Transcript: Morning Session, Part 1 – January 31

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Please standby for real-time captions. Please continue to standby. Your conference will begin momentarily. (Operator Instructions) Thank you.

Speakers, your lines are open.

Good morning, everyone. Welcome to the 29th meeting of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children. We are trying something new today. I hope everything works well. So far it seems that everyone is connected. Therefore, we will get the meeting started. First, we will start with some housekeeping notes. For committee members, your sound is coming through your phone lines. So please make sure that you have your computer speakers turned off. Secondly, we would like you to hold your questions and comments until the end of each presentation, and as you determine that you do have a question or comment, please press star 1 and you will be placed in queue for questions when that period is open. When you are invited to speak, please state your name each time to insure proper recording for the committee transcript and the minutes. If you have any problems with your phone line, press star 0 to make us aware of it. For the members of the public, your sound will come through your computer speakers, so please have your computer speakers on. Hold questions until the end of each presentation. To ask a question, go to the lower portion of the chat box, type in your question, and then click the send icon. It looks like the small balloon or cartoon adoption to the right of the area. For the subcommittee meetings for this afternoon, they're from 2:45 to 5:00 p.m. The links to subcommittee rooms will be listed in the webinar. So now we will conduct a role call for the committee members.

Okay.

So Don Bailey? Actually, this isn't going to work because you all are on mute until you go in. So please, as you can see in the chat box, Lisa is taking a roll call right there. I can see in box right now, Carla, Cate, Freddy, Jeff, okay. So type in and Lisa will take the roll call that way opposed to having you each hit star one and wait to be called on et cetera. Okay. Next is committee business.

Okay.

So as people log in, next item on the agenda is committee business. The first item is to introduce new organizational representatives. I would like to extend my warm welcome to these new organizational representatives and I look forward to working with them during their tenure on the committee. The first is Lisa Bujno, representative for the Association of Maternal

and Child Health Programs. She serves as chief of the Bureau of Public Health Systems Policy and Performance at the New Hampshire Department of Health and Human Services. In this capacity, she serves as the director's senior deputy, directs operational areas that promote access to health care services for all families and children. She has a Bachelor's and Master's of Nursing degrees from the University of Pennsylvania, and has practiced clinically in both private and public setting. So welcome, Lisa, to the committee. Next is Dr. Susan Tanksley, representative for the Association for Public Health Laboratories. She's manager of the laboratory operation at the Texas Department of State Health Services. She has worked with numerous internal and external partners such as legislative staff, medical associations and other nonprofit organizations. Doctor Tanksley has served as chair and co-chair of the APHL Committee for Newborn Screening and Genetics in Public Health and is a member of the Commission Review Workgroup for the Committee. She holds a Bachelor of Science in Genetics and Animal Science and a Ph.D. in Genetics. So welcome.

The third is Cate Walsh Vockley, who represents the National Association of Genetic Counselors. She's a site coordinator for the Inborn Errors of Metabolism Collaborative, a long-term follow up study for patients identified, or identifiable, through newborn screening. She has also worked extensively in cancer genetics and neurogenetics, such as Huntington's disease and dementias. Ms. Vockley has also been active with patient advocacy groups, particularly with the Niemann-Pick disease family organization and Save Babies Through Screening Foundation. She is a board certified genetic counselor, and has worked in clinical and research settings for over 25 years.

To our new representatives, thank you for your participation and we all look forward to your work on behalf of the committee.

Next item on the agenda is the approval of the September 2012 minutes. These minutes were included in the agenda book, and I would say that anybody who has any question or comment for the minutes, press star 1, if you want to make a question or comment as a committee member?

Operator, will you please open the lines?

Yes, ma'am. (Operator Instructions).

All right. If there are -- I am not seeing any -- I am not seeing any comments. Therefore, we will need to vote to accept is the minutes as they have been distributed. So, for a vote, how do we want to do this?

To do the vote, can each committee member sign their name with a yes?

They will have the chat.

Would you like me to open all of the lines at this time? I will watch all of the lines. If somebody gets too loud I will tone that line down for you. Hold on one moment. Again, participants I will open everybody's line. So if you have a mute feature on your phone, just mute it yourself. Hold on, please. All lines are open and interactive.

Okay. So, Don Bailey, you are first for acceptance of approval of the meetings. Yes or no.

Yes.

Thank you.

I approve. Jeff?

Approve.

Centers for Disease and Control Prevention, Carla Cuthbert.

Approve.

Agency for Healthcare Research and Quality, Denise Dougherty.

Approve.

Food and Drug Administration, Kellie Kelm

Approve.

Health Resources and Services Administration, Michael Lu he may not be present yet. Stephen McDonough.

Approve.

Dieter?

Approve.

National institute of Health, I guess Melissa is on at this point?

Approve.

Thank you.

Alexis Thompson.

Approval.

Catherine Wicklund.

Approve.

Andrea Williams.

Approve.

All right. Thank you all very much.

I think we figured out how to do the votes now.

Right. So now we can close whatever was open.

Yeah, operator, if you can close the lines now, please.

Yes, ma'am. I sure will.

Okay. Thank you.

Next on the agenda is discussion of the anticipated cancellation of the May meeting, Sara Copeland.

So bring up the slides?

So, some is of the things to consider and to discuss are this. The authorization for the newborn screening which authorizes the Secretary's advisory committee will be -- will run out on April 24th, 2013. While we can continue the work of the contracts we have in place and the grantees we have in place, after that if we have funds appropriated through Congress, we are unable to convene the committee or do any committee business after that time. Given the logistics of having FACA compliance committees such as the advisory committee, we are proposing to cancel the May 2013 meeting. At this point, unless the Newborn Screening Saves Lives Act is reauthorized prior to its expiration, we can get the logistics through, which is not simple since we do have to do a public Federal Register notice. We have to do the registration and we have to make arrangements for public comments, et cetera. So the likelihood of that happening is very small. The other option is we may be able to have a very abbreviated advisory committee meeting simply to discuss the vote for Pompe earlier in April if that is what the advisory committee would like to do. So we will need to hear from the advisory committee and representatives what your thoughts are about this. So, operator, if you can open the lines. If you would like to comment, please press star 1. Operator?

Yes, ma'am. I don't show anybody that's pressed star1.

Okay.

But again if you would like I can open up all lines again.

Yeah. Why don't you open up all lines?

If you want, we can keep them open during the entire call and I will watch over everything and just if anybody gets loud I can tone it out or tone it down, whatever you need me to do.

That sounds like a good plan so that people can comment.

Okay. And then I will watch the background noise for you.

All right. I appreciate that.

Again, participant, your lines will be open and interactive. One moment, please. All lines are open.

Are there any questions or comments?

One would be that the committee would be prepared earlier to provide the data that's necessary for the committee to make the decision that we are going to have an abbreviated short meeting before the authorization for the committee runs out. So, we just have to try to stay ahead of it and see if that is possible, and then hope that congressional action would take place enough to make things work.

What are your thoughts?

This is Cathy. So it seems like if we can get it together it might be worthwhile to try to have a vote so the Pompe people don't have to wait? Is that what I am hearing?

If at all possible, that would be one way to try to go forward. And so I think if it is the wish of the committee, we certainly would try to do that. But we would have to, as Sara said, meet all of the requirements for that meeting and that doesn't give us a big window to get that started. We would certainly try to do so if it looks like the evidence could be put together in a way that could be presented and reviewed by the committee. If it is the committee's wishes to try to do that, we would be more than happy to try to make that happen.

If we don't do that, you guys think the next meeting would be then in September?

If we have authorization, yes.

Right. And if we don't have authorization, then?

Then we can't meet.

And then no vote would happen to Pompe.

