explored because I think it is a responsibility that we are -- it’s hard, it’s really hard, and there are other things that the committee is required to do by mandate, but I think even though it’s hard, I think there’s nobody -- well, I shouldn’t say nobody else and it’s not the purview of the committee to do

professional guidelines, and that's not what I'm talking about. The ACMG is working, various other organizations are working, but I think that this committee is designed to have a role in that and I would like this committee to explore it.

DR. JOSEPH BOCCHINI: Thank you. Good comment. Any other new business to come before the committee? On the phone? Hearing none, that will conclude the agenda for this meeting. I want to thank everyone for their participation. I think we've had a really good meeting. A lot I believe has been accomplished or begun, so that we can move forward with a number of different projects. I want to thank HRSA for the organization and how this has gone. Catherine, thank you for the work that you've done, and look forward to seeing you all on the phone in August and we do want people to make comments about this survey and our public health approach, so we'll make sure that you have the website available so that you can contact us and make comments so that

we can get the best as we make this revision and get it through OMB. So, again, thank you all for your participation. Safe travels home and we'll see you again soon. Thank you.

(Whereupon, the above-entitled matter was concluded at 12:43 P.M.)