DACHDNC WEBINAR – FULL COMMITTEE DAY 1

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Female: Thank you for calling. May I have your passcode, please?

Male: Sure. It's 9591397 and this is the sound and recording line.

Female: This is the silent recording line?

Male: Yes.

Female: I will place the line in.

Male: Thank you.

Ms. Sarkar: Folks on the [unintelligible], we're having sound – the public can't hear us. So we're going to start over as soon as we are cleared and we know that the public can hear us.

Female: Hey, Debi?

Ms. Sarkar: Yes.

Female: I can hear through the computer speakers now.

Ms. Sarkar: You can?

Female: I can. Yes.

Ms. Sarkar: Great. All right. Let's start over.

Dr. Bocchini: All right.

Ms. Sarkar: Dr. Bocchini.

Dr. Bocchini: Good morning, everyone. We apologize for the – the initial problem where some – those of you who were on this webinar were unable to hear us, so we're going to start again. So I – as my first task, I will welcome

you all to the third meeting of the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children. We're going to start with opening remarks by me and followed by Debi Sarkar. This is our third meeting mentored by webinar format. We do have a full agenda today. We have a discussion and vote scheduled for the ALD nomination, an update from the Condition Review Team on MPS 1, a discussion on the challenges of transporting newborn screening specimens and some potential solutions to guide stakeholders, and various updates from our three subcommittees and workgroups. We also have scheduled public comments for 1:30 this afternoon Eastern time. Now I'd like to give you an update on the reauthorization of the Newborn Screening Saves Lives Act. The reauthorization won unanimous approval from the Senate Self-Education Labor Intentions Committee. The bill proposes to amend the Public Health Services Act to expand and improve programs at the Department of Health and Human Services related to newborn screening and reauthorizes this advisory committee. The bill also made timeliness of sending newborn screens a key component. The bill now moves to the full Senate for consideration and the House side action was still pending. So now I'd like to turn this over to Debi Sarkar for reminders and housekeeping items.

Ms. Sarkar: Good morning, everyone. I just wanted to go over a few friendly reminders and housekeeping notes. The first one is a gentle reminder to our committee members on lobbying. Government employees including special government employees are prohibited from lobbying and thus we can't lobby, not as individuals or as a committee. But if you lobby in your professional capacity or as a private citizen, it's just important for you to keep that activity separate from our work. Also I wanted to just give another reminder regarding questions that you may receive about the committee and the work that we do. Committee members, organizational representatives and subcommittee members can give presentations or grant interviews. However you must make it clear that you are expressing your personal opinions and/or you're representing your employer or professional organization and not speaking on behalf of Advisory Committee. If asked to give a presentation or interview as a representative of the committee, please let me know in advance of responding. Typically the DFO will ascertain the appropriateness of the presentation or interview and – and I'll identify the most appropriate person to speak on behalf of the Committee. Committee members and org reps may represent the committee and speak on committee matters, but only with the prior approval of the secretary or the DFO. Subcommittee members may not represent the committee or speak on behalf of the committee. So on to housekeeping items – for the webinar, members of the public, sound will be coming through your computer speakers, so please make sure you have your computer speakers turned on and I apologize for the glitch earlier but I think we've fixed that. So you should be hearing things well. Committee members and org reps, sound will be coming through your

phone lines, so please make sure you have your computer speakers turned off. Hold questions and comments until the end of the presentation and please remember when speaking to state your name first. We want to ensure proper reporting for the committee transcript and minutes. If you have any problems with your phone line, press start zero and the operator will be there to assist you. Just as a reminder, committee members will have the first discussion. We're going to try something new this time. In order to better facilitate the discussion, we're going to ask you to use the raise your hand feature in Adobe Connect when wanting to make comments or ask questions. Members, the – it's – there's a – a little person icon at the top of your screen in the middle section and you hit the down arrow and you can choose Raise Hand. This will allow Dr. Bocchini to identify who will speak next. After committee members have completed their discussion, we will invite the organizational representatives to speak and discuss. Again, org reps please use the Raise Hand feature and as time permits, we'll have a comment box available so that members of the public can ask questions and provide input and lastly I wanted to share some good news. Our next meeting will be a face-to-face meeting. We are currently working out the logistics, so please stay tuned. We should have information. We'll update the committee website with more information on the face-to-face meeting in the next month or so. So thank you very much for your attention and I'm going to turn it over Dr. Bocchini.

Dr. Bocchini: Thank you, Debi. I think everybody appreciates that good news that – that you gave us. Next I'd like to do a formal roll call for the committee. I'm going to go in alphabetical order, so please respond. Don Bailey?

Dr. Bailey: Here.

Dr. Bocchini: Here. Jeff Botkin?

Dr. Botkin: Here.

Dr. Bocchini: Colleen Boyle?

Dr. Boyle: I'm here and actually I'll be here until 2:00 today but I have – and – and Carla Cuthbert will be for me tomorrow.

Dr. Bocchini: All right. Thank you, Colleen. Denise Dougherty? [unintelligible] I know Denise was going to be here intermittently through the day. We'll get back and see if she's on in a little while. Charlie Homer?

Dr. Homer: Here.

Dr. Bocchini: Kellie Kelm?

Dr. Kelm: Here.

Dr. Bocchini: Fred Lorey? All right. And below here we have Michael Lu.

Dr. Lu: Here.

Dr. Bocchini: Steve McDonough?

Dr. McDonough: Here.

Dr. Bocchini: Dieter Matern?

Dr. Matern: Here.

Dr. Bocchini: Melissa Parisi?

Dr. Parisi: Here.

Dr. Bocchini: Alexis Thompson?

Dr. Thompson: Here.

Dr. Bocchini: Cathy Wicklund?

Ms. Wicklund: Here.

Dr. Bocchini: Andrea Williams?

Ms. Williams: Here.

Dr. Bocchini: And then our DFO, Debi Sarkar.

Ms. Sarkar: Here.

Dr. Bocchini: Once again, Denise Dougherty? And Fred Lorey. All right. We'll check them [unintelligible] be here later. Next we're going to do the organizational representatives. In the American Academy of Family Physicians, Freddy Chen?

Dr. Chen: I'm here.

Dr. Bocchini: Thank you. American Academy of Pediatrics, Beth Tarini? American College of Medical Genetics, Michael Watson?

Dr. Watson: Here.

Dr. Bocchini: American College of Obstetricians and Gynecologists, Mindy Saraco? Association of Maternal and Child Health Program, Kate Taft?

Ms. Taft: I'm here.

Dr. Bocchini: Association of Public Health Laboratories, Susan Tanksley?

Dr. Tanksley: Hey. I'm here.

Dr. Bocchini: Association of State and Territorial Health Officials, Chris Kus?

Dr. Kus: Here.

Dr. Bocchini: Department of Defense, Adam Kanis?

Dr. Bocchini: Genetic Alliance, Natasha Bonhomme?

Ms. Bonhomme: Here.

Dr. Bocchini: March of Dimes, Ed McCabe?

Mr. McCabe: I'm here.

Dr. Bocchini: National Society of Genetic Counselors, Cate Walsh Vockley?

Ms. Vockley: I'm here.

Dr. Bocchini: And Society of Inherited Metabolic Disorders, Carol Greene.

Dr. Greene: I'm here.

Dr. Bocchini: Let's go back. American Academy of Pediatrics, Beth Tarini?

Female: She could be out today.

Dr. Bocchini: Okay. And then Mindy Saraco? Okay. Thank you all very much.

Dr. Lorey: Hey, Joe?

Dr. Bocchini: Yes.

Dr. Lorey: Joe? It's Fred Lorey. Sorry. I had some audio problems.

Dr. Bocchini: Thank you, Fred. Glad to have you here. All right. There's one committee correspondence to make you aware of. We did receive a response from the secretary regarding the committee's recommendations on the retention and use of dried blood spot specimens at the newborn screening. A copy of the secretary's response is in the briefing book and – and for those of you who have gone through the briefing book, know that the secretary accepted four of the committee's recommendations and declined the other four. The primary reason she declined four of the recommendations was she took into consideration the ongoing review and possible revision of the common rules which as you know provides the requirements for human resource and so she – because of the possible

revision of the common rules and the ICC reports, she decided to decline four of the recommendations. You can see that she accepted the last four.

Female: Actually, we can't see the bottom page, at least some of us can't.

Dr. Bocchini: Okay. Can you see that – that they are available there? Okay. The next item is approval of the September 2013 meeting minutes. These minutes were distributed with the agenda book – briefing book, so are there any additions or corrections that anyone has to the – to the minute? Again, if you have an addition or correction, just go ahead and state your name and then discuss what you'd like to potentially have changed. If there are no additions or corrections to what was distributed, I would ask that some – that a member would vote to approve the – the meeting minutes.

Dr. Botkin: Jeff Botkin. I move approval.

Dr. Bocchini: All right. Jeff Botkin approve. Do we have a second?

Ms. Thompson: Alexis Thompson, second.

Dr. Bocchini: Thank you, Alexis. Now we'll have a voice vote for approval of the – of the minutes and then we'll go alphabetically. Don Bailey?

Dr. Bailey: Approved.

Dr. Bocchini: All right. Approved. Jeff Botkin?

Dr. Botkin: Approved.

Dr. Bocchini: Coleen Boyle?

Dr. Boyle: Yes.

Dr. Bocchini: Denise Dougherty. Has Denise had a chance to get on? If not, then Kellie Kelm? Kellie, are you on mute? All right. Charlie Homer?

Dr. Homer: Approved.

Dr. Bocchini: Fred Lorey?

Dr. Lorey: Yes.

Dr. Bocchini: Michael Lu?

Dr. Lu: Yes.

Dr. Bocchini: Steve McDonough?

Dr. McDonough: Aye.

Dr. Bocchini: Dieter Matern?

Dr. Matern: Approved.

Dr. Bocchini: Melissa Parisi?

Dr. Parisi: Yes.

Dr. Bocchini: Alexis Thompson?

Dr. Thompson: Yes.

Dr. Bocchini: Cathy Wicklund?

Ms. Wicklund: Approve.

Dr. Bocchini: And Andrea Williams.

Ms. Williams: Yes.

Dr. Bocchini: All right. Thank you all. The minutes of the September meeting are approved. The next item on our agenda is a presentation by Alexis Thompson on an update from the Sickle Cell Disease and Screening for Trait in Athletes Ad-hoc Workgroup and it looks like their slides are up, so Alexis I'm going to turn the meeting over to you for your presentation.

Dr. Thompson: Dr. Bocchini, thank you so much for giving me the opportunity to update the – the committee on the work of the ad-hoc committee. My presentation will be brief and certainly will stay within the time allotted to keep us on time. I wanted to first on the next slide present the objectives for my presentation, which will include reviewing – if someone can go to the next slide? Which – reviewing what – what's happened so far with reporting on – from the [unintelligible] advisor committee on screening for sickle cell trait in college athletes describing the impact of the NCAA policy on state health departments, work of the ad-hoc committee up to date and requesting feedback from the committee as we look toward next steps. The next slide presents the next questions that we – we were addressing in the ad-hoc committee. Next slide – the first one was to ask the question do the – the original recommendations in the white paper from the secretary's advisory committee, are they still relevant? Should they still stand? Another question is is this an appropriate use of newborn screening resources? Additional question is can or should the Discretionary Advisory Committee provide additional guidance to our secretary – the secretary and/or state agencies and how does this experience impact a broader discussion of notification of carrier status for other conditions? The next slide is just as a reminder for those who may not have been part of the committee when the – the – this was discussed initially and the next slide shows the summary of the four points that were

the conclusion from the deliberations of the committee and that's on the next slide. The first is that individuals should have the opportunity to find out their risk of medical disorders including carrier status of sickle cell disease, but this evaluation should take place in the medical home and should include counseling and assurances about privacy of genetic information. The testing should not be a prerequisite for participation in sports unless deemed medically necessary and finally as part of routine medical care, all potential athletes should be given education of state practices to prevent exercise and heat related illnesses and as noted these recommendations were accepted by Secretary Sebelius in the summer of 2011. Since that time, this was originally to address the recommendations for Division 1. At this time, the NCAA has moved forward and – and now all three divisions, Divisions 1, 2 and 3, had this mandate in effect as of the summer of 2013. The – the next slide – the secretary – the – the ad-hoc committee reviewed the statement and the consensus in the committee was that the recommendations that were made by the committee are still valid and are still relevant and no changes were proposed to the original statement by the – the broader committee. Next slide – we have a presentation that was very helpful and an update from Dr. Tarini on some of the information that she was gathering from state stakeholders regarding the request for sickle cell trait. What we – what we did find was that the information that's provided by states has been highly variable. There are some states that provide the entire newborn screening result, all of the tests that are done. Some of those states are attempting to provide additional educational materials. It – but it's not clear that – that any information is given besides the actual test results. There has been some anecdotal experience that some states were reporting that their efforts for providing additional information were rebuffed when that request came from universities or athletic departments. They had no interest in receiving any additional information regarding the test results. We also raised the question about the need for a disclaimer in that the – the [unintelligible] was not necessarily the intent of newborn screening and there really had been not much discussion about the risks of both false – false positive and false negative results, and also noting the difference between screening and diagnostic testing, that in its intended form that newborn screening is just that and that to apply risk that is defined by that test alone with no other additional diagnostic testing done puts many states in a very precarious situation. We also discussed the issues about accuracy of the test results and also focusing on matching, being certain that the results that are – even if they are accurate, making sure that they in fact match the individual for whom – that we – we – that is currently ask – requesting the results. There of course were some additional things that the committee has considered on the next slide. One question was is this an appropriate use of newborn screening? Dr. Tarini's original presentation demonstrated the burden and the costs that many states are bearing in order to meet these requests that have been initiated by the