Right.

It would be delayed until authorization was completed and then the next meeting scheduled subsequent to that.

This is Don Bailey. I think it is a good idea to try to meet early if we can, but I don't think we should if we have inadequate report, I mean an incomplete report, because that wouldn't be fair to Pompe either.

So --

So what we can probably do is that we will continue to meet with the condition review group throughout February and March as planned, which is what we have been doing anyway. And if it looks like the condition review group will be okay, we will try to get it started.

That sounds reasonable to me.

This is Jeff. I guess that I would support that, although I know probably we can't predict at this point is this just -- [inaudible]

Is there support for the advisory committee, or is there really a realistic possibility that it won't be reapproved? I am a little nervous about supporting a condition vote on a teleconference. We will see how this one goes. But I think it is a big step. And the quality of the discussion no doubt would be substantially greater at a face to face meeting. So, if it is a slam dunk then maybe it is not a problem. If there's some complicated issues to discuss I'm a little hesitant, at that particular time, about supporting that on a teleconference basis.

The other thing to consider is, from now on, most advisory committee meetings will be held via webinar. There may not be much variation there at all. So we can -- may be able, to bring in the advisory committee members to meet face to face, but do the rest of `it via webinar. We are still looking at that logistics but the likelihood of us having another face to face similar to what we have done in the past is low at this point in time given the state of the economy and the budgetary uncertainty, just for you guys to consider.

Hold on a minute.

Any other --

Go ahead.

It is Fred from the --

What is the status- about reauthorization? Is it pending? Is it something on the books and it is just a matter of congressional action getting there, or is there a real question about reauthorization?

From our side, we don't have much of a [inaudible]. There might be other org reps that know more. I can't comment on that. I don't know. March of Dimes or Genetic Alliance, if you have any comments or APHL, if you know of anything?

This is Natasha from Genetic Alliance. From what we can tell, it is still, we are kind of waiting to see if there are some sponsors letting up. March of Dimes has more on this, but with the climate; it is hard to tell what will happen. There have been other bills that have gone up for reauthorization that were a slam dunk and were very difficult, so it is just a waiting and seeing. Everything is very optimistic, but it is just kind of getting the process going. I welcome other people to chime in who have other information.

Thank you, Natasha.

Other comments?

This is Edward McCabe from the March of Dimes. I know that our Office of Governmental affairs is working very, very actively on this. I am not sure if they're on the call, but this is a priority for us.

Thank you.

Additional comments?

I think we are going to need an official vote on whether or not you want to try for the April meeting or not. Well, actually it is a logistics call on our end. We have heard the consensus, but let's just kind of run through it again. What would the preferences be?

With everything open, I will ask each person to indicate their preference for trying to expedite the process for Pompe and have a telephone conference before the end of the legislative authority of the committee while we wait for reauthorization. I will start with Don again.

I hear what Jeff was saying and I agree, but if the climate is such that if there's a low probability of face to face meetings, I think we should proceed with trying to have an earlier meeting to review Pompe. But again, only under the condition that we feel very good that we have done a

thorough due diligence on the review and we are comfortable with where we are, you know, with respect to the data.

I think that's a good point that both you and Jeff have made. I would think that if we decided to go forward, because of the data under review, in a telephone conference and we decided that we could not make the decision unless we were face to face, we could always amend the decision at that point, rather than not going forward and try and do what we think would be right. So I will take that as a go forward then, Jeff?

I agree. I would like to schedule a meeting or participate the meeting in April.

Okay. Carla?

I agree as well as long as the evidence review committee is prepared.

Okay.

And then Sara? Can we get a vote?

The logistics, if we can get the logistics of it together I think that's probably the prudent thing to do. We are having to look and see what we can do. Denise?

I agree.

Okay.

Melissa?

NIH?

Answer. Hello.

Hi. You were on mute, I think.

Okay.

Next would be Kellie Kelm.

I agree with all of the previous points.

Okay. And then Michael Lu, if you are on at this point?

Dr. Lu, are you on?

All right. Stephen McDonough.

I agree. I think it depends on what we are going to do with a vote on the matrix, but I think if we depending on what we do with the matrix, I am certainly happy to discuss April on Pompe.

Okay. Dieter?

I agree as well with what was said. I was wondering, are we able, if we voted and can give the review group the next condition to consider? Or is that on hold until we have this legislation done?

They already have, so they will start that no matter what.

Okay. Alexis Thompson.

Yes. I agree, but I have the similar reservations about the quality of the conversation and as well as the implementation of the matrix.

Catherine?

I agree as well. I just want to say also that I do agree about the face to face meetings and Jeff's point made at the beginning

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Okay. Thank you. Andrea Williams.

I agree.

Okay. Thank you all. I think that brings out the issues both as a committee and specifically about what kind of work we can get done ahead of the expirations of the legislative authority. Thank you. Sara, any additional comments relate today at that.

I don't this is so. I think that I have heard what the advisory committee would prefer, and for some reason it seems that for everybody, face to face is better which I concur. We will take that into consideration too as we look at going forward. However, if we do an early meeting it will have to be via webinar. I can guarantee that, but going forward after that we can take consideration as we get the instruction.

Thank you, guys.

Thank you, Sara. Next is the condition review decision matrix then we will discuss the review. So as a general pediatrician at Duke University, with research focuses on implementation and evaluation of the programs for children, including newborn screening, screening for visual impairment and screening for --

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Alex?

Thank you very much. Good morning everyone out there in Cyber space. What I am going to do this morning just very briefly highlight the document that was sent to you recently and Dr. Bocchini, I think you will make some comments as well. You will open it up for discussion. This is referring to the SACHDNC decision matrix. September 2012, the committee approved the use of a decision matrix to assist with the development of recommendations regarding conditions nominated to the RUSP. It is based on a 2-step process, first looking at net benefits or the differences between benefits and harms, then the capability of state newborn screening programs to adopt comprehensive screening. This is just a brief overview of the ratings that were developed for net benefit, A being there's a high certainty and will lead to a significant net benefit. B, which is where some of the issues have come up, if there's a moderate certainty that adoption screening for the targeting condition would lead to a significant benefit. The key thing here is around the term moderate, which implies that further research could change the magnitude of the direction of findings within any of the key questions such as the assessment and benefits would change to small to zero or even a negative net benefit. Again moderate meaning there's a chance that things could change. C being a higher moderate certainty of a small to zero net benefit and D being a high or moderate certainty of a negative net benefit, and L is low certainty about the net benefit. These are some key thoughts around the assigning net benefits or the difference between benefits and harms that were developed in the previous meetings that we've had and through the discussions that have ensued subsequent to the meeting. The most important consideration is the child being screened, and considerations include the overall public health burden including the birth prevalence and the severity of the condition, the benefits of early detection and treatments to the affected children, and then the harms related to screening diagnosis and treatment. It is important to consider both the harms to affected and unaffected children since all newborns would be exposed to screening. False positive screens are an important harm, however the impact of a false positive varies based on the condition and what things transpire after a positive screen, for example, the diagnostic process involved, sending another dry blood spot or whether or not there are more intensive and complex evaluation that has happened after a positive screen. There needs to be compelling evidence to justify screening for late onset disease, that is disease that doesn't manifest itself in the early childhood, and the key thing here is that the advisory committee doesn't use a single defined metric for that, so it is not like a simple point scheme that has been developed. These are complex issues, and it is reflected in the conversation that just occurred about the challenge of making decisions via webinar versus in person. I -- I think we all know how hard this can be.