NCAA mandate. If the results are provided without context, is this consistent with the intent of newborn screening is the question raised by the ad-hoc committee. It was recognized however that newborn screening is often driven by public policy or health legislation and that it is highly variable between states and so any additions or variations to their current actions may require new legislation and so perhaps a more protracted process. If the – if states, however, see this as a reasonable use of newborn screening, what recommendations are given and can the committee be useful in helping to craft those? Another question that continues to be raised is to whom should this information be – be sent? These are often now young adults. They are no longer children and the requests are often coming from either parents or third parties and under most circumstances, neither of those would be given access to this kind of health information without their being a clear reason why the individual is not in fact making the request themselves. Also the question is – is – was raised when that information is provided in terms of the screening test result, what other resources can we actually direct individuals or direct states to utilize that we believe gives the best current information on what the health concerns might be associated with sickle cell trait? So the next slide looks at some of the educational resources that we think may be coming out. There is a substantial amount of work and Althea Grant was kind enough to update the ad-hoc committee on work being done by the CDC to develop a full sickle cell trait education tool kit. This represents work by work groups on – on general information about sickle cell trait, complications and issues about sickle cell trait and athletic participation. The workgroups are made up by hematologists, by representatives from community-based organizations, from governmental partners, from the NCAA and from the – the National – National Athletic Trainers Association, so a fairly broad group. This has been a – a – an effort that's – that's been – that will be cobranded with the American Society of Hematology and the CDC is also requesting input from SCDAA, the Sickle Cell Disease Association of America, on their – their – on the materials. We can tell you – Dr. Grant could tell us that the general frequently asked questions materials have now – are now in CDC clearance. She hopes that those will actually be out shortly and the plans are for other items related to complications of athletics will be entering clearance soon and hopefully will be available by the spring of 2014. They anticipate most of these materials being downloadable from the CDC website which itself is being updated. The next slide – so our summary to date is that we believe that the secretary's advisory committee's recommendation should still stand. These late requests for newborn screening results solely to address the NCAA mandate is not an appropriate use of newborn screening resources, but the – still the question remains is how can the discretionary advisory community provide additional guidance to the secretary and/or state? The final slide is that what we believe is our next steps and that is to gather information from

states. We would like to get some clarification on the current guidelines on carrier notification from each state, understanding exactly how that guideline is created. Is this from internal work or is this based on health legislation? We'd like to understand what if any disclaimers about the results are given and determine the educational information if provided all with the results. The ad-hoc committee would like to eventually articulate their concerns – the concerns raised by the NCAA mandate considering drafting a report to the larger committee and potentially configure it into a paper and then we would like to consider methods by which the – the – the discretionary – I – I apologize – the discretionary advisor committee can offer assistance to states and with that, I hope that I've left some type for questions. I would certainly welcome them.

Dr. Bocchini: Alexis, thank you for an – an excellent summary and – and your leadership in – on this workgroup. This is now open for questions and comments first from committee members. So remember, we are going to try and use that icon in the middle of the – of your screen with – the little icon with the hand up, so first committee members if you would wish to participate on a discussion or ask a question, go ahead and – and put down that icon. As soon as I start seeing individuals, I will call them – call you for comments based on the – the preferred comment. Oh, the – their name in there first. Are the lines open for all committee members and organizational representatives, operator?

Operator: Yes, sir. All folks on the call have open lines at this time.

Dr. Bocchini: Okay. Thank you. So committee members first. Okay. I'm not seeing that there are any questions from committee members. Is this correct? All right. I – I think that what we would like from the committee is concurrence with Alexis' next step plan or comments that – of the – address any of the issues that she raised or committee work related to them. All right. I – I think the committee is in full agreement, Alexis, so let's go to the organizational representatives. Are there any questions or comments? Please again use that icon. Chris? Chris Kus?

Dr. Kus: Yes. Alexis, as I understand it, the – the NCAA mandate came as a result of a legal case. Is there – what are the possibilities of their changing this or entering in the discussion given our information?

Dr. Thompson: I think that's a terrific question, Chris. I – the challenge has been that – that this was a – a – a legal settlement that was not made public and so precisely the – the actual terms for this have never been made public. This NCAA has not said that that actually is their restriction, so ray – they – I do not get the impression from my discussions with them directly that they are completely tied to this – this legal settlement. This was certainly in the spirit of what this family wanted, but it was not clear that the absolute –

that there was an absolute requirement for them to in fact carry out – carry this out in the manner in which it's been done.

Dr. Kus: Thanks.

Dr. Bocchini: There's no questions or comments? Carol Greene.

Dr. Greene: Am I on mute? No.

Dr. Bocchini: No, we can hear you.

Dr. Greene: Okay, great. So we had – Alexis has been fabulous and it's been a very interesting process and I just wanted to point out that we have to be sure that we keep working on the – the issues related to carrier testing requirement separate from the issue of newborn screening because I personally think that we'll be able to stop the request to the newborn screening laboratories because the – the – the screening test result is not a diagnosis test and we talked about some strategies that could help to make that clear. CDC might be – might be – I – I think CDC is working on including that in their statement, APHL is probably considering some strategies to help guide the public health laboratories in how to put on disclaimers. So hopefully it will become clear very quickly that nobody should be acting on the result of a newborn screening without confirmatory testing which means hopefully the newborn screening labs will be out of it, but all the other questions still stand and this is a – a committee that deals with heritable disorders not just related to newborn screening.

Dr. Bocchini: Thank you, Carol. Comment, Alexis?

Dr. Thompson: I – I – I – no, I – I think that Carol, your point is very well taken and I – I think that certainly HP – APHL has always been a partner to this larger committee and – and I think their goal is – is vitally important in helping state labs configure their responses.

Dr. Bocchini: Dieter?

Dr. Matern: Dieter Matern. I have a question or a comment. Basically several states including Minnesota now will not have that information from the newborn screening laboratory anymore. So you actually have to go to the birthplace and ask them what the newborn screening result was. That is something that needs to be considered and it's probably true for maybe other states as well. I don't know what happened in Texas after they had to destroy all their samples.

Dr. Thompson: I think that point is very well taken and – and in fact there are some states, at least right now, that the newborn screening programs are recent enough that they are not 18-year-olds yet that were – were picked up by newborn

screening. The most notable one frankly is the state of Georgia. It has not yet reached that point. I do think that even as – as individuals recognize that the states cannot be used as a resource for responding to the mandate, it does not mean that the NCAA will not continue to ask for it which I think is a somewhat different issue, but it's certainly very related.

Dr. Bocchini: Natasha Bonhomme?

Ms. Bonhomme: Hi. Thank you so much for the presentation, Alexis, and one thing that I would like to add to that is really thinking about not only considering mechanics by which we can support and assist states, but there are other organizations and groups that will be getting questions about this including the community-based organizations that support the sickle cell community, birthing hospitals as well as other organizations that actually do do [unintelligible] education and so just to keep that in mind as well so that there is a multi-faceted approach to addressing this issue and the public may not necessarily know to go to their state lab. They may be going to other places to try to figure out this information including pediatricians, so just to kind of think about that in mind so that whatever strategies we pull can be really well rounded.

Dr. Thompson: I – I think that's an excellent point. Related – related to that, the hope is is that the materials that are being developed by the CDC will be the ones that are most commonly distributed. I should also mention and – because Althea mentioned it to our ad-hoc committee that the CDC has a standing relationship with the American Academy of Pediatrics and this is precisely the – the – the kind of thing that the CDC will be looking to the AAP for in partnership.

Dr. Bocchini: That would be Coleen Boyle?

Dr. Boyle: Yes. That was a great – great point in terms of trying to uniform – unify the message across various venues. So Alexis, I was just going to ask at your next steps slide, were you considering the first bullet, the gathering additional information and trying to clarify what's going on currently in terms of guidelines and education that's disseminated? Do you see that a function of the committee or, I mean, how do you see that rolling out? I guess I'm just trying to get some – some specifics here.

Dr. Thompson: That – that's a great question, Coleen. In fact, that was one of questions as I'm bringing it back to the larger committee, is trying to identify what the resources would be for gathering that kind of information. If this was beyond the – the – the purview of the work that Dr. Tarini had already been charged with doing.

Dr. Boyle: Right.

Dr. Thompson: But this was a question for – for me to actually get some input from the broader committee. We would hope to get some – some central resource to gather the information from states. My expectations are that this would end up being a series of calls or email communications that would eventually be organized into a spreadsheet and – and – and not much beyond that, but certainly would require some staff time.

Dr. Boyle: Okay. And then do you see the result then being recommendations, best practices, something like that?

Dr. Thompson: I – I – I don't know.

Dr. Boyle: Okay.

Dr. Thompson: I think we're trying to figure out what it is the states are doing. I think most states are doing the best they can but – but trying to understand exactly how broad that experience is and whether or not – it could very well be the states are already using – using their – their – their – their good resources for information or that they've already made decisions about how they will handle requests for – for results. But we – we just want to understand that and I don't think we have that right now.

Dr. Boyle: Okay.

Dr. Bocchini: And next I have Jeff Botkin. Jeff?

Dr. Botkin: Yeah. Thank you. I just wanted to pick up on that conversation with – because I think there may be an opportunity as we look at the trait issue here to get a lot more information about how states are dealing with carrier status more broadly. Maybe that's too tangential to the primary focus of this effort, but it seems to me there are sort of persistent questions about how carrier status is – is being communicated back to primary care providers and families, the adequacy of that information, how people are responding to that information. So I think that's sort of a long-standing issue in the newborn screening field, that this particular focus may offer an opportunity to sort of look at the carrier status situation a little bit more broadly.

Dr. Bocchini: Thank you, Jeff. I now have Carol Green and then Chris Kus.

Dr. Greene: Thanks. I am going to repeat a point I made earlier because I – I do see that with many people it does keep getting lost and so apologies for the repetition, but a screen is not a diagnostic test. Nobody should be making decisions about athletic – you – you don't even know if that was the right person or if the – if the screen was negative, the person still could have a hemoglobinopathy. If the screen was positive, it could have been a false positive and whatever states are doing, I think I'm interested in the whole question of how we handle carrier testing. But the state's response and it

should be the same if it's the birthing center. It should be the same if it's the pediatrician. The newborn screening result does not tell the NCAA what they need to know. It is not a diagnostic test. We talked when we were on the task force phone. We agreed that no geneticist and no hematologist would ever act on that information without a confirmatory test. So the newborn screening test by itself is not adequate. The person needs another test. So the state should not be asked, the birthing center should not be asked and if the pediatrician is asked, they should not be asked about the newborn screening report.

Dr. Thompson: It – I'll go a step further and say it would probably be malpractice to – at least a hematologist and a geneticist would consider it malpractice to counsel somebody about either being negative or positive based on a screen.

Dr. Bocchini: Thank you, Carol. Chris Kus.

Dr. Kus: Alexis, I don't know if you know this, but has this – has the NCAA mandate affected any athlete? Specifically, has any athlete refused to provide the information and then not be allowed to play?

Dr. Thompson: Great question, Chris. The NCAA as you can imagine is not an organization that's forthcoming with a lot of information. That's just not their style. That question has been raised. It – they have not been – been forthcoming with it. We do know, though, that there are – it was interesting in the early – in the early – the first year of this when it was just a vision one, that there are a subset of schools, in fact it's a significant minority of schools, where nearly all of the students opt out, where 90% of the students at some schools opt out. We don't – we've – we've asked repeatedly, I mean we're aware of it. The NCAA doesn't dispute that that's happened. They've – we want to understand what is it – what information or what message are those schools or those students using that – that actually results in sort of this mass – I – I think the fact that if you have 90% of your students that are not participating, what message are they getting that is different from the schools where they are almost requiring that students be tested? Again, you know, these are terrific questions. We – we are looking through other channels to get the NCAA to the table to get more information from them, but currently they have not been very open to providing that kind of information.

Dr. Kus: Thanks.

Dr. Bocchini: [unintelligible] addition I'd like – because we really don't have any feedback from the athletes themselves in terms of issues that may have arisen based on the results of the test.

Dr. Thompson: That's correct. The only thing that we do know is we know that there have been no deaths and that's the only information that we've been told. We don't – we know that there is a current project that the CDC is involved in to gather some information on what it is that athletes that have – have received counseling, what is their understanding of the information that they have received and Althea alluded to it – Dr. Grant alluded to on the call. But it wasn't clear to me yet what the timeline for that project will be.

Dr. Bocchini: All right. Thank you. I see no other hands up, so that'll conclude the discussion. I want to again thank Alexis for the presentation and – and for her leadership in this area and thank everybody who participated in the discussion. I think it's informed the next steps very nicely and so we'll look forward to the – the – the next board [unintelligible] from the ad-hoc committee. Thank you.

Dr. Thompson: Thank you.

Dr. Bocchini: Let's now go to Dr. Botkin's presentation. So we can put the flag up for the – the discussion on Introduction to Challenges When Conducting Pilot Studies and Possible Solutions and – and obviously based on the response from the secretary, there are some issues that – that – that may impact directly upon doing pilot studies. So Jeff, I'm going to turn this over to you. Thank you.

Dr. Botkin: Thanks, Dr. Bocchini and thanks to Debi Sarkar for giving me a few minutes to just raise this issue and I had raised this relatively recently, so I appreciate a few minutes on today's agenda with the hope that if the community is interested in pursuing this issue that we could raise this in much more detail at a future meeting. So I'm going to be very brief and make a couple of fairly straightforward points here and if I could have that next slide, please. I think all of us who are participating in this process recognize what a vast improvement it is over the relatively uncoordinated approach that has been the tradition for newborn screening for many years and that the evidence-based approach that this committee uses in terms of providing advice on the uniform screening panel is a major contribution to the field, but we obviously are quite dependent on the quality of the data that's been generated within the system broadly in order to make those recommendations and I know all of us who have the responsibility of coming forward with the votes on these conditions frequently would like better quality information and that we're struggling with data that in many circumstances is marginally adequate. We know that the data is difficult to acquire and this isn't so much a criticism as it is a recognition that data acquisition in this domain is complicated because we're dealing with population screening and we're dealing with uncommon conditions with which many clinicians out there aren't particularly familiar. So the evidence as we all know includes a number of elements. The test

characteristics and that's the test characteristics as they look in the context of a population screening context and once you get the volume and then require rapid turnaround times, then it's an educational experience to see what sort of challenges emerge with any particular test platform. Second point being natural history [unintelligible] from the conditions, population screening typically reveals positive results on a wider spectrum of the clinical condition than may have been previously recognized through clinical diagnosis. So it's a critical outcome feature of population screening. Thirdly and perhaps most importantly, important for the process to demonstrate that early detection and intervention has a meaningful and positive impact on child morbidity and mortality. Next slide, please. So because of the population nature of this and because the – the newborn screening programs are organized through public health programs in order to mirror the future conduct of any program, it's necessary to work in this context frequently with state health departments. However, many state health departments don't consider research to be part of their mission, understandably so. They're typically overworked and underfunded with their regular service obligations and research is oftentimes not perceived to be a poor function and in certain circumstances certain types of research are actually prohibited from being conducted within certain programs. In addition, everybody knows there is variability by IRBs in expectations for human subjects protections. It's been a – a significant challenge in this domain and here I would highlight a paper that is coming out in the February edition of Pediatrics Magazine that was a collaborative effort of the ethics and legal work group of the newborn screening translational research network that deals with parental permission for pilot studies that just make folks aware of. Next slide, please. So a number of states have very effectively collaborated with investigators to conduct these pilot studies for us and these have been absolutely critical to making high quality decisions about screening. Certainly Massachusetts and Wisconsin excellent examples of states that have done wonderful jobs in the past with conducting this type of work that's been critically important for our committee. A number of states, however, have been unable to support a number of valuable projects and we've involved with [unintelligible] brothers SMA project and that's been significantly hampered by states that had initially supported it at the time of grant application, a multimillion dollar grant having been awarded and then states decided that they had challenges with being able to support that project and I think that a fair point here is that these barriers are a factor, among many others, in states deciding to implement new tests through state mandates rather than through an evidence review process and at least speaking personally I think that's a reflection of an – an older style of decision making with newborn screening that ought to be inhibited and we would want to see a process by which we can support the evidence based approach that's been part of this committee's mandate. Next slide, please. So really the proposal here today is just to discuss these issues further.

Does the Discretionary Advisory Committee have a – a role in thinking through these issues, potentially providing recommendations to the secretary that might address these problems or issues that we see in this particular domain? From my personal perspective, the initial concept would be a – state-based programs that are organized into a national network of programs that are familiar with the conduct of research and might – funders may turn to those states as a platform for conducting this type of work when authoritative bodies like the Discretionary Advisory – Discretionary Advisory Committee have decided that a pilot study is necessary in order to make a decision based on – for addition of a new condition to the platform. So the proposal would be to pick up on these ideas and have a more detailed presentation and discussion at our next meeting. I'd say I've had some just pretty preliminary discussions with Mike Watson about these issues and there is activity going on in the field to address this particular set of issues and so it may well be that the – at this point the Discretionary Advisory Committee would be in a position to be informed about what's otherwise happening. It may well be that we could have a constructive role in encouraging moving along this particular direction. So I would hope to work with Mike and learn from Mike at our next meeting to hear about what are – what are activities that are occurring in this domain that would be important for us to – to know about. So I'm going to stop there and I guess if we have the opportunity, Dr. Bocchini, for any questions or comments?

Dr. Bocchini: We do, Jeff. We've got a couple of minutes. Let's go ahead and – and take comments first from the committee. So again, use the icon. Steve McDonough is the first so, Steve?

Dr. McDonough: Thank you, Mr. Chairman. Thank – I would like to thank doctor – Dr. Bocchini for the opportunity to make these comments and Dr. Botkin's excellent presentation. I'm fully in support of what you're suggesting and hope the committee supports it as well.

Dr. Bocchini: Thanks. Don Bailey?

Dr. Bailey: Yeah, I just want to second that and thanks, Dr. Botkin, for such a – for bringing this up. I think there's a critical need. I – I'd, you know, be interested to hear a little bit more about how you – how you think we should, you know, go about this in between – between meetings in addition to talking with Dr. Watson and the Translational Research Network. Also thinking about, you know, how – how this gets played out in the future, it may be that doing tests not just on a one disease at a time but maybe having – if we're – if we're going to be doing statewide pilots, maybe bundle some things together and try to get more bang for the buck in a single study.

Dr. Botkin: Excellent. Thank you.

Dr. Bocchini: All right. I don't see any additional comments or questions so – oh, Charlie Homer. Go ahead, Charlie.

Dr. Homer: Yeah. Thank you very much. I also think this is a tremendous idea, very excited about it. You know, like I still think about what kind of a coordinating center such a program might warrant. Also exciting to think about kind of what the data infrastructure would be and how we might use some of the newer forms of information exchanged to move it forward. But I think it's great and I'm looking forward to our elaborating on this at the next meeting. Thank you.

Dr. Bocchini: Melissa Parisi?

Dr. Parisi: Hi. This is Melissa from NICC. I just wanted to comment that I think this is a really worthwhile discussion and that there is some infrastructure in place through the Newborn Screening Translational Research Network, so any sort of future developments I think should involve a discussion about the role of some of the existing structures that are in place that could provide support to this sort of pilot studies because we think it's absolutely important, but we don't want to reinvent the wheel either.

Dr. Bocchini: Thank you, Melissa. I think that's a very important comment. It certainly I think gives us some direction. We could kind of look at the landscape and see what's out there and work together with you and others to kind of see what's available. So perhaps the next meeting, further information from Jeff, some review of the landscape and – and then perhaps maybe development of a – of a – of a workgroup within our Discretionary Committee to – to bring this forward in some way. So I think that – that sounds good. It's – Carol Greene is now next.

Dr. Greene: Also SIMD would fully support it and I wonder if there would be an opportunity at NIH to be helpful to – a related issue is how do you do things across multiple states dealing with IRBs? Natasha knows very well it took us more than a year to get something this – and not doing a new test, but just interviewing people for follow up, to get things through IRBs in three states. So that would be an important part of – of this very important initiative.

Dr. Bocchini: Thank you. Any additional comments or questions? All right. Again, Jeff, thank you for bringing this to the attention of the committee. I think this is something that should become a hot topic and – and something that we should move forward very quickly, so thank you.

Dr. Botkin: Great. Thank you.

Dr. Bocchini: The next item on the agenda is an update on the Newborn Screening TA Center – NewSTEPs and the presentation will be by two individuals. First Marci Sontag, PhD. Marci is the director of epidemiology of NewSTEPs

which is the Newborn Screening Technical Assistance and Evaluation Program, a program designed to support newborn screening programs across the United States through an innovative data repository and quality improvement initiatives. Dr. Sontag is an assistant professor of epidemiology in pediatrics at the Colorado School of Public Health. She has a PhD in epidemiology and an MS in biometrics from the University of Colorado Health Sciences Center. Dr. Sontag has studied clinical outcomes and newborn screening in cystic fibrosis since 1995. Her research in CAPUS has resulted in a better understanding of longitudinal progression of pancreatic damage and a new algorithm for CF newborn screening. Dr. Sontag is helping to lead the efforts to implement CCHD newborn screening in Colorado. In addition the presentation will be from Jelili Ojodu, M.P.H. Dr. Ojodu is the director for Newborn Screening and Genetics Program at the Association of Public Health Laboratories. He is also the project director for the Newborn Screening Technical Assistance and Evaluation Programs, the NewSTEPs program. Mr. Ojodu is responsible for providing guidance and direction for the Newborn Screening and Genetics in Public Health Program. He received his masters in public health from George Washington University and a bachelor of science degree in biological sciences from the University of Maryland, College Park. So with that, I'll turn the presentation over to the both of you. Thank you.

Mr. Ojodu: Thank you, Dr. Bocchini. Can you hear me?

Dr. Bocchini: Yes, we can. Go ahead.

Mr. Ojodu: All right. Lovely. So thank you for the introduction and the opportunity to present to the full committee on news that Marci and I are hopefully over the next 53 minutes will like to give you a comprehensive overview of the Newborn Screening Technical Assistance and Evaluation Programs, our current activities – which activities and what we have embarked on over the last 18 months or so and so next slide, please. So this is the, I guess, the obligatory funding acknowledgement. This is a HRSA-funded operative agreement program and we at APHL are collaborating with the Colorado School of Public Health to initiate and put out this particular program on NewSTEPs. Next slide, please. All right. So let's – a – a brief write down on NewSTEPs and I think we'll go into much more detail later. HRSA did put out a funding opportunity announcement in January of 2012 for a technical assistant in data repository program. We – we – we branded that to NewSTEPs which is the Newborn Screening Technical Assistance and Evaluation Programs, and our vision is noted on this slide here which was put together by a number of folks on our Newborn Screening Steering Committee. A good amount of them are listening to this particular presentation, but for the folks who do not have access to slides it notes that NewSTEPs vision is a dynamic newborn screening system and to have access to and utilize accurate, relevant information to

achieve and maintain excellence through continuous quality improvement. That's the only thing I'd like to highlight in this whole thing here, is that we're all about continuous quality improvement. Next slide.

Dr. Bocchini: Hello? Did we lose you?

Mr. Ojodu: You did. I have a back-up plan here.

Dr. Bocchini: Okay. Well, that's good.

Mr. Ojodu: One second. I'll send this to [unintelligible]. Can everyone hear me?

Dr. Bocchini: We can.

Mr. Ojodu: Can you hear me now?

Dr. Bocchini: Yes.

Mr. Ojodu: Thank you. Sorry about that. So what is NewSTEPs? NewSTEPs the [unintelligible] in it is a comprehensive newborn screening resource center for especially state newborn screening programs. We provide among other things the publicly available website that has a number of information whether it's state profiles as we move to collect in the future case definition then and of course the data repository that has varying levels of access to the public, state [unintelligible] schooling programs and public health decision makers. We as [unintelligible] served primarily to newborn screening programs across the country and other stakeholders which we will get into in a little bit more. Next slide, please. All right. So in reference to our mission, as noted here we are trying to achieve the highest quality for newborn screening systems by providing relevant, accurate tools and resources to facilitate collaboration between state programs and other newborn screening partners. This is very important. In the same age where there is, you know, we've heard that newborns can all be screened in the system, it has a number of components to it and all of those have to be working optimally to achieve, you know, end results which is to, you know, hopefully make a – a positive difference in the lives of these newborns and that are picked up from these different conditions that are on the recommended uniform screening panel and so that is our mission and that also was developed by the Newborn Screening Steering Committee. Next – all right. So we have four goals and let's talk briefly about them. The first one on information gathering and building relationships. When we started NewSTEPs, we wanted to make sure that we figured what the gaps and barriers are in preference to the [unintelligible] between education, communication, data collection and reporting and, you know, working with the newborn screening community, whether it's maybe more screening programs or the wider community in understanding what those gaps are. We wanted to be able to figure out how we can build trust and strengthen relationships. I should