Now, the next step as we talked about was the capability to screen and that was broken into four categories as well, ranging from high to moderate feasibility with newborn screening programs just ready to go, all the way down to four where there's low feasibility for screening. In terms of assigning to screen is the central issue. I think what nobody wants to do is overemphasize the issues of readiness because if it is all based on readiness, then things would never happen. But the feasibility of the screening is obviously important. However, careful

assessment of readiness can help identify needs that can be addressed and guide the implementation activities and you will see this in the later presentation that I make.

In terms of assigning to screen in terms of technical clinical feasibility, there should be an established screening test, clear approach to diagnostic confirmation, accepted treatments and plans for what needs to happen regarding long-term follow up. The issues related to readiness include the availability of resources for diagnostic confirmation and all of the components of long-term follow up, including treatment. Then, of course, newborn screening programs have to be authorized so I went back and looked at some of the decisions that the advisory committee had made, and I tried to classify it. I think that, you know, reasonable people can disagree with how classified this is. But it was an important exercise to go through this test, how well things worked and looked like when it was evaluated. It was a net benefit but there were questions about the feasibility of the screening because large screening programs haven't been done yet. There were questions about the test and so forth. That went from a 4 to a 2 after Wisconsin. Yeah, Wisconsin. I was suddenly blanking on which did the screening from a four to a two with CCHD. I think that there was consensus that there was an A net benefit. But over time, the capability to screen, I keep saying ability, it is really capability to screen really went from a four to a three to a two with the disease in 2006 when that was reviewed, that was classified as it being Pompe disease, around issues of screening and there were positives that screening would generate. Also issues around treatment including the issues of CRIM status, and the screen test hadn't been implemented in the United States. At that time, that was a four. With hemoglobin H disease that is correct -- I have that an L net benefit because it was unclear about the benefits of early intersense. Because of at that we didn't look at the ability to screen. Hemoglobin H disease is interesting because California screens it. And it could be picked up by the way a lot of states do screening. But it is not something that we explicitly considered at the time. Hyperbilirubinemia, in terms of the ability to screen for it. We didn't exclusively address that, but what would have been a point of care screening test that had lots of challenges. Then Krabbe disease, it was listed as an L. We didn't explicitly evaluate the ability to screen. So that is, I think, an example of how things could be done. Again, people might disagree about how I rank things. I would be interested to hear what people have to say about that. These are the lessons I learned in my process of grading things. First, that can be rated as a D or L should include guidance about what's needed to resolve the uncertainty. A score doesn't need be assigned if it is unlikely to be recommended for a screen based on net benefit. If it is an L, I don't think, for example, a lot of work needs to be done to sort out how feasibility screening is. And then, the final point is there's a lot of overlap between readiness and feasibility and, you know, tabbing it can be difficult figuring out which is feasibility and which is readiness. They're not meant to be exclusive but it is a frame work makes sure we consider all of the distinct components, and again I think it is really feasibility that drives most of this.

With that I would like to open things up to questions and comments. I think you are going to lead the conversation.

I would like to hear from committee members first.

I was hoping you would say we were going to open up comments for doctor --

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We will take questions as well.

Operator, you can open all of the lines, please.

All of the lines are open.

It is clear it is an evidence-based committee. We need a frame work in which to make our decisions and I think that one of the questions that the committee members raised in terms of using this matrix and in subsequent call that is we've had is to provide examples. And I think that what Alex has done very nicely is to take the previous decisions of the committee and put them in a decision matrix in such a way it shows us this matrix is providing us with a transparency within which we make our decisions based on the evidence that's available to us. And so I will start with that comment, and then let's hear from the committee.

This is Jeff. I want to thank Alex for the work and the things he does for the committee on newborn screening. A question about feasibility - I think we are seeing this illustrated with the Pompe disease materials. But will you comment on what the evidence-based process is for assessing feasibility and capabilities for state programs?

Yeah. So you know, there is -- [inaudible] one is and obviously one principle thing is the ability to screen, so there has to be a good test out there. So in the process of evidence review, we are able to evaluate the test characteristics. But, there's sort of an overview, you know, there's a lot of aspects to the feasibility and also readiness that come out in the process of evidence review. That's why we are working with APHL who's going directly to states to evaluate what it would take to implement comprehensive screening. So, again why I think you will see this when we talk about Pompe later, that there's clearly some aspects of feasibility that come directly from the evidence. But then there are other things at that are going to rely on the work that APHL can do within the states. Did I capture that?

That's a really important partnership that has been established. It will provide us the opportunity to really get a feel for what is going on in the laboratories and what the impact would be to attempt to implement a new screening test or a new protocol or algorithm so that it is going to strengthen our ability to really test feasibility and readiness. I asked this question before to the laboratory themselves. What happens with the schedule -- [inaudible] dealing with the results.

The APHL is going to be looking at this. In the laboratory, that is. Really I apologize for being imprecise, but the whole process of newborn screening.

Okay. Great. Thank you.

Can I make a comment?

Yes, Stephen

I feel that the matrix is, in large part, push back from the committee's recommendations on Critical Congenital Heart Disease and the considerable stress base placed on state health departments and their ability to implement, in addition to SCID, in the greatest recession since the great depression. It was difficult on health departments to do this. We have to be careful not to overreact and place unreasonable burdens on rare conditions at health departments that will be able to quickly screen for in the future, conditions so uncommon that conventional evaluations may not be easily designated as either A or B, program versus in between. I continue to have concerns about the need to approve it at this meeting. A 1 or A 2 will be approved by the committee. I'm unclear why the committee would want to approve an A 4 but should send a recommendation for the health departments. I believe that many A 3 should be approved and the role of our committee is to set a direction for the state health departments to be able to screen A 3 conditions as resources become available to them. Last week the definition of category B was changed, and I would like to hear from medical researchers if the current metabolic disorders being studies out there in research will easily fit into our A or B or fall somewhat in between. And I would like to hear from them before we make that decision. How many of the 31 core and 26 secondary disorders are on the RUSP are category A 1 and category B 1? So the category B 1 condition be removed from the -- and if not, why should conditions meeting the upcoming definition of B 1 in the future not be considered added to the rough? Is there a grandfather clause for children who have B # 1 conditions in the future that they won't be able to be added to the, where children who had B 1 conditions before 2013 are currently being screened? To me there are too many remaining questions to be answered about the matrix. I believe more work needs to be done and the written comments should be requested from public group researchers and advocacy groups. I would like to hold off until the next meeting whenever that would be. However if the committee decides to vote today I will be voting no. I appreciate the opportunity to make these comments.

Thank you, Stephen. I think that those are important comments, and I would like to hear some views from the rest of the committee members. I think that, you know, essentially, what we are trying to do is to take the evidence that's available and place it in a category for the transparency we need to make the decision for the best interest of the public health and for the whole community. I certainly would agree with you that A, at guilt or innocence, the committee might decide for the A categories. I think that we need to have a definite situation of something that may show promise but is not, but that there's not enough evidence that going forward with additional research that we might find that the benefit that we think is there may not actually be there.

And so I they need the opportunity to have conditions fit into that category.

I think it is very clear that the committee has made recommendations on the laboratory and the general care of the heart disease that were A recommendations and think that it taught us in terms of a pint of care recommendation that we have to think about other things. That's why

those are being added not to be a debt are limit to having that done, but to pay attention to the impact because we make that decision. That's why that is been there. So, I think those are my comments. I would like to hear comments from the rest of the committee.

If I might interject, we have always had a matrix. It was just differently configured and the legislation has always said to have a public health impact. That's what the Secretary was pointing out in the letter. This is not a new requirement. It has been there since the inception. We are just trying to quantitate the ability to do that. So this is done, this is Don Bailey. So a couple of questions. My understanding of what we would be voting on is the frame work for us to be kind of putting all of the cumulated evidence across a variety of different domains into some kind of consistent format, but that we are not voting on where to draw a line in terms of may recollecting a decision. Am I correct on that?