say that we had the trust of 61 screening programs through most of our relationships that we've had over the past 13 years or so through our corporative agreement that we had, that we continue to have with the Centers for Disease Control and Prevention, primarily in newborn screening and molecular biology branch, and so state newborn screening laboratories especially and HHRs had a long-standing relationship. The scope of NewSTEPs is broadening, you know, in – in the newborn screening systems and, you know, our activity does go all the way up until at least short-term follow up. So we really did want to fill out those kinds of relationships and, you know, strengthen those relationships apart from both – both the need to know our national stakeholders. Second thing is to – on education and networking. We wanted to be out there everywhere. State level, local level, regional level, whether it's through the national collaborating within the regional collaborators to understand, you know, and create those newborn screening networks available for communication and other kinds of activities that have been brought to our attention by the newborn screening stakeholders in general. The third goal is the data repository. This is a major goal for us. We have a national data repository that's fairly – we wanted to design something that was a little bit innovative. Actually, that was very innovative, build and validate the contouring system of, you know, newborn screening system quality improvement activities, monitoring trends in the system, collect as a – as we're going to talk about in a – in a minute, Marci will, the things I was talking about. It's a quality indicator that we developed and over the past couple of years that we're using to collect information into the data repository and then address needs of the newborn screening programs. Needs that have been brought a number of times over the past several months and we'll talk about that later in the future are on – on how we can help individuals take newborn screening programs in addressing these, you know, continuous quality improvement and their – and then one screening programs and then technical assistance. As part of our name, we wanted to be able to provide a comprehensive way of, you know, technical assistance to newborns screening programs whether it's in the form of education, training opportunities, working with the folks in the newborn screening personnel to figure out what their needs are from pre-analytic, analytic and post-analytic activities, all the way up until instruction and follow up competence and then, you know, work with states to be able to – to figure out how we can address any one of these, you know, either deficiencies or work with those states that have those best practices to be able to share with them across, you know, statewide screening programs. This is our team. I believe this is the Newborn Screening and Genetics in Public Health department seen together with our collaborators from the Colorado School of Public Health. Next slide, please. So who are they? So it's myself as the director of the program. Sikha is the manager. She manages pretty much everything related to NewSTEPs. Careema Yusuf is the senior specialist and is pretty much

responsible for anything related to the data repository. Thalia Wood is responsible and most of you know her from Alaska. She is here with us in Silver Spring, Maryland now. She is responsible for everything related to all of the committees, subcommittees, work crew and task force and we – we have plenty of them which we'll talk about in a minute. But her main responsibility is to manage all of those as well. Elizabeth Jones is the liaison that bridges the gap between all of the things that we do in NewSTEPs and the newborn committees, the genetics and public health committee that is funded under the auspices of CDC to make sure that we are coordinated on everything that's cross-cutting the newborn screening especially that, you know, since we have funding from two major federal entities right there. Marci Sontag is the associate director for NewSTEPs. Among other things, she is my right-hand person, makes sure that – she keeps me straight on a number of things, and she also works with Careema very urgently on our activities related to our data repository and everything that has anything to do with just epidemiology related to the program, and then Dr. Yvonne Kellar-Guenther is the program evaluator. Everyone of HRSA grants now has to have – does have to have some kind of evaluator that, you know, evaluates the overall, you know, program and Yvonne has done a great job from Colorado School of Public Health in making sure that everything that we do not only it is, you know, we can measure it, but also, you know, the extent at the end of the day and then my boss is Jane Getchell, who is looking across from the envelope. Yes, she is the senior director here at APHL a part of public health program and she pretty much advises us on all activities related to [unintelligible]. So I talked a little bit about the NewSTEPs steering committee and – and that does comprise of folks from the Newborn Screening Systems or the collaboratarians, follow up coordinators, nurses, physicians, IT specialists. We even brought together folks pretty much from everywhere around the country to be part of the Newborn Screening Steering Committee and I will make applied or on the – the – the list of committee members available to everyone on – on the economic – and economic layer, but the committee is broken down into several workgroups and we created these workgroups to help accomplish the activities, you know, that, you know, are very important to making sure that we are touching upon like this linking on all of the – the objectives of NewSTEPs in general, whether it's a quality indicators workgroup and most of you have heard or seen from slides from us whether it's from past secretary's advisory committee presentations on our quality indicators and work that we've done in trying to harmonize our quality indicators that we can put into our data repository, our data repository workgroup, our website work group, evaluation to workgroup so going to states to evaluate their newborn screening program. We needed a group of folks that can better help us understand what are the needs, you know, that we need to be focusing on whether it's, you know, developing a pre-evaluation to collect information form state newborn screening programs before we go into the state

newborn screening programs to do a complete evaluation of their newborn screening systems and then of course technical assistance workgroup. So we'll talk in depth about this. STFU being short-term follow up and of course CCHD workgroup – we also added another workgroup on health information technologies which is one of those cross-pitting activities not only in APHL but just newborn screening systems. Next slide, please. So this is a diagrammatic representation of NewSTEPs' activities across the board. So NewSTEPs is in the middle of it. I talked a little bit about the types of services that we are currently providing to state newborn screening programs. We're going to [unintelligible] that later. The quality indicators work that we've done over the past almost three years now in vetting through the system and the community on what kind of indicators we should be collecting as I mentioned, as a collective or a state with one screening program together with the case definitions. The website and data repository, if you have not logged onto our website, please do so – www.newsteps.org. A lot of information is on there about everything that I'm talking about and more, current events, eight profiles and – and other things that Marci will go into later. These specific activities, whether it's on CCHD, ID or any other condition that may be added in the future by the right [unintelligible] by the secretary's advisory committee, we would be able to provide a comprehensive resource to every state newborn screening program, you know, now and in the future. Then as I noted in one of my slides earlier, continuous quality improvement [unintelligible] onscreen with this and a certain mark of major activities of NewSTEPs and from looking at the newborn screening community as an embarking on those or a pass [unintelligible]. I'm jumping [unintelligible].

Dr. Sontag: Thank you, Jelili, and now I'm going to go start with Goal 1 and just go into a little more detail into our current activities. As Jelili nicely outlined, our first goal for our collaborative agreement was to look at information gathering, building relationships and identify the gaps and barriers in NewSTEPs giving education to coast – coast to coast leaders across the nation and the newborn screening follow up personnel as to – as it relates to new disorders, new assays, follow up strategies, then the gaps and barriers in communication across the newborn screening system and then data collection and reporting, how – where – where our gaps were, really look at that all over gaps and barriers and then build and strengthen the relationships across the newborn screening system with our state – local, state, regional and national newborn screening stakeholders and then private partners and with NewSTEPs. We have had a really comprehensive network that we have used to gather information. We've gone to the genetic regional collaboratives and other HRSA-funded projects. We've attended national meetings across [unintelligible] diseases, across things like [unintelligible] meetings [unintelligible] who've had a national presence really for the last 18, 19 months that we have been funding to [unintelligible] information making a connection with having our colleague conversations, giving presentations so we can

gain that information of how we can best support state newborn screening programs as they are implementing the work that they're doing. Coming back to the program evaluation community input we have sought feedback from the community on many different aspects, on the quality indicators for newborn screening. We'll talk about that in more detail later, but this is really – the quality indicators are really developed by the community. Case definitions for newborn screening authority, newborn screening data use – how will we be using these data, what specifically best provides these data back to the states to give them the known information that they can gain from this, newborn screening continuous quality for the potential [unintelligible] to describe this is what we're all about, improving the newborn screening system and newborn screening data collection and how we provide newborn screening to infants throughout the nation. Identifying components of an evaluation tool – we've used other evaluation tools that are already inclusive to the Delphi Survey of our steering committee members and activators of newborn screening and identifies the key things that we would need to have for an evaluation tool that we'll talk about again in a bit. Getting input on specimen transport – the Milwaukee Journal Sentinel has recently had an article or a series of articles out about specimen transport and we've been working with our APHL group to identify information related to specimen transport and how we can best support states to shorten the transport time and I'll talk about that again later, too. And then newborn screening aware – awareness, we did a series of [unintelligible] interviews with Title V directors across the nation to understand their understanding of newborn screening and the newborn screening system and how the Title V program interacts with newborn screening. One of our goals and I [unintelligible] is a small slide to read, but what we'd like for you to get from this is looking at state representation in NewSTEPs. One of our goals is to have all of the states participate. They are all participating in one form or another and these are different ways across the top here in which they can participate, whether it be on our steering committee, our various other committees, in our workgroups, participating in some of our webinars, so on the left side there is the difference [unintelligible] is confirmation that we really are getting state wide in our activities and getting feedback from all of the states that have NewSTEPs can best support their work. So our second goal is related to education and networking and within this we want to create and – and support a university network for educational communication again at the local, state and national level and we do this knowing that networks with individuals can be utilized to improve newborn screening outcomes. If we're all working in silos or working by ourselves, we're not going to get as if we're all working together. So to develop that network has increased the networking, increasing the virtual networking where we have lots of webinars and chances for people to discuss and then across that sharing our successes and challenges. How can we learn from the successes and challenges across our [unintelligible]?

One of the key forms of our educational program is our interactive website. This is a dynamic website that continues to grow. We're gaining resources from the community that we're adding to this. We're adding best practices from the community. A lot of it's broken down by different types of individuals who come to our website. Jelili said again this is at newsteps.org and we have it broken down across the newborn screening and laboratory personnel and follow up personnel, parents and caregivers and then policy makers and administrators and that parent and caregivers group, we have some basic information there and so we encourage them to visit Babies First Paths who is our partner organization that really is good at educating that group of individuals. This is another web shot of our – another screen shot of our website, the short-term follow up page, but we really would encourage you all to go onto our website and see all of the information that's there and [unintelligible] this is a dynamic website and we're going to continue to add information as we grow and get resources from the community. This is screen snapshot of our website hits that we debuted our website in May at the Newborn Screening and Genetic Testing [unintelligible] in Atlanta and so we got a lot of hits in May and that's continued to grow to this is the end of last year, and it continues to grow now as its out of our short-term follow up at the CCHC pages. So we continue to – we really are growing into what people are seeing as the resource to first head to for newborn screening and information, especially for those people working in newborn screening at the follow up and lab levels. Another example of educational outreach, we have had two follow up workshops, one general follow up workshop with all of the people working in follow up and this is an area that really has not been tapped into very much previously. But we really want to make sure the people working with [unintelligible] have the network to be educated and to connect with each other. One of the general follow up workshops and one of the follow up workshops directly related to [unintelligible]. So we've had eight attending each of those workshops, small groups that can really dive into the issues, and the workshops will continue to happen through NewSTEPs. We have a dedicated listserv specifically for newborn screening with almost 400 members. We've got a website. You can see now this is our – as of the end of last year, over 3,500 hits to our website and approximately 50% of our new hits last month. That's a lot of hits coming to our website. And then webinars – we have just had a series of webinars for many different activities that relate to newborn screening and really use those for training and information dissemination and all of these webinars are archived and then put back onto our website. So if you miss one, you can go back and listen to it again later. This is a brief snapshot of the webinars that we've participated in just in the fall of 2013 and we're [unintelligible] a little bit more detail about what we cover in some of these, that they were related to our medals of understanding, related to training for the data repository between [unintelligible] for us really giving the space to understand how to enter data into the data repository. We've

had a short-term follow up webinar which was attended by – the initial webinar was attended by over 100 people and then we had CCHD [unintelligible] webinar as well that were well attended and well received by that community. This is just a snapshot of ways that we're providing education to the [unintelligible]. And now goal 3. This is kind of our – has been our bread and butter the last year. We have spent a lot of effort to really develop and innovative data repository and the goal of the data repositories are to evaluate newborn screening systems and this evaluation was not meant to be a punitive evaluation. This is an evaluation to provide feedback to the states so they can improve their own programs. They can say oh, here's how we compare to the rest of the country. That leads to the quality improvement and monitoring of changes in the system and this will also [unintelligible] disorder occurrences and practices related issues in newborn screening disorders. The website can also be reached on our website at newsteps.org. There is a [unintelligible] here to provide tools to the newborn screening programs to evaluate their systems and provide benchmarks and we had thought of the components of the data repository as really being in three different [unintelligible] the state profiles, the case definitions and the quality indicators. So we see here a map of the states. You can go to that map, click on your state, find out some information about your state. There is quite a bit of information there now and in the coming months we will have much, much more information available so you can print out more information about the state profiles for giving state newborn screening programs. The [unintelligible] state profiles, you see the state there in the middle and what types of elements to collect related to the state profiles becomes demographic information of the babies who are born in the state, [unintelligible] disorders that are screened for, what are their policies where they do newborn screening, the newborn screening program structure so we can understand how within their state health departments do they organize their newborn screening so we can learn from each other in that area, what their IT and laboratory systems are, the information systems as well as their actual laboratory testing systems, and this is just HIT elements. Now this is a slide where it lists the components of the state profile. I'm not going to read through each of these, but many details go behind each of these data elements. So just take a look at those. You can see how the depth at which we're trying to understand the newborn screening system and under the state program you say oh, my gosh. This is a lot of information to enter. We recognize [unintelligible] is a lot of information to enter and what we're doing is introducing this in a staged approach, so they'll look at it and say hey, can't this chunk it requires me to enter by this stage and then another by this stage, another by this stage and then it'll all be there for them to be able to update once per year. They won't have to reenter any of it. This is updated as things change and we're also working with them, which we'll talk about in a little bit, of how we can transfer data where that's appropriate as well. And then the next