We are drawing a line as to where to make decisions. And maybe I should go through the slides next, just to give you that information about where we think we need to draw the line. So, if there are additional comments, on these comments, I would like to hear those first. If not, I will go ahead with the proposed committees Press Release for the matrix and we will generate further discussion.

Okay. Can I make one point about evidence? There's always uncertainty when you look at evidence, and it is a matter of looking at the whole chain of evidence. So, if you remember we have a whole series of key questions we tease out separately. Any given question, there's always going be uncertainty. The issue is what the magnitude is. When you look at the whole chain of evidence, are you confident that adding this condition to newborn screening for all newborns in the country is going to make a difference? Or is there still uncertainty where the harms might be greater than you're certain of or that the benefits might not be as good? That's where I think in most cases statewide pilot studies come into play. If you look at historically what has happened where states have been great laboratories to find out whether or not things work out or not. Certainly that's what happened with it and I am sure Sara can come up with other examples. In terms of the things that are currently on the screening panel, again I am not knowledgeable enough to go through all three dozen of them or however many there are depending upon how you count. But those are the things in the future that might come up, if the data that is being collected by state shows that there's more harm and expected benefit is not as great. But the thing I wanted to point out is within any of the key questions, these are rare conditions. And in most cases, newborns have been identified with the conditions, because you know treatments are new and those kinds of things. But it is really a matter of whether or not the benefits really do out weight the harms. And so, again, things that are added to the RUSP are those things we think that every newborn in the country not be exposed to. I think that is where the difference between the A's and B's really -- and I am just -- I am not telling you this just without saying this, but that's what grew out of the meetings that occurred. So I will just leave it there.

Other questions from committee members?

This is Dieter.

Yes, Dieter.

I wonder whether we can hold off with the vote until we have heard from Alex on the Pompe review since he indicated that there's basically an example of how this matrix would be applied and how APHL is looking at the states. I kind of maintain my concern that the matrix as it is proposed and if we were going back six or seven years and look at the work that SACHDNC did at the time, if anyone at that time would have looked at the states, probably all of the conditions that were added would have been considered as low feasibility, given at that no other screening lab had any. This makes it too easy not to screen for conditions.

And if we look at the current example, I mean Illinois for example, a few years ago; they said they couldn't do screening -- storage issues because it requires too much equipment. They don't have money and space. Then they went with a small footprint technology, and decided that doesn't work. Now they implement. So it is a constantly fluid situation. That's why I am interested to hear how the states are currently prepared to screen for Pompe disease.

The fact we can categorize things as threes and fours that the committee could make a strong recommendation for the conclusion of the condition on the RUSP, in spite of the fact that the labs are -- or the states are not, ready. And yet make a strong argument that this is something that should be done by state laboratories and that these sources should be placed into that area so that it could be done. I mean to me, that gives some additional strength to the committee's decision to say we think this should be done. We think it should be done as soon as possible. We know the states aren't ready. But we think they should put resources in to do this. That would probably be A 4, so it gives the committee the opportunity to really push to make this happen.

This is Jeff. I guess I would say that heart disease was a little bit different because it had more to do with whose responsibility it was. If there was a blood spot screening for Congenital Heart Disease, I don't think anybody would have had the same sort of anxieties around bringing one on board. I accept the distinction between the feasibility and not wanting to over-interpret that. If tests are out there, and it can be brought in a reasonable period of time, we should be voting positively even though states aren't ready to do it today, within a reasonable period of time. I am not too concerned about that aspect of it. I think Stephen makes good points about the history here, and I think we are with how we think about these issues. I certainly, among others, was critical of the evidence review that went into the original uniform panel. I think part of the responsibility of the
secretary's Advisory Committee is to review some of those issues as they go along, the quality of what it has been in the past. I see that as a good set of developments. I don't think that I would hold the matrix hostage to the fact at that we are improving the thoughtfulness and care that we make these sorts of decisions. I accept Stephen's concerns but I don't think it would make me disapprove the matrix at this point.

All right.

Additional comments on the committee.

This is Don Bailey again. This may -- I don't want to -- this discussion today. It may be more relevant to the next part of the discussion on where we draw the line. But I would like for the committee in the future to take on the questions of benefit. If for, let's say, a condition like -- syndrome where there's no medical treatment now for children, but children would be eligible for early intervention programs, would we expect every new condition to approve early intervention through, you know, special education, physical therapy, speech therapy and so forth. Would therapy and so forth be effective for that particular condition, which I think is probably not a reasonable expectation. I would like to ask that, you know, future meetings if we are still a committee, who actually devotes time to thinking directly about this issue, that's an important condition. We should consider that.

Thank you.

Other committee members' comments? Questions?

If not let's open it. Carol?

My comment or question is actually not directly related to the matrix. But I would like to say that the last couple of points of discussions, if the matrix makes sense, you still have to define feasibility and define benefits. So including feasibility doesn't mean that you can only do something if states are ready to hit the ground running right now. You still have to work on and there's still opportunity for feasibility. I don't personally see that, from that point of view, as any argument against the matrix. It still means we have to discuss those elements. What I wanted to say is something that we need to consider, in implementing whatever matrix we go forward with, is mention the pilot studies. That's really important, just thinking practical, and we have been there. If we say that we need pilot study, some states consider pilot studies experimental. Others consider pilot studies improvements of their services and moving forward. And if we are not careful about some language around the implementation, we could be at risk for making, setting up a situation where any progress a state might be ready to move forward, to actually screen and to report back on the data: but if we set up a situation with experimentation, we get a rather important wall in terms of state's attorney general, in terms of consent, not be able to do population, so I think we must be careful as we move forward with a description and not have everything except the rough experiment.

Thank you. Additional comments from organizational representatives?

Yes, hey, Mike. -- I tend to somewhat. To me feasibility is very poorly defined because it could be, you know, the impediments to feasibility that we really need to know. So we can determine whether or not they're surmountable or not. An example of something that, you know, wasn't there when this started, may say that it is not feasible to operate. The real issues are what are

the impediments to bringing on board if we think that the conditions are important enough to be screened?

I agree. That's a good way to put it.

Additional comments.

This is Susan representing APHL.

Yes, Susan.

I just wanted to comment a little bit on feasibility from a laboratory perspective, and I am laboratory operations unit manager at the Texas lab. It is fortunate to gather the information from the states to kind of, as Mike was just saying, find out what the impediments are. In the case of SCID, for example, Texas and many other states were nowhere close to ready for implementation of SCID. However, without the advisory committee adding that, making that recommendation to add it to the panel, many states still would not have added SCID to panel or be in the process of adding SCID to the panel, when you know, there was obvious evidence that we should be screening for SCID. And so I think that it is very important to understand the perspective of the states and where they are it doesn't mean you shouldn't recommend it be added to panel. But it should provide a perspective of where the states are and what those impediments are and how long it will take. Just because it may take a long time for a state to add it to the panel it doesn't mean that it shouldn't necessarily be added to the panel.

Thank you. That's a parent comment. That's in part why the partnership has been developed with the public health laboratories with the evidence review group, so that information can be available to the evidence review group and be presented today at the committee, so that those kinds of thing can be addressed and the committee can push forward, based on the recommendation for the laboratories to make the adjustments to include the new testing, like the case of SCID, would have a better feel for what they could or could not do when the decision was made. Additional comments.

This is Freddy.

Yes.

Just, we are supportive of using the decision matrix of the logical extension of evidence-based reviews, and the requirement really that you need to grade the evidence and come up with. I think we are supportive of having decision review matrix, and look forward to that discussion next about how the committee will use it.