bucket of our data repository goes to the quality indicators. There are eight quality indicators that have really been developed by the newborn screening community. It has been a series of in person meetings followed by webinars followed by calls for public comment where we got a lot of feedback from them. The eight quality indicators that are listed here, these are the very high level descriptions of the quality indicators. You can go to our website and pull up the details and the definitions related to all of those quality indicators. You could understand them in more depth. Specifically, one of the quality indicators that has come to our attention in the past month with the Milwaukee Journal Sentinel article is that time elapsed from birth to screening and then follow up testing, confirmed diagnosis, etc. How long is it taking to get these babies screened and diagnosed and the [unintelligible] testing? So this, as I said, has been a quality indicator that's been developed years – in the last couple of years and I want to know specifically about how we'll use this information. So you can see we're looking at each number of different quality indicators here related to that time elapsed, so we can really dive into what's happening with these babies? When are they being screened? When is that sample arriving at the state lab? So here's a sample report and the sample report shows time from birth to specimen collection if you present the same kind of report of birth to – to the lab, etc. and this data provided an aggregate by each state. Each bar here represents a state. So you can look at it and see what that distribution is for each state. When is the specimen collected? In this case, it's collected 24 to 48 hours as recommended and then some of the samples were collected before that and some after, so you can look at what the [unintelligible] division is across all states and then each state would then report that depicts where they are. Where in that [unintelligible] is how they compared to the national average. So we will be looking – reaching out to those states who are at one extreme and say hey. How can we help you get closer to that national [unintelligible]? How can we get – get you to that – the outcomes that are more desirable and also we're going to promote [unintelligible] doing that really allows us to understand their data. I wanted to [unintelligible] that these babies presented here are all completely fictitious. It's just a sample form. But these are the types of reports that we will be presenting with our repository. This is just a quick [unintelligible] of how states will enter data into their repository from our website. They'll go in [unintelligible] in this case [unintelligible] for states that don't have, you know, near California or near Colorado, but the year they're entering data for and then [unintelligible] which quality indicator. Finally the last bucket of our data repository is the baby level or case data and this is disorder – disorder specific newborn screening data brought basic demographic information about the baby and then the timing of diagnosis, specimen transport, the follow up, all of those [unintelligible] aggregate we want to know about those babies who are diagnosed with specific disorders and to do that we really need some information from a

case definition worksheet. Case definitions are an effort that was really led by HRSA over the past several years and we have taken that and developed them and implemented them into a data repository. So we have taken the case definitions for the try [unintelligible] heart condition. We're looking at the last couple. I'm looking at CDCHD and we unfortunately are variable. Set the stage with data collection but [unintelligible] definitions will allow us to compare data from state to state. So we will be able to understand if a case is called cystic fibrosis in Utah and is called cystic fibrosis in Florida, you know it's the same definition of cystic fibrosis or have that same level of certainty. And again just a brief snapshot of our data repository, what it looks like. One important note here is it looks as if we are collecting date of birth on these babies and we are not collecting date of birth. Our vendor, 5AM Solutions, has done a very nice job in allowing us to calculate those date differences. So we become the [unintelligible] data first and enter data second in collection, it would calculate the date difference but then when you hit save those dates are erased, so no dates are then transmitted to recess. A little bit more information on what that diagnostic workup looks like and in the interests of time I'm not going to go into a lot of detail here, but you can see [unintelligible] categories and how they were diagnosed [unintelligible], not specific information but enough information is available for public health reform to allow us to determine that this case is truly a case. [unintelligible] to the state lab [unintelligible] their [unintelligible] to confirm that this case was a case. This [unintelligible] got back for [unintelligible]. So the data confidentiality, just want to remind you no babies are identified at this stage with [unintelligible] repository. To reemphasize this, this non – no baby level data, no dates of birth are stored within our repository. So as I said earlier, dates of birth and all those sorts of things are entered on the screen and then erased, never saved up to our server. So here's a plot overview of how we look at our user roles within NewSTEPs. That you see at the top you have that public web user. You can see the state profiles. You can see the public information, but you can't see specific information related to a case. You might be able to see the policies and procedures related to a case, but you would not be able to see any baby level data or any specific quality indicators related to a case. You would be able to see overall how often quality indicators all across the entire country. How – what's the performance of the entire country look like, but not your – not any specific state. Registered users can see de-identified aggregated QI data, access basic reports. Then the next number down we have the state's profile data manager and the state's baby level data manager. In many states these people may be the same people that are accessing this data. The [unintelligible] manager will be able to enter, edit and read the profile data. QI data [unintelligible] by – this is just specifically to their state, which leaves the other data for [unintelligible] be able to see that specific information for the baby. The system administrator [unintelligible] to all

of the data and then give access to the individuals of the [unintelligible] so we have [unintelligible] administrators for each of the 50 states and those are the people we've got to get back to [unintelligible] give that access to the state people. Then there's a super administrator and the super administrator, they're the ones who will have the access [unintelligible] into the overall database access. Now I wanted to talk just a little bit about [unintelligible]. Is this data research level data? So [unintelligible] the Colorado – do this in Colorado, we went to the RIRB and asked them to grant us permission to review this. They reviewed and said you know, we don't feel comfortable with this. We're not [unintelligible] because they had additional conversations with HRSA and their OHRP, the office of Human Research Protection and [unintelligible] conversations that really spanned many, many months, in-depth conversations. This project would seem to be non-human centered research. So actually under that umbrella, the non-human centered research is a way we're plucking the data. We actually from a regulatory standpoint could cross additional information about these babies but loaded [unintelligible]. We have decided not to as it is really in the best interests of the states not to have that information. But the IRB, the Colorado IRB, has written a letter explaining this decision and the process that we have undergone to really make sure we are treating this data in the most adequate and responsible way. It's important for you to know, though, that we are not engaged in human centered research. Anyone who puts data into our program is also not engaged in human centered research which should conclude that [unintelligible] were concerned about do we need to go to IRB to [unintelligible] data. So under that same realm, we have the memorandum of understanding that all 50 states have now received this memo with MOU just between NewSTEPs and specifically APHL to hold up the cost of an agreement in each state and [unintelligible] include issues related to data ownership, data sharing, data recording with security records to make sure we are holding the data secure and then the IRB and [unintelligible] language that we just looked at. So we are working each of the 50 states now to get these signed and we've had many cultures come back from the states and we're having to mark the pages on the memos of understanding. We are working to get them signed within the next coming months so we can enter data. The [unintelligible] understanding earlier committed to the data for the case definitions and the quality indicators. The state profile information is publicly available data and states were able to enter that already.

Mr. Ojodu: And all of this information is on our website.

Dr. Sontag: Thank you, Jelili. All of the information [unintelligible] to all of this is on our website if anyone would like to get more information about the memos of understanding or any of [unintelligible]. Now back to once they get that memo of understanding signed, how are states going to enter data? Right now it's manual data collection. There should be some screen shots

of our data repository people – you could go in and type that in. However, we are currently working on methods to be able to electronically transfer data. That would allow states to use the newborn screening LIMS, Laboratory Information Management System, to transfer data into NewSTEPs. So we're using volunteer state newborn screening programs to help us facilitate this and we're also looking at application programming interface which I didn't know what that meant until the last two months, but it reduces the burden for multiple data entry points. So this is something where it's – people enter data into our website, they will – it could potentially be updated on NSTRN or Baby's First Steps website, so state [unintelligible] complaints and to update the data and make sure it's up to date but with – with two sectors and lab [unintelligible] we're going to see programs do the work that they need to be doing in the states now. So before I leave this topic of our newborn or data repository, I think it's important to note that the legacy data that was collected by NMSIS before June 1, 2012 has not been provided to NewSTEPs in a way that will allow us to do more of the [unintelligible] data transfers or data comparisons. So all of the data that we will be looking at will be from 2012 forward given our current data structure. I want to briefly talk about the HIT technology – health information technology activities that we're doing. We have this here to show you really how complex the HIT system is, that we are working in many different areas to help defer to E1 screening programs as it relates to HIT. We have HIT workers that we'll talk about briefly. Well we'll look at this in a moment, but we're really working to support [unintelligible] transfer and how can we understand the data to make it easier and very consistent across all local, state and [unintelligible] programs. With that, I'm going to hand it back to Jelili who is going to just finish up with our typical [unintelligible].

Mr. Ojodu: So going forward [unintelligible] noted earlier and we plan and already are building on existing technical assistance and training opportunities for individuals any [unintelligible] programs in general. It spans the scope of actually because I know that whether it's pre-analytic, analytic, post-analytic, all the way up until short-term follow up, point of care testing conditions are part of the recommended uniform screening panel, so that does include CCHD and we're certainly planning to work with CDC to address issues and activities relating to hearing screening as well and then of course in the future, hopefully in the coming years we plan to open Stage 2, [unintelligible] newborn screening quality certificate program. [unintelligible] go into the details of that later because that's in the future, future, future. On the [unintelligible] that I noted earlier which is a comprehensive part of what we plan to do in the – in the – we've started doing already and – next slide, please – and then it's – we plan to go into statement one screening programs. We already had a site evaluation in – in New Jersey already and we have one coming up in another state in the coming months. Providing technical assistance on congenital heart defect – this is a program that was started under the auspices of HRSA that's

been transferred to us in NewSTEPs arriving in opportunities for folks in the community to the described workgroups, webinar series and webpages which is on our website which will be on the next slide that I will talk about. Short-term follow up [unintelligible] of think about the need to engage everyone in the system and at least in our opinion we felt that, you know, that folks that beyond the laboratory screening, the folks that are working either short-term follow ups or follow up in general, you know, can be engaged and certainly are compassionate in, you know, working with us on certain activities. So we have a workgroup, a webinar series and a number of webpages to address issues on a monthly basis on activities related to short-term follow up. That is actually being led by Dawn Thompson in Washington and Carol Johnson in the state of Iowa and then HIT surveys and listservs and workgroups. This is something that was newly instituted. I think we had our first call a couple of months ago. There were a number of people from the newborn screening community but – but most importantly there were also folks from the newborn screening vendors that were participating on this. We need their buy-in as well [unintelligible] from picking up on screening programs in the future. Next slide, please. That's just a snapshot – a screenshot of our congenital heart disease website. If you need more information about education, just go to the website. We have a number of activities, [unintelligible] and educational resources related to what we are doing and most of you know, HRSA funded six states – six states to actually enhance – expand their newborn screening – recommended newborn screening panel to include congenital heart defect. Dean Adroy, actually February 27 – 28, we are going to be hosting an interesting meeting between – and have invited one person from every state in the newborn screening program to attend. The meeting is going to be – as noted here, the purpose of the meeting is to talk among the states, the pertinent stakeholders, the partners to help facilitate CCHD screening throughout the United States of America, and so we're looking forward to hosting this meeting. If you have any questions about this, feel free to contact us. It's an open meeting although seats are very limited, and the deadline to apply for this is actually February 1. Thank you. [unintelligible] Site visits – we have created a tool and we talked a little bit about this earlier in which we are providing states to collect information on what their needs are. These site visits are invited kind of in evaluations that, you know, we would get an invitation from either the commissioner of health or deputy commissioner of health or someone from the newborn screening program to do a comprehensive peer review of the newborn screening system, everything – laboratory, follow up, hospital, you know, specialists, everything that's involved in that. A report is generated four months, three to four months after the inside evaluation, and it contains a number of recommendations that are – are provided to the state on bettering or assisting them in addressing its quality improvement issues across the board there. So finally, what is it that – I'm sure everyone knows what NewSTEPs is right

now, but if you don't please also just go to our website and look that up. Comprehensive newborn screening resource center for state newborn screening programs primarily and stakeholders in general. We are partners with state newborn screening programs in this initiative. I'm going to show the beautiful slide of the collaboration of participation from state newborn screening programs across every single state on the different workgroups that we've instituted here. That's very important. Provide technical assistance and resources to state newborn screening programs. Collate and summarize data in aggregate – we won't be providing any specific state information to the public. Certainly it would be – all that information will be ideated and only provided to the individual states for them to compare to the state of origin or the states across the country. Again, as noted earlier, develop our communities for continued quality improvement locally, regionally and nationally. In collaboration with all of the activities that we do, whether it's funded by CDC or the HRSA-funded activities, National Collaborating Center, ECMG, Babies First Steps, making sure that we're all in synchrony to, you know, address the – the – the needs of the – the newborn screening community as a whole and I think that's it. Do we have another slide there? Oh, yeah, contact information – I've highlighted and put this website a number of times. If you have a question, feel free to email any of us. Our email is newsteps@aphl.org and we certainly look forward to questions from this community, collaboration with the newborn screening community in general in the future. So I think that's it.

Dr. Bocchini: Well, first of all, I want to thank Marci and Jelili for this presentation. Really just kind of remarkable effort and – and incredible progress in a few year period of time, so just truly will bring significant benefits overall to all of us. I want to open this discussion to questions or comments, first from the committee. So again if you will first of all let's make sure that all the committee members' lines and the organization representatives' lines are open. Operator, is that the case? Okay. So the lines are open. Then committee members, I'd like to hear from you first for comments and questions and then the organization representatives to follow. We do have a few minutes for Q&A and comments. All right. I see nothing yet from the committee, so organizational representatives? All right. First from committee we have Dr. Parisi. Melissa?

Dr. Parisi: Hi. This is Melissa and I just want to thank the NewSTEPs team for putting together a very impressive series of – of resources. I was really pleased to see the quality indicators and the case definitions moving forward. That – that's a really nice bit of work. Just wondering if there's an opportunity to partner with some of the resources that are part of the NBSTRN, particularly around some of the – the data resource that you were referring to and the longitudinal pediatric data resource that's part of the NBSTRN and the R4S system that a lot of the states have been contributing data towards and again, which I guess my recurring theme of

not duplicating effort but making sure that we're coordinating some of our efforts in these regard.

Dr. Sontag: Excellent. And actually going – by the [unintelligible] can see, we've actually thought big about how we do connect with the other federally funded partners and NBSTRN really has a long-term follow up piece that – their registry is for long-term follow up and [unintelligible] diagnosis. You see at the bottom close diagnosis through the rest of life and we are at the short-term follow up piece. We're looking of course the newborn screening program. [unintelligible] there are any data elements that could connect from one system into the next system, so we have had some conversations with NBSTRN about could we have a global unique identifier that could be entered on the state level and then once the states tell us the baby has consented, it should be a longitudinal repository. At NBSTRN, we could link that data between the two so that data that was collected on a newborn screening program about when the baby was diagnosed and tested and all of those things could be transferred over to [unintelligible] and then conversely NBSTRN then has to be long on their follow up because they get and some of those long-term follow up components respond to the date program. So we could say oh, this baby has been seen two times and is doing well. They [unintelligible] information but that'd be a nice service to give back to the state to allow them to really understanding yes, this baby is – is doing well and is in follow up. So we're in those conversations and we're very aware of [unintelligible] our role is and how NBSTRN fits into that.

Dr. Parisi: Great. Thank you.

Dr. Bocchini: Next is Natasha Bonhomme.

Ms. Bonhomme: Hi. Good job, Jelili and Marci. That was a lot of information and really, really good to hear. Can you give a little bit more detail about the CCHD meeting that you're having in February and as part of that, are – are – so that's kind of question number and the subquestion is are you going to be talking about any kind of public education or kind of consumer input as part of that meeting seeing that a big driving force of CCHD being adopted in states came from the advocacy organizations? Thank you.

Mr. Ojodu: [unintelligible]

Dr. Sontag: Thank you, Natasha. That was an excellent question. So the purpose of our meeting at the end of February is really to move every state forward in CCHD. So whether it's the states who've been screening for a couple of years and are already implemented and ready to go, how do we help them with quality approvers so they're moved further along and can improve their systems and the states who are really at that very beginning stage trying to figure out, as you said, the advocacy and putting it

[unintelligible] stage are moving forward. So our target in this particular meeting really is the state and [unintelligible] program. But you bring up an excellent point as far as the family organizations and other advocacy groups that really helped to move forward CCHD screening and while [unintelligible] these [unintelligible] representatives such as yourself, Natasha, could come to this meeting and really help us think about ways to include that as we move forward.

Ms. Bonhomme: Thanks.

Dr. Bocchini: All right. Next we have Michael Watson. Mike?

Mr. Watson: Yeah. Thank you. I only wanted to clarify one aspect of NBSTRN, which is, you know, I think we certainly deal with long-term follow up as relates to conditions that are part of newborn screening because they're not well understood and we certainly need that data to better understand clinical histories, penetrance and all those sort of things, but from a research perspective which is really where the NIH's focus is, NBSTRN has interests across screening, diagnosis, follow up where new technologies, new methodologies, new conditions and pilots and such may come into play because that's certainly going to cover everything, certainly in pilots everything from screening right out to outcomes and all of that coming together to make decisions about what's appropriate to add in newborn screening.

Dr. Bocchini: Thank you, Mike. Are there any additional questions or comments from committee or liaisons? [unintelligible] we are right on – on schedule for us to close the morning session and for those of you on the East Coast, it's lunch time. For those of you on the West Coast, perhaps you can get a late breakfast and we'll see you back in one hour at 1:30 East Coast time. Thank you all for your contributions this morning. We'll talk to you within – in an hour. Thank you.

. . . Committee on Heritable Disorders in Newborn and Children January meeting. I first will need to conduct a roll call. So let's begin. Don Bailey?

Dr. Bailey: Here.

Dr. Bocchini: I'm here. Jeff Botkin? Coleen Boyle?

Dr. Boyle: I'm here and just a reminder that I'm going off at 2:00 and – and Carla will be representing CDC, Carla Cuthbert.

Dr. Bocchini: Okay. Thank you. Denise Dougherty?

Dr. Dougherty: I'm here. I actually was there earlier today, but not for long. I had self-inflicted audio problems.

Dr. Bocchini: Oh, okay. Thank you, Denise. Charlie Homer? Kellie Kelm? Fred Lorey? Michael Lu? We have Joan Scott here for Michael Lu. Steve McDonough?

Dr. McDonough: Here.

Dr. Bocchini: Dieter Matern?

Dr. Matern: Here.

Dr. Bocchini: Melissa Parisi? Alexis Thompson?

Dr. Thompson: Here.

Dr. Bocchini: Cathy Wicklund?

Ms. Wicklund: Here.

Dr. Bocchini: Andrew Williams?

Ms. Williams: Here. I'm here.

Dr. Bocchini: Okay. Thanks. And Debi Sarkar?

Ms. Sarkar: Here.

Dr. Bocchini: Let's just go back and check. Jeff Botkin? Charlie Homer?

Dr. Homer: Here.

Dr. Bocchini: Okay. I heard that. Okay. Kellie Kelm?

Dr. Kelm: Here.

Dr. Bocchini: All right. Thank you. Fred Lorey? And Melissa Parisi. All right. Let's go to the organizational representatives. Freddie Chen? Beth Tarini? Michael Watson? Mindy Saraco?

Ms. Saraco: I had audio problems, too.

Dr. Bocchini: Okay. Who was that?

Ms. Saraco: This is Mindy Saraco.

Dr. Bocchini: Okay. Thank you, Mindy. Kate Taft? Kate Taft? Susan Tanksley?

Dr. Tanksley: I'm here.

Dr. Bocchini: Chris Kus?

Dr. Kus: Here.

Dr. Bocchini: Adam Kanis?

Dr. Kanis: Here.

Dr. Bocchini: Natasha Bonhomme?

Ms. Bonhomme: Here.

Dr. Bocchini: Ed McCabe? Cate Walsh Vockley?

Ms. Vockley: I'm here.

Dr. Bocchini: Carol Greene?

Dr. Greene: Here.

Dr. Bocchini: And let's go one more time for both Melissa Parisi?

Dr. Parisi: I'm here.

Dr. Bocchini: Okay. And Fred Lorey? And Freddie Chen? Beth Tarini? Michael Watson? Kate Taft. Ed McCabe? Okay. That'll conclude the roll call.

Dr. Homer: Charlie Homer joined. Thank you.

Dr. Bocchini: Okay, Charlie. We caught you the last time.

Dr. Homer: Thanks.

Dr. Bocchini: Okay. All right. We're first going to start with a couple of comments. We have a 15-minute period within the schedule to – for the public comment. We have six individuals who wish to make a comment, so please try and limit your presentation or your comments to about two minutes. So those of you who are going to make plural comments, please make sure you have your computer speakers turned off. Keep your phones on mute unless speaking. If you don't have a mute button, press star six and mute your phone and before speaking, please state your name and organization if applicable. So operator, if you'll open the phone line for Sarah Wilkerson, board member for Save Babies Through Screening Foundation.

Dr. Thompson: Dr. Bocchini, may – may I interrupt you just for a moment? I – I – I neglected this morning just to make a request for additional participants in the ad-hoc committee. If there is anyone on the call today that represents either APHL or the state – state newborn screening programs that we would really welcome that additional expertise. If they wouldn't mind

identifying themselves perhaps to Debi, we would love to have them join us.

Dr. Bocchini: Thank you, Alexis.

Dr. McCabe: Joe, this is Ed McCabe. Sorry. I was having some technical difficulties.

Dr. Bocchini: Okay.

Dr. McCabe: But I am on the call.

Dr. Bocchini: Thank you, Ed. Appreciate that.

Dr. Lu: And Joe, I'm here as well.

Dr. Bocchini: I'm sorry, who?

Dr. Lu: Michael Lu.

Dr. Bocchini: Okay. All right. Okay. All right. I have adjusted the roll call.

Dr. Tarini: Dr. Bocchini?

Dr. Bocchini: Yes.

Dr. Tarini: It's Beth Tarini. I'm on the line now.

Dr. Bocchini: Okay, Beth. Thank you. Okay. So first person then is Sarah Wilkerson. Operator, is Ms. Wilkerson on line.

Female: Yes, her line is open.

Dr. Bocchini: Okay.

Ms. Wilkerson: Hi.

Dr. Bocchini: Go ahead.

Ms. Wilkerson: Can you hear me okay?

Dr. Bocchini: Yes, we can.

Ms. Wilkerson: Great. Well, thank you so much. Again, my name is Sarah Wilkerson. I'm here as a mother and as a member of the board for the Save Babies Through Screening Foundation. I'm also a mother of an MCAD child, my son Noah, who would be 4 years old if he were still alive today. Noah passed away before we learned of his illness. He was born at 3:00 a.m. on a Friday and died quite simply because he was born on the wrong day of the week here in Colorado. The state lab in Denver was closed for the

weekend, which added a couple of unnecessary days of delays in getting his newborn screening test results in time. His [unintelligible] cards that useless at the hospital over the weekend and wasn't couriered to the state lab until Monday. It was received on Tuesday at the lab and on Wednesday we got the call letting us know of his disorder, but it was too late. Noah had gone into metabolic crisis and died the night before. I can't tell you what it was like as a mother to learn that my child had died of an illness that was treatable nearly all of the time. We were never given the opportunity to fight for his life with the very well established treatment plan for MCAD children and even a day would have made a difference in saving his life. It isn't just Colorado that has limited weekend hours. 27 states in the U.S., more than half, are either closed completely or have limited weekend hours and functionality despite the fact that babies are born every day of the week and all deserve timely testing. I implore you today to consider the issue of weekend hours in labs as you begin to examine the many ways that newborn screening test results can be sped up. There's no way to regulate what days of the week babies are born, but labs can be kept open to meet the demands of families like mine. Thank you so much for your consideration.

Dr. Bocchini: Ms. Wilkerson, thank you for your comments. As you know, based on your comments at the September meeting, this committee went forward to work with APHL and the CDC to evaluate of the timeliness of newborn screening and as you'll hear tomorrow, that process is underway and – and certainly we'll take into consideration your comments. Thank you.

Ms. Wilkerson: Thank you.

Dr. Bocchini: Next on the – on – on the list is Kate Kelly, parent of a child with MCAD. Operator, please open the line for Ms. Kelly.

Female: Her line is open.

Dr. Bocchini: Thank you. Go right ahead, Ms. Kelly.

Ms. Kelly: Hi. Can everyone hear me?

Dr. Bocchini: Yes, we can.

Ms. Kelly: All right. Well, thank you. My name is Kate Kelly and my son has MCAD. I'm here to share with you what timely screening and follow up has meant for my family. Our son was born on a Tuesday morning after a healthy and uneventful pregnancy. We were discharged from the hospital on a Friday afternoon when he was three days' old. As far as we knew, he was a perfectly healthy little boy. We received a call from our pediatrician later that evening as we were getting out son ready for bed, telling us that his newborn screening was off the charts for MCAD. It didn't take us long to realize how fortunate we were to have received our son's results so

quickly, before he was allowed to sleep for too long and risk serious health consequences. Thanks to his rapid newborn screening, we had information that was saving his life and it was as simple as setting an alarm, waking him up and feeding him. If only every family were so lucky. Our story was included in the recent Milwaukee Journal Sentinel feature on newborn screening. We were a happy story and that the stories of too many other families who did not receive this lifesaving information about their babies until it was too late. I urge this committee to fix these issues that are endangering babies across the country. In particular, I am advocating for improved education for hospitals about the dangers of batching samples, mandated use of courier services to ensure that samples make it to the labs in a timely and traceable manner even on weekends and holidays, and assistance for state laboratories to help them identify any technologies or resources that will allow them to process samples seven days a week because babies are born each and every day and days matter. I'm proud to say that our son is now a happy, active, 22-month-old thanks to newborn screening. We have shared his first smile, first steps, first words and every milestone has been celebrated with an extra measure of gratitude for although every child is a blessing and a joy beyond words, our son gives us a little extra reason to know that we have been blessed. From the bottom of my heart, thank you for all you have done to advance newborn screening. Thank you for giving us the opportunity to know our son and for the knowledge to keep him healthy each and every day. Newborn screening does save lives and all families deserve a happy newborn screening story like ours. The action of this committee to ensure timely screening and follow up is crucial to achieving that goal. Thank you for your time and for your consideration.

Dr. Bocchini: Okay. Thank you for sharing your personal story and showing us how effective newborn screening can be when it's done in the most effective way. Thank you. Next is Dr. Gerry Raymond, director of children neurology, University of Minnesota. Operator, please open Dr. Raymond's line.

Female: Dr. Raymond's line is open.

Dr. Bocchini: Thank you. Go right ahead.

Dr. Raymond: Okay. Good afternoon. I'm Gerald Raymond, professor of neurology at the University of Minnesota, and I'm a researcher in the field of adrenoleukodystrophy. I thank the committee for allowing us to make comments this afternoon. I'll try to keep my oral comments brief since I've already presented before the committee before and some of this material is also in my written comments. As you all are aware, X-linked adrenoleukodystrophy is a genetic disorder that results from ABCD1 mutations as a result of an accumulation of very long chain fatty acids. It affects approximately 1 in 17,000 individuals and affects all ethnic groups.