This is Jeff. Just one other quick comment. This feasibility is really such a new concept for us to think through and I am not sure with how we make decisions about that because there are lots of circumstances. I will take congenital heart disease in Utah as an example. We describe the

cut offs established. So there are particular challenges with bringing that on in our state environment. But the same challenges may not exist in the other states. The Secretary's Advisory Committee could say it is just as good for all of testify other states. -- all of the other states, but how we express that needs to be flexible in a way to realize individual states may have particular circumstances that may it less feasible there. It doesn't mean the test is or the implementation isn't feasible, it just means it shouldn't be an implication that you say is behind the times if we are not up and running to go along with the other state colleagues.

Thank you. That's another important point. Other comments?

All right. If I go through the slides on the proposed committee use of the matrix. Just as background information, this committee has always worked with a decision matrix based on the evidence that was available -- on the evidence that was available. And I guess it is about two years ago the committee began the process of revising that matrix and incorporating some of the newer information about how to evaluate evidence in a transparent fashion, and grade it some way, to help not only make the decision transparent but also to clarify and a better way to make the decision, and perhaps stronger decision. And so that this committee did meet with leadership of the U.S. public service task force and other people who have been involved in grading evidence and to come up with this revised matrix. And the committee has come along the way in discussions and we have reached a point we have finalized the matrix and the committee did approve it and now the question is for final vote is how to use the matrix because the question came up at the September meeting about where we drew the line. We have had a couple of meetings with the committee by telephone to try to, you know, hash out some of the issues and then we have modified the categories as such. We didn't change what they meant, but we have clarified them in such a way that I think that the use of the matrix is fairly clear, so, we can go forward. Okay. So this is the current matrix. And again it is -- we have net benefit, feasibility and then readiness many the center. And then down in in left column, those that have significant benefit, those at that are small to zero benefit, negative benefit, and have categorized the A decision, A 1-4, and B decision which is where the data has moderate certainty. But again I think that a short cut of this line here is what caused a little bit of difficulty in terms of the interpretation that changed and what that meant. And then, whether a decision was to go forward with the recommendations with that in particular. So in the process for evaluating the condition for the recommended uniform screening panel, we -- the way we define the certainty of evidence was in these three categories. Low certainty was that available evidence was insufficient to have [inaudible] in the assignment of the net benefit because of significant limitations in the availability evidence. For moderate certainty, as Alex mentioned earlier, further research could change the magnitude or direction of findings within any of the key questions, such that the assessment of net benefit would change.

So here we have a condition for which there is some evidence of benefit, but not enough to be certain enough that additional data would not change that -- not change that benefit, and then high certainty. The net effects, net benefit is unlikely to be strongly affected by the results of future studies.

And so for a benefit, the conditions that fall below an A rating then are not added to the RUSP. And again, as Alex mentioned, category B designation and reviews will include is suggestions related to the gaps in evidence and what could be done to make an A rating. And so this would have a targeted or expedited condition review. For example, the process that occurred with the addition of SCID falls into this category that there would be some direction, given, that would enable others to study or provide additional data that might solidify the benefit or ultimately change it. They solidified it from a B to an A.

Then for categories C, D and L. Resubmission would be required for consideration to the RUSP.

Now, the conditions that would be A 1 or A 2 would require little to no further discussion. There would be significant benefit and readiness and feasibility. So the committee would believe that they should be added to the RUSP. High certainty of significant benefit, screening has high or moderate feasibility and health departments are ready or have developmental readiness to implement the screening process. As mentioned earlier, that would also mean that the follow up and the rest of that would be replaced as well.

-- in place as well. Categories A 3 and A 4-may be added to the RUSP but requires decision about what makes them less feasibility or ready for the addition, and could further demonstration projects make this more feasible, or is there a missing algorithm that might move it to a higher category?

And again, here is the matrix.

So I think that the, this is up for any additional discussion, and then a motion for the vote to accept the matrix and its use by the committee.

Operator, can you open the lines?

Operator: Yes, ma'am. The lines are open and interactive.

Thank you.

Any discussion or comments?

Dieter.

Yes, Dieter.

I apologize. I wasn't on the phone call last Friday so I have a question. So if the A 4, this is in internal discussion -- [inaudible] or what are the limitations for is that? Is that Secretary -- A 4.

No, no, it is the committee's discussion and decision. So we bring that forward as a recommendation to the Secretary based on the discussion and the final vote by the committee.

With the stipulation as to what that means and what the recommendation is for correcting the A 3 or A 4.

You would tell or recommend to the Secretary to include this condition on the RUSP. But be aware that for an A 4, health department versus low feasibility of actually following the recommendation?

No, no. That at the present time, they are unable to -- they're not ready or they may not be feasible. But the recommendation of the committee would include what we believe that it is important enough that they put resources or whatever is necessary to bring the labs up to the level and follow-up et cetera up to the level where it should be added. And again, for example, the SCID, it would be as soon as possible. And for others, it might have a different timetable. Does that clarify your question, Dieter?

Yes. -- [inaudible] I just wonder in the case of SCID for example, the second tier – what would the Secretary have done if it come with the stipulation there's work that needs to be done. Would she have recommended it, or said come back and let's figure it out, or whatever?

Yeah. That's actually what happened with the initial letter to the Secretary saying I can't remember the language. But that it was essentially a promising thing, associated with SCID, but that states needed extra support to be able to exhaust the -- and that started happening. So it was just a -- I think that it is actually what happened, SCID, when I went back and looked at the letters to the Secretary.

So this is Ed from the March of Dimes. I would just -- I think it was Jeff that mentioned that really this would have been the situation for -- but you know, the system wasn't in place at the time with these categorizations. But I think that we need to really look at what's best for the health of the babies and they may have to push the state health department to be thinking in areas like -- before.

I agree. I think that is the committee can help make that happen with the three or four. But the important point is that we will have, because of working with the labs and having a clear understanding of where they are, we may be able to provide the Secretary with what the state health department needs to get this done, or what the laboratories need to get this done. So I think it is strengthens our ability to make specific recommendations or change to implement a new task or a new program.

Yes, I agree completely.

Thank you.

Dieter again, if I may. How -- there are 51 programs in this country, and do we say well, if 51% of those are ready to go then it is an A 2? Or because it might be very different from California. North Dakota might not have a problem with the technical implementation, the laboratory

because if Iowa is ready, apparently North Dakota would be particularly. But they may not be ready to see five false positives for Pompe a week.

Dieter, the question you have --

It is one of the concerns that we had about the process. [inaudible] to authorized legislation we have to look at this readiness and feasibility. But what I didn't want there to be was like a point system, where you've added up this many states, and say do this and this many can do that and then add things up and divide it and come up with a simple metric. It is much easier to leave the ratings many hands had of experts like you. That's why there's a committee, because there are nuances that aren't captured by the numbers you are talking about. I am not a voting person. I am just having the conversations have gone. But it is my strong opinion that the final classification requiring deliberation, and not just a simple metric.

I think we have the committee -- if no state was ready, or two or three state windshield pilot program, we indicated that it should be done and all states should work toward doing it. And as you said, do it more recently, than it appears it is committee, task resources to be provided to enable that to happen. So I think the history of the committee is that we are basically doing without a rating, but now we are finding a way to categorize so that the committee has the data that's needed to really make a more, a clearer recommendation.

I'm all for data, but my concern, maybe we should just go through Pompe example before we vote so that we, or at least I, get a better understanding of how we do this.

I can tell you, you will probably be disappointed when we are done with the Pompe because we are still in the process of working with the states and that kind of thing. So I don't -- I mean it is ultimately which direction hinges going and stuff like that. But I don't think that listening to the Pompe is going to resolve all of your concerns.