There are predominantly two major manifestations in childhood, Addison's disease or primary adrenal insufficiency which affects her in the first year of life, and does result in significant morbidity and mortality for these boys. With the identification [inaudible] can be monitored for development of Addison's disease and if they develop this can be referred for diagnosis and treatment and treatment [inaudible] is really simple using oral clinical steroids. The other manifestation is some [inaudible] which is a devastating event. Unfortunately it can also be monitored for and detected by MRI and again surveillance allows referral for stem cell therapy. Given the – the incidence of disease and potential to monitor and intervene, we have always been very eager to improve diagnosis in individuals. Me and others have developed a method to use newborn screening in tandem aspect. We've shown it to be sensitive and specific for proximal betaoxidation defects and we have now published several papers on this. The most recent is our pilot study on 5,000 newborns in Maryland. Recently the New York State newborn screening program added ALD to their panel and I would like – certainly like to acknowledge all of those ALD families who have lobbied strongly to the legislature to do that. We worked – worked closely with the newborn screening program to develop the framework to screen and follow up positive results. The system went live on December 31 and so it's been in place for only two weeks. There have already been two referrals by this program and these individuals are presently being assessed and confirmed. We certainly look forward to advancing ALD newborn screening and we look – we continue to be actively involved in this development. We hope that the committee will look favorably on the proposal today and how to be available to answer any questions. Thank you.

Dr. Bocchini: Thank you, Dr. Raymond, for your comments. We appreciate them. Next on the agenda Dr. Amber Salzman, president of the Stop ALD Foundation. Operator, if you will please open Dr. Salzman's phone line.

Operator: The line is open.

Dr. Bocchini: Thank you.

Dr. Salzman: Hi.

Dr. Bocchini: Hi.

Dr. Salzman: Hi. This is Dr. Amber Salzman. I lead the Stop ALD Foundation. The purpose of my comments are to provide further context to the updated ALD newborn screening nomination. So in the September 2012 Advisory Committee Meeting, the ALD newborn screening nomination was reviewed. The committee recognized a compelling case. However, we were asked for more prospective data from the Mayo pilot study that was going forward. This has now been included in the revised nomination.

The results further support the validity of the test. With this as a backdrop, patient advocates supported by ALD physicians and scientists have been working with several states to prepare for implementation of ALD newborn screening and as Dr. Raymond mentioned, this has begun implementation in New York. So in summary, there's a reliable approach to doing a biochemical screen of blood spots. Mechanisms are in place to do the molecular screening on the samples that come up positive by the biochemical screen. The ALD community is poised to work through the process to support families with an affected newborn. It has been published in several studies and reinforced by experts in the field that early warning is the only way to assure children are treated in time for a therapy to be effective. I have personally suffered the loss of my nephew, Oliver, due to a late diagnosis. At the time of his diagnosis, we screened the extended family and found that my 1-year-old son and 7-year-old nephew were also affected. Due to the early warning from Oliver, they were both treated. My son is now a healthy teen and my nephew is a sophomore in college. Had newborn screening been in place when Oliver was born, he too could have been spared. Several hundred babies will be born in the U.S. with ALD this year. We really don't want any more families to unnecessarily suffer the devastation ALD can cause when it is diagnosed too late to intervene. Given the compelling case as well as screening, diagnostic and treatment protocols, we urge the committee to move the nomination forward to the External Condition Review Group. Thank you so much for your time.

Dr. Bocchini: Thank you for your comments, Dr. Salzman. As you know, we have received your information that was – additional information as requested by the committee. It's gone to the Nomination and Prioritization Review Committee and we'll hear the results of their evaluation later this afternoon. Next on the agenda is Ann Moser, a research associate at the Kennedy Krieger Institute. Operator, please open Ms. Moser's line.

Operator: I don't show Ms. Moser has joined the call at this time.

Dr. Bocchini: Okay. Then let's go down to the – the next individual, Mr. Dean Shure, president of the MLB Foundation. Let's open Mr. Shure's phone line.

Operator: Dean's line is open.

Dr. Bocchini: Go right ahead.

Mr. Shure: Thank you Mr. Chairman, committee members and those that are tuned in. There's actually an additional 50 or 60 people that have come on since your remarks when you opened the meeting, and I'd like to remind everyone from the advocacy side that the defendant has made progress on

the ongoing funding for the Newborn Screening Saves Lives Reauthorization Act. The House still has a lot of work to do, so we need to continue that pressure and we're all in support of the work that the committee does and we thank you for that. So that's the part of the job that – that we can carry on. I'm going to repeat just very briefly some comments I've been sharing for the past couple of meetings of this committee. I'm continuing to garner interest to call a summit hopefully for later this year, hopefully adjacent to your September meeting to discuss the dynamics around changing the criteria that exists for us today that you have to have a viable therapy in order to implement a newborn screen. It's a very complicated issue. I acknowledge I don't understand all of the perspectives on it and I'm sure that in the ten years or so since the rust has – has been around, that – that's something that perspectives may have changed on. It's – there are social issues, ethical issues, financial issues, care issues, public health issues, and so on related to the potential of a newborn screen without a viable therapy and I would just like to remind folks that – that there – that we're trying to put this summit together. If they want to reach out to me through the website or email, we'll be sure to include them in the attendance. It would be an open meeting and I'm – I'm looking for funding for that and – and making some progress in that too. So with that, I thank you and keep up the good work.

Dr. Bocchini: Thank you, Mr. Shure. We appreciate your comments. Is Ann Moser on the line, operator?

Operator: Let me check. One moment. I don't show she has joined, no.

Dr. Bocchini: All right. Thank you. That will conclude the public comments, so we appreciate the efforts of all of you who have come forward to make comments to the committee. We do appreciate your input. Next on the agenda is the X-linked adrenoleukodystrophy discussion and update from the Nomination and Prioritization Workgroup and Dr. Dieter Matern, committee member, will lead the presentation. Dieter?

Dr. Matern: Thanks. And I don't know if I can drive this, but we'll see. So I'm representing the Nomination and Prioritization Workgroup here and give a report on X-linked adrenoleukodystrophy and I would like to start with acknowledging the proponents, the primary proponents being Dr. Charles Peters, and then several advocate organizations that are supporting this nomination as well starting with the Stop ALD Foundation, the ALD/AMN Global Alliance, Be A Hero Become A Donor, Cure ALD, Fight ALD, The Myelin Project, Run4ALD, ELA and ULF. So first a – a little bit of background, basically a repeat of what Dr. Raymond just shared with the – with us. X adrenoleukodystrophy, the X stands for the X chromosomes with an X-linked recessive condition which typically means that only males are developing symptoms. The prevalence is 1 in 21,000 males depending on where you look. Dr. Raymond mentioned 1 in 17,000

and the important part is in spite of what I just said, female carriers actually will develop symptoms by about 60 years old in about 65% of them. It's the most common peroxisomal disorder and as was mentioned earlier it's caused by mutations in the ABCD1 gene. This gene encodes the peroxisomal membrane protein ALDP, which is a transmembrane transporter for very long chain fatty acids or VLCFA with their carbon chain lengths of more than 22. The pathophysiology next ALD again is due to the ALDP deficiency, which results in impaired very long chain fatty acid peroxisomal beta-oxidation and it leads therefore to accumulation of very long chain fatty acids CoA in cells, which causes oxidative stress, oxidative damage to protein microglial activation and apoptosis and that leads to the phenotype and the phenotype is not a simple phenotype. There are top categories and we heard already about the adrenocortical insufficiency as Addison only, variant cerebral demyelinating form of X adrenoleukodystrophy, cerebral ALD adrenomyeloneuropathy and then the important part is that there's no genotype phenotype correlation and even within the same family, you can see different phenotypes besides having the same genotype. A phenotype in cerebral X-ALD starts slowly. Patients are often diagnosed as attention deficit hyperactivity disorder and typically do not present clinically before 2 ½ years of age. It is a progressive inflammatory demyelination process in the brain and goes along with severe cognitive and neurologic disability leading to a vegetative state and death within two to five years after the diagnosis is made or the onset of symptoms. The diagnosis in the laboratory is based on an elevation of very long chain fatty acids in the plasma sample and it can be confirmed by molecular genetic analysis if these states look in and see ABCD1 gene and this is particularly important that you are looking for carrier females because 15% of those have normal plasma very long chain fatty acids. [unintelligible] we heard already from Dr. Salzman when reinvestigate – investigations can lead to early identification of patients today. In adrenomyeloneuropathy, the etiology is somewhat different with a noninflammatory prototype affecting distal [unintelligible] the total root nervous system so that phenotype goes along with a progressive spastic paraplegia which is also often misdiagnosed initially as multiple sclerosis or hereditary spastic paraparesis, but what also is important is that 20% of males with adrenomyeloneuropathy will develop cerebral ALD later in life. The diagnosis is basically confirmed in the laboratory the same way than X-AL – X-ALD. The – the question then of course must be raised for newborn screening. It's – it's actually then for the condition under consideration. So as you also heard there are treatment options, hormone replacement, Lorenzo's oil and then hematopoietic cell transplantation and what I'm showing here is part of a graph from a paper from the University of Minnesota group published a couple years ago which basically shows you in – on the left side the – the finding of the survival rate of patients with ALD based on the Loes score. The Loes score is based on MRI patterns, the radiological features of the

brain, and Loes score is – has a better prognosis. From what you can see here, if you have a score that's less than 10 at the time of transplantation, survival is better as opposed to when you have higher Loes scores and more progressed disease, your survival is not as good. The chain loads if you were to do neurologic function and have a score based on that, if you have a better score meaning you have better neurologic function, the survival after transplantation is better than if you have more progressive disease and this of course means that there could be made a case for newborn screening so that you identify patients before they develop any symptoms and can treat them. The next question then if you consider a condition for newborn screening is you want to have a test available to do on blood spots looking at a marker that you can do very quickly on a large number of locations as its required for population newborn screening. So as you also heard the Kennedy Krieger Group, including Dr. Raymond, works the – this – this up initially looking at lysophosphatidylcholines as the biomarkers and found that you can measure those in blood by using – using liquid chromatography tandem mass spectrometry. My colleague here at the Mayo Clinic, Dr. Silvia Tortorelli, has been somewhat involved with that and also the work of the Kennedy Krieger Group to – to improve this – this assay. The goal was here to – on our end was to move away from the LC-MS/MS part to a more simple flow injection analysis tandem mass spectrometry which is how we do amino acid nasopiatines already in – in newborn screening. Liquid chromatography adds some degree of – of complexity to the test and the goal in newborn screening is to do it as simple as possible. So we should also reduce the time – the instrument time on the – of each sample from 2 to 1.5 minutes which means you basically double your throughput which means you have that equipment in your laboratory needed to do the testing and then we also multiplexed it with six [unintelligible] storage disorders so you can basically do more than just the lysophosphatidylcholines now but also measure any line activities of some of the [unintelligible] storage disorders such as [unintelligible] and NPS 1 that are already recommended were under consideration for inclusion in the one screening panel. This again also was brought to our advisory committee about two years ago and this is the letter that the proponents received back from our committee and I just show this here because it points out that we at that point did not feel that the evidence review was appropriate and the reason was given that despite this being an important condition and worthwhile condition, this large pilot study that is presently under way at the Mayo Biogenetics Laboratory had nothing complete. So that brings me of course to talk a little bit about our study. Just as a reminder, this was a study not just for X-ALD but also for several other [unintelligible] disorders with [unintelligible] Friedreich ataxia. We tested 100,000 key identified [unintelligible] that we received from the California newborn screening laboratory to figure out the most effective and patient tested approach to these conditions. Also figure out how to quickly confirm the presumptive positive [unintelligible] and kind

of emulate the reading for genetic collaborative [unintelligible] on this data project to help [unintelligible] that am I going to use any of the assays that we tested in – in doing this in the [unintelligible] performance. Just quickly just to make sure that I acknowledge and particularly financial support from NICHD and NBSTRN and the Legacy of Angels and then the [unintelligible] collaborators and supporters. So this was our approach and at the bottom you can see X-Adrenoleukodystrophy looking at the [unintelligible] choline this is not a specific marker. It also is elevated in Zellweger spectrum disease with [unintelligible] oxidate but under protein deficiency these are all [unintelligible] and then on top of the LPC markers we can see that [inaudible] disorders that are screened using this test. Here you can results. We are looking at particularly P24 and P26 that are helpful in picking up X [unintelligible].

Female: Somebody is moving stuff around.

Dr. Bocchini: [inaudible] mute the line who is working on some other project? Thank you. Go ahead, Dieter.

Dr. Matern: Yes. So on the left right here you see panels for C24 and C26. These are the results from the flow injection analysis and on the right side you see the same analyzed with the T2. T2 stands for second tier. So we do the flow injection analysis and if that isn't normal, we do a second tier test, a reinjection of the prepared specimen in the liquid chromatography to separate particularly C26. C26 there is in some blood spots an interfering substance in the filter papers. It doesn't come from the patients, in the filter paper that could cause false positive results. So synthetic – not in every case, we use the LTMS as a second tier and if that isn't normal then you would consider it presumptive positive and we'll follow up on this. Now the green that you can see here is basically the reference range in the – in unaffected newborns. The – the red boxes are true positive cases with ten cases VS if you can read that, it's – the red box on the left is Zellweger spectrum diseases. These are not picked up by the newborn screening pilot study that we did. These are retrospectively analyzed and for strong known patients and we have 51 X-ALD males and 24 X-ALD carriers that were tested. Again, these are not all picked up among the 100,000. These are retrospectively tested to determine within these ranges where we can figure out what works best. You can see that T24 it newly identifies Zellweger spectrum disease and you see that the – the X-ALD cases are not totally separated from the normal control but it means there's no significant overlap for T24. There is some overlap for T26 with normal and then the carriers have overlap with T24 normal range and for T26 normal range and that is not entirely remedied by the second tier test. So how did it go? Among the first 85,000 samples tested and I cannot reveal the numbers yet for the full 100,000 because we have not completed molecular testing on – on those that were found normal by the first tier, the second tier test for the last 15,000 because we unfortunately fell into

the situation that NICHD told us they wouldn't give us a no-cost extension. So the study funding ended in September of last year and now we're trying to finish this study more slowly and at as – as little cost as possible. So – but among the first 85,000, you have an abnormal rate of 1% for the first tier test. So there were 640 females with an elevation and 274 males. The second tier however the patients we remedied is quite significantly so that we have only a second tier abnormality on 25 of the 640 females and 10 of the 274 males and genotyping at that point revealed 1 female carrier and 2 male XLD patients. Now this included only genotyping for HABTD 1, so any of the other peroxisomal disorders are not excluded at this point. So what is the standard of newborn screening currently? We heard already that in the U.S. in New York newborn screening for X-ALD was started on December 30 of last year, so about two weeks ago, and they identified two cases. We apparently do not know yet whether these are – I don't know if these are males or females. I don't know what medication status they have. As far as I know in New York, they do basically our assay. I don't know if they do the second tier test, but I do know that they do as a – either a second or third tier test molecular testing for – off the ABCD1 gene. So if they reported both cases out, it is likely that they carry imitation ABCD1 gene. In Connecticut, in New Jersey, legislation both passed to include new X-ALD into the new one screening program, but it's not done yet and in California the legislature is considering the one screening for X-ALD. Elsewhere in the world in the Netherlands I am aware that in April the newborn screening chronically in the Netherlands will determine whether they want to screen for X-ALD. The suggestion there is that they would screen only for males which I do mean that they look at the screening part and whether if it's a female, they will not do the test. If it's male, they will do it. So in summary, I believe that X-ALD is a serious medical condition. I think the natural history of X-ALD is fairly well understood. The – the – the thing that is – that I think needs some discussion is that it does not require initiation of treatment in the newborn period, which at least in the past was somewhat of a – something you would assume that if you'd screen for something that early, you want to do it for conditions that need immediate attention. The – there are blood spot based assays available using LPTs as disease markers but again, LPTs are not specific to X-ALD but are also elevated in other peroxisomal disorders which I would consider them at least secondary targets and also it will be normal in female carriers. However, I don't think it will identify all carriers. Also again we did the study. We hope to complete this by the end of next month. We took the two-tier approach, however not one including [unintelligible] testing. We – the preliminary findings with respect to the performance suggested we do identify by 1 in 25,000 boys which is kind of expected based on the literature. Our false positive rate is .02% and the positive [unintelligible] value is 18%. Now one of the things that I think our committee at some point should address because it comes up

repeatedly that people talk about an acceptable false positive rate is that nobody defines ever a false positive rate, either how it is calculated or what is actually acceptable. So I'm showing you here a comparison to the amino acinase akonotine screen done at – in our [unintelligible] at Mayo. Our false positive rate is .02% and the positive liquid value 68% so that's 40 plus additions that we screened with this test. The – so the false positive rate if we consider .02 acceptable, I think X-ALD will be fine. If we compare the national average for the same screen amino acinase akonotine the false positive rate is .46% which apparently we feel all to be acceptable. Otherwise the screen wouldn't be done. The positive predictive value nationwide is 18% so that it's consistent with the X-ALD. So we get – we have a check that – that would work. So what would our group's recommendation be to the SACHDNC? We believe that it is time and justifiable to initiate the external evidence review. As I mentioned, SACHDNC already stated that this is an important condition and the pilot study that we were waiting for I think suggested there is an appropriate newborn screening approach. We should also I think recommend to the newborn screening program that I already screened for this, that they participate in the region for laboratory performance database. There is already a portal on the NBSTRN website for X-ALD screening and then recommendation to ACMG would be to develop and achieve algorithms for X-ALD and relevant peroxisomal disorders that are also identified by history and this is all I have. Are you guys still there? Hello? Can you guys hear me?

Female: I'm here, Dieter. I don't know if you can hear me.

Dr. Matern: Now I can hear you.

Dr. Bocchini: Can you hear us? This is Joe Bocchini. Can you hear us?

Dr. Matern: Yes, I can [unintelligible]. I – I can hear you.

Dr. Bocchini: Okay. I'm not sure what happened, but is everybody back on?

Female: Um-hum.

Female: Yes.

Male: Yep.

Male: Yes.

Dr. Bocchini: All right. Great. Well, again, I don't know if you heard me say, but I wanted to thank Dieter for an excellent presentation and summation of the considerations of the – of the nomination prioritization workgroup. So this is now open for discussion. So and actually if you could – if the – his

last slide can be put back up and then again from the committee members first, if you'll press the icon, let's go ahead and start the discussion.

Dr. McDonough: This is Dr. McDonough. I can't push the icon. It doesn't work right now.

Dr. Bocchini: Okay.

Dr. McDonough: But I'd like to move that X-ALD go forward for evidence review.

Dr. Bocchini: All right. I'll accept a second if that's appropriate and then we can have discussion following the second of that.

Dr. Lorey: It's Fred Lorey. I'll second.

Dr. Bocchini: Okay. Thank you, Fred. So let's have a discussion if there is one from the committee. It appears if no one can – okay, Jeff Botkin. So we're back with the – being able to raise the hand. So Jeff, go ahead.

Dr. Botkin: Okay. Thanks. Nice presentation. I – it wasn't clear to me or isn't clear to me what we know about the spectrum of the disorders. You talked about different subtypes, but what do we know about the spectrum of those subtypes from more severely to less severely affected kids.

Dr. Bocchini: Dieter, are you able to answer that?

Dr. Matern: Yes. Sorry, I – I had myself muted. Okay. Well, again I think the spectrum of disease is – is basically the – the cerebral [unintelligible] AMN and Addison's disease. I think – and again I'm not the expert on – on X-ALD, but – and – and newborn screening, of course, will certainly or I would expect it to feature a little bit more about the conditions and see whether there are other milder variants, but again the – the spectrum, I mean, this – this is a slowly progressive condition meaning over several years and – and from – so that we – I – I think you develop the symptoms and it might be sooner or later and – and most patients I think are symptomatic by – by 4 years old.

Dr. McDonough: Okay. Thank you.

Dr. Bocchini: Someone needs to mute their line. We've got some background discussion. Okay. Thanks. Next, Melissa Parisi.

Dr. Parisi: Hi, Dieter. Thanks for that presentation. I just had two questions for you. One of them is related to the lack of necessity for starting treatment in the newborn period. For those with Addison's disease, isn't it relatively important to start treatment so they don't go into an adrenal crisis? I don't know again the – the time course typically for those boys. But it seems like there could be some benefit in starting treatment as early as possible and I guess I'll go ahead to my second question which is for those who

screen positive after your second tier liquid chromatography step but did not have an ABCD1 mutation and presumably some of those may have other peroxisomal disorders. How are you triaging or following up on – on those cases or does anyone have a plan in place for them?

Dr. Matern: Yeah. So the first question about Addison only disease, again I don't think that it's – most patients I also think do not present based on the literature in the first couple years of life. So again it's – it's – overall it doesn't appear to be a neonatal condition. The other question was about what to do with the abnormal – abnormal results that we have in the screening but did not do ABCD1 – did not do any other molecular testing of ABCD1 gene. Our goal is to still complete and work those cases up completely. So we will look at other peroxisomal conditions by molecular means, but again I just don't have that data yet.

Dr. Bocchini: Any follow up, Dr. Parisi?

Dr. Parisi: No. Thank you very much.

Dr. Bocchini: Okay. Next is Steve McDonough?

Dr. McDonough: Oh. Thank you, Mr. Chairman. I think it's really important that we consider conditions that don't need treatment right at birth. Addison's disease with X-ALD often doesn't present until after age 2, but it is a very sneaky condition that as a primary care provider I want to know if a child is at risk for Addison's disease so we begin treatment ahead of time and before the child presents in crisis. So even though there's a condition that doesn't need treatment right at birth, it's very important that physicians taking care of these children or working with those families have a heads up about what's coming and what we can do to prevent problems.

Dr. Bocchini: Thank you, Steve. Next, I have Jeff Botkin followed by Don Bailey.

Dr. Botkin: Thank you. I think that – I believe you said it was the Netherlands who is pursuing a protocol on which the female carriers would not be identified. So a couple questions about the carrier status. How prevalent is carrier status and has anybody made any sort of recommendations about any management for females who are carriers? I understand from the presentation that these are people who may have manifestations many decades later that may have reproductive implications for them, but is there anything to be done in the pediatric age group for female carriers?

Dr. Matern: I – I – I'm not aware of any specific recommendations. I think the – the Dutch basically decided not to screen for carriers because of the much later onset of symptoms and even then not a – I mean, still a good number of – of carriers who would never have any symptoms. The – the incidence, I mean, based on our study, overall incidence three and we had [unintelligible] we had one carrier among 85,000, but again we would not

pick all of them up. So I would assume that there are more that we miss than we identify. Part of the evidence review unless we would be able to have Dr. Raymond comment during this discussion would certainly be a review I think of the New York protocol that the Kennedy Krieger and [unintelligible] Dr. Raymond were involved in putting together. At this point I have no idea how the further follow up is – is going on for, for example, these two referrals that they have in New York in the last few weeks. It seems to be maybe just statistics, but I mean that would be an unexpected timing to – to get to in the first basically 12,000 babies screened.

Dr. Bocchini: This is Dr. Bocchini. I think that that would certainly be something that would be evaluated by the condition work group as it – as it evaluated the data if we were to choose to bring that forward rather than trying to solve at the present time by our committee. Don?

Dr. Bailey: You know, I'll just remove my – put my hand down. Jeff asked just exactly what I was interested in and that was a – didn't know if now is the time to discuss that or if it would be something we would just make sure that the evidence review addressed and I suspect we will have quite a bit of discussion about that once they come back with a – with a report.

Dr. Bocchini: Okay. Thank you. I see no other questions from the committee. Are there questions or comments in the [inaudible]? Again, please use the icon if you have a question or comment [inaudible]. All right. Having no additional questions or comments from the liaisons or the committee, I think with the – we are ready now to vote on whether to move this condition to the condition for review group and I will go again in – in alphabetical order. Don Bailey?

Dr. Bailey: Yes.

Dr. Bocchini: I would vote yes. Jeff Botkin?

Dr. Botkin: Yes.

Dr. Bocchini: Coleen – I guess Carla, are you representing Coleen at this point?

Dr. Cuthbert: Yes, I'm representing CDC and I vote – we vote yes.

Dr. Bocchini: Okay. Denise Dougherty?

Dr. Dougherty: Yes.

Dr. Bocchini: Kellie Kelm?

Dr. Kelm: Yes.

Dr. Bocchini: Charlie Homer?

Dr. Homer: Yes.

Dr. Bocchini: Fred Lorey?

Dr. Lorey: Yes.

Dr. Bocchini: Michael Lu?

Dr. Lu: Yes.

Dr. Bocchini: Steve McDonough?

Dr. McDonough: Yes.

Dr. Bocchini: Dieter Matern?

Dr. Matern: Yes.

Dr. Bocchini: Melissa Parisi?

Dr. Parisi: Yes.

Dr. Bocchini: Alexis Thompson?

Dr. Thompson: Yes.

Dr. Bocchini: Cathy Wicklund?

Ms. Wicklund: Yes.

Dr. Bocchini: And Andrea Williams.

Ms. Williams: Yes.

Dr. Bocchini: Okay. So it's unanimous to move this condition forward to the – to the workgroup for the commission review and I want to thank Dieter for his presentation, the Nomination Prioritization Workgroup for its efforts and certainly the individuals who have brought this forward to us to bring us to this point and now we will then hear over the next couple of meetings the efforts being completed by the Commission Review and then we'll go from there. So again thank you all very much for getting us to this point. So we are now – all right. So this concludes day one of the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children third meeting. Next up will be the subcommittee meetings so before we start the subcommittee meetings please take a five minute break so that the subcommittees can be set up. You can see on your screen the – where you can go to participate in the subcommittee meetings and those of you who

are members of the subcommittee have already received your agendas and the issues that will be discussed at each of those meetings. Those subcommittee meetings, there are three of them. It's Education and Training, Follow Up and Treatment, Laboratory Standards and Procedures will meet from starting in about five minutes for approximately two hours. We will then hear from the subcommittees tomorrow morning or sometime tomorrow, tomorrow afternoon, and so we look forward to that as well. So thank you for a good first day and we look forward to hearing and seeing you tomorrow. Thank you.