Dieter again, actually, maybe that is just already one of problems, that it might too long to get to point where we have that information from all # A 1 programs.

-- all 51 programs.

It is not looking at all 51 programs. You will see for example. But again, it is just; there just need be enough information for you to be able to make an informed decision about whether or not you think that this is something at that could be reasonably done by a state.

I just want to reiterate my concern there may be some B 1s that will come up that we ought to be able to approve that look good, very rare. It will take forever to get the amount of research to get them A. The health department has the tech speak, they're ready to go: we won't be able to approve them. If you go back and look at conditions in rough you will find a lot of B 1s are there that were approved because we got the technology to do them but there was just no research whatsoever that would make them an A. The other point I would like to make is that

when we do a B recommendation. If the committee, going forward, is reauthorized that someone should come back annually, give us an update on the status of the research that is going on all of the conditions that are in the B category, where they are, what things are going on. I would like that actually to be part of the letter that would come from or the decisions the committee would make if we make a B 2 or 3 that we would cause the Secretary to designate someone to come back and update us annually on where that is at.

This is Don. Can I respond to that?

Yes, Don. So Stephen I didn't really fully appreciate all that you were suggesting in the previous calls. And now that I am thinking through this a little bit more, the comment you make about B I think is really something we should consider. I am in agreement with all aspects of the matrix, all of the A 1 through 4s and C, D, L and with the decisions with that. I am just worried about saying never that we would never consider, never approve a B because going back to my comment about, you know, other conditions for which if we can show that early intervention or, you see the point. I think there are conditions, that is, will never really be able to meet the high standard for certainty of benefit. But for which there's a reasonable expectation for benefit. And if it was feasible. And if it's a 3, we wouldn't be doing it. I am wondering can we just have a little amendment here so we are not saying never say never to B? That this is the frame work that we are following, but that B, it gives us a little flexibility on B's because I would hate to come up with a rule that basically then we would have to change our scoring system later if we ever wanted to consider a B.

Well, you know, the way is that B includes suggestions related to gaps in evidence and what could be done to make an A rating. As an evidence-based committee, it would be really difficult for us to go forward with a recommendation that affects public health and the laboratories and families without being sure that there's a benefit for those families and especially for the patient. I think that there has to be a level of evidence that you must meet to go forward, that is the difference between A and B. This is not unlike an evidence-based committee. So I think that it would be really difficult to draw a line and then say but we can go down as far as you want in a particular set of circumstances. You have to be clear that you are going to have benefits for patients before we're clear with going to the Secretary with a recommendation.

Well, I agree. I think that I understand that. I think that there's a little bit of confusion about within the benefit. And again I apologize for not having thought this through more thorough earlier. But it is moderate certainty of benefit or is it moderate certainty that, you know, that it might be coming in the future? That would support that? I think there are conditions where we would have an accumulated set of evidence that there is a net benefit for screening. I'm just thinking this through for a committee discussion. If we set a precedent right now we will never approve a B, my point earlier about more specificity about what we mean by benefit is might be pertinent, maybe I am not -- maybe I am the only one who feels the way.

So, if I can -- Don, you have mentioned a couple of times you are concerned about enrolling a child into early intervention and looking at the outcomes from early intervention would be

considered to be a benefit? And I can tell you that from the evidence review process, we would look at any benefit that would accrue to the affected child involvement. I don't consider early intervention to be different from any other therapy. It is just that when we have looked at so far, early intervention hasn't come up as a, you know, as a major treatment. So, I don't think that's a particular concern, what I think about getting back to B is we have these questions that create a chain of evidence. If there's one key question, one thing that the benefits really hinge upon, and there's significant uncertainty about that key question in a way that if the committee thinks that the answer to that key question might be such, that's where something would become a B. So it is important to look at the whole chain of evidence and then if there's a key question where there's so much uncertainty that you were concerned that the -- risk no longer outweighed the harm, it would get a B. The recommendation would be that that whatever issue is around that is resolved. Certainly there's rare conditions there's never going be strong evidence throughout. If a key question is where the kind of structure that everything is buildup upon would fall apart, if the answer were different than what we have and if the advisory committee felt strongly it was an important area of uncertainty. I don't know if I said that well or not.

I think it did. Let me just add what I think is the answer. I think that, as Alex said, that you create these questions. If one of the key questions many terms of benefits is outcome of a specific intervention and there are only a few question, but the outcome is pretty dramatic, that may be 90% of all of the questions and result in an A rating even though it is a small number of patients. So you can make an A rating with incomplete data as long as key question has a very strong outcome.

So I think that the kind of thing he's talking about, limited data but a really strong likelihood, a really strong benefit based on a key question might make something an A. The committee has the final -- so I think that the kind of thing that is we both are talking about are thing that is could potentially have an A net benefit because of the impact on the question.

I would just respectfully disagree slightly, Joe. I think that it will never show the early intervention has a dramatic impact in the ways that you are talking about. And I don't think that it will be reasonable to expect each condition to conduct a trial for that condition specific. Now, this is taking us off on a different path. And I don't think -- well, I think I have said it. I don't think that we would, the conditions that I am talking about would ever meet that criteria until there's a medical treatment for it.

It seems to me the whole matrix is embedded if -- background with a lot of times in this situation that it is not going to be ideal. I think the As aren't going to be that we would ideally want. So, particularly given the fact that the evidence review group doesn't put the letter on it, a B into an A category because we think it ought to go forward. I think the other aspect -- the whole research infrastructure. So I'd like to see the Secretary's advisory committee look into thinking through the really serious challenges that are out there for conducting research in this domain. So we shouldn't simply limit the quality of the data. We should make more of an effort

to develop infrastructure to get these kinds of studies done if a reasonable fashion. -- in a reasonable fashion.

Can I bring up a much, much smaller point? That's the A 2, can someone explain to me the word however?

Thank you. By the way, I do go with the much larger, before that would be a real utility to have the committee think about how we might make research in this area more robust. I want to, that was a much more major point with which I hardly agree.

-- I don't think that is a matrix question, but it is an important question and one we should discuss as a separate, you know topic I think is really important. We are on an advisory committee, and our primary goal is to determine but I think that we can look at other aspects of the whole process, and -- research I am not sure, question, direct the Secretary to what would be the research priority. So I have some difficulty with that, but I think on the other hand, I think that we can play a role.

Okay. Are there questions?

This is Alexis. I had one question similar to the last speaker. For both A 2 and A 3, just a friendly amendment to add the worst, in terms of public health department, so it is clear we are not asking for an absolute statement from all public health departments.

Add most.

Yeah. That’s what I meant to say.

Then it will be noted in the minutes.

It will be noted in a minute. So the next question now is.

So I need a motion from committee members to vote on use of the matrix as indicated.

This is Jeff. I move approve the matrix as amended.

Is there a second?

-- I second it.

Okay. So it has been moved and seconded. And now we will go through a vote. Let me find the vote. I have it. Let's start with it. Vote for or against.

I vote for it.

For?

Catherine.

For, approve.

Alexis.

Approve.

-- I am sure whether Melissa or Alan is on?

Alan is on. I vote for.

Okay, Alan. Welcome.

Dieter

Against.

Stephen?

No.

Dr. Lu?

Approve.

Kellie Kelm

Approve.

Denise Dougherty.

Approve.

Carla.

We approve.

Jeff.

Approve.

I will vote yes. Don Bailey?

I am going to vote no because of lack of clarity for B, and I just don't think we are at a point where we should be reducing all B conditions.

.Well I really appreciate the discussion and your comments. I think it is a very important issue. I think as we go forward, I think that some of the issues have been raised which are really, you know, substantial, we will in the process of use thing matrix clarify. And clearly, the committee can clarify in the future if it does look in a way that we don't like. So I do believe -- we can modify further as we go along as needed. I appreciate the comments and the work of the committee and getting to this point.

We now have a 15 minute break. You can get up from the computer and walk around the office or whatever you need to: get a cup of coffee. We will return at 11:25. Thank you all very much.

11:25 eastern time.

Eastern time, yeah. That's not for you, Stephen.

Okay. Thank you, all. [Captioners transitioning]

Please continue to standby. There is going be silence until the conference resumes in about three minutes. Thank you.

Hi, hello.

Operator, are we back on?

Yes, ma'am. Your line is live. All people are on listen only for now.

Okay, great. Thank you. We are going to wait one more minute and then we are going to get started again.

Okay, welcome back, everybody. We are now going to hear public comment. So, um, what I would like to remind you is that when you are invited to speak, please state your name and the organization or affiliation, and then the comment. It has been mentioned, to you, that you should be limited to two minutes so that each individual who is on the list has a chance to make their comments for the committee. So, with that, we are ready to start. On my list of individuals who wish to make public comment, the first is Christie Weiss who is a parent advocate and is with Baby' s First Steps.

Yes, I am here.

Thank you. Please go forward.

Members, thank you for this chance to present public comment today. I am the parent of a child and an advocate who was on the 2012 Babies First Test task force and a chemist. I would like to commend the panel of the scope of newborn screening which provides early detection and a chance to intervene early. Today though, I would like to ask for your attention to those children not identified at birth. According to the European disease network, one third of children with disorders are late onset. The symptom free period is over one year. But they exist, and it suggests that the general [Inaudible] are not the only factors involved. Environment must play a role and [Inaudible] of the populations of those affected. I would like to ask the committee that you consider environmental influences going forward. My daughter's case was not found when she was a newborn. We reported to her pediatrician as early as with [inaudible] weeks of age that she was not well, nearly four years later and nearly $100,000, she is still undiagnosed. The fact that her symptoms get worse with antibiotics and improves when the toxins are removed points to her condition. It is convenient in the information driven world to focus only on genes. But as noted, almost all human diseases are from modifiable environmental factors. Environment may seem like a broad term but some of the areas include food additives, preservatives, pesticides, pharmaceuticals, vaccinations, and chemicals from flame retardants to solvents. I will assume that some of you will agree that these are some fragile children in the country and they may be the most impacted by toxins in their bodies because they are unable to process them, and also those from the outside which they are also unable to process, leading to a greater burden. Thank you.

Thank you. We appreciate those comments. Thank you. Next on the site is Dean Suhr.

Yes, good morning Mr. Chairman and committee members - thank you for giving me this time to speak. And thank you for this format or broadcasting that meeting for those of us on the west coast. It saves us a day of travel and some money, and we can get that much more done; your prior discussion has been about the benefits for early detection for diseases with therapies, and that is the criteria. I am just continuing my efforts in a discovery phase and conditioning to reach out in the hospital, to the panel members, but to other organizations to consider the lag time. I think it is a multiyear process and getting rid of therapy as a criteria on the uniform panel. And the basis is that quality of life is really important as viable therapy and for those folks, most of the rare diseases that do not have a therapy today, and will not have one in the next five or ten years, providing quality of life by knowing what you are in for. I am not underestimating the complexity of the task. It is a big change for the panel and their consideration and it is a change in terms of support for families that are diagnosed and do not have a therapy to go to. They need to get to another support system and that may involve the medical services, it is not going be what we are looking for therapies. This is just a road that I am on. I am going to be contacting some of you. And we are going to work with other organizations to try and understand the complexity of the issues before we come back. You can e-mail me if any of you would like to reach out before I contact you. And also, under the MLD condition banner but not specifically for MLD, I am working on a project that has to do with providing supports for families. But for those that are diagnosed typically most severe

symptomatic. And that program is [Inaudible - Static] may or may not overlay to screen. Thank you for the ongoing interest and look forward to chatting with you.

Thank you, we appreciate your input. Next on the list, Jane Larkindale. She is from the Muscular Dystrophy Association.

Hi, on behalf of the Association as a whole, I would like to thank you. As [Inaudible - Low Volume] and my comment is [Inaudible - Heavy Accent] community. I also want to point out that families are affected by more than 40 diseases which includes [Inaudible - Heavy Accent] and we would like to thank for your efforts today on behalf of multiple stake holders. Tomorrow doctor is going to pre-information about [Inaudible] including information [Inaudible - Heavy Accent] in the past few years. MDA has been leading the research and how to treat. These affect diseases cost and recent studies show that [Inaudible - Heavy Accent] outcomes for the patients. And it is not curable - It is treatable. Dr. Mandell, I understood they have [Inaudible] and robust. At the same time, it is going to [Inaudible - Heavy Accent] and we are ready to act. Our Association is ready to support your committee and any other partners as we work towards a shared goal. Thanks.

Thank you. We certainly look forward to the presentation tomorrow as well. Next is Amber Saltzman, an advocate of the Stop ALD Foundation.

Hi, good morning. Good afternoon. Can you hear me?

Yes, we can. Thank you.

Okay, thank you. Good morning, good afternoon. I am Dr. Amber Saltzman and I am the President of the Stop ALD Foundation. We were very grateful for the review of the adrenoleukodystrophy (ALD) newborn screening nomination at the September 2012 meeting. At that meeting, we learned that sufficient prospective data was not yet available from the large pilot study presently underway at the Mayo Biochemical Genetic Laboratory (MBGL). I thought it worthy to update the group that approximately 50,000 of the 100,000 samples have been screened and we have arranged, along with Kennedy Krieger Institute and Mayo, for the confirmation sequencing of the samples that came up ALD positive to date. We have planned to submit the data and scientific details at the next committee meeting in May, and had looked forward to receiving an expedited review at that time. However, we were greatly disturbed to learn that the meeting will likely not occur. We very strongly and respectfully request that the additional ALD data be reviewed when Pompe is voted upon on April 2013, outside the standard meeting, so that ALD may be placed in the queue for expert review. Please let us know what would be required for this to be considered so that we make appropriate preparations. Also, we would greatly appreciate guidance on who are the decision makers to approach relative to ensuring continuance of the committee in the context of reauthorization of the Newborn Screening Saves Lives Act and endorsing the value of at least some meetings been done face to face. One last comment. It would be very much appreciated if speakers are

identified by-the closed captioning or by the person speaking so that it is easier to follow the meeting. Thank you very much for your dedication and pressing forward to save the children.

Thank you. I think we are too learning about how to do this meeting this way. So, I will remind everyone to go ahead and identify themselves as they speak. And we certainly share your concerns about the May meeting and obviously, what is going to happen is not in our hands. It is in the hands of Congress and we'll just have to see what happens. We'll keep you in touch with individuals within this committee to be able to have the data submitted and then evaluated as quickly as possible when it is available. We'll certainly want to keep you posted of things as they change.

Thank you, kindly.

Next is Ms. Tiffany House, an advocate for the Acid Maltase Deficiency Association.

Hello, my name is Tiffany House. I am the president and I am also the vice chair [Inaudible - Static]. I am speaking to you today on behalf of all patients to request that Pompe Disease be added to the newborn screening panel. We are lucky enough to have an approved treatment with enzyme replacement therapy that has been proven to slow, and sometimes reverse, the effects of this devastating disease. [Inaudible - Static] with enzyme replacement therapy, the consensus among Pompe Disease experts is that earliest intervention usually leads to the best results. Unfortunately, the path to diagnosis is often hard and long. In late onset patients, this is usual because it is hard to see the symptoms. By the time diagnosis is made, there can be damage that is irreversible. If newborn screens are started, the significant awry in diagnosis would be removed. I know there would be concern and so I would love to focus the rest of my presentation on addressing this concern. The average time it takes a patient to get a diagnosis is ten years. I was born in 1983. At 8, I struggled to keep up with my peers. My parents took me to many doctors. Every doctor said it was normal for me. It wasn't. It continued until I was 11. A pediatrician saw me, and I went through the Mayo Clinic a month later. By the time I was diagnosed, my lung function had been affected. They were at 40% of normal. And I was starting to have difficulties with talking and was starting to get scoliosis. We didn't know I had this for the first 11 years of my life, it destroyed my muscles. Today even with treatment, my lungs function at 20% and I am in a wheelchair. Even late onset patients with a much shorter diagnostic journey have a lot of damage. One patient I know was diagnosed, and her lung function was to the point that nighttime ventilation was required. Patients can be identified at first and closely monitored so treatment can be started.. As a patient myself, I ask you to please add Pompe. That will save lives. It will allow patient treatment to start before it is too late, [Inaudible - Heavy Accent] only to find the answers after there has been damage. Screening would cure the lives of people for the better. Thank you for your time.

Thank very much or your personal story and I think all of us are aware of the issues related to diagnostics and as it was talked about, the determining of specific diagnosis is helpful for a family has well. So thank you for your comments. Thank you. Next is Mr. George Fox, a parent advocate. Are you on the line?

Yes, sir. Can you hear me?

Yes, go right ahead.

Yes, my name is George Fox. I am a parent. And I wanted to thank Tiffany for her presentation and for the advisory committee. For my family; there is no question that early diagnosis would have resulted in a better quality of life for our son. While I know every patient responds differently, it has been my observation that the earlier treatment is started, for the most part, the better the prognosis. I have observed this in the last ten years not just with my son but with the population as a whole. Our son started ERT in March of 2003. It is important to know that when he was born the doctor labeled him as strong in his exam. However, he had already started to slowly regress. At first, his regression was hard to see. At three months of age, during a routine exam, a heart murmur was detected. So from three months to six months we sought the cause of the problem. It was during this three month period that a dramatic weakening revealed itself, so after three long months and a battery of tests it was determined. From six months to eight months, our son's vent went down quickly to the point where we were barely able to save his life. However, had we started before that six month period when he declined, and he was still strong, it is very safe for me to say we would have had a much stronger son today. I have seen countless videos and testimony from families around to world to help support this. Our son is 10-years-old and 100% defendant for his movements. He is on a Ventilator 24 hours a day. He cannot sit up on his own or roll over in bed. He must always have one of us or a nurse by his side. I understand there are issues that need to be resolved when it comes to newborn screening, in every disease really. To me, though, the issues need to take priority. They pale in comparison to the positives that will come from newborn diagnosis of children. Not only will newborn screening maybe save some lives but it will most certainly preserve a quality of life that will be lost forever otherwise. In the most severe forms of the disease, sorry, this is still hard for me after ten years. It is very hard;--in the most severe forms of the disease, treatment is a must before the symptoms show up. I would say that the goal is to reduce morbidity in newborns and children, and then this disease is a great candidate to achieve this goal. So please add this. In addition, I know there are always questions of funding as well. And there needs to be a hierarchy of saving a child's life verses funding. It seems like funding is eliminating you getting to the next step. I know there has been a lot of work done and you guys are doing a great job. But, I feel like if we do not expose all of the conditions because, newborn screening is going to explode with all of the technology, and we need to expose the problem. Otherwise, I don't feel a resolution will ever be solved, we'll just be sweeping the problems under the rug. So once again, thank you for everything that you do. Thank you.

Thank you, Mr. Fox. And thank you for sharing your personal story and your passion as well. Next on the agenda is Sarah Wilkerson through Save Babies Through Screening.

Yes, I am here. Thank you for having me today.

Could you speak up a little bit? You are not coming through very well.

Okay. Is this better?

Not really. Are you right next to the--

Can you hear me now?

Oh, much better. That is it.

All right, well thank you for having me today. I am here as a parent and a board member, my second time speaking to you all the about my son. He lived for only a few days in 2009 before he slipped into a coma and passed away. A day later it showed that he had MCAT. In the years since his passing, I have committed myself to speeding up the screening test time. It could mean life or death. I spoke to you about the policy changes I was able to get going in Colorado, including getting the test samples to the lab via a courier service. Hospitals used the U.S. Postal Service a lot. It is still condoned in at least 30 states. Tennessee, Texas, Washington, and wise. As a rule, hospitals in the area bunch test results together. This caused a delay to the screening process, days that babies like my son Noah just do not have. We were started because of the death of our founder's son 14 years ago because of batching. Therefore, I ask you to look at the timing of tests and using the courier service. At end of the day, each state can test for everything under the sun but if the test results are not turned around quickly, the test may as well not have been run at all. Thank you.

Thank you for your comments and we appreciate your input into the committee. Next is Dr. Priya Kishnani from Duke.

Yes, this is Dr Kishnani. [Inaudible] can you hear me?

Yes, we can. Go ahead.

Thank you so much for giving me, yours truly, another chance to speak to the committee. I have spoken in the past and I just wanted to state that I have been involved in the care of individuals of this disease for the past 30 years and have managed more than 250 cases. It has been a humbling experience, you know, learning from when there was no treatment to now having a treatment in the form of enzyme replacement. And I have to admit that myself, who I consider to be an expert, this has been a very big learning curve for me. In the past, even as Mr. Fox said, we always took starting babies under six months of age as a good thing to do. In fact, after trials, which actually led to FDA approval of the drug ,was based on data from children less than six months age when they started. The outcome was changed in the first year of life and in the first several years of life. But [Inaudible - Static] today is that this is already too late. We are now seeing a clinical decline in the children. Some of them have not done as well as they should have done, as in the case of Mr. Fox and now for the infantile disease, I think the need for treatment is not a question of weeks and months. It is really a question of days. And even there

is a difference between starting someone three days since diagnosis to someone treated eight days later. I think this is very well understood from the Taiwan data and dealing with patients through the world. So this is my first point. We think we have a good handle and that a quick diagnosis is already extremely late. The second point is on late onset disease, and I think the term itself could be a [Inaudible - Heavy Accent] or is opened up for misunderstanding because of the word late. I think it represents a spectrum from children to adults, and it includes the ones that are supposed to be doing well. Now when we look at his tollage and MRI, getting a better glimpse at muscle, it is already too late. Knowledge that we did not have when we entered into this arena of treatments, the knowledge that we have today, it is already often too late in the treatment rhythm. Once the muscle is damaged, it is a point of no return. So I really want to look at importance of early diagnosis notice for the infants and each for what we consider, you know, the [Inaudible - Heavy Accent] loss of functionality is for adults. I want to clarify that I think we have clinical rhythms in place for the infants and late onset forms of the disease . We've the tools today to manage once we identify someone. And so with this, I really ask the committee, and I hope that the report that comes out from here goes for public and expert comment before it goes to vote. I am an advocate for the patients and a care clinically for anything because of a delay in diagnosis and in start of therapy. Thank you for listening.

Thank you for your presentation and the information. That will conclude the public comments part of the meeting. We now have lunch. I guess if you are on the west coast, maybe a late breakfast. But since we were only about ten minutes behind, we are going to reconvene at 30 minutes after the hour. So you have about 35 minutes for lunch. So please enjoy it and then be back at 30 minutes after the hour. Thank you, all. [The event is on a recess. The session will reconvene shortly.

[End of morning session, Part 1, for Thursday, January 31]